IASLC 2022
Asia Conference on Lung Cancer

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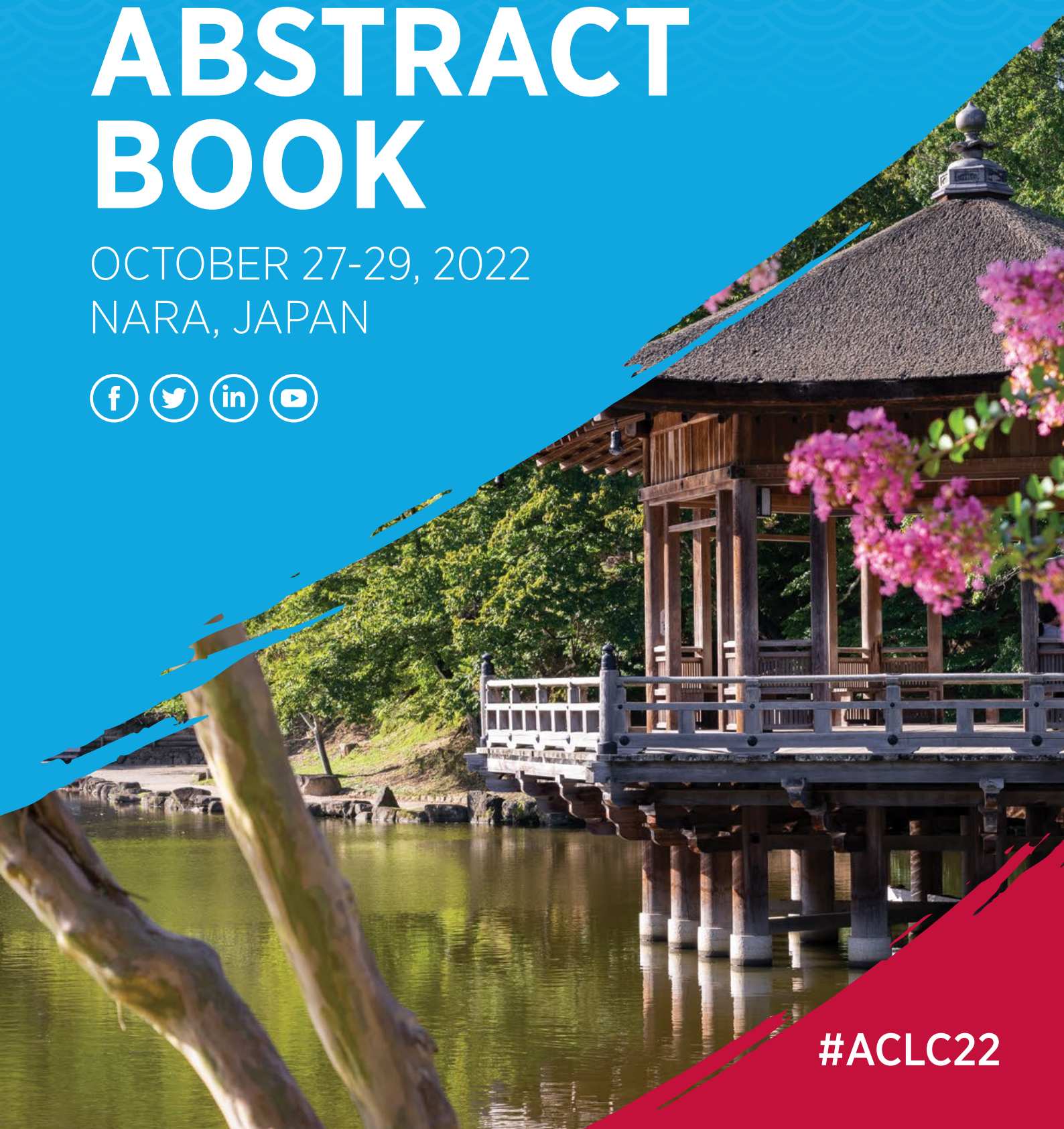
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TABLE OF CONTENTS

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Oral Sessions

Oral Abstract Session 1
October 27, 2022, 17:00 - 18:00

OA01.01:
Is Computed Tomographic Screening for Lung Cancer Associated with Lung Cancer Overdiagnosis Among Asian Women?

Prof. Hsiu-Hsi Chen[1], Professor Pan-Chyr Yang[2], Prof. Robert Smith[3]

[1]National Taiwan University, Taipei, Taiwan, [2]National Taiwan University, Taipei, Taiwan, [3]American Cancer Society, Atlanta, United States

In 2022, Gao et al. reported significant overdiagnosis of lung cancer (LC) in Taiwanese women associated with LC screening. Their conclusion is based on: 1) increased incidence of stage 0-1 disease without a decrease in stages 2-4; and 2) a higher 5-year survival rate for female LC in Taiwan compared with Western countries after the introduction of LC screening. Their methodology, presentation, and interpretation of LC overdiagnosis should be considered with great caution because important data from the cancer registry and changes in therapy were not addressed.

We used Taiwan Cancer Registry data to examine: Age-standardized incidence rates (ASR) of LC in men and women from 1979-2019; Time trends of LC ASRs between 2004-2019 by histological type; Stage-specific time trends of LC ASRs between 2004-2019; Stage-specific time trends of LC (ASR) between 2004-2019 by gender; and a comparison of overall incidence between 2004-2011 and 2012-2019, adjusting for increasing LC incidence before LDCT screening began.

There has been an increasing time trend of female LC in Taiwan from 1979-1997 before the introduction of LDCT screening and their reported baseline time period from 1998 to 2003. Only looking at trends in LC stages 0-I and stages 2-4 from 2004 and 2018 is prone to mistakenly ascribing excess incident stage 0-I cancers to overdiagnosis rather than early detection of stage 0 & 1 with screening. Second, increasing incidence before the introduction of screening warrants examination of stage-specific time trends to differentiate stage-shifting from overdiagnosis. After age-standardization, there is an increasing trend of stage 4 from 2004 to 2011 and a declining trend after 2011, whereas stage 0-I cancers increased. Third, we observed high incidence of stage 0-I and lower incidence of stage 3 and 4 for females, in contrast to trends in males. Fourth, the higher five-year survival rate of female LC in Taiwan is not attributable to the contribution of a denominator inflated with overdiagnosed cases but due to more effective targeted therapies for EGFR mutation+ tumors, such as the introduction of Gefitinib in 2003 and Erlotinib in 2006, coincident with the introduction of LDCT screening. In Taiwan, 62% of women diagnosed with lung cancer carry an EGFR mutation, compared with 20% in White populations.

We find no evidence for LC overdiagnosis in Taiwanese women. Crude analyses of registry data can lead to erroneous conclusions when the underlying increase and heterogeneity of LC incidence and changing patterns of therapy are not considered.

OA01.02:
Operational Management Challenges in Continuing Lung Cancer Screening during COVID-19 Pandemic

Dr. Prerna Gautam[1]

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Background: COVID-19 has affected the cancer care delivery system and prevention and screening services for cancer was one of the worst affected domains of cancer care. Lung cancer screening (LCS) reduces mortality in high-risk individuals and millions of people could not continue their screening in view of COVID pandemic. This study was planned to assess the operational management challenges in lung cancer screening amidst COVID-19 pandemic.

Methods: This was a cross sectional questionnaire-based study in which responders were health care professionals working in cancer care facilities who were also running lung cancer screening. They were asked to know the challenges related to various aspects of operational management concerns in lung cancer screening i.e. locating screening facilities, evaluating process changes to screening services, following up screening tests, improving measurement of screening effectiveness, scheduling screening appointments amidst COVID-19 pandemic.

Results: LDCT for lung cancer screening was suspended at all the centers and all screening visits were cancelled. Total monthly mean ± SD LDCTs (73 ± 16 vs 9 ± 5; $p < 0.01$) and new patient monthly LDCTs (28 ± 7 vs 2 ± 1; $p < 0.01$) were significantly decreased during the COVID-19 period. New patient monthly LDCTs have remained low despite resuming full operations. During the COVID peak period, annual LCS LDCT volume and baseline LCS LDCT study volume decreased by approximately 72% and 78%, respectively, from the pre-COVID peak period, whereas follow-up LCS LDCT volume decreased by approximately 50%. Major reasons for this decrease in LCS were inability to locate working screening facilities (80%), no change in process during pandemic (84%), no follow up of screening tests (100%), no improvement in measurement of effectiveness (20%), and inability to schedule appointments (100%).

Conclusions: COVID-19 caused significant disruption in lung cancer screening, leading to a decrease in new patients screened in view of various challenges encountered in the continuation of lung cancer screening. Early reports showed that the unfavorable consequences related to the pandemic for screening programs and lung cancer care.

OA01.03:
Safety of Lung Cancer Surgery in Patients with History of SARS-CoV-2 Infection in the Post-vaccination Era: A Single Center Experience

Dr. Somin Im[1], Dr. Kwon Joong Na[1], MD Ji Hyeon Park[1], MD Bubse Na[1], MD Samina Park[1], Prof. In Kyu Park[1], Prof. Chang Hyun Kang[1], Prof. Young Tae Kim[1]

[1]Department of Thoracic and Cardiovascular Surgery, Seoul National University Hospital, Seoul, Republic of Korea

Background: SARS-CoV-2 pandemic poses an unanticipated challenge in lung cancer management. Although the number of infection cases has increased, there have been more mild illness cases recently since the SARS-CoV-2 vaccine shown great efficacy and effectiveness in real-world data. Here, we sought to explore the postoperative outcomes of lung cancer surgery in patients with SARS-CoV-2 infection and to determine the timing of lung surgery should be performed following SARS-CoV-2 in the post-vaccination era.

Methods: This study is a retrospective single-center study, which included patients with lung cancer who underwent curative resection from June 2021 to May 2022. Depending on their history of SARS-CoV-2 infection prior to surgery, the patients were divided into two groups. The postoperative outcomes of the two groups were compared.

Results: A total of 876 patients underwent lung cancer surgery during this period, of which 41 patients had a history of SARS-CoV-2 infection. In SARS-CoV-2 group. All patients received at least two doses of vaccination, and the most common symptoms were cough (73.2%), sore throat (65.9%), and chills (56.1%). Five patients had preoperative CT scans that suggested SARS-CoV-2 sequelae, yet surgery was nonetheless performed on them as they had no respiratory symptoms. There was no patient whose surgery was canceled due to SARS-CoV-2 infection. Minimally invasive surgery was performed in 36 patients (87.8%). The types of operation performed included wedge resection (N = 3, 7.3%), segmentectomy (N = 2; 4.9%), lobectomy (N = 33; 80.5%), bilobectomy (N = 1; 2.4%), and pneumonectomy (N = 1; 2.4%). The interval between SARS-CoV-2 infection to surgery was < 4weeks (13 patients), 4-6 weeks (9 patients), 6-8 weeks (7 patients), and > 8weeks (12 patients). The complication rate (15.4% vs. 11.1% vs. 0 vs. 8.3%) and length of stay (median 5 vs. 4 vs. 4 vs. 3 days) were not different according to the interval between infection and surgery. We compared postoperative outcomes between SARS-CoV-2 group and non-SARS-CoV-2 group. There was no statistical difference regarding complication rate (19.5% vs. 17.8%; p = 0.83), respiratory complication rate (14.6% vs. 11.1%; p = 0.45), and length of stays (7.0±2.4 vs. 7.7±5.9; p = 0.43).

Conclusion: In the post-vaccination era, lung cancer surgery can be safely performed after SARS-CoV-2 infection, even in a short period of less than 6 weeks after infection.

OA01.05:
Biomarker Analysis from a Phase II Alternating Therapy with Osimertinib and Afatinib for EGFR-Mutated NSCLC (WJOG10818L)

Assoc. Prof. Kimio Yonesaka[1], Hidetoshi Hayashi[1], Atsushi Nakamura[2], Yuki Sato[3], Koichi Azuma[4], Shinya Sakata[5], Motoko Tachihara[6], Satoshi Ikeda[7], Toshihide Yokoyama[8], Kentaro Ito[9], MD.PhD Yukihiro Yano[10], Hirotaka Matsumoto[11], Haruko Daga[12], Akito Hata[13], Kazuko Sakai[14], Yasutaka Chiba[15], Kazuto Nishio[14], Nobuyuki Yamamoto[16], Kazuhiko Nakagawa[1]

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Background: Epidermal growth factor receptor-tyrosine kinase inhibitor (EGFR-TKI) is a key drug for EGFR-mutated non-small cell lung cancer (NSCLC). However, all tumors ultimately develop resistance to EGFR-TKIs via multiple mechanisms. EGFR secondary mutations, especially that causing T790M amino acid substitution, confer resistance to EGFR-TKIs. Third-generation EGFR-TKI osimertinib could conquer cancer cells harboring the T790M mutation, but alternatively induces C797S, another resistance-causing mutation. A preclinical study revealed that while osimertinib or afatinib alone induced drug-resistant clones harboring C797S or T790M, respectively in Ba/F3 cells activating EGFR mutations, both drugs in combination prevented the appearance of such resistant clones, suggesting that their combination suppresses the emergence of both T790M and C797S as secondary mutations.
Based on these observations and considering tolerability, alternating therapy with osimertinib and afatinib was examined for treatment-naïve patients with EGFR-mutated advanced NSCLC as a single-group, phase II trial (WJOG10818L). Here, we present updated data for survival and a genomic analysis.

Methods: Treatment-naive patients with stage IV NSCLC harboring an activating EGFR mutation (L858R or exon-19 deletion) were enrolled. Alternating cycles of osimertinib at 80 mg/day for 8 weeks followed by afatinib at 20 mg/day for 8 weeks were administered. CtDNA was extracted from the plasma prior to therapy and post acquired resistance. Genomic alteration was examined using the AVENIO ctDNA surveillance panel. Soluble HER3 ligand heregulin was measured using ELISA.

Results: Forty-six patients were enrolled and treated with the alternating therapy. After a median follow-up time of 3 years, the median progression free survival was 20.2 months (95% CI: 14.5–25.8 months). The overall response rate was 69.6% (95% CI: 54.2–82.3%). The median overall survival was not reached. Among 26 plasma samples obtained after acquiring resistance, three had MET amplification. However, no EGFR secondary mutation between exon 19–21, including T790M and C797S, was detected. EGFR compound mutations G665C, E709G, L62R, and S957T observed prior to therapy disappeared after acquiring resistance. No HER2 amplification, HER3 mutation, or genomic fusions were observed. The levels of soluble HER3 ligand heregulin did not change significantly between pre-treatment and post acquired resistance.

Conclusion: Alternating therapy with osimertinib and afatinib for treatment-naïve patients with EGFR-mutated advanced NSCLC demonstrated encouraging efficacy. The advantages of this therapy are prevention of acquired resistance via secondary EGFR mutations, including T790M and C797S, and a broadened efficacy against various compound EGFR mutations.

Oral Abstract Session 2
October 28, 2022, 13:15 - 14:30

OA02.01:
Differential Diagnosis of Rare Thoracic Tumors Characterized by Gene Rearrangement Using RNA Pan-Cancer Panel

Dr. Harumi Nakamura[1], Dr. Yoji Kukita

[1]*Osaka International Cancer Institute, Osaka, Japan*

Background: NUT carcinoma, Ewing sarcoma, rhabdomyosarcoma, CIC-rearranged sarcoma, Synovial sarcoma, Solitary Fibrous Tumor and Salivary gland-type tumors are rare thoracic tumors. Among them, NUT carcinoma and CIC- rearranged sarcoma are particularly high-grade tumors with an average life expectancy of 6 months, therefore rapid and accurate differential diagnosis is very important. However, diagnosis is often difficult with conventional methods. We believe that the RNA pan-cancer panel will be an effective tool for the rapid and accurate differential diagnosis of rare cancers by gene rearrangement, including these high-grade tumors.

Methods: Fusion gene analysis was performed on 44 cases, including 6 thoracic tumors, of rare cancers with unclear or undetermined diagnoses that underwent biopsy or surgery at the Osaka International Cancer Institute from January 2012 to April 2022. We used to construct a sequencing library using the TruSight RNA Pan-Cancer Panel which includes 1385 genes (Illumina Inc., San Diego, CA) and this library was sequenced on an Illumina NextSeq 550 Instrument. The fusion analysis was done using the BaseSpace app RNA-Seq Alignment tool. Finally, a molecular pathological diagnosis was made based on a comprehensive evaluation of the tumor histopathological feature, immunostaining results and fluorescence in situ hybridization (FISH) method results and fusion gene analysis.

Results: Of the six thoracic tumors analyzed in the RNA Pan-Cancer Panel, five tumors (NUT carcinoma, Ewing sarcoma, tow Synovial sarcomas, Adenoid cystic carcinoma) had fusion genes of diagnostic significance, and one tumor had no fusion gene detected. Although CIC-rearranged sarcoma was not included in the thoracic tumors in this time, it was possible to detect CIC-rearranged sarcoma in other tissue.

Conclusion: The lung is not only the primary organ, but also the most common metastatic site of sarcoma. The RNA Pan-Cancer Panel is expected to be a very effective tool for rapid and accurate differential diagnosis of thoracic tumors caused by gene rearrangement.

OA02.02:
The Association of Tumor Metastatic Score and Overall Survival in Patients with Stage IV Non-Small Cell Lung Cancer Bearing Extra-Thoracic Metastases

Dr. Yen-lin Chen[1], Dr. Yao-Wen Kuo[2], Dr. Jei-Yie Huang[3], Dr. Kuan-Yu Chen[1]

[1]Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan, [2]Department of Integrated Diagnostics & Therapeutics, National Taiwan University Hospital, Taipei, Taiwan, [3]Department of Nuclear Medicine, National Taiwan University Hospital, Taipei, Taiwan

Background: Nearly half of the patients with non-small cell lung cancer (NSCLC) had stage IV disease at diagnosis. The prognoses of patients with stage IV NSCLC seem attributable to the extent of metastases. To elucidate the dissimilarity of outcomes in these patients, we proposed a novel scoring method, the tumor metastatic score (TMS), for evaluating the extent of metastases.

Methods: This retrospective cohort study was conducted at a tertiary teaching hospital in Taiwan. Stage IV NSCLC patients were included from the Integrative Medical Database. The patients were excluded if having misclassified stage, unavailable histologic reports, concomitant active malignancy other than lung cancer, treatment at other hospitals, and incomplete staging workup. The TMS summated the count of metastases in 11 organ systems, with each organ scored from 0 to 3 points at most. The clinical characteristics, genetic alteration profiles of tumors, and overall survival (OS) were recorded and analyzed. The OS was plotted by the Kaplan–Meier method and the difference between groups were analyzed by log rank test. A multivariable analysis using Cox proportional hazards model was performed for prognostic factors assessment.

Results: From May 2011 to April 2018, a total of 726 patients (399 patients were men, 55%) diagnosed with stage IV NSCLC bearing extra-thoracic metastases were included. The median age was 64.8 (IQR 56.9–75.2) years old. The most common histologic subtype was adenocarcinoma (n=616, 84.9%). Whole body PET was performed in 157 (21.6%) patients. Of the 444 subjects with available genetic testing, 186 (41.9%) had druggable oncogene. The patients with single metastasis were our reference group (n=111, 15.3%). All patients with more than one metastasis (n=615, 84.7%) were divided into 4 groups by the distribution of TMS value in quartiles. The patients in group 1 (TMS value 2–5) (n=181) had similar prognosis as the reference group (19.4 vs. 20.2 months; HR=1.00, 95% CI=0.77–1.29, p=0.994). The patients in other groups all had worse survival outcome compared with the reference. Age > 70 (HR=1.66, 95% CI=1.35–2.05, p<0.001), no oncogene alteration (HR=1.64, 95% CI=1.33–2.00, p<0.001), TMS score > 5 (HR=1.61, 95% CI=1.31–1.99, p<0.001), smoking (HR=1.34, 95% CI=1.04–1.72, p=0.023), and male sex (HR=1.29, 95% CI=1.03–1.62, p=0.028) were independently associated with a shorter survival than their counterpart.

Conclusion: The TMS provides an unconventional scoring method, which may be applied for prognosis prediction in stage IV NSCLC patients with extra-thoracic metastases. Further investigation is warranted to validate the clinical implication of TMS.

OA02.03:
AKT Pathway as a Therapeutic Target to Constrain Lineage Plasticity Leading to Histological Transdifferentiation

<u>Dr. Alvaro Quintanal-Villalonga</u>[1], Dr. Hirokazu Taniguchi[1], Dr. Yingqian Zhan[1], Mrs. Fathema Uddin[1], Mrs Viola Allaj[1], Mrs Parvathy Manoj[1], Mr. Nisargbhai Sha[1], Dr. Metamia Ciampricotti[1], Dr. Umesh Bhanot[1], Mrs. Jacklynn Egger[1], Mrs Juan Qiu[1], Dr. Elisa de Stanchina[1], Dr. Natasha Rekhtman[1], Dr. Brian Houck-Loomis[1], Dr. Richard Koche[1], Dr. Helena Yu[1], Dr. Triparna Sen[1], Dr. Charles Rudin[1]

[1]*Memorial Sloan Kettering Cancer Center, New York, United States*

Background: In lung adenocarcinomas (LUADs), lineage plasticity drives neuroendocrine (NE) and squamous cell (LUSC) transdifferentiation in the context of acquired resistance to targeted inhibition of driver mutations, with up to 14% and 9% incidences in EGFR-mutant tumors relapsed on EGFR inhibitors, respectively, leading to poor survival. To date no specific therapies aimed to prevent transformation are available for patients at high risk.

Methods: We performed genomic (whole exome sequencing), epigenomic (bisulfite sequencing), transcriptomic (RNAseq) and protein (antibody arrays) characterization of LUAD-to-LUSC and LUAD-to-NE transdifferentiating clinical samples. Clinical findings were validated in cell lines as well as LUSC- and NE-transdifferentiation patient-derived xenograft (PDX) models.

Results: Our data supports that histological transdifferentiation is driven by epigenetic remodeling rather than by mutational events. Integrative multi-omic analysis revealed divergent biological pathways dysregulated for each histological outcome, such as upregulation of genes involved in Hedgehog and Notch signaling and MYC targets in LUSC-transdifferentiated tumors. Most interestingly, these analyses identified commonly dysregulated pathways in both NE- and LUSC-transdifferentiating tumors, including remarkable downregulation of a variety of immune-related pathways and upregulation of genes involved in AKT signaling and in the PRC2 epigenetic remodeling complex. Concurrent activation of AKT and MYC induced a LUSC phenotype in EGFR-mutant LUAD preclinical models characterized by increased P40 and CK5/6 expression, further accentuated by EGFR inhibition. AKT inhibition in combination with osimertinib delayed LUSC relapse in an EGFR-mutant PDX model of LUSC transdifferentiation. Additionally, pharmacological targeting of AKT in combination with osimertinib delayed NE relapse in a PDX model of NE transformation.

Conclusion: These results identify common and divergent dysregulated pathways in NE and LUSC transdifferentiation, and nominate AKT as a therapeutic target to prevent the acquisition of resistance to EGFR-targeted therapies through histological transdifferentiation.

OA02.04:
A Phase Ib Study of AK112, a PD-1/VEGF Bispecific Antibody, in Combination with Etoposide and Carboplatin in First-Line Treatment of Extensive-Stage Small-Cell Lung Cancer

Dr. Shun Lu[1], Dr. Zhiwei Chen1, Dr. Lin Wu[2], Dr. Qiming Wang[3], Dr. Yan Yu[4], Dr. Rui Ma[5], Dr. Xianling Liu[6], Dr. Tao Li[7], Dr. Yan Li[8], Dr. Wei Zhao[8], Dr. Xia Song[9], Dr. Lin Li[10], Dr. Xiao Xu[11], Dr. Wei Liu[11], Dr. Zhongmin Wang[11], Dr. Baiyong Li[11], Dr. Yu Xia[11]

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Background: The current stand of care for extensive-stage small cell lung cancer (ES-SCLC) is PD-L1 antibody combined with etoposide and carboplatin. Either chemotherapy combine with immunotherapy or anti-VEGF antibody have shown encouraging clinical benefit. AK112 is a humanized IgG1 bispecific antibody that simultaneously binds to PD-1 and VEGF. This study evaluated safety and tolerability of AK112 in combination with etoposide and carboplatin, and explored preliminary anti-tumor efficacy of this regimen in first-line ES-SCLC patients. (NCT05116007)

Methods: This is an open-label, multi-center, phase Ib study, including dose escalation and dose expansion. In dose escalation part, safety of AK112 was assessed at 3 dose levels (3, 10, and 20mg/kg q3w) in a "3+3" design in combination with etoposide (100mg/m2, d1-3, q3w) and carboplatin (AUC 5mg/ml/min, d1, q3w) for up to 4 cycles treatment, followed by AK112 monotherapy maintenance. The assessment period of dose-limiting toxicities (DLTs) was 21 days. In dose expansion part, 2 doses of AK112 were selected to enroll no more than 30 patients in each cohort. Adverse events were graded per CTCAE 5.0 and efficacy were evaluated per RECIST Ver 1.1.

Results: At date cut-off on June 1, 2022, total 35 patients were enrolled, the median follow up time was 7.2 months. Average treatment time was 179 days. TRAE occurred in 32 (91.4%) patients, 19 (54.3%) patients experienced grade ≥3 TRAEs.The most common grade ≥3 TRAEs were neutropenia 8(22.9%), leukopenia 5 (14.3%), anaemia 4 (11.4%), thrombocytopenia 2 (5.7%). 12(34.3%) patients experienced irAE, and grade ≥3 irAE were reported in 3(8.6%) patients such as colitis 1(2.9%), enteritis 1(2.9%), paraneoplastic associated peripheral neuropathy 1(2.9%). AK112 related SAE were reported in 7 (20.0%) patients. 2 (5.7%) patients discontinued the study medication due to TRAEs. No new safety signal was observed. Among 35 patients, 3 patients did not get tumor assessment result because of AE and withdrawal of informed consent form, analysis based on 32 patients's confirmed tumor assessment result found that 29 patients achieved PR, 28 of which were confirmed, 3 patients achieved SD, with a confirmed ORR of 87.5% (28/32) and DCR of 96.9% (31/32). The mPFS was 6.9 months, 6 month PFS rate was 52.1%. OS data are not mature. Details of efficacy was shown in Table 1.

Conclusion: AK112 in combination with etoposide and carboplatin showed favorable safety profile and promising anti-tumor efficacy as first-line treatment in patients with ES-SCLC and may potentially be a very promising treatment option.
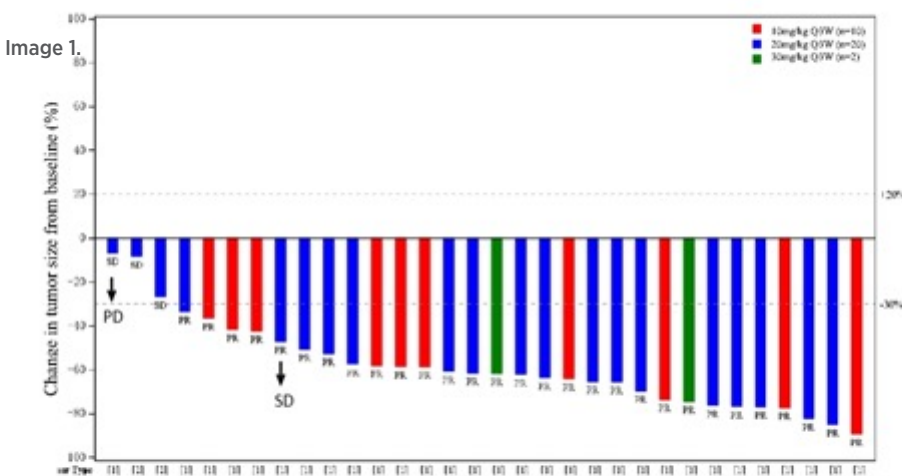
Image 1.

Figure 1. Best objective response in patients completed at least 2 times of tumor assessment (n=32).

Table 1.

Table 1. Summary of tumor response and survival benefit.

	3 mg/kg Q3W (N=2)	10 mg/kg Q3W (N=10)	20 mg/kg Q3W (N=20)	Total (N=32)
Confirmed ORR n(%)	2 (100.0)	10 (100.0)	16 (80.0)	28 (87.5)
[95% CI]	[15.8, 100.0]	[69.2, 100.0]	[56.3, 94.3]	[71.0, 96.5]
Confirmed DCR n(%)	2 (100.0)	10 (100.0)	19 (95.0)	31 (96.9)
[95% CI]	[15.8, 100.0]	[69.2, 100.0]	[75.1, 99.9]	[83.8, 99.9]
CR n(%)	0	0	0	0
PR n(%)	2 (100.0)	10 (100.0)	16 (80.0)	28 (87.5)
SD n(%)	0	0	3 (15.0)	3 (9.4)
PD n(%)	0	0	1 (5.0)	1 (3.1)
NE n(%)	0	0	0	0
Median DOR [95% CI]	NR[3.06, NE]	6.44[2.79, NE]	5.55[2.83, NE]	5.62[3.06, 7.69]
Median PFS [95% CI]	NR [4.3, NE]	7.0 [4.2, NE]	6.9 [4.1, 8.0]	6.9 [4.3, 8.5]
6-month PFS rate [95% CI]	50.0 [0.6, 91.0]	54.5 [22.9, 78.0]	51.2 [25.4, 72.0]	52.1 [32.8, 68.3]

This analysis included all subjects who had received at least one study drug, had a measurable lesion at baseline (as defined by RECIST V1.1), and had at least one post-administration tumor evaluation.

OA02.05:
Fear of Cancer Recurrence and its Predictors among Patients with Non-Small Cell Lung Cancer (NSCLC)

Dr. Wonyoung Jung[1,2], PhD Genehee Lee[3,4], PhD Danbee Kang[3], Dr Young Mog Shim[5], Dr Hong Kwan Kim[5], Ansuk Jeong[6], Dr Junhee Park[1], PhD Juhee Cho[3,7,8], MD, MBA, DrPH Dong Wook Shin[1,3,9]

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Background: We aimed to identify the prevalence of fear of cancer recurrence (FCR) and its predictors in patients with non-small cell lung cancer (NSCLC) in Korea.

Methods: We conducted a cross-sectional study using prospectively collected data. Participants completed survey questionnaires including the Korean version of Fear of Cancer Recurrence Inventory-Short Form (K-FCRI-SF), and the European Organisation for Research and Treatment of Cancer Quality of Life Core Questionnaire (EORTC QLQ-C30) from January to October 2020, at Samsung Medical Center, Republic of Korea. Logistic regression was used to determine the potential predictors associated with FCR.

Results: Of the total 949 study population (mean age 63.4 ± 8.8 years, female 44.3%), 55.8% were found to have high levels of FCR ($\geq$ 13). Among the nine items of K-FCRI-SF, the three greatest fears were 1) fear of disease progression (55.7%), 2) being afraid of recurrence (41.5%), and 3) being anxious about the possibility of recurrence (41.5%). Multivariable logistic regression showed that female sex (adjusted odds ratio [aOR] 1.49, 95% confidence interval [CI] 1.12-1.99), poor emotional (aOR 3.97, 95% CI 2.74-5.74), social (aOR 1.79, 95% CI 1.26-2.53), role (aOR 1.44, 95% CI 1.04-2.00) functioning, and severe dyspnea (aOR 3.14, 95% CI 1.13-8.74) were independent predictors of high FCR. Aged 70 or older were 43% less likely to have higher FCR (aOR 0.57, 95% CI 0.35-0.92), compared to patients aged under 55.

Conclusion: Our data demonstrated that high FCR was prevalent in NSCLC patients in Korea. Predictors of high FCR included younger age (< 55), female sex, poor emotional, social, role functioning, and severe dyspnea. Screening and early detection should be implemented in NSCLC patients with predictors of FCR.

Image 1.
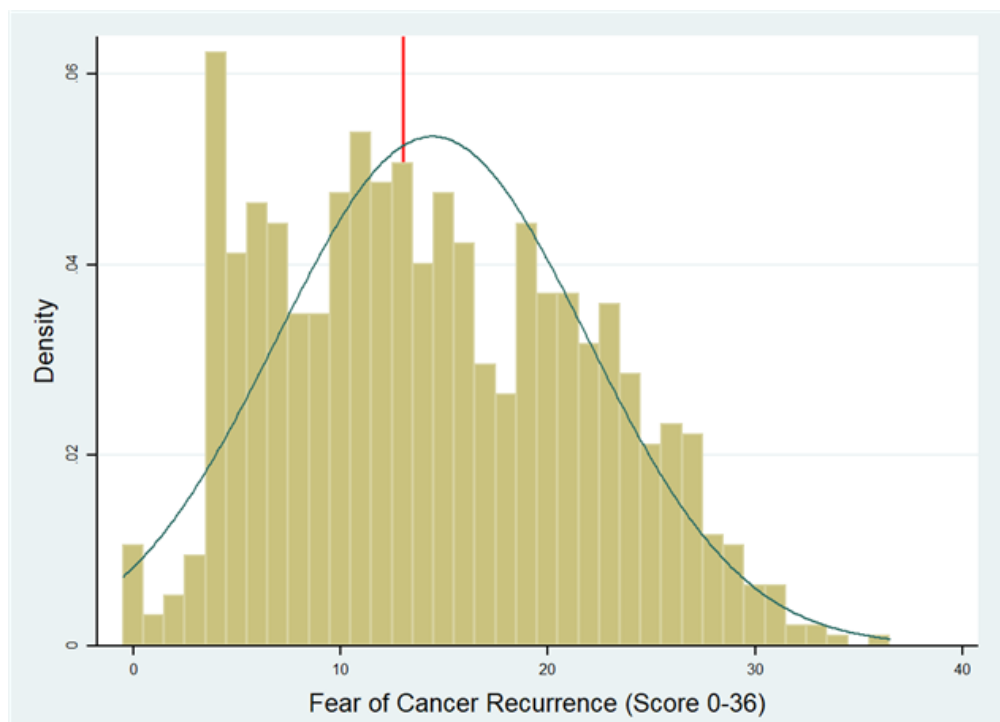
OA02.06:
CRESTONE: Initial Efficacy and Safety of Seribantumab in Solid Tumors Harboring NRG1 Fusions

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Background: NRG1 fusions are rare oncogenic drivers found in ~0.2% of all solid tumors that elicit HER3/ERRB3 overactivation to drive tumor growth. Currently there are no approved targeted therapies for NRG1 fusion-positive tumors. Patients (pts) with tumors harboring NRG1 fusions have poor outcomes with standard therapies. Seribantumab is a fully human anti-HER3 IgG2 monoclonal antibody that suppressed tumor growth in NRG1 fusion-driven preclinical models.

Methods: CRESTONE is a Phase 2, global, multicenter, open-label study of seribantumab in adult pts with locally advanced or metastatic solid tumors harboring NRG1 fusions. A dose ranging phase established the RP2D as a 3g once weekly (QW) intravenous dose administered until treatment discontinuation criteria are met. In the expansion phase, cohort 1 will enroll at least 55 pts who had received at least one prior therapy and are naïve to ERBB-targeted therapy. The primary endpoint is objective response rate (ORR) by independent central review per RECIST v1.1. Initial data from pts treated with seribantumab 3g QW on cohort 1 from the CRESTONE study (NCT04383210) with investigator (INV)-assessed response are reported.

Results: As of the data cut-off (APR 18, 2022), 15 pts have received seribantumab 3g QW in cohort 1. Median age was 61 years (range 44–76), 67% were female, and median number of prior therapies was 1 (range 1–5). 93% of pts had non-small cell lung cancer (NSCLC); 5 NRG1 fusion partners (ATP1B1, CD74, ITGB1, SDC4, SLC3A2) were reported. Among 12 pts evaluable for INV-assessed response, the confirmed INV-ORR was 33%, and the disease control rate was 92% with INV-ORR in NSCLC of 36% (including 2 complete responses, 2 partial responses). 53% of pts remain on study treatment, including 2 pts with NSCLC with an ongoing duration of response of 9.7 and 11.5 months. Seribantumab 3g QW was well tolerated with no drug discontinuations due to adverse events. Among the safety population (n = 35), the most frequently (≥20%) reported treatment-related adverse events (TRAEs) were diarrhea (40%), fatigue (29%), and rash (26%). Two grade 3 TRAE of vomiting and diarrhea were reported; no Grade 4 or 5 TRAEs. Initial efficacy and safety data will be presented and was previously presented at ASCO 2022.

Conclusions: Initial data indicate seribantumab induced durable responses in advanced solid tumors harboring NRG1 fusions with a favorable safety profile. These data support the evaluation of seribantumab in NRG1 fusion-positive solid tumors in the ongoing CRESTONE study.

Poster Tours

Poster Tour 1 & 2
October 27, 2022, 18:00 - 19:00

PPT01.01:
Protein Changes during Immune-Related Adverse Events and Corticosteroid Treatment in Cancer Patients Receiving Immune Checkpoint Inhibitors

Dr. Hiroaki Kanemura[1], Dr Satomi Watanabe[1], Dr, Kaoru Tanaka[1], Dr Soichi Fumita[1], Dr Seiichiro Mitani[1], Dr Koji Haratani[1], Dr, Yusuke Kawanaka[1], Dr, Takashi Kurosaki[1], Dr Shinichiro Suzuki[1], Dr Takeshi Yoshida[1], Dr Hisato Kawakami[1], Dr, Kimio Yonesaka[1], Dr, Tsutomu Iwasa[1], Sumire Shimada[2], Kimio Terao[2], Kazuhiko Nakagawa[1], Hidetoshi Hayashi[1]

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Background: Immune checkpoint inhibitors (ICIs) often cause immune-related adverse events (irAEs), but the exact mechanism underlying irAE has yet to be fully elucidated. The aim of this study was to identify circulating proteins that were associated with the development of irAEs.

Methods: The study included cancer patients who developed systemic irAEs during therapy with ICIs at Kindai University Hospital between 2019 and 2021. In this study, systemic irAEs were defined as meeting one of the following criteria: (1) serum CRP positive ($\geq$ 3mg /dL and more than 4 times higher than baseline) (2) with fever greater than 38°C (3) the presence of irAEs in multiple organs (4) receiving steroid therapy. We investigated 1460 proteins known to be involved in inflammation, cardiometabolism and carcinogenesis using the Olink panels in serum samples from 34 cancer patients. Serum samples were longitudinally collected at baseline (collected prior to ICI therapy initiations), at onset of irAEs, and after irAEs improved. Serum D-dimer, ferritin, heparan sulfate, hyaluronan, IL-6, and syndecan-1 were measured in all collected samples. Baseline protein levels and longitudinal change was compared with incidence and grade of irAE, ICI treatment, and responsiveness to corticosteroids.

Results: Among the 34 studied patients, 14 patients who developed grade 3-4 irAEs had significantly elevated baseline serum concentration of IL-6 (median 3.665 vs 1.700 pg/mL, p = 0.03) compared to 20 patients who developed grade 1-2 irAEs. Furthermore, there was significantly elevated serum concentration of IL-6 (median 26.33 vs 4.145 pg/mL, p = 0.03; median 32.89 vs 5.49 pg/mL, p = 0.04) in pneumonitis patients (N = 6) and hepatitis patients (N = 7), respectively. Of the 14 patients who had sufficient longitudinal protein measurements at 3 points, 9 patients received corticosteroid treatment. Although there was a trend toward decreased concentration of IL-6 after corticosteroid administration, one patient who developed steroid-resistant irAEs had the elevated change in IL-6 from 51.1pg/mL to 382.48 pg/mL. Based on the 1460 proteins we analyzed, pneumonitis patients (N = 6) had significantly higher level of SCGB3A2 (p = 0.02) compared to patients who did not develop pneumonitis. In addition, patients who received anti-CTLA-4 (N = 5) had significantly higher level of SRP14 (p < 0.0001) and XCL1 (p < 0.0001).

Conclusion: Baseline and longitudinal change of circulating proteins was associated with grade of irAEs, specific irAEs and responsiveness to corticosteroids, which may help in the management of irAEs.

PPT01.02:
Study on Tumor Immune Microenvironment of Pulmonary Lymphoepithelial Carcinoma Using Multiplex Immunohistochemical Staining

Dr. Wei-Hsun Hsu[1,2,3], Dr. Chia-Chi Hsu[1,3,4], Min-Shu Hsieh[5], Pei-Chen Tai[1,3], Dr. Derek De-Rui Huang[2], Jih-Hsiang Lee[1,2,3], Dr. Chia-Chi Lin[2], Yih-Leong Chang[4,5,6], Prof. Chih-hsin Yang[1,2,3,4]

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Background: Pulmonary lymphoepithelial carcinoma (LEC) is a rare type of lung cancer. The driver mutations in LEC are infrequent, so there are no available targeted therapies for LEC. Though the clinical outcomes of patients with LEC are better than those for patients with other types of lung cancer, tumors frequently recur. Evidence has indicated that the measurement of immune microenvironment factors may predict outcome of cancer therapy; however, the composition of immune microenvironment in LEC remains largely unknown. Here, we investigated the association between the immune microenvironment and clinical outcomes of LEC.

Method: We used surgical samples of LEC for multiplex immunohistochemical (IHC) staining. The densities for tumor-infiltrating CD4+ T lymphocytes, CD8+ T lymphocytes, CD68+ macrophages, CD20+ B lymphocytes, and CD4+/FoxP3+ Tregs in LEC were determined. Besides, we investigated the amount of each infiltrating immune cell spatially proximal to the closet tumor cell. The PD-L1 tumor proportion score (TPS) was examined using Dako 22C3 IHC staining. The relationship between the immunological profile and clinical outcomes of LEC was analyzed.

Results: By using multiplex IHC, 7 markers were stained and represent different cell subsets (Fig 1). There was no significant correlation between the clinical outcome of LEC and the density of each tumor-infiltrating immune cell type. Alternatively, we found that the amount of CD4+ T lymphocyte proximal to tumor was trended to longer disease-free survival in LEC (Fig 2). Additionally, the PD-L1 TPS was highly correlated with the amount of CD8+ T lymphocyte proximal to tumor, suggesting that immunotherapy might be beneficial for patients with advanced LEC.

Conclusion: In addition to the density of tumor-infiltrating immune cell, the spatial proximity of tumor-infiltrating immune cell measurement is useful for investigating the tumor-immune cells interaction. The spatial proximity of tumor-infiltrating CD4+ T lymphocytes might serve as a good prognostic factor for LEC.
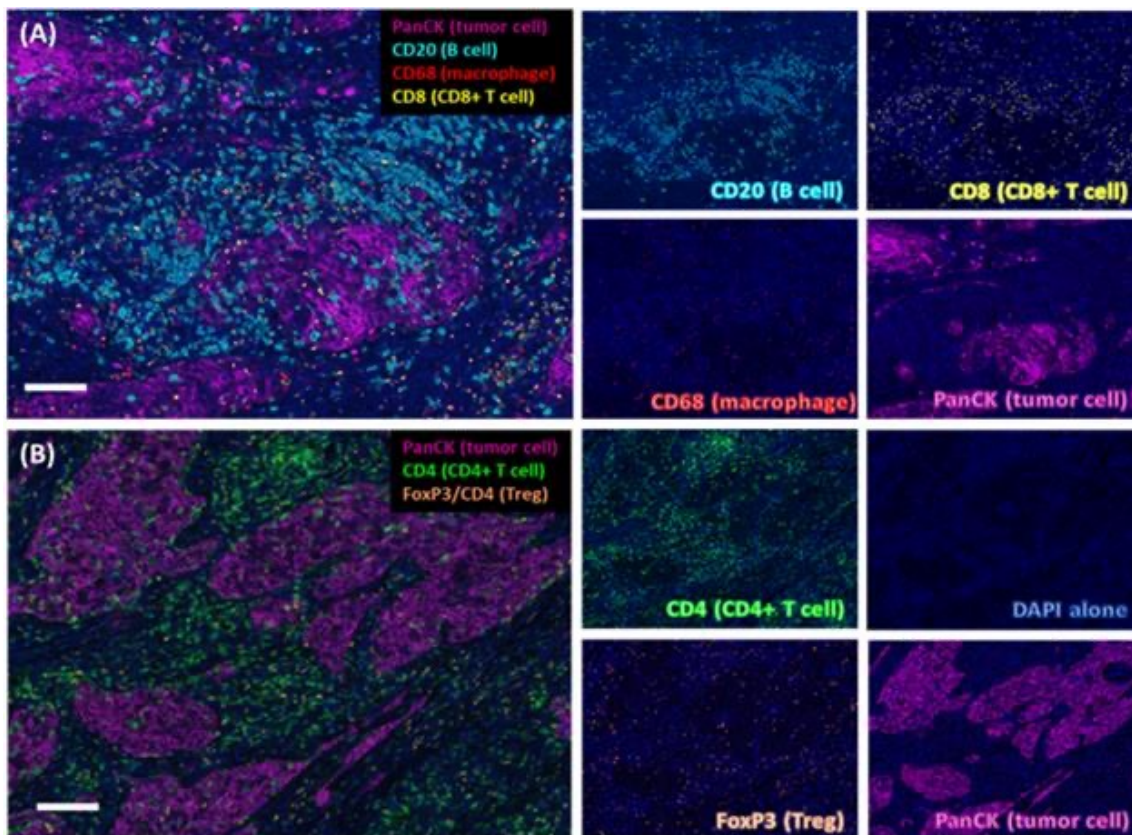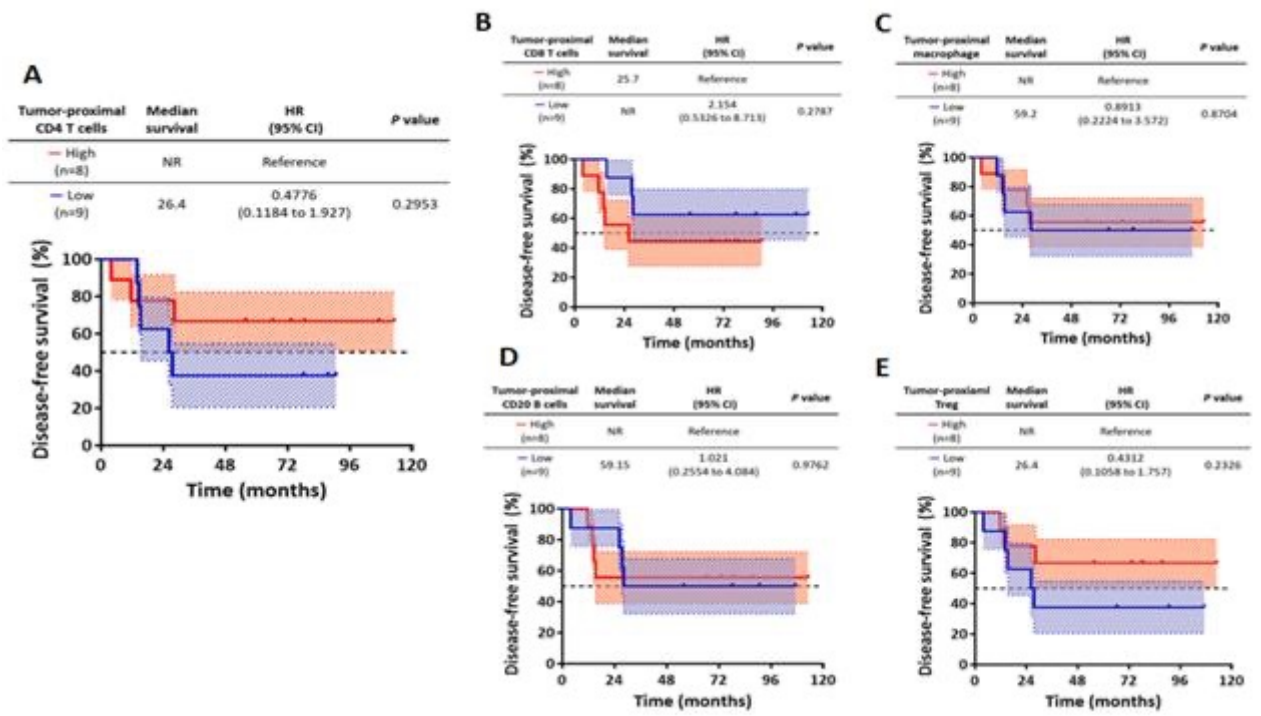
Image 1.

Image 2.

PPT02.01:
Risk of Thromboembolism in NSCLC with Different Oncogenic Drivers, Including ROS1, ALK and EGFR Mutation

Dr. Hsin-Yi Wang[1,2], Assoc. Prof. Shang-Gin Wu[3], MD Yen-Ting Lin[3], MD,PhD Chung-Yu Chen[1], Dr. Jin-Yuan Shih[4]

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Background: ALK and ROS1 positive lung cancer was reported to associate with an elevated risk of thromboembolic events. The study aimed to assess the long-term risk of developing thromboembolism in ROS1 positive lung cancer and compared to lung cancer with other oncogene drivers in the Asia population.

Methods: We retrospectively enrolled a cohort of ROS1 positive lung adenocarcinoma in a medical center in Taiwan and collected comparison cohorts of ALK+ and EGFR+ lung cancer. Events of venous and arterial thromboembolism throughout the cancer course were identified and the incidence rate was calculated. Characteristic and risk factors of thromboembolic events were also evaluated.

Results: Forty-four ROS1+, 98 ALK+ and 168 EGFR+ NSCLC patients were enrolled in the analysis. A total of 11 (25%), 36 (36.7%) and 38 (22.6%) patients in the ROS1, ALK and EGFR cohort respectively had a subsequent diagnosis of thromboembolic events throughout the follow-up course of the disease (p=0.042). The incidence rate was 99.0, 91.9 and 82.5 events per 1000 person-years for the 3 groups respectively. The majority of thrombosis events in the ROS1 (91.6%) and ALK (85.4%) cohort were venous. On the contrary, nearly half (43.2%) of thromboembolic events were arterial in the EGFR cohort. Most of the patients had thromboembolic events at the status of disease progression. A higher proportion of thromboembolic events were noted while cancer diagnosis in the ROS1 group (36.3%) than in ALK (16.7%) and EGFR (10.5%) group. Stage was the only clinical variable associated with thromboembolic risk both in univariate and multivariable analysis. More advanced stages resulted in a significantly higher risk of thromboembolic events. (OR: 1.62; 95% CI: 1.18–2.22; p=0.003) There was statistical significance in survival difference between patients with and without thromboembolism only in the EGFR group, but not in ALK or ROS1 group.

Conclusion: ROS1 and ALK-positive NSCLC had similar risks and incidence in venous thrombosis across the cancer course. EGFR mutated NSCLC had fewer venous thrombosis events but more arterial events probably related to the elder population.

Table 1 Absolute and relative rates of TE event by different molecular driver cohorts

	N	Patients with events	Events	Person Time (years)	Absolute rate – arterial and venous (per 1000 person years)	95% CI Lower	95% CI Upper	Relative rate *	95% CI Lower	95% CI Upper	Absolute rate - venous (per 1000 person years)	Absolute rate - arterial (per 1000 person years)
ROS1	44	11	12	111.1	99.0	56.5	173.4	1	-	-	99.0	9.0
ALK	98	36	41	391.8	91.9	67.3	125.4	1.192 (P=0.61)	0.60	2.36	79.1	12.8
EGFR	168	38	44	460.6	82.5	60.8	111.9	0.956 (P=0.90)	0.47	1.94	49.9	34.7

* Hazard ratios were estimated using Cox proportional hazards regression adjusted for sex, age, smoking and stage

\# Only first TE event in one specific patient were included in the analysis of absolute rate. There was one patient in ROS1 and EGFR group respectively representing arterial TE and venous TE at the same time as their first event.

Table 2 Characteristics of thromboembolic events

Mutation cohort	ROS1	ALK	EGFR	P value[&]
Number of patients	44	98	168	
Number of patients with thromboembolism events	11 (25%) *	36 (36.7%)[※]	38 (22.6%) [#]	P=0.042
Sex				
Male	2	18	13	
Female	9	18	25	
Type				
Arterial events	1	6	19	P=0.12
Location				
Coronary	0	3	2	
Cerebral	1	3	12	
Both coronary and cerebral	0	0	2	
Other	0	0	3	
Venous events	11	35	25	P=0.001
Location				
Pulmonary embolism	3	10	4	
Deep vein thrombosis	3	20	13	
Both PE and DVT	2	2	5	
Trousseau syndrome	2	0	0	
Other	1	3	3	

*One patient had both arterial and venous thrombosis

[※]Two patients had both arterial and venous thrombosis, one of them had both coronary and cerebral embolism. Two patients had recurrent venous thrombosis events.

[#] Four patients had more than one arterial TE events. Two patients had both arterial and venous thrombosis. One patient had recurrent venous thrombosis.

[&] by Chi-square Test

PPT02.02:
Computer-Assisted Flagging of Never Smokers at High Risk of NSCLC in a Large US-Based HMO Using the LungFlag Model

Mr. Eran Netanel Choman[1], Mr. Alon Lanyado[1]

[1]Medial Earlysign, Hod Hasharon, Israel

Background: Smoking is considered to be the major cause of lung cancer, but lung cancer is not just a smokers' disease. The prevalence of lung cancer in never-smokers is gradually rising with around 20% of lung cancers in the UK and US occurring in people who have never smoked. This figure rises to around 50% in some Asian countries.

Methods: A machine-learning algorithm based on routine EHR and laboratory data, previously developed and validated on an ever-smoker population was used to evaluate the accuracy in detection of Non-Small Cell Lung Cancer (NSCLC) among individuals who never smoked. The cohort was from a large US HMO and included 509 case patients with NSCLC and 50,001 contemporaneous NSCLC-free controls.

Results: Data were analyzed using the area under the receiver operating characteristic curve (AUC), Positive Predictive Value (PPV), and diagnostic odds ratio (OR) as measures of model performance for the age group 40 and above. The risk predictor was calculated for multiple time windows prior to the diagnosis date (Dx) using cut-offs yielding specificities of 95%, 97% or 99%.

Conclusion: The model demonstrated high accuracy in early detection of NSCLC among never-smokers.

Table 1.

Time Window (Months before Dx)	AUC	Specificity Level					
		99%		97%		95%	
		PPV %	OR	PPV %	OR	PPV %	OR
3-6M	0.805 [0.773,0.840]	3.7 [2.3,5.6]	12.0 [7.1,19.5]	2.3 [1.7,3.3]	8.3 [5.7,12.7]	2.2 [1.7,2.9]	8.8 [6.5,13.5]
6-9M	0.821 [0.793,0.850]	2.6 [1.1,4.3]	8.2 [3.6,14.1]	2.3 [1.5,3.1]	8.0 [5.1,11.6]	2.0 [1.5,2.5]	7.7 [5.2,10.5]
9-12M	0.799 [0.771,0.832]	3.2 [1.6,5.2]	8.7 [4.7,15.2]	2.4 [1.7,3.4]	7.0 [4.8,10.7]	2.1 [1.6,2.8]	6.4 [4.6,9.7]

PPT02.03:
Preoperative Localization Technique Using Mixture of Indigo-Carmine and Lipiodol of Pulmonary Nodule via Transbronchial Approach

Dr. Soojin Lee[1], Prof. Na Hyeon Lee[2], Prof. Jung Seop Eom[3], Prof. Jeongha Mok[3]

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Background: As the number of minimally invasive surgeries, including video-assisted thoracoscopic surgery increases, small, deeply located lung nodules are difficult to visualize or palpate; therefore, localization is important. We studied the use of amixture of indigo-carmine and lipiodol coupled with a transbronchial approach to achieve accurate localization and minimize patient discomfort and complications.

Methods: Total of 60 patients were enrolled from May 2019 to April 2022, and surgery was performed after the bronchoscopy procedure. Wedge resection or segmentectomy was performed, depending on the location and size of the lesion (Fig.1). Bronchoscopy was performed using a 4.0-mm flexible bronchoscope (BF-P260F; Olympus,Tokyo, Japan)under conscious sedation using fentanyl and midazolam. After airway inspection, the bronchoscope was advanced to the target lesion using virtual bronchoscopic navigation (Bronchus Technologies, Inc., Mountain View, CA, USA). Thereafter, under X-ray fluoroscopic guidance, a 20-MHz radial probe EBUS (UM-S20-17S; Olympus, Tokyo, Japan) was inserted into theguide sheath (K-201; Olympus, Tokyo, Japan) and pushed through the working channel towards and as close to the lesion as possible (Figure 1). After the lesion was targeted, the radial probe was removed, and the mixture was injected through the guide sheath

Results: In 58/60 (96.7%) patients, surgery was successful after localization (Fig. 2), and 2/60 required c-arm assistance. None of the patients complained of discomfort during the procedure, and in all cases, margins were found to be free from carcinoma as determined by final pathology results.

Conclusion: We recommend this localization technique using mixture of indigo-carmine and lipiodol in concert with the transbronchial approach because the procedure time is short, patient's discomfort is low, and success rate is high.

Image 1.
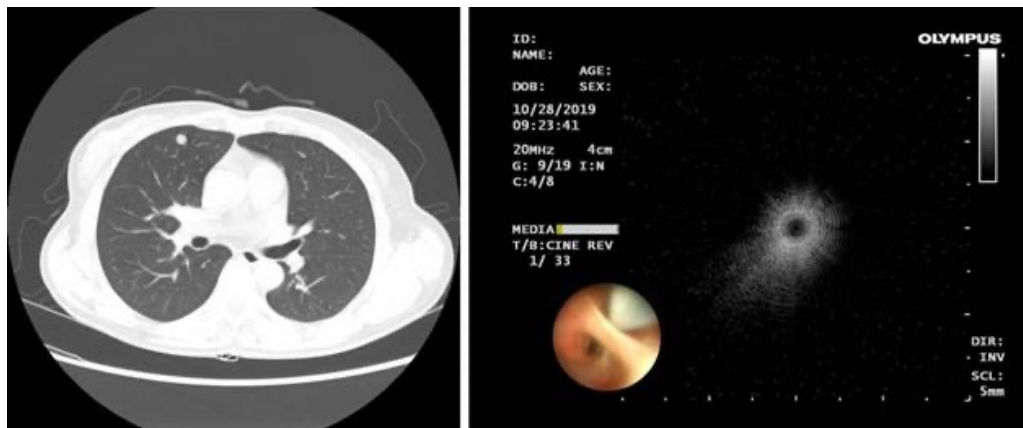
Image 2.
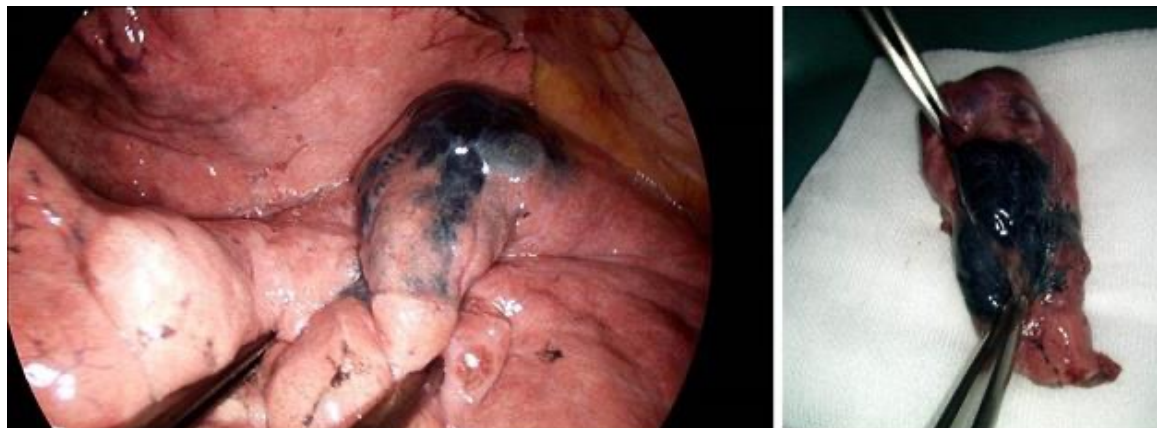
PPT02.04:
Analysis of Pre-Analytic Factors Affecting the Success of Next-Generation Sequencing of Non Small Cell Lung Cancer

Dr. Naoki Shiraishi[1], Dr. Takayuki Takahama[1,2], Dr. Kaoru Tanaka[2], Mr, Yuzuki Nakagawa[1], Dr. Yusuke Kawanaka[2], Dr. Takashi Kurosaki[2], Dr. Shinishiro Suzuki[2], Dr. Tsutomu Iwasa[2], Dr. Junko Tanizaki[2], Dr. Masayuki Takeda[3], Hidetoshi Hayashi[2], Dr. Kimio Yonesaka[1,2], Dr. Kazuya Fukuoka[1,4], Kazuhiko Nakagawa[1,2]

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Background: The Japanese Lung Cancer Society guidelines recommend biomarker testing to determine the treatment strategy for advanced non-small cell lung cancer (NSCLC). For biomarker testing, we have used the Oncomine Dx Target test (ODTT), an NGS-based assay. However, the initial success rate of the ODTT was low in our hospital. In several cases, ODTT failed due to insufficient nucleic acid extracted from the sample. Therefore, we report on our efforts to increase the success rate of NGS testing, including the introduction of rapid on-site cytologic evaluation (ROSE) and in-house testing and validation in our hospital.

Methods: Between June 2019 to March 2022, 240 patients who underwent ODTT in our hospital were included in the analysis. The 40 patients who received ODTT from June 2019 to June 2020 were defined as the "pre-review group," and the 200 patients who received ODTT from June 2020 to March 2022 were defined as the "post-review group." To identify the causes affecting the success rate of the ODTT, we have investigated sample type, sample size, and the quantity and quality of extracted DNA/RNA in the pre-review group. We have identified several factors affecting the success rate of the ODTT in the pre-review group. In the post-review group, we examined the success rate of ODTT testing after introducing remedial measures.

Result: We examined the causes of ODTT failures in the pre-review group. We found that the inconsistent quality and quantity of samples and the lack of standardized NGS testing procedures were the reasons for the test failures. Starting in June 2020, the specimen collection process was performed by introducing ROSE. In addition, the quality check process and thin slice process were improved through in-house testing. In the pre-review group, the success rate of ODTT was 55%, and the test submission rate was 82%. In the post-review group, the success rate of ODTT was 98%, and the test submission rate was 97%, with a marked improvement. Compared to the pre-review group, the success rate and test submission rate for biopsy samples such as TBB and TBNA increased in the post-review group with the introduction of ROSE. In addition, the in-house testing process improved the mutation detection rate, turnaround time (TAT), and the uniformity of nucleic acid extraction concentrations among specimen types.

Conclusion: The success rate of ODTT testing improved after the introduction of ROSE and the implementation of the test at their facility.

Poster Tour 3
October 28, 2022, 17:00 - 18:30

PPT03.01:
Phase II Study of S-1 and Cisplatin with Concurrent Thoracic Radiotherapy Followed by Durvalumab for Unresectable, Locally Advanced Non-Small-Cell Lung Cancer in Japan (SAMURAI Study)

Dr. Kazuhiko Shibata[1], Dr. Shigeru Tanzawa[2], Dr. Hisashi Tanaka[3], Dr. Megumi Inaba[4], Dr. Jyunya Nakamura[5], Dr. Takayuki Kishikawa[6], Dr. Masanao Nakashima[7], Dr. Keiichi Fujiwara[8], Dr. Tadashi Kohyama[9], Dr. Hiroo Ishida[10], Dr. Toshihiro Misumi[11], Dr. Kenshiro Shiraishi[12], Dr. Noriyuki Matsutani[13], Dr. Nobuhiko Seki[2]

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Background: The standard treatment for patients with unresectable, locally advanced NSCLC (LA-NSCLC) is chemoradiotherapy (CRT) followed by durvalumab, based on the PACIFIC trial. However, the transition rate and the reasons for failure to proceed to durvalumab after CRT were not evaluated, prospectively. Furthermore, although phase II studies in Japan have shown high efficacy and tolerability of CRT with cisplatin + S-1 (SP), no prospective study using durvalumab after SP-based CRT has yet been reported. We therefore conducted a phase II study to verify the efficacy and safety of durvalumab following SP-based CRT.

Method: This study was prospective, single arm, multicenter, phase II clinical trial. Eligibility criteria included patients with unresectable stage III LA-NSCLC, ECOG PS 0-1, aged over 20. Patients with EGFR mutation or ALK rearrangement were allowed. Cisplatin (60 mg/m2, day1) and S-1 (80-120 mg/body, day1-14) were administered with two 4-week cycles with concurrent thoracic radiotherapy (60Gy) followed by durvalumab (10 mg/kg) every two weeks for up to one year. The primary endpoint was 12-month PFS rate from first registration assessed by the investigators. The planned sample size was 58 with a threshold value of 47% calculated from TORG1018 study in Japan, an expected value of 63% calculated from PACIFIC trial, α = 0.10 (one-sided) and β = 0.8 in 12-month PFS rate.

Results: From December 2019 to August 2020, 59 patients were enrolled from 22 institutions. Median age was 68 (range: 42-81). 7 patients had driver mutation (EGFR mutation; n=3, ALK rearrangement; n=4). All patients received CRT after the first registration, and of whom 86.4% (51/59) proceeded to durvalumab after the second registration. Median follow-up time was 21.9 months. The 12-month PFS rate from first registration was 72.5% (80% CI: 64.2–79.2, 95% CI: 59.1–82.2). The 12-month PFS rate from second registration was 70.1%. Median PFS and MST were not reached. The 12-month OS rate and the 18-month OS rate were 91.5% and 86.4%, respectively. The ORR in CRT phase and consolidation phase were 62.7% and 45.1%, respectively. The progressive disease rate in each phase were 3.4% and 21.6%, respectively. Grade 3 common adverse events are neutropenia (20.4%) and anorexia (10.2%) in CRT phase, and pneumonitis (2.0%) in consolidation phase. An all-grade common immune-related adverse event in consolidation phase was thyroid dysfunction (21.6%).

Conclusions: Our study met the primary endpoint. SP-based CRT could be a candidate for the further evaluation.

PPT03.03:
Prognosis and Efficacy of Adjuvant Therapy in Post-Surgical NSCLC Patients with WES-Based Genetic Profiling

Dr. Akiko Tateishi[1], Dr. Hidehito Horinouchi[1], Dr. Takaaki Mizuno[1], Dr. Yu Okubo[1], Dr. Yukihiro Yoshida[1], Dr. Shun-Ichi Watanabe[1], Dr. Mototaka Miyake[1], Dr. Masahiko Kusumoto[1], Dr. Koji Inaba[1], Dr. Hiroshi Igaki[1], Dr. Yasushi Yatabe[1], Dr. Masami Mukai[1], Dr. Naoki Mihara1, Kouya Shiraishi[2], Takashi Kohno[2], Dr. Yuichiro Ohe[1], Ryuji Hamamoto[2]

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Background: Only a few reports conducted whole exome sequencing (WES) for genomic profiling in large scale non-small cell lung cancer (NSCLC) cases.

Method: We conducted WES and analyzed the clinical course of patients with NSCLC who underwent surgery between 1985 and 2019 in the PRISM project of our institute. We evaluated the patients' characteristics, recurrence-free survival (RFS), overall survival (OS), and postoperative adjuvant chemotherapy (Adj). The patients (pts) were divided into those without any druggable gene alterations (Pan-negative; PN) and with some gene alterations such as EGFR mutation (MT).

Results: A total of 1351 pts were included in the study. The histological types were adenocarcinoma (1111 pts, 82.2%), squamous cell carcinoma (189 pts, 14.0%), and others (51 pts, 3.8%). WES revealed the presence of the following genetic mutations: EGFR MT (585 pts, 43.3%); ALK fusion (32 pts, 2.4%), KRAS MT (124 pts, 9.2%), BRAF MT (21 pts, 1.6%), MET exon14 skipping (17 pts, 1.3%), RET fusion (22 pts, 1.6%), and ROS-1 fusion (13 pts, 1.0%), The median RFS and OS of the PN and MT groups were as follows: PN, 36.0 months (m) and 149 m; EGFR, 53.8 m (hazard ratio (HR) 0.81, p=0.01) and 124 m (HR 0.75, p=0.01); ALK fusion, 23.7 m and not reached (NR); KRAS, 27.2 m and 79 m (HR 1.42, p=0.03); BRAF, 32.0 m and 153 m; MET exon14 skipping, 36.5 m and NR; RET fusion, 121.1 m (HR 0.47, p=0.04) and NR; and ROS-1 fusion, 32.0 m and 78 m. A total of 90 pts received Adj, 23 pts were PN, 41 pts were EGFR MT positive, and 26 pts had other MTs. In patients who received Adj, the median RFS of the PN and EGFR MT groups was NR and 22.5 m (HR 5.64, p<0.01), respectively, and the median OS was NR for both.

Conclusions: Compared with the PN group, pts with EGFR MT and RET fusion tended to have a better RFS and patients with EGFR MT, ALK fusion, and RET fusion tended to have a better OS. Moreover, EGFR MT pts with Adj seemed to have a poorer prognosis than PN pts with Adj.

PPT03.04:
AI-based Quantitative CT Analysis for Prediction of Radiation Pneumonitis after Stereotactic Body Radiotherapy for the Lung

<u>Mr. Masahiro Yoneyama</u>[1], Dr. Yukinori Matsuo[1], Dr. Noriko Kishi[1], Dr. Ryo Itotani[2], Dr. Tsuyoshi Oguma[2], Dr. Hiroaki Ozasa[2], Dr. Kiminobu Tanizawa[2], Dr. Tomohiro Handa[2], Dr. Toyohiro Hirai[2], Dr. Takashi Mizowaki[1]

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Background: The association between chest CT features and radiation pneumonitis (RP) has been shown, and CT-based predictive models of RP are warranted. However, those have not been put into practical use due to the difficulties in quantifying CT features. Here, we applied AI-based quantitative CT analysis (AIQCT) to pre-treatment high-resolution CT (HRCT) in patients who received stereotactic body radiotherapy (SBRT) for the lung to evaluate the relationship of CT features with RP.

Method: Patients who received SBRT to stage I non-small cell lung cancer were enrolled between January 2011 and June 2020. AIQCT automatically categorized lung parenchyma and airways as percentages of the total lung volume. Four (composite) regions were categorized: reticular + honeycomb (Ret+HC), bronchi (= airways within the lung, Br), consolidation + ground-glass opacities (Con+GGO), and normal lung (NL). We collected the percentages of these regions and the mean dose (Dmean) for them obtained from dose distributions on simulation CT using deformable image registration. The patients were divided into training (first three-quarters of patients) and testing (last quarter) cohorts. We applied the recursive partitioning and regression tree (RPART) to the training cohort to build a predictive model of grade 2 or worse radiation pneumonitis (G2+RP). Model performance was assessed using the testing set.

Results: We enrolled 207 patients (154 for training and 53 for testing). G2+RP occurred in 26 patients (12.6%). Univariate analysis showed significant differences in volumes of Ret+HC and Br, and Dmean of NL between patients with and without G2+RP, with medians [IQRs] of 0.3% [0.1–0.6] and 0.2% [0.1–0.4] (P = 0.04); 1.9% [1.6–2.5] and 1.7% [1.4–2.1] (P = 0.04); and 4.3 Gy [3.2–6.3] and 3.5 Gy [2.5–4.6] (P < 0.01), respectively. The RPART identified the following three risk groups: NL-Dmean $\geq$ 6.6 Gy (high risk, n = 8); NL-Dmean < 6.6 Gy and Br-volume $\geq$ 2.5% (moderate risk, n = 13); and NL-Dmean < 6.6 Gy and Br-volume < 2.5% (low risk, n = 133). The incidence of G2+RP was 62.5%, 38.4%, and 7.5% in the three risk groups, respectively (P < 0.01). In the testing cohort, the incidence according to the risk groups was 50.0%, 27.3%, and 5.0%, respectively (P < 0.01).

Conclusions: AI-based quantitative CT analysis identified CT features related to radiation pneumonitis after SBRT for the lung. A predictive model of RP was proposed based on AI-detected bronchial volume and the mean dose to the normal lung.

PPT03.05:
Afatinib + Bevacizumab vs Afatinib Alone as First Line Treatment of Patients with EGFR Mutated NSCLC: Subgroup Analysis of a Randomized, Phase II Study: AfaBev-CS

Dr. Toshiyuki Kozuki[1], Dr Nobuhisa Ishikawa[2], Dr Shoichi Kuyama[3], Dr Nobuhiro Kanaji[4], Dr Kouji Inoue[5], Dr. Toshihide Yokoyama[6], Dr Masayuki Yasugi[7], Dr Takuo Shibayama[8], Dr Keisuke Aoe[9], Dr Kazunori Fujitaka[10], Dr Masahiro Kodani[11], Dr Nobuaki Ochi[12], Dr Yutaka Ueda[13], Dr Kazuhiko Watanabe[14], Dr Akihiro Bessho[15], Dr Keisuke Sugimoto[16], Dr Shoichiro Yamamoto[17], Dr Yoshihiro Amano[18], Dr Hiroshi Ohnishi[19], Dr Nobukazu Fujimoto[20], Dr Hirohisa Ichikawa[21], Dr Takashi Ninomiya[1], Dr Isao Oze[22], Prof Katsuyuki Kiura[23]

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Background: Adding bevacizumab to erlotinib prolonged PFS in NEJ026 and CTONG1509 trials, but limited data are available adding bevacizumab to a second-generation EGFR-tyrosine kinase inhibitor. AfaBev-CS is a Japanese no-profit, randomized, open-label, multicenter phase II trial of afatinib plus bevacizumab vs afatinib alone as first-line treatment for EGFR-mutated advanced NSCLC. We reported result of primary endpoint in ASCO2022 (Abst#9112).

Methods: Untreated patients of advanced non-squamous NSCLC harboring EGFR sensitizing mutation (Del19 or L858R) and without symptomatic brain metastases were enrolled. Eligible patients were randomized in a 1:1 ratio to receive either afatinib (30 mg, daily) plus bevacizumab (15 mg/kg, every 3 weeks) (AfaBev arm) or afatinib (40 mg, daily) monotherapy (Afa arm), and stratified according to stage, EGFR mutation status and institution. The primary endpoint was PFS and the secondary endpoints were OS, tumor response and adverse events. The sample size was set in terms of feasibility. The power is greater than 50% under the assumptions of a median PFS of 12 months for the Afa arm and HR of 0.6 for the AfaBev arm, with an accrual of 2.5 years and a minimum planned follow-up period of 2 years with the type 1 error of 0.05 (two-sided).

Results: Between August 2017 and September 2019, 100 patients were enrolled (each arm, 50 patients). At a median follow-up of 31.3 months for all randomized patients, total 69 events occurred. Median PFS was 16.3 months for AfaBev arm and 16.1 months for Afa arm, with a hazard ratio (HR) of 0.865 (95%CI, 0.539 – 1.388; log-rank p=0.5476). Median PFS was 21.9 months for AfaBev arm and 16.4 months for Afa arm (HR 0.724; 95%CI, 0.353 – 1.483) in EGFR exon19 deletion. Median PFS was 16.1 months for AfaBev arm and 16.0 months for Afa arm (HR 0.840; 95%CI, 0.380 – 1.857) in EGFR exon21 L858R. In terms of OS, result was immature because number of events was still small. Objective response rate was 77.6% in AfaBev arm and 72.0% in Afa arm. Severe adverse events were observed in 11 patients for each arm. Grade 3 or more diarrhea, hypertension, rash acneiform, paronychia and stomatitis were frequently observed in AfaBev arm.

Conclusions: This study failed to show the efficacy of AfaBev arm for improving PFS in untreated patients with EGFR mutated non-squamous NSCLC. There was no significant difference in both EGFR exon 19 deletion and exon 21 L858R subgroups. Clinical trial information: jRCTs061180006

PPT03.06:
The Case Fatality Rate of COVID-19 Infection and Effect on Systemic Treatment of COVID-19 Infection in Non-Small Cell Lung Cancer

Ms. Yeji Jung[1], Dr. Daeho Choi[1], Dr. Sehhoon Park[1], Dr. Hyun Ae Jung[1], Dr. Jong-Mu Sun[1], Dr. Se-Hoon Lee[1], Dr. Jin Seok Ahn[1], Dr. Myung-Ju Ahn[1]

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Background: In the outbreak of COVID-19, the case fatality rate was higher, especially in advanced cancer patients. The Omicron variant was well known that had high transmissibility but a lower risk of mortality. It has not been revealed whether the current systemic treatment could be retained or not in advanced non-small cell lung cancer (NSCLC) patients with a COVID-19 infection.

Methods: We retrospectively reviewed the medical record of NSCLC patients who were diagnosed with COVID-19 infection at the Samsung Medical Center between 2020 and April 2022. We analyzed the case fatality rate and risk factors for case fatality rate. In patients with palliative systemic treatment, we investigated the COVID-19 infection' effect on their systemic treatment.

Results: Among 1,072 NSCLC patients who were diagnosis with COVID-19 infection, 570 patients who were cured after surgery, and 143 patients had stable disease after concurrent chemo-radiotherapy. Among 452 advanced NSCLC patients, 387 patients received systemic treatment in palliative setting. Of them, 188 patients who received targeted therapy, 111 patients received cytotoxic chemotherapy, 58 patients received immunotherapy +/- chemotherapy, and 19 patients received the systemic treatment of clinical trial. Among them, 94.6% of patients (338 of 387) continued their systemic treatment after the COVID-19 infection. Only one patient discontinued their treatment due to complication of COVID-19 infection and 18 patients changed their systemic treatment due to disease progression. The case fatality rate was 3.8% (17 of 452) in advanced NSCLC patients. The risk factor of the case fatality rate was old age (≥75 years), history of previous lung radiotherapy, current cytotoxic chemotherapy, and underlying lung disease (interstitial lung disease or chronic obstructive pulmonary disease). Among the total patients, 58 patients were infected with COVID-19 during PD-1/PD-L1 inhibitor alone or PD-1/PD-L1 inhibitor with chemotherapy. Six of them ceased treatment due to disease progression, but 52 patients continued their treatment even after COVID-19 infections. Among 188 patients with targeted therapy such as EGFR-TKI and ALK-TKI, there was no case with treatment discontinuation.

Conclusions: In the Omicron wave, majority of advanced NSCLC patients continued systemic treatment and had low case fatality rate compared to other variants. However, patients with risk factor such as old age (≥75 years), history of previous lung radiotherapy, current cytotoxic chemotherapy, and underlying lung disease need careful management. Majority of patients who received PD-1/PD-L1 with or without chemotherapy, or targeted therapy continued their treatment after COVID-19 infection.

Poster Sessions

Poster Viewing Reception A
Exhibit and Poster Hall | October 27, 2022, 18:00 - 19:00

PP01.01:
A Meta-Analysis for Treatment-Related Adverse Events of Combination Chemoimmunotherapy vs Chemotherapy in First-Line Treatment for NSCLC

Dr. Kazuki Takada[1], Dr. Shinkichi Takamori[2], Mr. Fumitaka Mizuki[3], Dr. Naoko Miura[1], Dr. Yasunori Shikada[1], Prof. Mototsugu Shimokawa[4,5]

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Background: Many meta-analyses have been conducted on adverse events (AEs) of immunotherapy in non-small-cell lung cancer (NSCLC). However, only one meta-analysis of AEs with combination chemoimmunotherapy versus chemotherapy alone in the first-line treatment of NSCLC has been published, and that report did not show what toxic symptoms and hematologic toxicities occurred more frequently with the addition of immune checkpoint inhibitors (ICIs) compared with chemotherapy alone.

Methods: We searched the PubMed and Scopus databases and conducted a meta-analysis of randomized clinical trials (RCTs) comparing ICI + non-ICI versus non-ICI as a first-line therapy in NSCLC. The aim was to investigate the treatment-related AEs of combination chemoimmunotherapy versus chemotherapy alone in first-line treatment for NSCLC and what toxic symptoms and hematologic toxicities were more frequent with the addition of ICIs compared to chemotherapy alone. We calculated the relative risks (RRs) and 95% confidence intervals (CIs) from the data of RCTs and estimated the pooled RRs and 95%CIs using common- or random-effects models.

Results: A total of eleven trials involving 6,757 patients were included. Combination chemoimmunotherapy was significantly associated with higher risk of any treatment-related AEs, grade 3 or higher treatment-related AEs, treatment discontinuation due to treatment-related AEs, and deaths due to treatment-related AEs than chemotherapy alone. Moreover, patients receiving combination chemoimmunotherapy had a significantly higher risk for some toxic symptoms (all grade: vomiting, diarrhea, and constipation; high grade: fatigue and diarrhea) and hematologic toxicities (high grade: thrombocytopenia) than patients receiving chemotherapy alone.

Conclusions: Combination chemoimmunotherapy was significantly associated with higher risk of treatment-related AEs than chemotherapy alone in the first-line treatment of NSCLC. The results provide an important reference of toxicity of combination chemoimmunotherapy for our clinicians in the management of lung cancer care, and we need to be aware of the results when treating lung cancer.

PP01.02:
Central Nervous Systemic Efficacy of Immune Checkpoint Inhibitors and Concordance Between Intra/Extracranial Response in Non-Small Cell Lung Cancer Patients with Brain Metastasis

Ms. Sora Kang[1], MD Hyehyun Jeong[2], MD Ji Eun Park[3], MD, PhD Ho Sung Kim[3], MD, PhD Young-Hoon Kim[4], MD, PhD Sang-We Kim[2], MD, PhD Jae Cheol Lee[2], MD, PhD Chang Min Choi[2], MD, PhD Shinkyo Yoon[2], MD, PhD Dae Ho Lee[2]

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Background: Immune checkpoint inhibitors (ICIs) markedly improve the clinical outcomes of advanced non-small-cell lung cancer (NSCLC). However, the intracranial efficacy of ICI is not well elucidated, and previous studies showed discordant outcomes of ICI between intracranial and extracranial diseases. We aimed to evaluate the clinical outcomes and the intracranial and extracranial response of patients with NSCLC and brain metastasis who were treated with ICI in the real-world setting.

Methods: A total of 55 patients (median age, 63 years [range, 42–80]; male, 78%) who had NSCLC with brain metastasis and treated with ICI monotherapy were retrospectively analyzed. We separately assessed the response rates of brain lesions and systemic lesions, and estimated the overall survival (OS) and progression-free survival (PFS).

Results: The median OS and overall PFS were 17.0 months (95% CI, 10.3–25.6) and 3.19 months (95% CI, 2.24-5.03), respectively. The intracranial objective response rate and disease control rate of ICI were 36% and 54%, respectively. Among the 44 patients who showed disease progression, only 32% (n = 14) showed concordant outcomes and 9 patients (20%) showed opposing discordant outcomes. Eight patients continued ICI with local brain therapy after intracranial progression, and their median extracranial PFS and OS were 15 months (95% CI, 5.0–not assessed [NA]) and 23.8 months (95% CI, 14.7–NA), respectively.

Conclusions: ICI monotherapy had a clinically meaningful intracranial efficacy in NSCLC patients with brain metastasis. Watchful waiting and close monitoring without local radiotherapy might be feasible in NSCLC patients with asymptomatic active brain metastasis.

PP01.03:
Effectiveness of Adding Chemotherapy to ICI for First-Line Treatment of Advanced NSCLC with PD-L1 Score Around 50%: Regression Discontinuity Analysis

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Background: : Selection between immune checkpoint inhibitor monotherapy (ICI-mono) or combined with platinum-based chemotherapy (ICI-chemo) is determined by PD-L1 expression with a cut-off value of 50% as the first-line treatment for patients with metastatic non-small-cell lung cancer (NSCLC). However, the effect of adding chemotherapy to ICI with PD-L1 score around 50% is unknown. We compared clinical outcomes with ICI-mono versus ICI-chemo using a quasi-randomized study design known as regression discontinuity analysis.

Methods: 159 patients with advanced NSCLC who received first-line ICI-mono (n=80) or ICI-chemo (n=79) from January 2016 to April 2021 in our institution were retrospectively analyzed. PFS (progression-free survival) and overall survival (OS) were evaluated. PD-L1 expression was evaluated using the PD-L1 22C3 pharmDx (Dako).

Results: Patients with PD-L1 $\geq$50% received ICI-mono (n = 68) and patients with PD-L1 <50% received ICI-chemo (n = 44). ICI-mono showed nonsignificant improvement in PFS at the cutoff 50% versus ICI-chemo by 9.5 months (95% CI [confidence interval], -4.7–23.7; P=0.18) in the model without covariates and 9.8 months (95% CI, -4.5–24.0; P=0.17) in the model with covariates. ICI-mono showed nonsignificant improvement in OS at the cutoff 50% versus ICI-chemo by 6.0 months (95% CI, -2.8–14.8; P=0.17) in the model without covariates and 6.39 months (95% CI, -2.4–15.2; P=0.15) in the model with covariates.

Conclusions: In a quasirandomized study design, sparing the chemotherapy in first-line ICI treatment does not appear to impact survival outcomes in NSCLC patients with PD-L1 score around 50%. Due to the small patient numbers in the current analysis, larger studies are warranted to validate our findings.

PP01.04:
Association of Thyroid Transcription Factor-1 with the Efficacy of Immune-Checkpoint Inhibitors in Patients with Advanced Lung Adenocarcinoma

Dr. Kenji Nakahama[1], Dr. Yasuhiro Kaneda[2], Dr. Motohiro Izumi[3], Dr. Naoki Yoshimoto[4], Dr. Akira Sugimoto[1], Dr. Hiroaki Nagamine[1], Dr. Koichi Ogawa[1], Dr. Yoshiya Matsumoto[1], Dr. Kenji Sawa[1], Dr. Yoko Tani[2], Dr. Shigeki Mitsuoka[2], Dr. Tetsuya Watanabe[1], Dr. Kazuhisa Asai[1], Dr. Tomoya Kawaguchi[1,2]

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Background: Thyroid transcription factor (TTF-1) is expressed in most lung adenocarcinomas and is associated with the prognosis and sensitivity to chemotherapy. However, little is known about the association between the expression of TTF-1 and immunotherapy. We aimed to identify the relationship between TTF-1 expression status of lung adenocarcinoma and the efficacy of immune-checkpoint inhibitor (ICI) therapy.

Methods: This retrospective multicenter study comprised patients with advanced lung adenocarcinoma treated with ICI monotherapy between December 2015 and July 2020 at Osaka Metropolitan University Hospital, Ishikiriseiki Hospital, and Bell Land General Hospital. We collected clinical medical records including data on TTF-1 expression and analyzed the relationship between TTF-1 expression and programmed death-ligand 1 tumor proportion score (PD-L1 TPS), objective response rate (ORR), progression-free survival (PFS), and overall survival (OS).

Results: : In total, 108 patients with lung adenocarcinoma were analyzed. The rate of PD-L1 TPS ≥1% and TPS ≥50% in patients with positive TTF-1 expression was significantly higher than that in patients with negative TTF-1 expression (88% vs. 60%, p <0.001; 65% vs. 24%, p <0.001). The ORR was significantly higher in TTF-1 positive patients than in TTF-1-negative patients (38% vs. 8%, p = 0.003). Among patients with PD-L1 TPS ≥50%, the ORR in TTF-1 positive and negative patients was 48% (26/54) and 17% (1/6), respectively (p = 0.21). Among patients with PD-L1 TPS <50%, the ORR in TTF-1-positive and negative patients was 21% (6/29) and 5% (1/19), respectively (p = 0.22). The median PFS and OS was significantly longer in TTF-1-positive patients than in TTF-1-negative patients (5.4 vs. 1.6 months, p <0.001; 18.2 vs. 8.0 months, p = 0.041). Even in patients with PD-L1 TPS ≥50%, the median PFS was significantly longer in patients with positive TTF-1 expression than those with negative expression (10.5 vs. 1.4 months, p = 0.007). Multivariate analysis revealed that TTF-1-negative status was an independent unfavorable prognostic factor for PFS (HR 2.09, 95%CI 1.19–3.57, p = 0.011) and tended to be a poor prognostic factor for OS (HR 1.57, 95%CI 0.87–2.76, p = 0.13).

Conclusions: Patients with TTF-1-positive status receiving ICI monotherapy showed better outcomes than those with TTF-1-negative lung adenocarcinoma.

PP01.06:
Efficacy and Safety of Immune Checkpoint Inhibitors with Chemotherapy for Patients of Performance Status 2 with Advanced NSCLC

Dr. Hirohisa Kano[1], Dr. Eiki Ichihara[2], Toshihide Yokoyama[3], Dr. Koji Inoue[4], Dr. Chihiro Ando[5], Dr. Tomoki Tamura[6], Dr. Keiichi Fujiwara[7], Dr. Daizo Kishino[8], Dr. Naohiro Oda[9], Dr. Masaaki Inoue[10], Dr. Nobuaki Ochi[11], Dr. Haruyuki Kawai[12], Dr. Nobukazu Fujimoto[13], Dr. Hirohisa Ichikawa[14], Dr. Akihiro Bessho[1], Dr. Katsuyuki Hotta[15], Dr. Yoshinobu Maeda[5], Dr. Katsuyuki Kiura[2]

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Background: : Immune checkpoint inhibitor (ICI) with platinum-based chemotherapy is one of the standard treatments for advanced non-small cell lung cancer (NSCLC). However, its efficacy and safety in patients with performance status (PS) 2 are not clear because most clinical trials exclude poor PS patients.

Methods: We conducted retrospective analysis of PS 2 NSCLC patients who received ICI with chemotherapy at 13 centers from December 2018 to December 2020.

Results: Among 480 patients who received ICI with chemotherapy, there were 40 patients with PS 2. The median progression free survival (PFS) for these patients was 5.9 months [95% Confidence interval (CI): 3.8-9.0] and the median overall survival (OS) was 14.2 months (95% CI: 8.2-17.1). Immune-related adverse events with any grade occurred in 13 cases (32.5%), and grade 3 or higher in 8 cases (20%). The mPFS and mOS in the PD-L1 high group (PD-L1≥50%, n=13) were 5.9 months and 15.5 months, respectively. The mPFS and mOS in the PD-L1 low group (PD-L1<50%, n=20) were 4.3 months and 9.0 months, respectively. The PD-L1 high group tended to have better PFS and OS compared to the PD-L1 low group, although there was no significant difference (PFS; p=0.188, OS; p=0.160). In the PD-L1 high expression group, 1-year PFS and 2-year PFS were 34.6% and 26.0%, respectively, and 1-year OS and 2-year OS were 66.6% and 45.7%, respectively, indicating durable efficacy of the treatment in the PD-L1 high NSCLC.

Conclusion: ICI with chemotherapy showed promising efficacy in PS 2 patients. In particular, the tail plateau was observed in the group with high PD-L1 expression.

PP01.07:
Prognostic Factor of TTF-1 Expression for Lung Adenocarcinoma Patients Received Chemotherapy Plus Immune Checkpoint Inhibitor

Dr. Reina Goshono[1], **Dr Ryo Morita**[1], **Dr Mio Kikuchi**[1], **Dr Yoshimi Shibuya**[1], **Dr Tatsuya Yokoyama**[1], **Masato Watanabe**[2], **Dr Masato Takahashi**[2], **Dr Shin Fukui**[1]

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Background: Previous study reported that thyroid transcription factor 1 (TTF-1) expression is prognostic marker for advanced lung adenocarcinoma patients received cytotoxic chemotherapy. Recently cytotoxic chemotherapy and immune checkpoint inhibitor (ICI) is one of the treatment strategy for advanced non-small cell lung cancer. We investigated the role of TTF-1 as a prognostic marker in lung adenocarcinoma patients received chemotherapy and ICI.

Methods: This study is single center retrospective study. We evaluated the medical records of lung adenocarcinoma patients in Akita Kousei Medical Center from January 2019 to December 2021. TTF-1 expression is determined by immunohistochemistry using antibody 8G7G3/1 (DAKO), and divided TTF-1 positive group and negative group. We assessed the patient's characteristics, treatment regimens, progression free survival (PFS) and overall survival (OS). The data cutoff was March 31, 2022.

Results: 122 patients were defined as adenocarcinoma from 216 patients who received bronchoscopy as suspected of lung cancer. Total 46 cases were received chemotherapy with ICI. Twenty eight patients were TTF-1 positive and 18 patients were negative. In TTF-1 positive group, median age was 73 (range, 57-85), including 22 males and 6 females. In TTF-1 negative group, median age was 72 (range, 54-84), including 16 males and 2 females. Median PFS was 48 weeks in TTF-1 positive group and 20 weeks in TTF-1 negative group. TTF-1 positive group is significantly longer PFS than negative group (Hazard Ratio (HR)=0.4937; 95% confidence interval (CI), 0.2191-1.113; p=0.05). Median OS was 56 weeks in TTF-1 positive group and 24 weeks in TTF-1 negative group. TTF-1 positive group is significantly longer OS than negative group (HR=0.4364; 95% CI, 0.1884-1.01; p=0.0279). Moreover, TTF-1 negative group, the patients who received chemotherapy without Pemetrexed is more effective than those who received chemotherapy with Pemetrexed.

Conclusion: TTF-1 expression was one of the prognostic indicator for PFS and OS in lung adenocarcinoma patients received chemotherapy and ICI.

PP01.08:
Analysis of the Effect of Mediastinal Lymph Node Dissection on the Efficacy of Immune Checkpoint Inhibitors in Non-Small Cell Lung Cancer.

Mr. Yohei Kawaguchi[1], Ms Nanako Nishioka[2], Pharmacist Takahiro Tomi[2], Dr. Taiyo Nakamura[1], Dr. Hiroaki Kato[1], Dr. Kentaro Imai[1], Dr. Takuya Aoki[3], Dr. Naohiro Kajiwara[1]

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Background: It has been suggested that mediastinal lymph node dissection may affect the efficacy of immune checkpoint inhibitors (ICIs) by altering lymphatic flow pathways and other factors. We examined the effect of ICIs in patients with postoperative recurrence of non-small cell lung cancer.

Methods: From 2016 to April 2022, we investigated 96 patients with postoperative recurrence (rec group) and advanced lung cancer (ad group) who treated with ICIs. Patients of rec group were undergoing lung resection with mediastinal lymph node dissection at our hospital. Patients with recurrence after chemoradiotherapy were excluded.

Results: 19 patients were in the rec group and 77 patients were in the ad group. 2-year survival rates in the rec and ad groups were 60.1%:51.6% (p=0.254), respectively. 2-year progression-free survival rate of ICIs, which was used for the first time in the treatment sequence, was 17.5%:23.9& (p=0.456). The overall response rate in the rec and ad groups was 47%: 48%(p=0.957) and the disease control rate was 74%:63% (p=0.409) respectively. In the analysis of the patients treated with ICIs in the 1st line, there were 73 patients (14 in the rec group and 59 in the ad group). The 2-year survival rate was 48.7%:48.5% (p=0.459) and the 2-year progression-free survival rate was 25.8%:29.8% (p=0.459) respectively. The overall response rate was 57%:54% (p=0.844), and the disease control rate was 86%:61% (p=0.080). In terms of considering the range of lymph node dissection for the ad group, selective dissection was performed in 5 patients and systematic dissection were performed in 14 patients. The 2-year survival rates were 66.7%:58.9% (p=0.504) and 2-year progression-free survival rate was 33.3%:11.4% (p=0.049). The overall response rate was 80%:36% (p=0.089), and the disease control rate was 100%:64% (p=0.120).

Conclusion: In this study, there was no difference in the efficacy of ICIs between patients with postoperative recurrence and those with unresectable advanced lung cancer. Although this was a small number of cases, it was suggested that the extent of lymph node dissection may have affected the efficacy of ICI in postoperative recurrent cases.

PP01.09:
Analyses of the Outcome of Immune Checkpoint Inhibitors for Postoperative Recurrent Disease in NSCLC

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Background: Immune checkpoint inhibitors are often administered to patients with unresectable non-small cell lung cancer (NSCLC). However, it is expected that the response to ICIs will differ between unresectable advanced cases and recurrent cases after surgery, because of differences in both the tumor volume and lymph node status. We therefore compared the response and outcomes of ICI therapy between postoperative recurrent cases and unresectable advanced cases in NSCLC.

Methods: Between Dec. 2015 and May 2022, we experienced 34 patients with postoperative recurrent NSCLC and 110 patients with unresectable advanced NSCLC. We examined the clinicopathologic factors, response rate of ICIs, effect of the lymph node status and the survival rate between them.

Results: No significant differences in age, gender, histology, PD-L1 expression (22C3), EGFR/ALK mutations or the presence of brain metastases were observed between the two groups. There were more cases with ECOG-PS 2 or worse in the advanced group (p=0.01). Pembrolizumab was used in 98 cases (78 in advanced group and 20 cases in recurrent group), nivolumab in 28 cases (22 in advanced group and 6 cases in recurrent group.) and atezolizumab in 18 cases (10 in advanced group and 8 in recurrent group). The ICI selection and rate of combined therapy did not differ between the two groups. In the advance group 3 CR and 29 PR were observed, in comparison to 7 CR and 7 PR in the recurrent group. The ORR was 29.0% in the advanced group and 41.2% in the recurrent group (p=0.21). A multivariate analysis for overall survival did not show any significant difference in the postoperative recurrence with HR 0.64 (95%CI: 0.39-1.07, p=0.09), whereas for ECOG-PS more than 2 was significant with HR 1.51 (95%CI: 1.18-1.94, p=0.001). Regarding the extent of lymph node dissection, the overall survival was 42.3 months for cases with ND2a-2 dissection, which was significantly longer than that of 10.8 months for cases with ND2a-1 or a smaller dissection (p=0.01). Postoperative recurrence cases tend to include many patients with a good PS, and ICI treatment is expected to result in a better response and longer survival than in advanced cancer cases.

PP01.10:
Long-Term Progression-Free Survival after Discontinuation of Immune Checkpoint Inhibitors

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Background: There has been reported that patients who experienced long-term progression-free or survival after discontinuation of immune checkpoint inhibitors (ICIs).

Methods: We evaluated the clinicopathological characteristics of the 20 NSCLC patients who were treated with ICIs and subsequently terminated for reasons other than progression disease.

Results: There were 18 males, 2 females, 4 non-smokers, 14 adenocarcinomas, 5 squamous cell carcinomas, and 1 other. The median duration of ICIs administration was 2 months (1-7 months), and the median course of administration of ICIs was 2 (1-8). Of the 20 patients, 4 patients experienced no progression of disease or death for more than 6 months after completion of ICIs, and one patient was alive without progression for 48 months. The median age of those patients was 74 years, 3 male, and one female. Pembrolizumab was used in all four cases. Histologic types were adenocarcinoma in three cases and squamous cell carcinoma in one case. The median duration of ICI administration was 5 months (2-8 months), the number, of course, was 5.5 (2-8), and the median recurrence-free period was 10 months (1-48 months). In the 16 patients with short-term exacerbations, the median duration of ICI treatment was 1.5 months (1-7 months), the number, of course, was 2 (1-7), and the median relapse-free period was 2 months (1-5 months).

Conclusions: We report the clinicopathological characteristics of patients with long-term progression-free survival after discontinuation of ICI compared with those with short-term progression after completion of ICI.

PP01.11:
Success of Tepotinib Therapy in Overcoming Resistance to Osimertinib in a Patient with EGFR-Mutant Lung Adenocarcinoma with a Potential Acquired MET Exon 14 Skipping Mutation

Dr. Shinkichi Takamori[1], Dr. Takashi Seto[2], Dr. Fumihiko Kinoshita[2], Dr. Masafumi Yamaguchi[3], Dr. Tatsuro Okamoto[2], Dr. Asato Hashinokuchi[1], Dr. Kyoto Matsudo[1], Dr. Taichi Nagano[1], Dr. Kenji Watanabe[1], Dr. Mikihiro Kohno[1], Dr. Tomoyoshi Takenaka[1], Dr. Tomoharu Yoshizumi[1]

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Background: Osimertinib is a standard therapy for the treatment of advanced non-small cell lung cancer (NSCLC) harboring epidermal growth factor receptor gene (EGFR) mutations, but most patients with EGFR-mutant NSCLC develop secondary resistance to osimertinib. Mesenchymal-epithelial transition gene (MET) alterations and oncogene fusions have been identified as the most common mechanisms of resistance to osimertinib. However, MET exon 14 skipping mutation (METex14del) as an acquired resistance to osimertinib has rarely been reported.

Methods: A non-smoking 76-year-old woman was diagnosed with lung adenocarcinoma in the right lower lobe (cT2bN2M1c [pulmonary and bone metastases], cStage IVB). The primary tumor was submitted to cobas® EGFR Mutation Test v2 (Roche Diagnostics Ltd.,), next generation sequencing (Oncomine Comprehensive Assay v3; Thermo Fisher Scientific,), the AmoyDx® Essential NGS panel (Amoy Diagnostics, Xiamen, China), all of which were positive for EGFR L858R and de novo T790M. We administered daily osimertinib (80 mg/day), and achieved a partial response. However, after 14.0 months, computed tomography showed progression of the primary tumor and lung metastases. Re-biopsy of the primary tumor was conducted, and the specimen was submitted to Archer®MET companion diagnostic for detection of METex14del.

Results: Although the primary tumor was negative for METex14del, the re-biopsy specimen was positive for METex14del. We validated that the biopsy specimen of the primary tumor before osimertinib administration was negative for METex14del using local reverse transcription PCR (Figure a). We administered daily tepotinib (500 mg/day) to the patient as third-line therapy, and achieved a partial response (tumor shrinkage rate: 34.5%; Figures b and c) after 2.0 months. The partial response had lasted for 6.0 months.

Conclusion: We described a patient with lung adenocarcinoma harboring METex14del as a potential acquired resistance to osimertinib, who responded to subsequent tepotinib therapy. Re-biopsy and re-analysis of genetic profiles should be considered in NSCLC patients who develop osimertinib resistance.

Image 1.
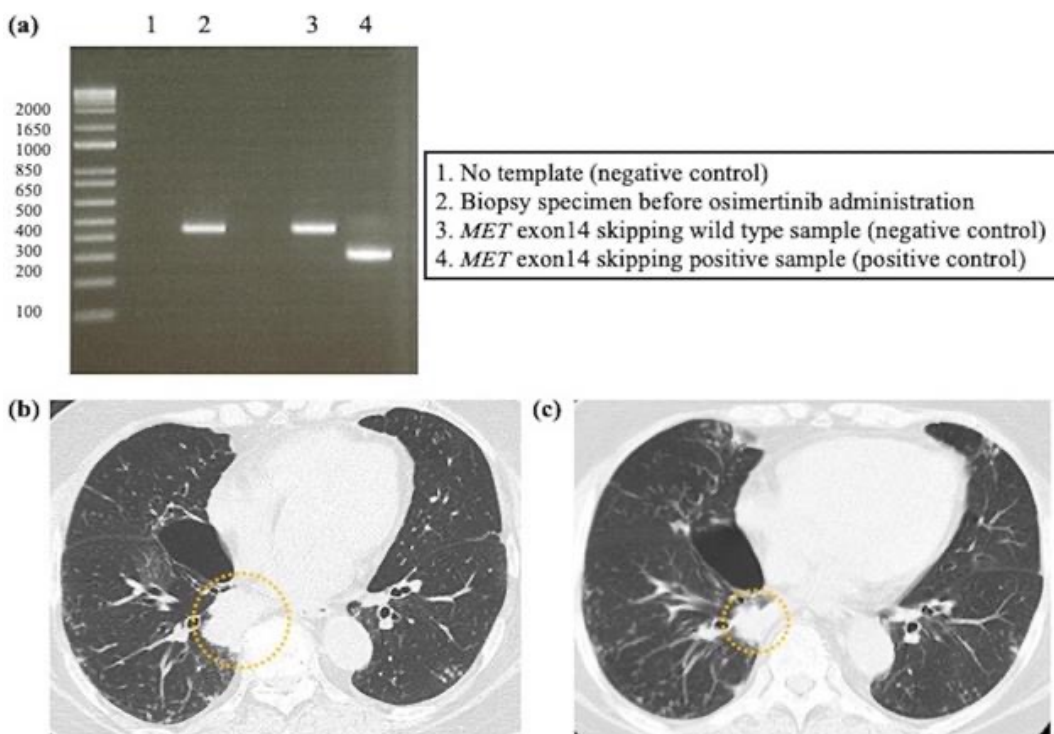
PP01.12:
A Project to Investigate the Actual Status of Biomarker Testing in Unresectable Advanced or Recurrent Non-Small Cell Lung Cancer: WJOG15421 L (REVEAL)

Dr. Toshihide Yokoyama[1], Dr. Tomohiro Sakamoto[2], Dr. Taichi Matsubara[3], Dr, Takayuki Takahama[4], Atsushi Nakamura[5], Dr. Takaaki Tokito[6], Dr. Tatsuro Okamoto[7], Dr. Hiroaki Akamatsu[8], Dr. Masahide Oki[9], Yuki Sato[10], Dr. Kazunori Tobino[11], Mr. Kunihiro Nishimura[12], Mr. Manabu Hiraoka[13], Hirotsugu Kenmotsu[14], Dr. Junya Fujimoto[15], Prof. Mototusgu Shimokawa[16], Nobuyuki Yamamoto[8], Prof. Kazuhiro Nakagawa[3]

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Purpose: The treatment selection for non-small cell lung cancer (NSCLC) is based on the results of biomarker testing. However, there are a certain number of patients with advanced or recurrent NSCLC in whom driver genes have not been sufficiently searched before initial treatment. The purpose of this study was to investigate the actual status of biomarker testing and drug therapy, and to identify the problems in lung cancer treatment.

Methods: This retrospective, multicenter study registered patients with advanced or recurrent NSCLC diagnosed between July 1, 2020 and June 30, 2021. The primary endpoint was the actual status of biomarker testing. [Results] 1,500 pts were enrolled from 29 institutions. The multiplex gene testing was performed in 705/1,478 pts (48%), and OncomineDxTT was performed in 474/1,478 pts (32%). The implementation rate of biomarker testing was EGFR 84%, ALK 79%, ROS1 73%, BRAF 54%, MET 54%, and PD-L1 82%. The presence of background factors such as squamous cell carcinoma, comorbid diseases such as interstitial pneumonia or serious organ disorders, and poor performance status, tended not to use the multiplex gene testing. In addition, biopsy sites also affected the implementation rate.

Conclusions: The implementation rate of multiplex gene testing was 48%. The results of implementation rate of biomarker testing, and analysis results of factors related to the success rate of biomarker testing will be reported at this meeting. We hope that the results of this study would contribute to the establishment of a system where all patients with lung cancer can receive appropriate personalized medicine.

PP01.13:
Efficacy and Intracranial Activity of Tepotinib in Japanese Patients with MET Exon 14 Skipping NSCLC (VISION)

Dr. Masahiro Morise[1], Dr. Hiroshi Sakai[2], Dr. Terufumi Kato[3], Shingo Matsumoto[4], Takako Inoue[5], Tomohiro Sakamoto[6], Takaaki Tokito[7], Shinji Atagi[8], Dr. Toshiyuki Kozuki[9], Hiroaki Takeoka[10], Kenichi Chikamori[11], Naofumi Shinagawa[12], Hiroshi Tanaka[13], S Peter Eggleton[14], Rolf Bruns[15], Gordon Otto[16], Paul Paik[17],[18]

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Background: Tepotinib is a highly selective MET inhibitor, approved in Japan for advanced MET exon 14 (METex14) skipping NSCLC, which occurs in 3–4% of NSCLC patients. Brain metastases (BMs) are reported in 20–40% of patients, representing a high unmet need with a poor prognosis. Tepotinib crosses the blood-brain barrier and has demonstrated intracranial activity in preclinical MET-driven lung cancer. Accepted and presented at JSMO 2022.

Methods: In the Phase II VISION study (NCT02864992), patients in Cohorts A+C with METex14 skipping NSCLC, detected by liquid or tissue biopsy, received 500 mg QD oral tepotinib. The primary endpoint was objective response per RECIST v1.1 by independent review committee (IRC). An ad hoc retrospective analysis of brain lesions was conducted by IRC using Response Assessment in Neuro-Oncology Brain Metastases (RANO-BM) criteria.

Results: Of 38 patients enrolled from Japan at data cut-off (February 1, 2021), 68.4% were male, median age was 73 years (range: 62–87), 63.2% had an ECOG PS of 1, 55.3% had smoking history, 76.3% had adenocarcinoma, and 47.3% were treatment-naïve. Objective response rate (ORR) across treatment lines was 60.5% (95% CI: 43.4, 76.0) and disease control rate was 78.9% (95% CI: 62.7, 90.4), with a median duration of response of 18.5 months (95% CI: 8.3, not estimable [ne]), median progression-free survival of 19.9 months (95% CI: 8.3, ne), and median overall survival of 20.4 months (95% CI: 16.3, ne). Tumor shrinkage was observed in more than 90% of evaluable patients. Thirteen patients with tumor responses had dose reductions; six remained on treatment at data cut-off. Of 34 patients with METex14 skipping detected by tissue biopsy, ORR was 58.8 (95% CI: 40.7, 75.4) and in 14 patients detected by liquid biopsy, ORR was 71.4% (95% CI: 41.9, 91.6). Of all patients in Cohort A (n=152; data cut-off; Jul 1, 2020), 15 patients were evaluable by RANO-BM (12 received prior radiotherapy), of which two patients were Japanese. Intracranial disease control was achieved in 13 of 15 patients. 5 of 7 patients with target lesions had intracranial responses (all partial responses), and 7 of 8 patients with non-target lesions had intracranial control.

Conclusions: Tepotinib demonstrated robust systemic activity in patients with METex14 skipping NSCLC in Japanese patients and showed intracranial activity in patients with BM.

PP01.14:
Tepotinib in Asian Patients with Advanced NSCLC with MET Exon 14 (METex14) Skipping

Dr. Terufumi Kato[1], Prof. Chih-hsin Yang[2], Dr. Myung-Ju Ahn[3], Dr. Hiroshi Sakai[4], Dr. Masahiro Morise[5], Dr. Yuh-Min Chen[6], Dr. Ji-Youn Han[7], Dr. Jin-Ji Yang[8], Dr. Jun Zhao[9], Dr. Jason Huang[10], Dr. Karin Berghoff[11], Rolf Bruns[12], Helene Vioix[13], Gordon Otto[14], Dr. Xiuning Le[15], Paul Paik[16],[17]

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Background: Tepotinib is a highly selective, potent MET inhibitor approved in several Asian countries for the treatment of advanced METex14 skipping NSCLC. In the VISION study, tepotinib demonstrated robust and durable efficacy in patients across treatment lines. Here, we report outcomes in Asian patients. Previously presented at ASCO 2022.

Methods: Patients with advanced METex14 skipping NSCLC, detected by liquid (L+) or tissue (T+) biopsy, received tepotinib 500 mg (450 mg active moiety) QD. The primary endpoint was objective response by independent review committee. Efficacy was assessed in Asian patients with ≥3 months' follow-up. HRQoL was assessed in patients enrolled in Asia only. Safety was assessed in Asian patients who received tepotinib by data cut-off (February 1, 2021).

Results: In 79 Asian patients assessed for efficacy (38% female, 42% smoking history, 34% treatment-naïve [1L] and 77% adenocarcinoma), ORR was 54.4% (95% CI: 42.8, 65.7), mDOR was 18.5 months (8.3, ne), mPFS was 12.1 months (6.9, ne) and mOS was 20.4 months (19.1, ne). Meaningful activity was observed irrespective of therapy line or METex14 skipping detection method. ORR was 66.7% (46.0, 83.5) in 1L patients (n=27) and 48.1% (34.0, 62.4) in previously treated patients (n=52). ORR was 57.9% (44.1, 70.9) in T+ patients (n=57) and 51.4% (34.4, 68.1) in L+ patients (n=37). In patients enrolled in Asia analyzed for HRQoL (n=73), mean change from baseline for EORTC QLQ-C30 GHS (4.06), EQ-5D-5L VAS (−0.53), and EORTC QLQ-LC13 for cough (−6.77), dyspnea (−0.98), and chest pain (−7.00) symptom scores demonstrated stability in QoL. Median time-to-deterioration (months) was 9.4 for EORTC QLQ-C30 GHS, 8.3 for EQ-5D-5L VAS, and 11.1, 6.8, and ne for EORTC QLQ-LC13 for cough, dyspnea, and chest pain, respectively. HRQoL outcomes were similar across therapy lines. Patients with tumor responses had more pronounced symptom improvements than patients without responses.In 88 Asian patients analyzed for safety, the most common adverse events (AEs) were peripheral edema, increased blood creatinine, and diarrhea. 29.5% of patients had Grade ≥3 treatment-related (TR) AEs. TRAEs led to permanent discontinuation in 14.8% of patients.

Conclusions: In VISION, tepotinib showed robust and durable clinical activity in Asian patients with METex14 skipping NSCLC, and HRQoL outcomes remained stable during treatment with a meaningful time to deterioration of QoL. TRAEs were manageable with few leading to treatment discontinuation.

PP01.16:

Resistance Mechanisms to Osimertinib in Advanced EGFR-Mutated NSCLC: An Update from a Single Institution Prospective Cohort Study

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Introduction: Osimertinib is a recommended first-line treatment for advanced EGFR–mutated (deletion in exon 19 and exon 21 L858R) and EGFR-TKI pretreated T790M-positive non-small cell lung cancer. Resistance to osimertinib inevitably developed after a period of treatment and this study aims to evaluate the mechanisms of resistance. Parts of the results were presented previously (WCLC 2022).

Methods: We prospectively collected tissue samples from patients having advanced EGFR-mutated NSCLC previously treated with osimertinib as first-line or later line treatment who developed resistance to osimertinib. Tissue sample was analyzed utilizing the FoundationOne platform.

Results: Among 39 eligible patients, 4 received osimertinib as first-line therapy and 35 patients received osimertinib as a later line treatment. The original activating mutations were detected in 94.9% and T790M was detected in 15.4% of the patients (including 2 patients with de novo T790M). Alterations in TP53 (69.2%), Rb1, PIK3CA, CDKN2A (17.9%) and MTAP (15.4%) were detected. Amplification of MET (23.1%), NKX2-1 (20.5%), NFKBIA (17.9%), EGFR (15.4%), CCNE1 and MYC (12.8%) were detected. Five patients developed acquired EGFR C797S (n = 3) and L718V/Q (n = 2) mutations. Five patient developed histological transformation of squamous cell (n = 2), small cell (n = 1), sarcomatoid (n = 1) and pleomorphic (n = 1) carcinoma. Nine of the 14 patients harboring potentially druggabble MET amplification or acquired EGFR mutation received correspondent targeted treatment and the overall survival of these patients was 8.2 months.

Conclusions: In patients with EGFR-mutated advanced NSCLC who received osimertinib therapy, subsequent treatment for potentially druggable MET amplification or acquired EGFR mutation required further investigation.

PP01.17:
Phase 1/2a Study Evaluating Alectinib Pharmacokinetics and Efficacy in Hispanic Population with Advanced ALK-rearranged Non-Small-Cell Lung Cancer.

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Background: Alectinib is a standard treatment in advanced ALK-rearranged NSCLC in the first-line setting. Six hundred milligrams twice-daily (BID) dose has been adopted as the recommended starting dose in almost all regions, even though half of the recommended dose has proven similar efficacy in the Asian population. Ancestry studies have suggested a marked genetic heterogeneity in Latin Americans and unearthed ancestry related to present-day groups from East Asia. Hence, this study assessed alectinib PK and efficacy in the Hispanic population.

Methods: This single-arm, phase 1/2 trial recruited 40 patients with advanced (clinical stage IIIB-IV) ALK-rearranged NSCLC between February 2019 and August 2021. In phase 1, patients received alectinib orally in fasted conditions, starting with 300mg BID in 21-day cycles and dose escalation in 150mg increments until 600mg BID. Primary endpoints (phase 1) were dose-limiting toxicity (DLT) and PK parameters (Cmax; Tmax; and AUC1-10). In phase 2, the 300mg BID was the chosen dose based on plasma concentrations within the therapeutic range (572-665ng/ml) and administered until disease progression or development of unacceptable side effects. The primary endpoint (phase 2) was the overall response rate (ORR), and secondary endpoints were progression-free survival (PFS), overall survival (OS), intracranial response (ICR), and duration of response (DOR).

Results: Thirty-eight patients have completed PK analysis Table1. Two DLTs were observed in the 600mg BID dose and none in lower doses. Efficacy was assessed in 39 evaluable patients; 19 (47.5%) received alectinib in the second or further lines (2-5) of treatment. The median age was 46.5 years (39.7-56.0), and brain metastases at baseline were observed in 56.4%. The ORR was 76.3% [95%CI (59.8-88.6)], 53.8% reached partial response, and 20.6% complete response. In those with measurable disease (n=18), ICR was 73.7% [95%CI (48.8-90.9)], and four patients (22.2%) reached a complete ICR. At the data cut-off date (February 15, 2022), the median follow-up was 17.8 months. The 12-month PFS was 74% [95% CI (55-100)], and the median PFS was non-reached [95% CI (13.44-NR)]. The 12-month OS was 85.7% [95% CI (69-100)]. Any grade adverse events occurred in 66.7%, and grade ≥3 occurred in 7.7% of cases.

Conclusions: Alectinib PK analysis in the Hispanic population demonstrated significant variation and was effective and safe with a 300 mg twice-daily dose. This study suggests that an individualized dose guided by plasmatic concentrations might be attractive to optimize therapy, improving access and avoiding unnecessary toxicity without compromising clinical outcomes.

Image 1.

Table 1. Pharmacokinetic parameters across different alectinib doses.

Alectinib dose (mg) BID	Food	Tmax (h)	Cmax (ng/mL)	AUC$_{1-10}$ (ng*h/mL)
300	Fasted	2.84 (1.8-3.4)	598±137.1	5011±1332
450	Fasted	3.26 (1.9-3.1)	702±255.2	6089±1610
600	Fasted	3.14 (2.2-3.6)	1077.2±403.1	9745±4210

*Tmax is median (range)
Fasted conditions were two hours before and one hour after alectinib administration.
AUC= area under the curve. Cmax= maximum concentration. Tmax= Time to reach maximum concentration.

PP01.18:
Clinical Outcomes for EGFR and HER2 Exon 20 Insertion-Mutated Advanced Lung Cancer

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Background: Exon 20 insertion mutations (ex20ins) in EGFR and HER2 are uncommon driver mutations in NSCLC with poor prognosis and few targeted therapy options. There is limited real-world data for patients with these rare mutations. We report clinico-pathologic features and outcomes for 131 patients with ex20ins NSCLC across British Columbia, Canada.

Methods: NSCLC patients who had tumour testing from Jan 1, 2016-Dec 31, 2021 (n=7233) were identified via the provincial database. Patients with ex20ins in EGFR or HER2 were included. Survival analyses were performed using the Kaplan-Meier method using log-rank test to assess subgroup differences.

Results: 131 patients were identified: 84 EGFR, 47 HER2. Median age was 66. In the EGFR group, 61% were female, 49% were Asian, and 75% were never/light smokers. In the HER2 group, 57% were female, 40% were Asian, and 64% were never/light smokers. 33% of patients had brain metastases (mets). For met EGFR ex20ins patient (n=71), mOS was 7.1 months. 39/71 (55%) patients had palliative systemic therapy (ST), of which, 20/39 (51%) received ex20ins-specific TKI (ie. poziotinib, mobocertinib, or afatinib). mOS was 18.6 months for patients who received any ST vs. 2.6 months for patients who did not (P<0.001). mOS was similar for patients treated with ex20ins TKI vs. other (18.6 vs. 15.9 months, P=0.463). In the 1L setting, mPFS was 7.1 months for all patients; mPFS was 4.1 vs. 7.4 months for patients treated with TKI vs. other (P=0.744). Grade 3 toxicity was 15.4% (6/39) for all ST patients, and 20% (4/20) for TKI patients. For met HER2 ex20ins patients (n=41), mOS was 7.3 months. 25/41 (61%) patients had ST; 11/25 (44%) received ex20ins-specific TKI. mOS was 9.0 months for patients who received any ST vs. 4.9 months for patients who did not (P=0.015). mOS was 23.0 months for patients treated with ex20ins TKI vs. 5.6 months for patients who were not (P=0.019). In the 1L setting mPFS was 4.5 months for all patients who had ST; mPFS was 5.4 vs. 2.1 months for patients treated with TKI vs. other (P=0.343). Grade 3 toxicity was 16% (4/25) for all ST patients, and 9% (1/11) for TKI patients.

Conclusion: In this large, population-based retrospective review of EGFR and HER2 ex20ins NSCLC patients, there was improvement in survival for patients who received any ST vs. those who did not. Overall survival was significantly better among HER2 ex20ins patients who received ex20ins-specific TKIs.

PP01.19:
Overall Survival Benefits of First-Line Treatments for Asian Patients with Advanced Epidermal Growth Factor Receptor-mutated Non-Small-Cell Lung Cancer Harboring Exon 19 Deletion: A Systematic Review and Network Meta-analysis

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Background: Randomized-controlled trials (RCTs) have investigated different first-line treatments for patients with advanced epidermal growth factor receptor (EGFR) mutated non-small-cell lung cancer. However, their efficacy, in particular, the long-term overall survival (OS) benefit in Asian patients with exon 19 deletion remains unclear.

Methods: We performed a systematic review and frequentist network meta-analysis by retrieving relevant literature from PubMed/MEDLINE Ovid, Embase, Cochrane Library, trial registries and other sources. We included RCTs comparing two or more treatments in the first-line setting for Asian patients with exon 19 deletion. This study was registered in the Prospective Register of Systematic Reviews (CRD 42022320833).

Results: Eighteen trials involved 2715 Asian patients and 12 treatments: including EGFR TKIs (osimertinib, dacomitinib, afatinib, erlotinib, gefitinib, and icotinib), pemetrexed-based chemotherapy, pemetrexed-free chemotherapy, and combination treatments (gefitinib plus apatinib, erlotinib plus ramucirumab, erlotinib plus bevacizumab and gefitinib plus pemetrexed-based chemotherapy). Asian patients with exon 19 deletion had no significant OS benefits from all these treatments. Erlotinib plus bevacizumab, ramucirumab plus erlotinib and osimertinib were shown to be consistent in yielding the best progression-free survival benefit (P-scores = 94%, 84% and 80%, respectively). Combination treatments caused more toxicity, especially gefitinib plus apatinib and erlotinib plus bevacizumab, resulting in the greatest incidence of grade ≥3 adverse events. Icotinib and osimertinib had the fewest grade ≥3 adverse events. Different toxicity spectrums were revealed for individual treatments.

Conclusions: In Asian patients harboring exon 19 deletion, EGFR TKIs and combination treatments demonstrated no OS benefit when compared with conventional chemotherapies. Further studies are warranted to investigate the resistance mechanism with TKIs and potential combination strategies in patients with this common mutation.

PP01.20:
Prevalence of Central Nervous System Metastasis in EGFR Mutated Advanced Non-Small Cell Lung Cancer in Thailand: A Multicenter Study

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Background Central Nervous System (CNS) metastasis is common in patients with advanced stage non-small cell lung cancer (NSCLC), which impacts their survival and quality of life. Nearly Half of NSCLCs in Thailand are EGFR (Epidermal Growth Factor Receptor) mutated NSCLCs. The aim of this study was to define the prevalence of CNS metastasis in EGFR mutated advanced NSCLC in Thai patients and their survival during the year 2013-2019.

Methods We retrospectively conducted a multicenter study of EGFR mutated advanced NSCLC from 9 government hospitals in Thailand from January 2013 to December2019. Demographic data and cancer treatment were recorded with previous reports of overall survival data in all cohorts. Brain imaging was performed upon neurologic signs and symptoms. Treatment of CNS metastasis and overall survival data in CNS metastasis group were reported here.

Results There were 254 patients with advanced EGFR mutated NSCLCs. The prevalence of CNS metastasis was 32.28% (82 patients). Brain metastasis at first diagnosis was 41.5% (34 patients). In all CNS metastasis patients, EGFR TKIs was given as first line 42.7% (35 patients), second line 30.5% (25 patients), third line 13.4% (11 patients). Whereas four others received EGFR TKIs as switch maintenance. Most of EGFR TKIs treatment was first generation for 91.46% (75 patients) while 17.07% (14 patients) received Osimertinib as subsequence line of treatment. However, 17.6% (7 patients) did not receive any EGFR TKIs. The onset of CNS metastasis before EGFR TKIs was 53.3% when compared to 21.3%, 25.3% during EGFR TKIs and after EGFR TKIs, respectively. Treatment of brain metastasis was whole brain radiation for 76.82% (63 patients), followed by surgery with whole brain radiation for 8.53% (7 patients) and whole brain radiation with third-generation EGFR-TKIs for 1.2% (1 patients). The median survival of CNS metastasis and non-CNS metastasis groups was comparable (21 months VS 21 months; p= 0.286). The median survival of EGFR-TKIs and non-EGFR TKIs groups was 12 months and 9 months, respectively (p=0.281). The median survival of those with EGFR TKIs as first line, non-first line and non-EGFR TKIs was 13 months,12 months and 9 months, respectively(p=0.281).

Conclusion The prevalence of CNS metastasis for EGFR mutated NSCLC was 32.28%, compatible to other previous reports. Despite only the widely affordable first-generation EGFR TKIs treatment can prolong the median survival of CNS metastasis. Moreover, the first line setting of EGFR TKIs results to the longest median survival time.

PP01.21:
Clinical Characteristics and Real-World Progression-Free Survival of Patients with EGFR Mutation-Positive Adenocarcinoma Lung Cancer Treated with EGFR as the First Line: A Retrospective Cohort Study from Indonesia

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Background: First, second, and third-generation epidermal growth factor receptor tyrosine kinase inhibitors have been recommended for first-line treatment of EGFR mutation-positive metastatic non-small cell lung cancer (NSCLC) by the Indonesia Association for the Study of Thoracic Oncology (IASTO). This study describes the clinical characteristics and real-world progression-free survival of patients with EGFR mutation-positive adenocarcinoma lung cancer treated with EGFR as the first line.

Methods: This is a retrospective cohort study. Clinical characteristics and data were collected from medical records from 14 respiratory service centers nationwide between 2017 and 2021. The Kaplan-Meier method and log-rank test were used to estimate PFS, and the Cox proportional hazards model was used for multivariate analyses.

Results: A total of 505 patients were enrolled. EGFR-TKI treatments were given gefitinib 66%, erlotinib 19%, and afatinib 15%. The median age was 59 years old. Male 49.1%, female 50,9%. Smoking history (never smoker 59.8%, current/ex-smoker 40.2%), and with ECOG 0-1 83.2%. EGFR common mutations were 96.6%, and EGFR uncommon mutations were 3.4%. No history of cancer was 93.7%, and the advanced stage was 99.2%. Median PFS was 9 months (0.44% CI: 8.1-9.8). Patients with exon 19 deletion, never smoker, and ECOG 1 had the longest PFS of nine months. Other demographic characteristics had no impact in PFS including gender (p=0.50), smoking history (p=0.60), history of family cancer (p=0.90), pleural effusion (p=0.13), staging (p=0.58), ECOG (p=0.09).

Conclusion: Based on the study result we can conclude the EGFR-TKI treatment can only prolong the survival of patients with common mutation for up to 9 months.

PP01.22:
The Detection Rate of EGFR Gene Mutations in the Cobas EGFR Mutation Test and the Oncomine Dx Target Test Multi-CDx System in Our Hospital.

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Background: In Japan, the Oncomine Dx Target Test Multi-CDx System has been approved for use as a companion diagnostic platform for targeted therapies to identify alterations in four driver genes: EGFR, ALK, ROS1, and BRAF since Feb, 2019. Prior to that, the Cobas EGFR mutation test has been used for detection of EGFR mutation; however, the minimum detection sensitivity of Oncomine Dx and Cobas EGFR is considered to be different.

Method: In this study, we examined the frequency of EGFR mutation detection in consecutive patients who underwent Cobas EGFR from August 2021 to April 2022 and Oncomine Dx from the start of the contract to April 2022 in clinical practice.

Result: Of the 60 patients who received Cobas EGFR only, 23 patients were positive for activating EGFR mutations, and of the 62 patients who received Oncomine Dx only, 8 patients were positive for activating EGFR mutations. There were 10 cases in which both Cobas EGFR and Oncomine Dx were performed (of which only 4 patients had Cobas EGFR performed between August 2021 and April 2022), and 1 case of discordant EGFR gene mutation results (only Cobas EGFR was positive).

Summary: The detection rate of EGFR gene mutations was higher in Cobas EGFR and lower in Oncomine Dx. One possible reason for this could be due to the difference in minimum detection sensitivity between Cobas EGFR and Oncomine Dx.

PP01.23:
Differences in First Generation EGFR-TKI Responses in Advanced Stage Lung Adenocarcinoma with EGFR Mutations.

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Background: Gefitinib and erlotinib are superior to chemotherapy in Adenocarcinoma with epidermal growth factor receptor (EGFR) mutation patients. Both drugs can be accessed as first-line therapies. However, the determination of the choice of gefitinib or erlotinib is not yet clear.

Aims: To compare the PFS of Adenocarcinoma with epidermal growth factor receptor (EGFR) mutation patients who receiving first-line gefitinib versus erlotinib.

Methods: This is a retrospective study used a medical record of patients who treated with first-line gefitinib 250 mg once daily versus erlotinib 150 mg once daily at Dr. H. A. Rotinsulu hospital from 1st January 2019 to 31th December 2021.

Results: There are 258 consecutive Adenocarcinoma with epidermal growth factor receptor (EGFR) mutation patients but only 139 cases were had the inclusion and exclusion criteria. We have found that 103 patients (74,1%) received gefitinib and 36 patients (25,9%) received erlotinib as first-line treatment. All baseline factors (except smoker status) were balanced between the arms. Median progression-free survival in gefitinib and erlotinib group was 26 months and 17 months (P = 0.184), respectively. Based on univariate analysis, gander affects PFS (HR1.7; CI 95 % 1.0-3.4; P =0.049) it was confirmed by bivariate analysis (HR 1.9; CI 95 % 1.0-3.4; P =0.033).

Conclusions: Based on the results of this study, there was no difference in PFS between gefitinib and erlotinib in the treatment of pulmonary adenocarcinoma patients with EGFR gene mutations.

Keywords: gefitinib, erlotinib, non-small cell lung cancer, EGFR mutations.

PP01.24:
Survival Difference of EGFR Exon 19 Deletion and Exon 21 Mutation in Asian Patients with Advanced Non-small Cell Lung Cancer

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Background: Epidermal growth factor receptor (EGFR) mutation status is a good predictor of response to EGFR tyrosine kinase inhibitors (TKI) in non-small cell lung cancer (NSCLC). The existing data on the difference in survival outcome between EGFR sensitizing mutations are limited and conflicting. This study reported the survival differences between EGFR exon 19 deletion and exon 21 mutation in advanced NSCLC patients. The authors added in this study the differences in response rate to initial targeted therapy.

Method: Fifty-eight patients with advanced NSCLC harboring EGFR exon 19 deletion (25 patients) and exon 21 mutation (33 patients) from January 2012 to December 2018 were retrospectively reviewed in our institution. Using Kaplan-Meir curves and log-rank test, we compared the progression-free survival (PFS) and overall survival (OS) between the two sensitizing mutations.

Results: The median age at diagnosis was 66 years old (range 53-77). All patients were Asian and received EGFR-TKI as first line treatment. Patients with EGFR exon 19 deletion had 3 cases (12%) of partial response (PR), 20 cases (80%) had stable disease (SD), and 2 cases (8%) had progressive disease (PD). Patients with EGFR exon 21 mutation had 7 cases (21.2%) of PR, 24 cases (72.7%) had SD and 2 cases (6.1%) had PD. No significant difference was found in the objective response rate (ORR) (12% vs 21.2%; p=0.358) and disease control rate (DCR) (92 vs 93.9%; p=0.772) between the two groups. The median PFS in patients with exon 19 deletion was 19.0 months (95% CI 10.7-27.3) and 32.1 months (95% CI 23.3-40.9) in patients with exon 21 deletion (p=0.048). The median OS was 28.0 months (95% CI 26.4-29.6) in the exon 19 deletion group and 36.0 months (95% CI 15.7-56.3) in the exon 21 mutation group (p=0.207). Cox multivariate analysis indicated that EGFR exon mutation status and smoking history were factors that affected PFS but not OS. Gender and Osimertinib affected OS.

Conclusion: In our study, PFS was significantly longer in Asian patients with EGFR exon 21 mutation as compared to exon 19 deletion after first line EGFR TKI treatment in contrast to published studies. No significant difference was found in the OS between the two groups. This is the only study who reported a better PFS in EGFR exon 21 mutation. Additional research are needed to further investigate whether a difference in the tumor biology between exon 19 deletion and exon 21 mutation exists especially in Asian population.

PP01.26:
Impact of AXL Expression on the Efficacy of Osimertinib in Untreated EGFR-Mutated NSCLC

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Background: The initial therapeutic interventions for non-small cell lung cancer (NSCLC) patients with EGFR mutations have a critical impact on their clinical outcomes. Preclinical studies have reported that drug tolerant factors have an impact on EGFR-TKI sensitivity. This study investigated the impacts of drug tolerant-related protein expression in tumors on the efficacy of osimertinib in the first-setting of EGFR-mutated advanced NSCLC patients.

Methods: This was a prospective observation study, in which 92 patients were analyzed who had EGFR-mutated advanced or postoperative recurrent NSCLC and were treated with osimertinib, at 14 institutions in Japan. The expression of AXL, p53, and PD-L1 in patient tumors was determined using immunohistochemistry. The AXL signaling pathway was investigated using a cell line-based assay and AXL-related gene expression in the Cancer Genome Atlas (TCGA) database.

Results: High levels of AXL expression were detected in 26.1% of the pretreatment EGFR-mutated NSCLC tumors. Tumor AXL-high expression was significantly shorter in the progression free survival of osimertinib than those with AXL-low, irrespective of EGFR activating mutation status (p = 0.026). Cell line-based assays demonstrated that that the overexpression of AXL proteins accelerated PD-L1 expression, which elicited an insensitivity to osimertinib. In the Cancer Genome Atlas database, AXL RNA levels were positively correlated to PD-L1 in the lung adenocarcinoma cohort.

Conclusion: The results show that high levels of AXL expression in tumors impact clinical predictions when using osimertinib to treat EGFR-mutated NSCLC patients.

PP01.27:
Exploration of Secondary Resistant Mutations against Mobocertinib - in Vitro Study with Various EGFR Exon 20 Insertion Models

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Background: Approximately 10% of non-small cell lung cancers (NSCLCs) that harbor epidermal growth factor receptor (EGFR) gene mutations have in-frame insertions in exon 20 of the EGFR gene. These tumors do not usually respond to currently available EGFR-tyrosine kinase inhibitors (TKIs). However, a novel EGFR-TKI, mobocertinib, was approved by the US FDA for lung cancer with EGFR exon20 insertion mutations.

Methods: We examined efficacy of mobocertinib in Ba/F3 cells harboring one of five most common EGFR exon 20 mutations (EGFR A763insFQEA, V769insASV, D770insSVD, H773insH and H773insNPH mutations). We also examined growth inhibitory effect of poziotinib, afatinib, CLN-081, erlotinib, osimertinib, brigatinib and BI4020 using the same Ba/F3 models. We then established acquired resistance cells against mobocertinib via chronic drug exposure after N-ethyl-N-nitrosourea mutagenesis, and we explored secondary mutations in the EGFR.

Results: Among tested EGFR-TKIs, mobocertinib showed the highest efficacy in all tested Ba/F3 cell lines including H773insH, which was less sensitive to other EGFR-TKIs. As secondary resistant mutations to mobocertinib, we identified T790M or C797S depending on the original EGFR exon 20 mutation. In Ba/F3 cells with A763insFQEA and D770insSVD, all mobocertinib-resistant clones developed C797S mutation. On the other hand, we identified either T790M or C797S secondary mutations in Ba/F3 cells with H773insH, H773insNPH, and V769insASV. In addition, we found a novel secondary mutation (F856V) in Ba/F3 cells with V769insASV.

Conclusion: These findings indicate that T790M or C797S, depending on the activating mutations, will cause acquired resistance to mobocertinib in NSCLCs with EGFR exon 20 mutations. We also found a novel secondary mutation (F856V) that may confer acquired resistance to mobocertinib.

PP01.28:
The Utility of the Anti-CKAP4 Monoclonal Antibody in DKK1-CKAP4 Signal-Activated Lung Cancer

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Background: Cytoskeleton-associated protein 4 (CKAP4) is a type II membrane protein that maintains the structure of the endoplasmic reticulum and a variety of cancers, such as pancreatic and lung cancer (LC), expresses CKAP4 on their plasma membrane (PM). We previously identified that CKAP4 functions as a receptor for Dickkopf1 (DKK1), a secreted protein that constitutes Wnt/β-catenin signaling, and promotes cancer cell proliferation through the activation of phosphatidylinositol 3-kinase (PI3K)/AKT pathway (DKK1-CKAP4 signaling) in pancreatic cancer. We developed an anti-CKAP4 monoclonal antibody and have shown that it inhibited tumor growth of pancreatic cancer-derived cells. In addition, we found that CKAP4 was secreted into exosomes triggered by the binding of DKK1. Serum CKAP4 levels measured by sandwich ELISA in pancreatic cancer patients were higher than those in healthy controls (HCs). However, there have been no reports of a similar study on LC. In the present study, we investigated the role of DKK1-CKAP4 signaling in LC and its potential as a therapeutic target.

Method: A total of 92 LC patients who underwent surgery at Osaka University Hospital were enrolled in this study. Immunohistochemistry (IHC) was performed on the surgical specimens. Serum CKAP4 levels in these patients and in HCs were measured by sandwich ELISA. The correlation between the serum CKAP4 values and the IHC staining with CKAP4 was examined. Furthermore, we overexpressed CKAP4 in H292 cells, an LC cell line that expresses DKK1 but does not express CKAP4 on the PM, and generated an H292/CKAP4 cell line that constitutively overexpresses CKAP4, including on the PM. We evaluated the function of the anti-CKAP4 antibody in vitro and in vivo using H292/CKAP4 cells.

Results: The patients who were positive for both DKK1 and CKAP4 by IHC showed significantly worse relapse-free survival than those with either DKK1 or CKAP4 positive or both negative (P=0.03). The serum CKAP4 levels were detected in 18 of 92 (19.6%) LC patients, whereas only 6 of 92 (6.5%) were detectable in HCs (P<0.01). The positive IHC with CKAP4 was associated with the serum CKAP4 positivity (P < 0.01). The anti-CKAP4 suppressed the growth of H292/CKAP4 but not H292 WT cells via the inhibition of the PI3K/AKT pathway both in vitro and in vivo.

Conclusion: Our anti-CKAP4 antibody was capable of detecting serum CKAP4 released from cancer tissue and inhibiting LC cell proliferation. These results suggest that the CKAP4 antibody may be useful for the diagnosis and treatment of DKK1-CKAP4 signal-activated LC.

Image 1.
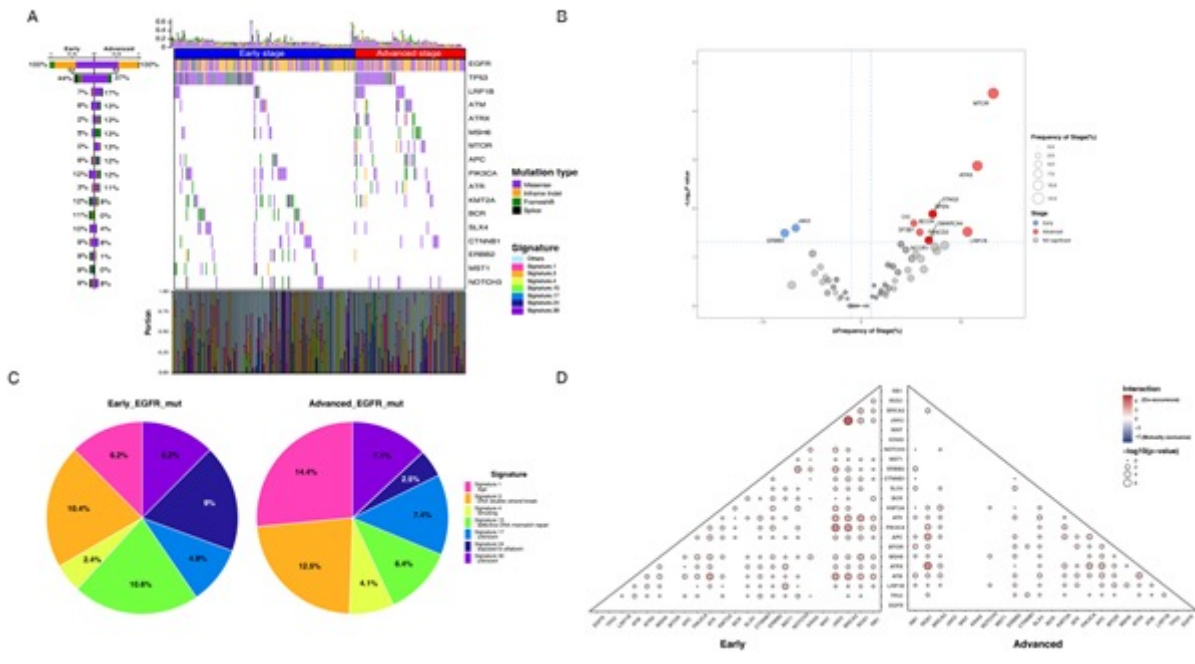
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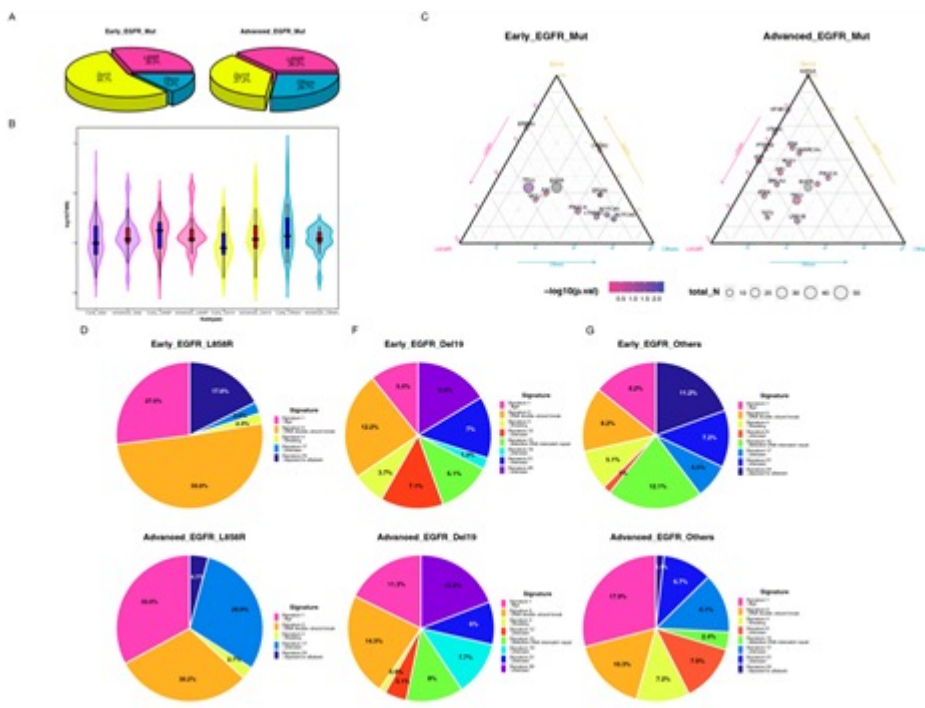
PP01.30:
MiR-503 Pleiotropically Regulates Epithelial-Mesenchymal Transition and Targets PTK7 to Control Lung Cancer Metastasis

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Background: Most deaths from lung cancer occur due to the metastatic spread of cancer cells. Epithelial-mesenchymal transition (EMT) and collective cell migration are distinct mechanisms involved in cancer invasion and metastasis. Moreover, microRNA (miRNA) dysregulation plays a key role in cancer progression.

Methods: We screened for miRNAs that were dysregulated in lung cancer cells with more invasive phenotype using the TaqMan human microRNA PCR array. We verified the direct target gene of specified miRNA using luciferase reporter assay. Gene-overexpressing or -knockdown lung cancer cells were generated, and their cell phenotype and expressions of associated genes were examined. The in vivo effect of miRNA in controlling distant dissemination of lung cancer was investigated using tail vein-based metastasis assay.

Results: Herein, we demonstrated that downregulation of miR-503 confers an invasive phenotype in lung cancer cells and provided in vivo evidence that miR-503 inhibits metastasis. We found that miR-503 inversely regulates EMT, identified protein tyrosine kinase 7 (PTK7, a Wnt/planar cell polarity protein that plays a crucial role in collective cell movement) as a novel miR-503 target, and found that reconstitution of PTK7 expression restored the functional effects of miR-503 on migration and invasion. However, PTK7 expression did not affect EMT induction, suggesting that miR-503 regulates EMT through mechanisms other than PTK7 inhibition. Mechanistically, we revealed that PTK7 activates focal adhesion kinase (FAK) and paxillin, thereby controlling cortical actin cytoskeleton reorganization. Collectively, these data suggested that miR-503 is capable of regulating both EMT and collective cell migration independently to control lung cancer metastasis.

Conclusion: MiR-503 is capable of governing EMT and PTK7/FAK signaling, indicating that miR-503 is a pleiotropic regulator of cancer invasion and metastasis and hence represents an attractive target for therapeutic intervention in lung cancer.

PP01.31:
Programmed Death-Ligand 1 Promotes Chemotaxis in EGFR-Mutant Non-Small Cell Lung Cancer through Regulating Cytokine Expressio

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Background: In Asian population, especially in non-smokers and women, EGFR mutations are the commonest driver gene that can be found in 50-60% of non-small cell lung cancer (NSCLC) patients. Although EGFR-TKIs were effective on against tumor with EGFR mutations, the resistance was inevitably occurred after a median of approximately 12 months of therapy. We and other groups recently found that expression of PD-L1 was highly associated with the short PFS of EGFR-TKI treatment in EGFR-mutant NSCLC. Most importantly, the role of intrinsic PD-L1 signaling in EGFR-mutant NSCLC, and the underlying mechanism of how PD-L1 promotes cancer progression as well as metastasis are still unknown.

Methods: Over-expression and knock-down of PD-L1 experiments were conducted using lipofectamine transfection and lentiviral infection, respectively. Cytotoxicity and chemotaxis experiments were conducted using SRB assay and trans-well analysis, respectively. The human cytokine assay was used to explore the cytokine profiling.

Results: We over-expressed PD-L1 in many EGFR-mutant NSCLC cells including NCI-H1975, HCC827, and PC9 cells. We found there is no difference in sensitivity to EGFR-TKI treatment. Interestingly, we found the conditioned media harvested from PD-L1 over-expressing cells can enhance the chemotaxis when compared to those harvested from control cells. Besides, the PD-L1 mediated chemotaxis in EGFR-mutant NSCLC can be rescued by lentiviral knock-down of PD-L1. Finally, we explored difference in the cytokine profiling between PD-L1 over-expressing and control cells using human cytokine array.

Conclusion: PD-L1 can induce cytokine storm which might contribute to the chemotaxis of EGFR-mutant NSCLC cells, and targeting cytokines might be the therapeutic strategy to overcome the progression of EGFR-mutant cancer.

PP01.32:
Activation of EIF2 Signaling and HIF-1α Signaling as Possible Mechanisms of NSCLC Tumor Cell Proliferation Through Induction of Autophagy

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Background: Lung cancer is responsible for the largest number of cancer-related deaths in the Philippines. Non-small cell lung cancer (NSCLC), the dominant type of lung cancer, makes up 85% of all lung cancer cases globally. Its high mortality rate underscores the demands for further understanding of the disease to improve its diagnosis and treatment.

Methods: The global proteome of tumor and adjacent normal tissue specimens from 7 Filipino NSCLC patients was analyzed to gain insights on the important pathways that may be involved in NSCLC. Protein identification and quantification was done through LC-MS/MS analysis of TMT-labeled tryptic peptides. Offline fractionation was done through basic reverse-phase liquid chromatography prior to LC-MS/MS to minimize co-isolation of peptides in MS2. Protein database search was done using the Sequest HT algorithm of Proteome Discoverer 2.5. Bioinformatic analysis through Ingenuity Pathway Analysis (IPA) was used for functional and pathway analysis.

Results: TMT quantification determined a total of 7,799 proteins with false discovery rate < 0.01 and abundance value in every patient sample. Two-sample t-test revealed 3,212 significantly upregulated and 1,428 significantly downregulated proteins in the tumor tissues. IPA analysis was done on the 1,195 proteins with at least 2-fold change difference. EIF2 and HIF-1α signaling pathways which are implicated in various cancer hallmarks were predicted to be activated. These pathways were known to contribute to the induction of autophagy, enabling cancer cells to survive amidst stress conditions such as nutrient starvation and hypoxia. EIF2A kinases observed to be upregulated in the tumor samples were known to be involved in the production of amino acids through autophagy in response to amino acid deprivation. Autophagy is also known to be induced in the hypoxic environment of the tumor. Under this condition, HIF-1α stimulates expression of phosphoglycerate kinase and lactate dehydrogenase A which are also found upregulated in the tumor samples. This enables the cells to adapt metabolically to oxygen deprivation. In addition, TNF which is known to also induce autophagy is predicted to be activated in the tumor cells.

Conclusion: Activation of EIF2 signaling and HIF1α-signaling contributes to sustained cell proliferation, induction of angiogenesis, and resistance to cell death. These pathways are involved in the stimulation of autophagy in response to amino acid deprivation and hypoxia due to sustained proliferative growth in tumor cells. Findings from this study add to the evidence of the tumor-promoting aspect of autophagy in NSCLC.

PP01.33:
Clinical and Molecular Characterization of Thoracic Inflammatory Myofibroblastic Tumors

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Background: Inflammatory myofibroblastic tumor (IMT) is a rare soft tissue neoplasm that has both malignant tumor and obvious inflammation. The pathological picture displays a wide morphologic spectrum. Generally, IMT has an indolent clinical behavior and surgical excision is the standard treatment for the local disease. The aim of this study is to analyze the clinical characteristics and molecular characterization of patients with thoracic IMT.

Methods: We retrospectively collected tumor specimens of IMT from the Pathology department in the National Taiwan University Hospital. ALK (D5F3) assay with a Ventana BenchMark XT automated staining instrument (Ventana, AZ) was used for ALK immunohistochemical (IHC) staining. To confirm the IHC result, fluorescence In Situ Hybridization (FISH) was performed by using commercial Vysis LSI ALK Dual Color, Break Apart Rearrangement Probe (2p23) (Abbott Molecular Inc., Des Plaines, IL). In addition, next-generation sequencing by Archer FusionPlex Lung Panel (ArcherDX) was used to detect the known and novel gene fusions in 13 genes. Patients' clinical characteristics, treatment course, molecular landscape, and overall survival (OS) were analyzed.

Results: From 2000 to 2020, there were 8 patients with thoracic IMTs. The median age was 33.8 (range: 18.6–58.7) years. There were 5 females and all of them were non-smokers. All tumor stages were early (6 stage I and 2 stage II). All patients received surgical tumor excision, and no tumor recurrence was detected. No patients received systemic chemotherapy or target therapy. Of them, 6 tumors harbored ALK rearrangement confirmed by IHC and FISH. The partners of ALK included 3 tropomyosin 3 (TPM3), 2 dynactin subunit 1 (DCTN1), and 1 echinoderm microtubule-associated protein-like 4 gene (EML4). In the other two tumors without ALK-positive, NGS showed neurotrophic receptor tyrosine kinase 3 gene (NTRK3) overexpression.

Conclusion: In Taiwan, the patients with thoracic IMT were young, and had early stages of disease status. ALK rearrangement and NTRK3 overexpression were the major genetic alterations. Different partners of ALK arrangement could be detected.

Table 1.

Patient No.	Sex	Age	Smoking	ECOG PS	Location	Size (cm)	TNM	Stage	ALK IHC/FISH	NGS	Recurrence	OS (mo.)	status
1	M	20.1	Non-smoker	0	LLL	2	T1N0M0	I	+	DCTN1 E26→ALK E20	No	59.7	Alive
2	F	26.7	Non-smoker	0	LUL	1.4	T1N0M0	I	+	TPM3 E8→ALK E20	No	17.2	Alive
3	F	58.7	Non-smoker	0	LLL	0.8	T1N0M0	I	+	TPM3 E8→ALK E20	No	32.5	Alive
4	M	18.6	Non-smoker	0	RLL	4.6	T3N0M0	IIB	+	DCTN1 E26→ALK E20	No	51.8	Alive
5	F	38.2	Non-smoker	0	LLL	2.5	T1N0M0	I	+	EML4 E7→ALK E20	No	4.9	Alive
6	F	51.2	Non-smoker	0	RUL	2.8	T1N0M0	I	-	NTRK3 overexpression	No	122.8	Alive
7	M	29.5	Non-smoker	0	LLL	1.65	T1N0M0	I	+	TPM3 E8→ALK E20	No	130.8	Alive
8	F	52.6	Non-smoker	0	RML&RLL	3.2	T1N1M0	IIA	-	NTRK3 overexpression	No	142.9	Death

PP01.34:
ACTN4 is Related to the Migration and Proliferation of Thymic Cancer Through β-catenin Pathway

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Background: The actin-binding protein ACTN4 belongs to a family of actin-binding proteins and is usually localized in the cytoplasm and participates in cytoskeletal organization. ACTN4 is known to be also associated with cancer development. While a functional association of ACTN4 with β-catenin has been confirmed in breast cancer, prostate cancer, cervical cancer, and so on. However, cancer-promoting factor of thymic cancer is not clear including ACTN4. In this study, we evaluated the expression of ACTN4 in thymic cancer specimens and examined the effects of ACTN4 knockdown and overexpression on the proliferation and migration ability of a thymic cancer cell line.

Methods: We performed immunostaining of surgical specimens obtained from thymic cancer patients (n=11) in our hospital. Next, we compared migration and proliferation ability in the thymic cancer cell line TY82. The knockdown of ACTN4 was performed by using siRNA and the overexpression of ACTN4 was achieved by transfection with plasmid. The human ACTN4 was cloned from lung cancer cell line A549 and inserted into CMV vector. To assess migration and proliferation abilities, the migration assay, WST-1 assay were used. β-catenin expression was confirmed by western blotting.

Results: By immunostaining, ACTN4 was positive in 10 of 11cases. Immunostaining revealed that ACTN4 stained more intensely at the tumor invasion margins and at the edge of the tumor, suggesting ACTN4 was associated with invasion ability of thymic cancer. The proliferative ability was suppressed by knockdown of ACTN4 compared to control cells. The ability of migration was also attenuated by the knockdown of ACTN4 in TY82 cells. Conversely, TY82 cells overexpressing ACTN4 had increased proliferative and migratory ability. Western blotting showed the expression of β-catenin was downregulated in ACTN4 knockdown TY82 cells and upregulated in ACTN4 overexpressing TY82 cells, as compared to control cells.

Conclusion: Our findings indicate that ACTN4 involved in the proliferation and migration ability of thymic cancer through β-catenin pathway. Further experiments are required to understand the molecular mechanisms that ACTN4 engages to promote tumor progression and metastasis in thymic cancer.

PP01.35:
Dysregulation of Lipid Metabolism Leads to Resistance of Lung Cancer Stem Cells to Reactive Oxygen Species-Induced Cell Death

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Background: Altered metabolism and resistance to reactive oxygen species (ROS)-induced cell death are well-known features of cancer stem cells (CSCs). Whether dysregulation of lipid metabolism plays an important role in CSC escape from ROS-induced apoptosis remains to be elucidated.

Methods: Spheroid culture was used to enrich CSCs of A549 and H1299 lung cancer cells. Qualitive and quantitative analyses of reactive oxygen species (ROS) were carried out using fluorescent probes (DCFDA, MitoSOX Red, HPF) and Flow-Cytometry. Mitochondrial oxidative phosphorylation on the basis of the oxygen consumption rate (OCR) was measured by using Seahorse XF24 Extracellular Flux analyzer. Lipid peroxidation products were detected by measuring malondialdehyde (MDA) and 4-Hydroxynonenal (4-HNE). Lipid profiles were investigated by using LC/MS-based lipidomics analysis.

Results: CSCs of A549 and H1299 lung cancer cells resisted to H2O2-induced cell apoptosis. Seahorse assay showed that lung CSCs had higher level of mitochondrial oxidative phosphorylation. Moreover, lung CSCs had lower levels of ROS and higher levels of cytotoxic end-products of lipid peroxidation 4-HNE and MDA. In addition, lung CSCs resisted to ferroptosis through upregulation of ACSL1, ASCL4 and GPX4 protein levels. To further investigate the causal relationship between lipid dysregulation and ROS resistance in lung CSCs, lipidomic analysis using LCMS (lipid class and amount) showed that CSCs increased in poly-unsaturated fatty acid (PUFA) and triacyglyceride (TAG) levels, compared to bulk cancer cells. More importantly, inhibition of ACSLs, GPX4, and TAG synthesis decreased lipid peroxidation and induced cell death in lung CSCs.

Conclusion: Lung CSCs exhibited unique lipidomic features including increased PUFA and TAG levels, which are important for their escape from ROS-induced apoptosis.

PP01.37:
Dynamic Alteration of Peripheral Immune Cells in Patients with NSCLC Received Anti-PD-1/PD-L1 Therapy and Clinical Efficacy

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Background: Little information is available about the association between dynamic alteration of peripheral immuno cells and the efficacy of immune checkpoint inhibitor (ICI) therapy and combination immunotherapy in patients with non-small cell lung cancer (NSCLC). We analyse the relationship between the peripheral immunocompetent cell of patients with NSCLC received ICI therapy or combination immunotherapy and the efficacy of them at multiple timepoints.

Methods: Patients with NSCLC who are scheduled to receive treatment with ICIs or combination immunotherapy are prospectively enrolled in this study. Peripheral blood samples are obtained every 3-8 week until disease progression.

Results: Twenty cases in which consecutive samples were obtained and clinical efficacy could be evaluated were included in the assessment. Twenty patients were analyzed separately for progression-free survival (PFS) of 6 months or less (n=13; group A), 6-12 months (n=3; group B), and 12 months or longer (n=4; group C). CD8+ T cells percentage were significantly higher at pre-treatment and during treatment in group C than group A). CD11b+CD14-CD15+ MDSCs percentage were significantly lower at pre-treatment in group C than group A).

Conclusion: High CD8+ T cells percentage and low CD11b+CD14-CD15+ MDSCs percentage may be predictive biomarkers of efficacy of ICI therapy, and require further study.

Image 1.
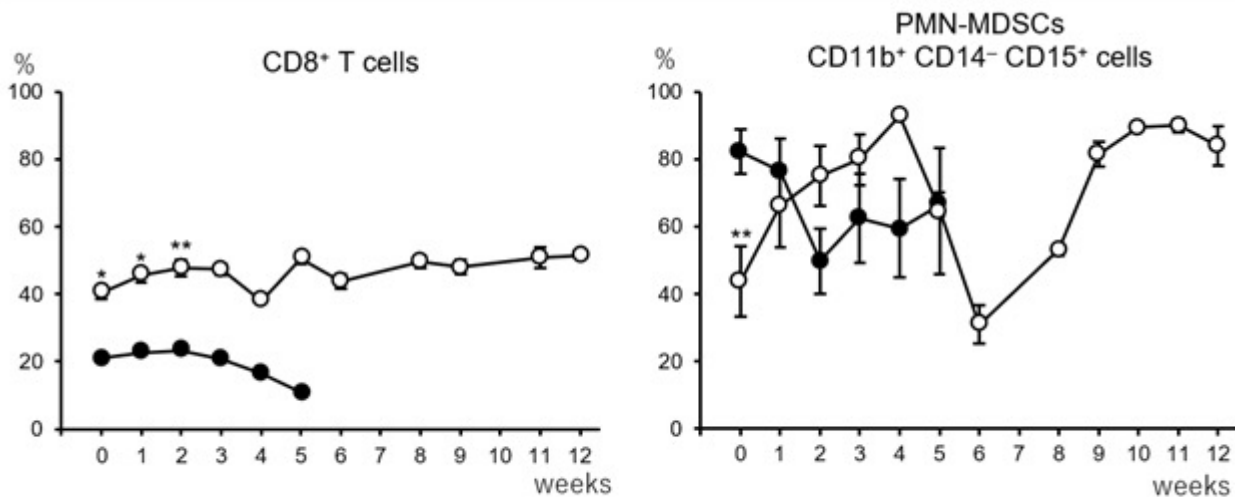
Fig. 1. Dynamic alteration of peripheral immune cells by anti-PD-1/PD-L1 therapy

PP01.38:
Cyclooxygenase-2 Expression Level in Primary Tumors is Associated with Vasculogenic Mimicry Formation and Survival in T1 Lung Adenocarcinoma

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Background: Vasculogenic mimicry (VM) is a special mechanism of tumor-associated angiogenesis. Little is known about the association between cyclooxygenase-2 (COX-2) expression and VM formation and survival in T1 lung adenocarcinoma.

Methods: From January 2009 to December 2014, 74 patients with surgically resected T1 lung adenocarcinoma were enrolled in this retrospective cohort study. Patient outcomes were followed up until December 2020. COX-2 level in primary tumors was assessed immunohistochemically and evaluated based on the staining intensity and percentage. Correlation between COX-2 and VM expression level and clinical outcomes were reviewed.

Results: High COX-2 expression was associated with increased VM events (p=0.035), and the COX-2 expression level was correlated with the level of VM formation (Spearman's coefficient ρ=0.261, p=0.025). Kaplan-Meier analysis revealed that high COX-2 expression level was associated with unfavorable recurrence-free survival and overall survival in T1 lung adenocarcinoma (log-rank p=0.03, and 0.01, respectively).

Conclusion: High COX-2 expression level in primary tumors was remarkably associated with increased VM events and reduced recurrence-free survival and overall survival in T1 lung adenocarcinoma. COX-2 may be a potential therapeutic target in T1 lung adenocarcinoma.

Image 1.
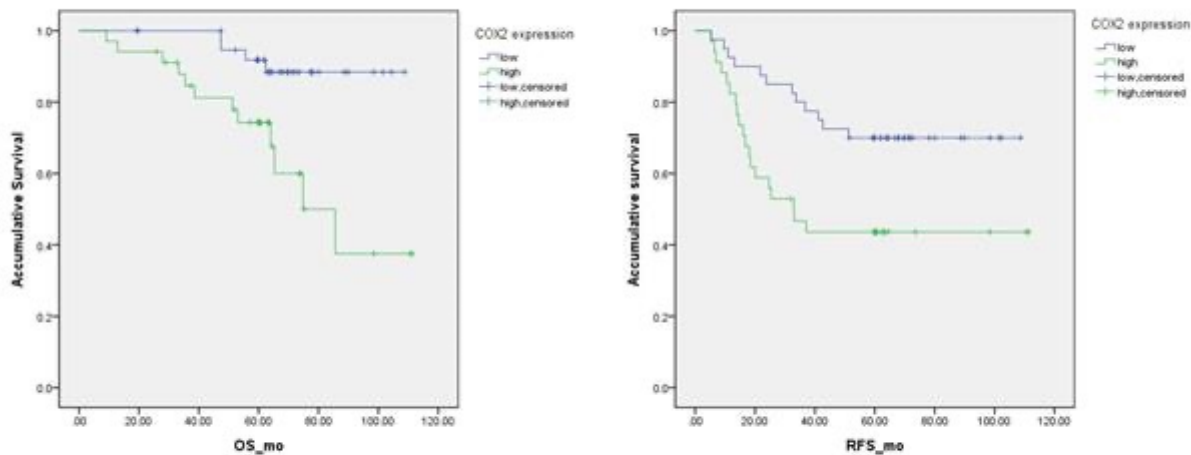
PP01.39:
Expression of Cluster Differentiation 109 Promotes Tumorigenesis and Is Associated with an Adaptive Immune Resistance in Lung Adenocarcinoma

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Background: Lung cancer is the leading cause of cancer death in Taiwan as it is hard for early diagnosis and shows a high capacity for metastasis. Immune checkpoint inhibitors are available as the first line of treatment for advanced lung cancer patients. Thus, identifying more reliable indicators of immune checkpoint inhibitors could benefit patient response to immunotherapy and therapeutic outcome.

Methods: We analyzed the transcriptome of lung adenocarcinoma patients from The Cancer Genome Atlas (TCGA) in conjunction with tumor immune infiltration databases. Immunohistochemistry staining of lung cancer tissues for the expressions of CD109, PD-L1, and CD8.

Results: We identified that cluster differentiation (CD)109, a glycosylphosphatidylinositol-anchored protein, was upregulated in lung adenocarcinoma patients. CD109 was positively correlated with several immune checkpoint molecules including programmed death-ligand 1 (PD-L1). Moreover, CD109 expression was associated with tumor-infiltration lymphocytes (TILs) and tumor burdens. Expression of CD109 was further identified as crucial for promoting stemness and metastasis of lung tumor cells. Immunohistochemistry staining of lung cancer tissues validated a significantly positive association between CD109 with PD-L1 and CD8.

Conclusion: Our study reveals the impact of CD109 on the immune component of the tumor microenvironment and CD109 may be a potential indicator of immune checkpoint inhibitors.

PP01.41:
Immunohistochemistry Techniques to Differentiate Adenocarcinoma or Squamous Cell Lung Cancer

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Background: Systemic therapy modalities for lung cancer are increasing, including chemotherapy, targeted therapy, and checkpoint inhibitors. Cancer cell type is a major determinant of therapeutic choice, especially in NSCLC. In certain situations, a marker is needed to determine the type of cancer cell. Immunohistochemistry plays an important role in the accurate diagnosis of different types of cell cancer.

Methods: This study has used 51 paraffin block lung cancer samples to determine the positive expression of thyroid transcription factor-1 (TTF-1), P40, and cytokeratin 5/6 (CK 5/6). Immunohistochemistry examination on TTF-1 expression using monoclonal mouse antibody 8G7G3/1, P40 expression using polyclonal rabbit antibody, and CK 5/6 expression using CK5/6.007 monoclonal mouse antibody.

Results: Of the 51 samples, we only managed to examine 47 samples, and that included 35 (74.5%) adenocarcinoma and 12 (25,5%) squamous cell carcinoma. In the adenocarcinoma group, our data have shown expression of TTF-1, P40, and CK 5/6   were positive in 25 (71.4%), 6 (17.1%). 4 (11.4%). in Adenocarcinoma samples. TTF1 expression was lower but P40 and CK5/6 expression were higher in Squamous carcinoma compared to the adenocarcinoma group. The bivariate analysis found a significant difference between the expression of TTF-1, P40, and CK 5/6 with adenocarcinoma cancer and squamous cell carcinoma (p < 0.05).

Conclusion: There were significant differences in TTF-1, P40, and CK 5/6 expressions between adenocarcinoma and squamous cell carcinoma, but the three expressions could not be used simultaneously. Thyroid transcription factor-1 expression was more accurate than P40 and CK 5/6 for differentiating adenocarcinoma from squamous cell carcinoma.

Keywords: adenocarcinoma, squamous cell carcinoma, TTF-1, P40, and CK 5/6.

PP01.42:
Diagnosis of MET Gene Alterations in Advanced NSCLC with Next Generation Sequencing

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Background: Biotransformations have caused by mesenchymal epithelial transformation (MET) of the cells on NSCLC also have contributed to cell proliferation, division, and metastasis. Our research on MET alterations has the following objectives:
    a. Detecting MET alterations with mRNA next generation sequencing diagnostic technique.
    b. Application in targeted therapy with the results obtained.

Methods: A research with retrospective, cross-sectional descriptive statistics. Analysis with SPSS 20.0 software, two-sided analysis with T-Test, test value with $P < 0.05$.

Results:
    — The detection rate of MET gene mutations: 34 cases # 9% is similar to many other studies in the world, about 4 - 10%.
    — Particularly, the rate of MET Exon 14 Skipping mutation, our research result is 4.26%, which is similar to many other studies in the world.
    — Expression of MET Exon 14 Skipping have been the most in two histological types: acinar adenocarcinoma (5 cases # 27.78%) and micropapillary adenocarcinoma (4 cases # 22.22%). Different from other studies in the world with most appearing in histological type of sarcomatoid carcinoma.
    — With the results of grouping of MET gene mutations: in addition to Exon 14 skipping and MET gene amplification, there are other point mutations. This is clinically applicable to a variety of TKIs targeting MET such as crizotinib, capmatinib, carbozantinib, savolitinib, tepotinib, glesatinib, merestinib or monoclonal antibody drug classes.

Conclusions:
    — MET gene alternations have many forms, now there are important targets for MET: MET Ex14 Skipping, MET Amplifications, MET point mutations.
    — There are many medecines suitable for these targets. This leads to the need to diagnose these MET gene mutations with next-generation sequencing techniques.

PP02.01:
Role of Bronchoscopy for Lung Cancer Diagnosis in Elderly Patients

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Background: A flexible bronchoscopy is a diagnostic tool for evaluating lung cancer. We aimed to review the bronchoscopy's role in the elderly lung cancer population.

Methods: Between 2017 and 2022, patients suspected of lung cancer and who performed bronchoscopy were reviewed. Patients aged ≥80 years were enrolled in the elderly population, and those aged 55 to 70 were enrolled as the comparable control group. The outcomes are a percentage of bronchial washing, biopsy, and complication in 1 week.

Results: A total of 431 patients were included, the elderly group was 211, and the control group was 220. The percentage of successful bronchial washings and endobronchial biopsy were not significantly different between the elderly group and the control. (Bronchial washing 123 (58.3%) vs. 114 (51.6%) $p=0.161$, and endobronchial biopsy 81 (38.4%) vs 70 (31.7%) $p=0.143$, respectively) the successfully performed number of transbronchial lung biopsies was even higher in the elderly group than in the control group. (16 (7.6%) vs 6 (2.7%), $p= 0.021$)

Conclusion: For lung cancer diagnosis, bronchoscopy in the elderly patients showed similar performance in bronchial washing and endobronchial biopsy to the adult patients. It showed even higher successful performance in trans-bronchial lung biopsy. We found that flexible bronchoscopy is a useful diagnostic tool for the elderly.

PP02.02:
Respiratory Sarcopenia Predicts Postoperative Outcomes in Patients with Non-Small Cell Lung Cancer

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Background: Emerging studies indicate that low muscle strength is a key characteristic of sarcopenia. The aim of this study was to evaluate the clinical utility of peak expiratory flow rates (PEFR), which reflects respiratory muscle strength, to predict the risk of postoperative outcomes.

Methods: This retrospective study included 460 consecutive patients undergoing lobectomy of non-small cell lung cancer from April 2013 to December 2018. Postoperative outcomes were compared between the lowest gender-specific quartile (respiratory sarcopenia) and the other quartiles according to the PEFR from preoperative respiratory function. The prognostic value of respiratory sarcopenia was evaluated in multivariate Cox proportional hazards model.

Results: PEFR was significantly higher in males than in females (median 7.5 vs 5.4 L/s, $P<0.001$). PEFR was positively correlated with pectoralis muscle area, but negatively correlated with advancing age (Pearson's r=0.59, $P<0.001$, Pearson's r=-0.31, $P<0.001$, respectively). Respiratory sarcopenia was associated with higher risk of postoperative complications and prolonged postoperative hospital stay (33.0% vs 24.1%, $P=0.058$; 10 days vs 9 days, $P=0.003$). Patients with respiratory sarcopenia exhibited the worse 5-year overall survival compared to those without respiratory sarcopenia (68.6% vs 82.0%, $P = 0.001$), although respiratory sarcopenia was not associated with recurrence-free survival ($P=0.56$). Multivariate analysis revealed that respiratory sarcopenia was an independent adverse prognostic factor for overall survival (hazard ratio, 1.54; 95% confidence interval, 1.04-2.29; $P=0.031$) after adjustment for gender, age, albumin, CEA, and pathologic stage.

Conclusions: Respiratory sarcopenia was significantly associated with prolonged postoperative recovery and poor survival in patients with localized non-small cell lung cancer after surgery. This may help assist preoperative risk stratification and optimize longitudinal care for patients.

Image 1.
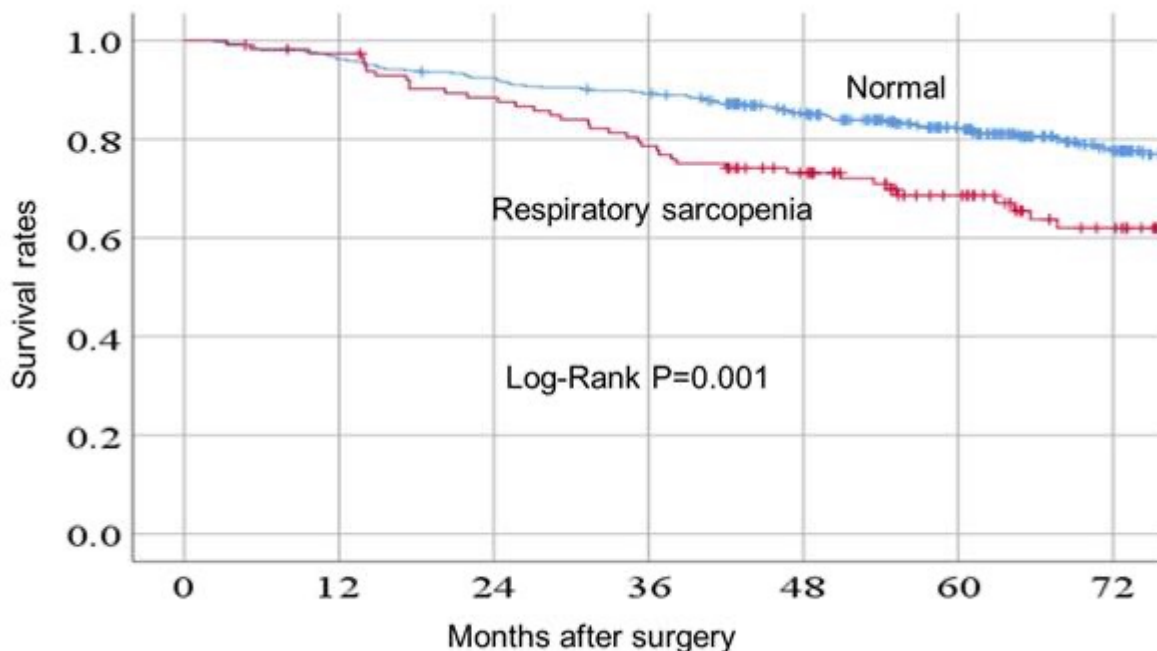
PP02.03:
Shared Presurgical Understanding for Lung Cancerin Patient's Acquaintances Using CT-Derived 3D Virtual Explanation Module

Dr. Kwon Joong Na[1], Prof. Soon Ho Yoon[2], Prof. Young Tae Kim[1], Prof. Chang Hyun Kang[1], Prof. In Kyu Park[1], Prof. Samina Park[1], Prof. Jin Mo Goo[2]
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Background: This study generated the patient-tailored standardized virtual explanation module for lung cancer from chest CT scans and evaluated whether the module improved the understanding of lung surgery in patients and their acquaintances who were physically apart.

Methods: We enrolled 66 adult patients who were suspected of having lung cancer on a preoperative multidetector chest CT and decided to undergo elective surgical resection. We excluded patients who were hard to communicate and read. Participants were randomly allocated to either group using a web-based randomization system. Only technicians in the company received the randomization list to deliver the module to intervention group, and investigators were blinded to group allocation. Pre-existing presurgical CT scans were segmented from using deep neural networks of commercially available software and transformed the structures as an anonymized interactive 3D virtual explanation module. The module comprised a standardized scenario beginning from patient-specific thorax outlook to inner thorax and lung cancer with explanation text. The link of the module was texted to patients' cell phone in the intervention group before admission for surgery. After admission, surgeons explained verbally about the same content using a standardized institutional document for informed consent. Control group received the verbal explanation without provision of the module. After obtaining informed consent, both groups answered a questionnaire that consisted of 9 items to test patients' understanding about basic anatomy, lung cancer, and surgery. Surgeons also answered the questionnaire, and it was served as reference. The Mann-Whitney and Fisher's exact tests were used to compare groups.

Results: Among 34 and 32 enrolled patients in intervention and control arms, one and three patients denied the surgery, each (adherence rate, 97% vs. 91%; p=0.35), resulting in 33 and 29 patients for analysis. The difference in understanding score did not reach statistical significance (7.2±1.6 vs. 6.5±1.8; p=0.12). 76% of patients in the intervention arms accessed the link, and the median access number among accessed patients was 14 (interquartile range, 7-18). 44% of the accessed patients texted the link to their acquaintances up to ten people. Nine acquaintances replied to questionnaire, and their scores were comparable to their patients' scores (6.9±2.0 vs. 7.1±2.6; p>0.05).

Conclusion: The 3D module failed to significantly improve patients' presurgical understanding but was actively accessed in three-fourths of the patients and texted to patients' acquaintances, successfully sharing the understandings.

Image 1.

The ribs and sternum are located underneath the skin.

Both lungs are connected to the airway.

There is 1 lesion of 2.5cm in the left upper lobe. The left lower lobe and right lung remain present after surgery.
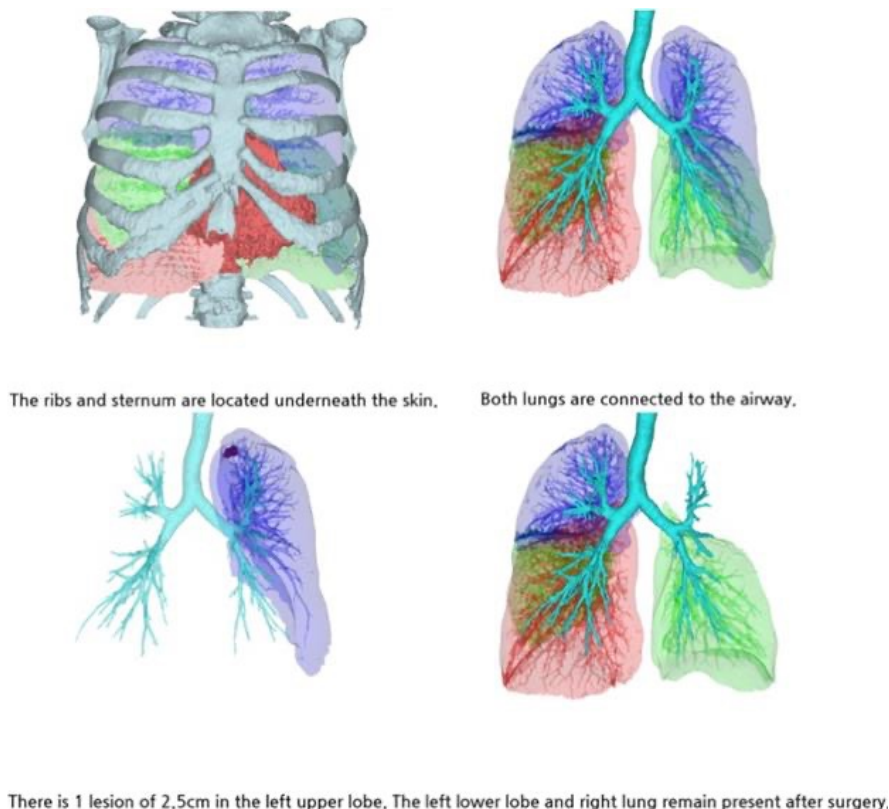
PP02.04:
Multiple Non-Small Cell Lung Cancers Including One Tumor with EGFR Mutation and Another Without That

Dr. Taisuke Matsubara[1], Dr. Eiji Nakajima[2], Dr. Tatsuo Ohira[1], Dr. Ikki Takada[1], Dr. Yuki Yazaki[1], Dr. Teruo Miyazaki[2], Dr. Jun Matsubayashi[1], Dr. Kinya Furukawa[2], Dr. Norihiko Ikeda[1]
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Background: Primary lung cancer is mainly caused by exogenous risk factors in one patient. The similar environmental factors lead multiple primary lung cancers (MPLCs), namely, field cancerization and carcinogenesis. However, one tumor has driver gene as the factor of carcinogenesis and another does not in MPLCs occasionally. We retrospectively investigated MPLCs including one tumor with epidermal growth factor receptor (EGFR) mutation and another without that in the patients with surgical treatments. When the patients had recurrent disease, the treatment decision was confirmed. Treatment depends on the driver gene mutation of the recurrent lesion.

Methods: Among 254 patients who underwent lung resection for non-small cell lung cancer (NSCLC) at Tokyo Medical University Hospital between July 2015 and December 2017, we selected cases with multiple operations for synchronous or metachronous multiple lung cancer. Cobas v2 as clinical PCR method was performed to detect EGFR mutation with each surgical tumor sample. The clinical courses were confirmed after surgeries.

Results: Three patients had synchronous multiple non-small cell lung cancers including one tumor with EGFR mutation and another without that. All tumors in three patients were histologically adenocarcinomas. One patient had left lung tumor with EGFR wild type and right tumor with exon 19 deletion. Another had left tumor with exon 21 L858R point mutation and right tumor with EGFR wild type. The other had quadruple adenocarcinomas including tumor with exon 21 L858R point mutation and EGFR wild type. The patient with adenocarcinomas of right exon 19 deletion and left wild type tumors had recurrent disease, as metastasis of right mediastinal lymph node and right pleural dissemination 10 months after surgery. EGFR tyrosine kinase inhibitor was administrated as recurrence of right tumor with exon 19 deletion. Two months later, swelling of right neck lymph node and left lung nodule emerged. Second line chemotherapy was carboplatin and pemetrexed. Two months later, the patient died of interstitial lung disease, and it was 9 moths survival after recurrent disease.

Conclusion: The patient with MPLCs has the similar environment factors. However, when MPLCs include one tumor with EGFR mutation and another without that, the carcinogenesis is heterogeneous and the decision for chemotherapy is difficult.

PP02.05:
Postoperative Pleuroparenchymal Fibroelastosis (PPFE) like Ipsilateral Upper Lung Field Pulmonary Fibrosis, Differentiation from the Lung Cancer Recurrence

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Background: Pleuroparenchymal fibroelastosis (PPFE) is a rare disorder characterized by predominantly upper lobe fibrosis. Few patients have progressive unilateral upper lung field fibrosis consistent with PPFE after lung resection, which could be challenging to differentiate from lung cancer recurrence.

Methods: Of 211 patients who had pulmonary resection for lung cancer in our institute from 2015 to 2017, the radiologic findings after surgery were retrospectively reviewed to extract patients having unilateral upper pulmonary fibrosis.

Results: We found four patients with upper pulmonary fibrosis, while one with bilateral preoperative fibrosis was excluded. All three patients (two males, two never smokers, mean age 66yrs) progressed ipsilateral (and all are right-sided) upper pulmonary fibrosis. The resected lung was the upper lobe, lower lobe, and S6. In the upper lobe resection case, the fibrosis progressed in the relocated S6. The mean time to detect the upper field fibrosis after surgery was 24.7 months, then the intra-alveolar fibrosis and fibrous thickening of the visceral pleura progressed time by time. These findings (pleural thickening in two and nodule-like alveolar fibrosis in one) imitate lung cancer recurrence, while PET-CT showed slight FDG uptake in all cases. Furthermore, bronchoscopic brush cytology resulted in the negative in alveolar fibrosis case. One patient died from acute empyema, and the other two cases were alive without any evidence of recurrence.

Conclusion: PPFE is a rare condition, and the proportion of association with lung cancer is unclear. Moreover, the dense shadow of PPFE could be difficult to differentiate from lung cancer, especially in postoperative care. The PET-CT would be beneficial in differentiating from lung cancer.

PP02.06:
Primary Pure Signet-Ring Cell Carcinoma of Lung with ALK Rearrangement – Case Report

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Background: A signet-ring cell carcinoma is a highly aggressive adenocarcinoma that usually arises in the stomach, colon, breast, prostate, or urinary bladder, with primary occurrence infrequent and usually appearing intermingled with other adenocarcinoma components. Very rare is a pure pulmonary signet-ring cell carcinoma, in which nearly all cellular components of the tumor are composed of signet-ring cells. Presented here is a case report of a pure pulmonary signet-ring cell carcinoma in an elderly patient.

Methods: An 81-year-old man was found to have an abnormal chest shadow in the left lung during an annual checkup. CT scan findings of the chest revealed a 20-mm sized mass in the lingual region of the left lung, while whole-body PET-CT showed an abnormal accumulation localized in the lingual region of the left lung, with no accumulation seen in other sites. Those results suggested primary lung cancer and partial resection of the upper lobe of the left lung was performed. The macroscopic appearance was a well-defined substantial mass. Histologically, tumor cells with eccentric nuclei and cytoplasm with abundant mucin had infiltrated the lung parenchyma, forming a substantial foci. Nearly all were signet-ring cells and a diagnosis of pure signet-ring cell carcinoma was decided. Immunohistochemical staining was performed to determine whether it was a lung primary tumor or metastasis from another organ, and for detection of ALK rearrangement in the adenocarcinoma with signet-ring cell features. In addition, multigene mutation detection test including the ALK fusion gene was performed.

Results: Tumor cells were positive for CK7, TTF-1, Napsin A, CK5/6, and p63, while CK20, CDX2, p40, PSA, ER, and GCDFP15 were negative. Based on CK7 and TTF-1 positivity, and CK20 negativity a diagnosis of primary lung carcinoma was made. Moreover, ALK staining was positive and further genetic analysis revealed ALK fusion gene expression. No other driver gene mutations or fusion, including the EGFR, KRAS, BRAF, MET, ROS1, NTRK and RET genes, were detected.

Conclusion: Primary pulmonary signet-ring cell carcinoma is considered to have a younger onset and poor prognosis. The present is an extremely rare case of an elderly patient with an early stage operable ALK fusion-positive primary pure pulmonary signet-ring cell carcinoma.

PP02.08:
The Usefulness of Liquid Biopsy When Biopsy Not Feasible in a Patient of EGFR Positive Non-Small Cell Lung Cancer (NSCLC), a Case Report

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Background: A third-generation epidermal growth factor receptor(EGFR), tyrosine kinase inhibitor(TKIs), Osimertinib, is effective against EGFR T790M positive non-small cell lung cancer(NSCLC). Identifying T790M mutation by re-biopsy is essential for proper use of osimertinib.[1] Both tissue biopsy and liquid biopsy can be useful in some of certain situations. Tissue biopsy is useful when biopsy is feasible. Liquid biopsy could be useful when biopsy not feasible or repeated inadequate samples (23% of cases).[2] Tissue biopsy is the golden standard to obtain tumor DNAs, but several factors limit its success rate.[3] The liquid biopsy with blood, using circulating tumor DNA, has been an alternative method. We report a 57-year-old woman who have destroyed lung by previous tuberculosis, and difficult to obtain proper amount of tissue from endobronchial ultrasound-guided transbronchial needle aspiration(EBUS TBNA). We eventually figure out T790M postivie by liquid biopsy and followed osimertinib use.

Case: 60-year-old woman diagnosed as stage IV (pleura metastasis). Result for positive EGFR, erlotinib was started as first line chemotherapy. Progression of the disease was confirmed after 16 months of treatment. Repeated biopsy for N2 node was performed by EBUS-TBNA but not enough tissue to confirom T790M mutation. After all, we alternatively use plasma genotyping(liquid biopsy) and mutation for T790M was confirmed. Followed second line chemotherapy with osimertinib was effective for the first 6 months of treatment. [Image 1.]

Conclusion: Tissue biopsy is golden standard to obtain adequate tumor DNAs. But liquid biopsy also have its role especially when biopsy not feasible. When it is difficult to access tissue due to structural problems such as destroyed lung(in this case, tuberculosis), liquid biopsy could be considered to help patient.

1. Keigo Kobayashi et al. Comparison of detection methods of EGFR T790M mutations using plasma, serum, and tumor tissue in EGFR-TKI-resistant non-small cell lung cancer. OncoTargets and Therapy 2018:11 3335–3343.
2. Laura Bonanno et al, Liquid biopsy and non-small cell lung cancer: are we looking at the tip of the iceberg? British Journal of Cancer 2022.
3. Hasegawa T et al. Feasibility of rebiopsy in nonsmall cell lung cancer treated with epidermal growth factor receptortyrosine kinase inhibitors. Intern Med. 2015;54(16):1977–1980.

Image 1.
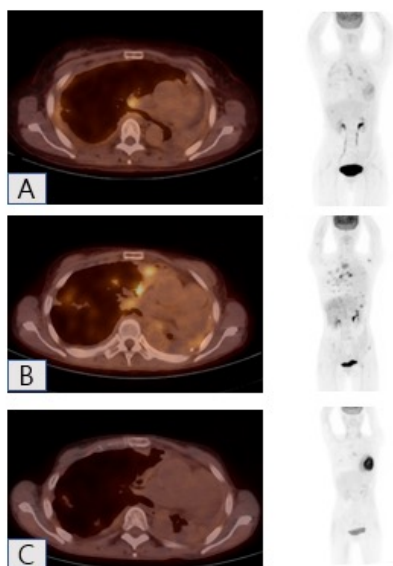
Image 1.
A : PET CT image before treatment. Activity is seen in the n2 node and pleura.

B: Progression of the disease was confirmed after 16 months of treatment. Multiple metastastic tumor in right lung, pleura, liver, spleen and bony structure

C : Followed second line chemotherapy with osimertinib was effective for the first 6 months of treatment. Remained metabolic active lesion in right lung, but much improved; partial response

PP02.10:
Perioperative Electrolyte Levels and Postoperative Atrial Fibrillation Following Robotic-Assisted Pulmonary Lobectomy

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Background: Atrial fibrillation (Afib) following robotic-assisted pulmonary lobectomy (RAPL) has been associated with increased length and cost of hospital stay as well as increased mortality rate. We investigated the effects of postoperative electrolyte levels on the incidence of new-onset postoperative Afib after RAPL.

Methods: We retrospectively analyzed consecutive patients who underwent RAPL from September 2010 to March 2022 by one surgeon. We collected perioperative serum levels of sodium, potassium, chloride, bicarbonate, anion gap, magnesium, phosphorus, calcium, corrected calcium, and ionized calcium. Independent samples t-test was used to examine relationships between perioperative electrolyte levels and incidence of new-onset postoperative Afib, defined as Afib not diagnosed preoperatively, with $p \leq 0.05$ as significant.

Results: Of 722 patients who underwent RAPL, 82 (11.4%) developed new-onset postoperative Afib. There were significant differences in post-anesthesia care unit (PACU) and highest postoperative potassium levels, highest postoperative bicarbonate and magnesium levels, and lowest postoperative and discharge phosphorus levels (Table 1).

Conclusion: Greater PACU levels of potassium, greater highest postoperative levels of potassium, bicarbonate, and magnesium, higher levels of phosphorus at discharge, and lower lowest postoperative values of phosphorus were all associated with new-onset postoperative Afib. Surgeons should be aware of these relationships and should correct electrolyte levels accordingly.

Table 1

Table 1: Statistically significant perioperative electrolyte values.

Variables	Patients with True PostOp Afib (n=82)	Patients without True PostOp Afib (n=640)	p-value
Potassium, PACU (mmol/L)	4.32 ± 0.06	4.19 ± 0.02	0.039
Potassium, Highest PostOp (mmol/L)	4.72 ± 0.04	4.59 ± 0.02	0.010
Bicarbonate, Highest PostOp (mmol/L)	29.5 ± 0.3	28.7 ± 0.1	0.006
Magnesium, Highest PostOp (mmol/L)	2.29 ± 0.03	2.21 ± 0.01	0.005
Phosphorus, Lowest PostOp (mmol/L)	2.52 ± 0.05	2.79 ± 0.02	<0.001
Phosphorus, Discharge (mmol/L)	3.64 ± 0.08	3.47 ± 0.03	0.044

*Mean ± SEM; SEM = standard error of the mean; PostOp = postoperative; Afib = atrial fibrillation; PACU = post-anesthesia care unit; Discharge = last value recorded during hospital stay.

PP02.11:
Effect of PM2.5 on Tumor Recurrence, Mortality, and Postoperative Complications in Resectable Non-Small Cell Lung Carcinoma: A retrospective Cohort Study

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Background: Particular matter 2.5-micron (PM 2.5) has recently become a global health issue. It leads to several negative health impacts, especially in lung cancer patients. The association between PM 2.5 and tumor-related mortality and recurrence are still controversial. This study aimed to identify the association between PM 2.5 and post-operative outcomes, tumor recurrence, and overall survival in resectable non-small cell lung cancer patients (NSCLC).

Methods: This retrospective cohort study included patients diagnosed with NSCLC who underwent pulmonary resection at Chiang Mai University hospital between January 2010 and December 2017. Patients were divided into two groups according to their residents' average PM 2.5 concentration; exposed (PM 2.5 > 50 µg/m3 24-hour mean) and unexposed group (PM 2.5 < 50 µg/m3 24-hour mean). The association between PM 2.5 and in-hospital mortality, tumor recurrence, and long-term mortality were analyzed by multivariable risk regression and Cox's regression analysis.

Result: A total of 587 patients were included (154 in exposed and 127 in unexposed group). Regarding characteristics, there were only baseline differences in tumor cell differentiation and intratumoral vascular invasion. Exposed group showed higher incidence of in-hospital and long-term mortality than unexposed group (4.55 % versus 0.79 % ,and 20.78 % versus 11.02 %, respectively). In multivariable analysis, patients in exposed group were more likely to have in-hospital mortality (Adjusted RR 7.26, 95% (CI), 2.05-25.74). However, no significant association was identified in terms of tumor recurrence (Adjusted HR 0.89, 95% (CI) 0.60-1.34) and long-term mortality (Adjusted HR 2.27, 95% (CI) 0.95-5.45).

Conclusions: Higher PM 2.5 concentration increases in-hospital mortality in resectable NSCLC patients and might affect long-term survival. Further studies with a larger sample size are warranted.

PP02.12:
A Trans-Omics Assessment of Gene-Gene Interaction in Early Stage NSCLC

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Background: Epigenome-wide gene-gene (G×G) interactions with non-small cell lung cancer (NSCLC) survival may provide insights into molecular mechanisms and therapeutic targets. To fill the gap, we proposed a three-step analytic strategy to identify significant and robust G×G interactions that are relevant to NSCLC survival.

Methods: In this study, we integrated epigenomic and transcriptomic data of multiple cohorts and utilized a three-step analytic strategy to identify robust G×G interactions. First, we performed an epigenome-wide G×G interaction study of lung cancer survival using samples from Lung Cancer Survival Epigenome Research Group (LCSERG) and further validated the selected signals using The Cancer Genome Atlas (TCGA). Second, we functionally evaluated the significant epigenetic G×G interactions and validated them at the gene expression level using transcriptomic data. Third, focusing on these G×G interactions having epigenetic cis-regulation of transcription, we conducted a trans-omics mediation analysis.

Results: In the first step, among 49 billion pairs of DNA methylation probes, we identified 175,775 G×G interactions with PBonferroni≤0.05 in the discovery phase of epigenomic analysis; among them, 15,534 were confirmed with P≤0.05 in the validation phase. In the second step, we further performed a functional validation for these G×G interactions at the gene expression level by way of a two-phase (discovery and validation) transcriptomic analysis, and confirmed 25 significant G×G interactions enriched in the 6p21.33 and 6p22.1 regions. In the third step, we identified two G×G interactions using the trans-omics analysis, which had significant (P≤0.05) epigenetic cis-regulation of transcription and robust G×G interactions at both the epigenetic and transcriptional levels. These interactions were cg14391855×cg23937960 (βinteraction=0.018, P=1.87×10-12), which mapped to RELA×HLA-G (βinteraction=0.218, P=8.82×10-11), and cg08872738×cg27077312 (βinteraction=-0.010, P=1.16×10-11), which mapped to TUBA1B×TOMM40 (βinteraction=-0.250, P=3.83×10-10). A trans-omics mediation analysis revealed that 20.3% of epigenetic effects on NSCLC survival was significantly (P=0.034) mediated through transcriptional expression. These statistically significant trans-omics G×G interactions can also discriminate patients with high risk of mortality.

Conclusion: In summary, we identified two G×G interactions at both the epigenetic and transcriptional levels, and our findings may provide potential clues for precision treatment of NSCLC.

Image 1.
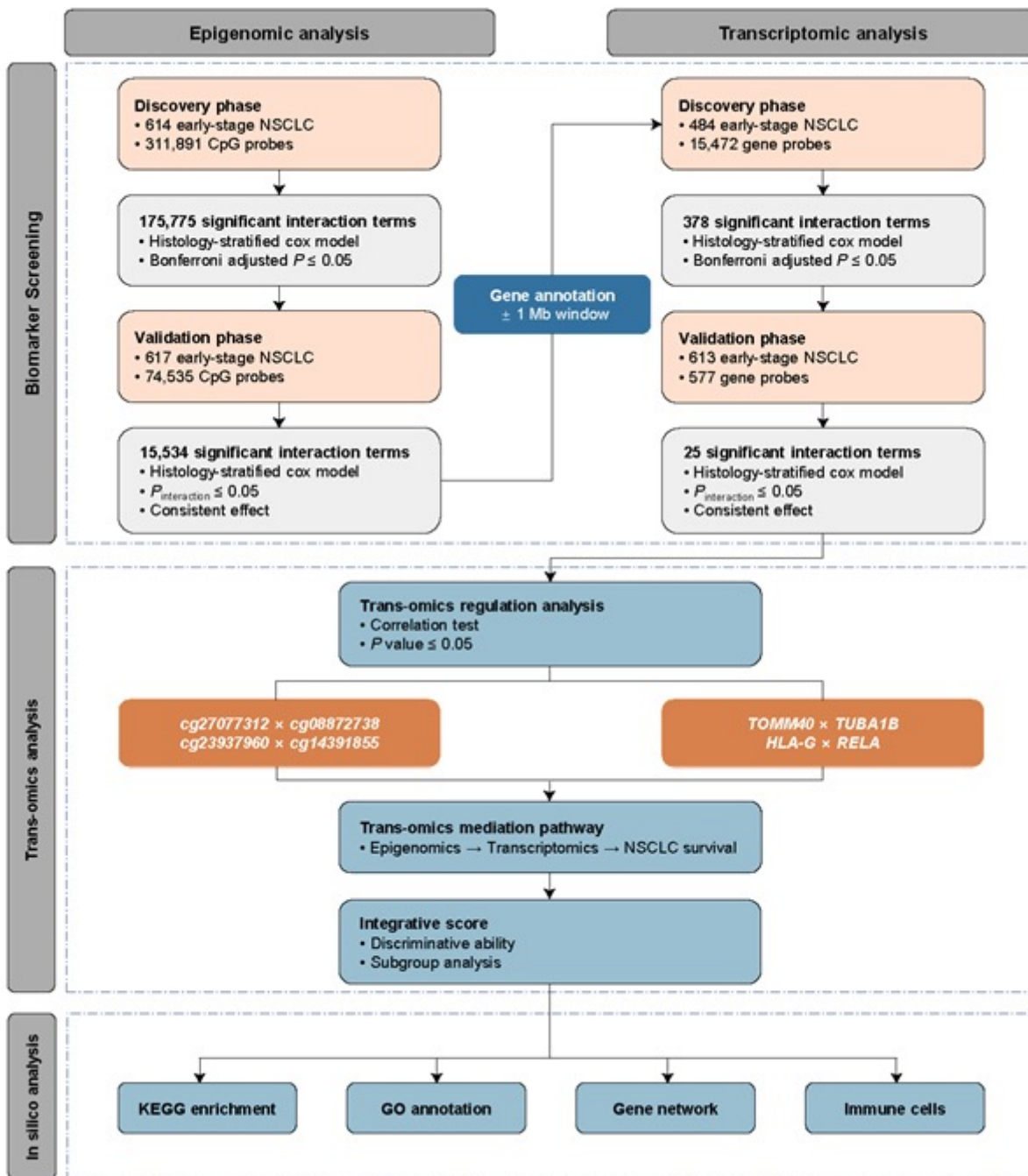
PP02.13:
Comparison Between Lobectomy and Proton Therapy for Confirmed Stage I Lung Cancer

Dr. Tadashi Sakane[1], Dr. Hiromitsu Iwata[2], Dr. Koichiro Nakajima[2], Dr. Tomoharu Nakano[1], Dr. Emi Hagui[1], Dr. Masanosuke Oguri[2], Dr. Kento Nomura[2], Dr. Yukiko Hattori[2], Dr. Hiroyuki Ogino[2], Dr. Hiroshi Haneda[1]
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Background: Lobectomy with systemic lymph node dissection remains the standard treatment for patients with clinical stage I non-small cell lung cancer (NSCLC). Stereotactic body radiotherapy has been proposed as a potential alternative to surgery for early-stage NSCLC in patients who are not ideal operative candidates. In recent years, an increasing number of lung cancer patients have been treated using proton therapy (PT).

Methods: We retrospectively reviewed data from 138 patients with histologically confirmed stage I NSCLC who underwent lobectomy (n=95) or PT (n=43) at our institution from July 2013 to December 2016. We compared local control (LC), recurrence-free survival (RFS), cause-specific survival (CSS), overall survival (OS), and adverse events between the lobectomy and the PT groups. Propensity score matching (PSM) was used to reduce selection bias in the two groups. Thirty-seven patients were identified from each group after performing PSM.

Results: In the overall cohort, patients who underwent lobectomy exhibited significantly lower age (p=0.04) and better performance status (p<0.001) compared to the PT patients. After PSM, the follow-up period in the whole cohort ranged 5 to 101 months with a median of 66 months. The study population included 38 male patients and 36 female patients with a median age of 70 years. In the lobectomy group, three patients (8.1%) had pathologic upstaging (stage I to II). Twenty-two patients (59.5%) received adjuvant chemotherapy, including three patients treated with platinum-based chemotherapy. In the PT group, there were 12 patients considered medically inoperable. No significant differences between the lobectomy and the PT groups were observed in 5-year LC (97.3% and 97.2%, p=0.98), RFS (86.5% and 80.4%, p=0.72), CSS (94.6% and 88.0%, p=0.22), and OS (89.0% vs 82.8%, p=0.22). Prevalence of significant adverse events (grade 2 or more) was 18.9% and 8.1% in the lobectomy and the PT groups, respectively (p=0.17).

Conclusion: In this study, we found no differences in disease control and survival between lobectomy and PT in patients with clinical stage I NSCLC. PT could be an alternative option to lobectomy for patients who cannot tolerate lobectomy. A prospective randomized trial will be needed in the future.

PP02.14:
Prognostic Impact of Ground Glass Opacity Component and Consolidation Size in clinical stage IA lung adenocarcinoma after sublobar resection: a quantitative analysis

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Background: The aim of this study is to perform a quantitative analysis of consolidation-to-tumor (C/T) ratio and maximal consolidation size for the risk of cancer recurrence after sublobar resection in clinical stage IA lung adenocarcinoma.

Methods: From 2010 to 2019, patients who underwent sublobar resection for clinical stage IA lung adenocarcinoma were analyzed. Sufficient resection margin was defined when the margin was ≥ 1cm or ≥ maximal consolidation of the tumor. Using a logistic regression model, risks of "within 5-year recurrence events" were analyzed quantitatively based on C/T ratio and consolidation tumor size.

Results: Of the 1,032 patients enrolled in this study, 523 (50.7%) and 509 (49.3%) patients underwent wedge resection and segmental resection, respectively. Patients with segmentectomy had significantly higher consolidation tumor size (p=0.002), C/T ratio (p=0.011), rate of sufficient resection margin (p<0.001) than those with wedge resection. In overall patients, estimated risks of cancer risk within 5 years showed a constant increase to 1.9%, 3.1%, 5.0%, 8.0%, and 12.6% at C/T ratio of 0, 0.25, 0.5, 0.75, and 1, respectively. This trend was similar for the maximum consolidation size, with sizes of 0, 10, 20, and 30 mm having a recurrence risk of 2.6%, 6.0%, 13.4%, and 27.2%, respectively. Patients who underwent wedge resection had an approximately two-fold higher risk of cancer recurrence than those with segmentectomy at the same C/T ratio (7.2% vs. 3.8% at 0.5) and consolidation tumor size (9.0% vs. 4.3% at 10 mm), similar to those with insufficient resection margin (6.7% and 9.0% at 0.5 and 10 mm).

Conclusion: Risks of cancer recurrence after sublobar resection were consistently increased according to the increase of C/T ratio and consolidation tumor size in stage IA adenocarcinoma. Segmentectomy is recommended to obtain sufficient resection margin in patients with C/T ratio > 0.5 or consolidation tumor size > 10mm.

Image 1.
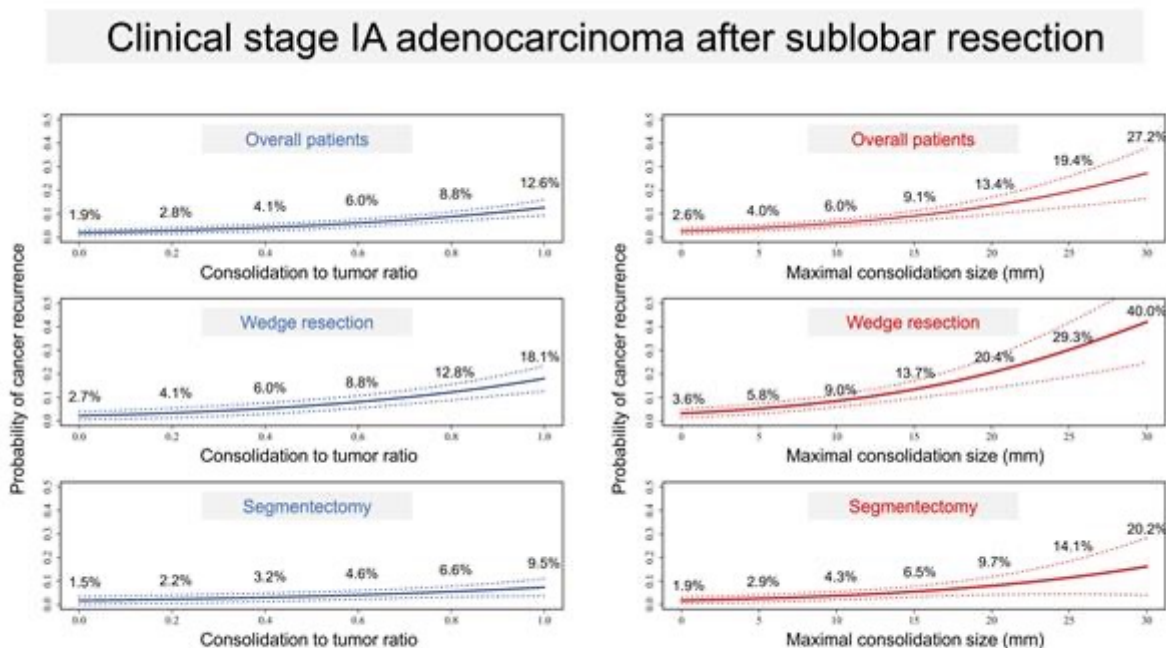
Image 2.
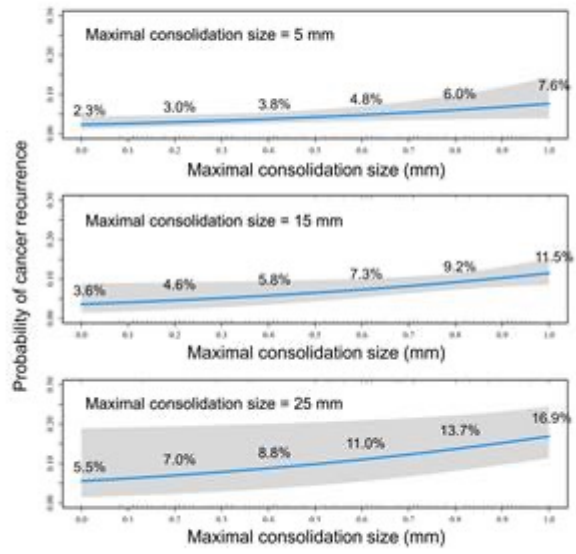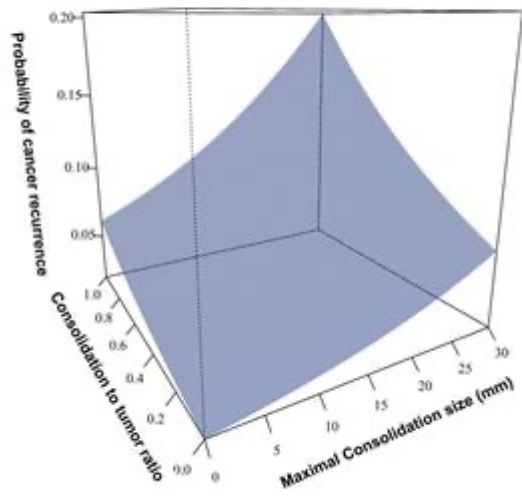
PP02.15:
Long-Term Results of Transbronchial ICG Administration in Limited Surgery for Early Stage Lung Cancer

Professor Yasuo Sekine[1], MD Hidehisa Hoshino, MD Eitetsu Koh, MD Takahiro Ochi
[1]Tokyo Women's Medical University Yachiyo Medical Center, Yachiyo, Japan

Background: Although margin preservation is important in peripheral small nonpalpable lung cancer, imaging analysis and surgical techniques based on this method are not widely used. Many centers use intravenous ICG to determine the extent of resection in segmentectomies. On the other hand, we have long practiced the bronchial infusion technique. In this presentation, we show the uniqueness and usefulness of the transbronchial infusion method.

Methods: A total of 55 patients (39 patients underwent aggressive segmentectomy and 16 patients underwent aggressive partial pulmonary resection) for primary lung cancer between September 2014 and September 2021. Indication for segmentectomy was a peripheral small lung cancer cT1a,bN0M0 with consolidation 2 cm or less, and indication for partial resection was a pure GGO or nodule with consolidation 1 cm or less and presenting within the outer 1/3 of the lung. The optimal resection area was defined that the margin distance should be 2 cm or more than the tumor diameter. The resection area was determined by CT simulation (VINCENT by Fujifilm Corp.) in advance. Then, transbronchial ICG was injected into the same area under general anesthesia, and the surgery was performed using a near-infrared camera. In some cases, ICG was injected intravenously into the segmental area and transbronchial ICG was injected into the subsegmental area or less.

Results: Mean age: 69.7±10.5, male: 28, female: 27, histology: AAH 1, Ad 37, AdSq 1, AIS 9, Carcinoid 1, MIA 3, Sarcomatoid 1, SCC 2, tumor diameter: 15.9±4.4 mm, consolidation: 6.0±5.6 mm, CTR 38.9±36.0%, tumor depth: 5.0±6.7mm, tumor to margin: simulated 17.8±9.9mm, actual measured 19.4±9.4mm (p=0.180.), pT: Tis 16, 1mi 6, 1a 22, 1b 10, 1c 1. Local recurrence: 2 cases for segmental resection, 0 cases for partial resection Local recurrence: 2 cases by segmental resection, 0 cases by partial resection, distant metastasis: 1 case by segmental resection. Long-term survival: 1 death (Sarcomatoid) from segmental resection. 3-year DFS: 94.3% for segmental resection, 100% for partial resection.

Conclusion: Aggressive limited surgery using transbronchial ICG infusion with a sufficient margin based on preoperative simulation may have the potential to improve recurrence-free survival. Its usefulness is particularly high for partial lung resection.
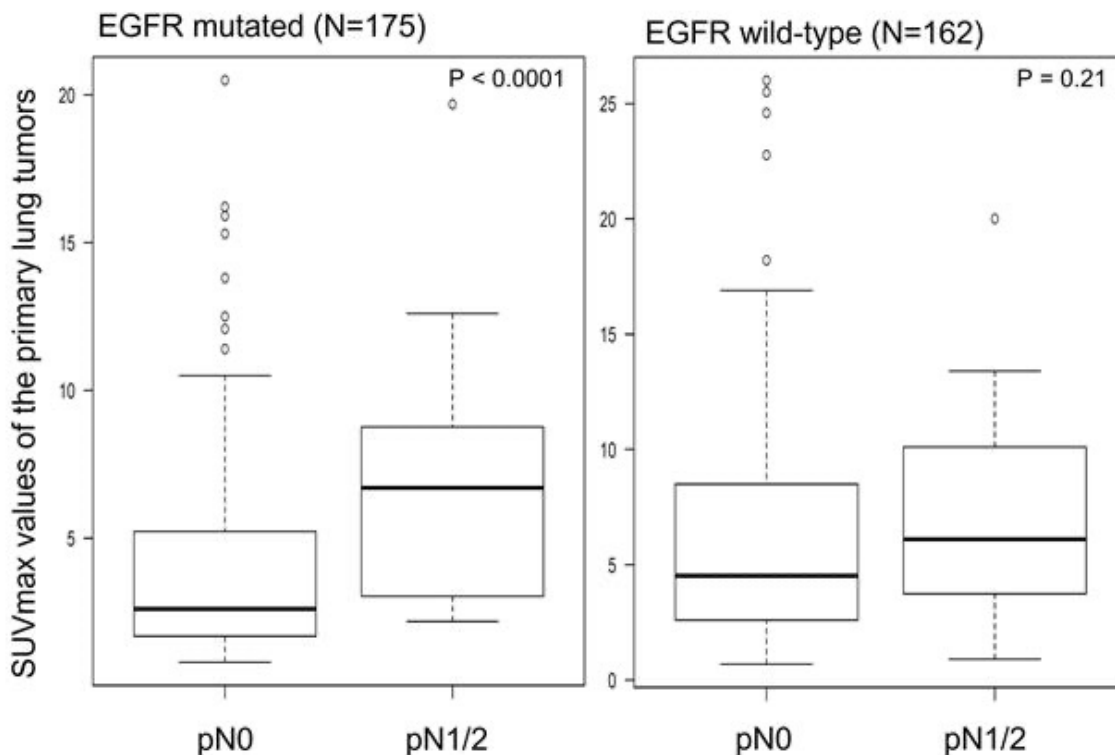
Figure 1. Correlation between pN status (pN0 vs. pN1/2) and SUVmax values of the primary lung tumors in EGFR mutated and EGFR wild-type subgroups.

PP02.16:
Correlation of SUVmax of Primary Lung Tumor and Occult Lymph Node Metastases in Clinical Stage I Lung Adenocarcinoma

Dr. Kenichi Suda[1], Dr. Shota Fukuda[1], Dr. Shuta Ohara[1], Dr. Akira Hamada[1], Dr. Masato Chiba[1], Dr. Masaki Shimoji[1], Dr. Toshiki Takemoto[1], Dr. Junichi Soh[1], Dr. Yasuhiro Tsutani[1], Tetsuya Mitsudomi[1]
[1]*Kindai University Faculty Of Medicine, Osaka-sayama, Japan*

Background: Prediction of lymph node (LN) metastases is sometimes difficult during preoperative examinations for NSCLC patients. Higher SUVmax of a primary lung tumor may suggest higher malignant potential of the disease. In this study, we explored correlation between SUVmax of the primary tumor and pathological nodal status in clinical stage I lung adenocarcinomas.

Methods: We retrospectively analyzed 337 patients with clinical stage I lung adenocarcinoma who underwent lobectomy plus mediastinal LN dissection between February 2008 through October 2021. Clinical factors (sex, smoking, total/consolidation tumor sizes, SUVmax of primary tumor, CEA, and EGFR mutation status) were extracted. Mann-Whitney U test and logistic regression analysis were used to compare SUVmax between pN0 and pN1/2 groups in univariate and in multivariate analyses, respectively.

Results: Occult LN metastases (pathologic N1/2) were found in 48 patients (14%). In univariate analysis of the entire cohort, SUVmax was significantly higher in patients with pN1/2 disease (median:6.4 vs. 3.2, p=0.0003). However, SUVmax was not an independent predictor for pN1/2 disease in multivariate analysis (p=0.42). In EGFR wild-type subgroup (N=162), we observed no significant difference in SUVmax between pN0 vs. pN1/2 patients in univariate analysis (4.5 vs. 6.1, p=0.21, Figure 1 right). In EGFR mutated subgroup (N=175), SUVmax was significantly higher (6.7 vs. 2.6) in patients with pN1/2 disease in univariate (p<0.0001, Figure 1 left) and in multivariate (p=0.020) analyses. Among pN0 patients, we observed that high SUVmax (>4.0) was significantly associated with EGFR wild-type (p=0.0001) and high peripheral WBC counts (median: 6,180 vs. 5,660, p=0.016), suggesting that high SUVmax in these pN0 tumors may be due to inflammation (but not high malignant potential).

Conclusion: SUVmax of the primary lung tumor was significantly higher in patients with pN1/2 diseases in clinical stage I lung adenocarcinoma patients, especially in those with EGFR mutation.

Image 1.
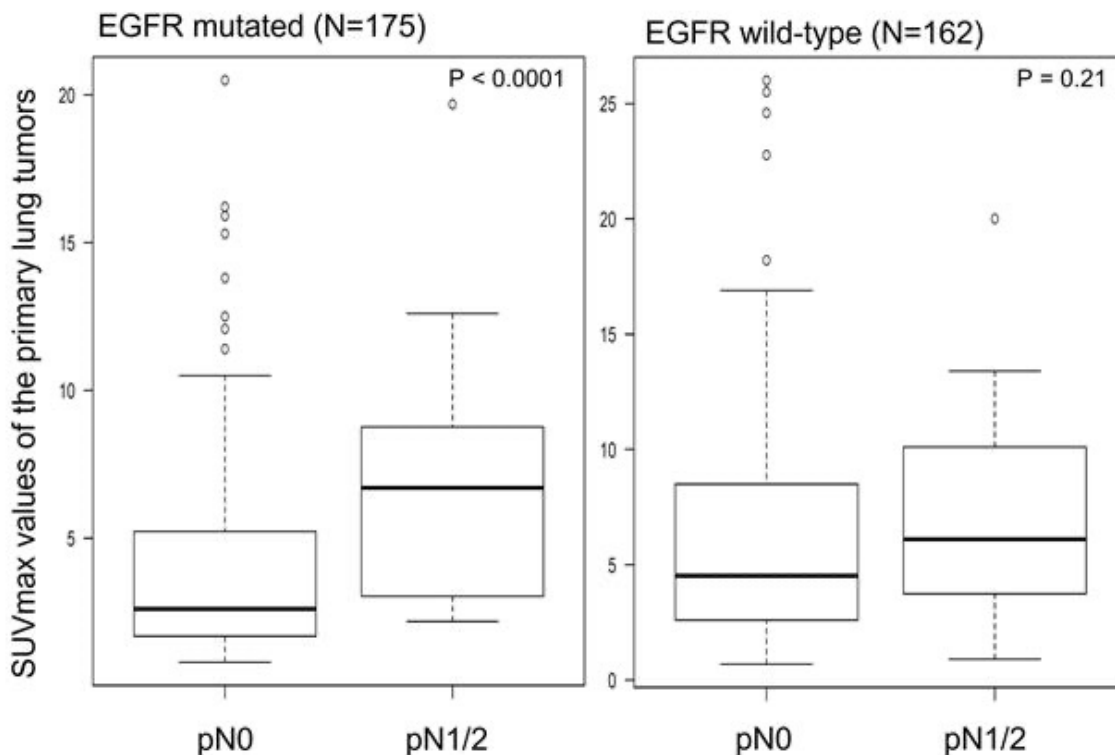
Figure 1. Correlation between pN status (pN0 vs. pN1/2) and SUVmax values of the primary lung tumors in EGFR mutated and EGFR wild-type subgroups.

PP02.17:
Challenges of the Eighth Edition of the American Joint Committee on Cancer Staging System for Pathologists Focusing on Early-Stage Lung Adenocarcinoma

Prof. Shiu-feng Huang[1], Dr. Yu-Ting Wang[2], Dr. Il-Chi Chang[1], Professor Chih-Yi Chen[3], Professor Jiun-Yi Hsia[3]
[1]Institute of Molecular and Genomic Medicine, National Health Research Institutes, Miaoli, Taiwan, [2]Department of Anatomical Pathology, Chung Shan Medical University Hospital, Taichung, Taiwan, [3]Department of Thoracic Surgery, Chung Shan Medical University Hospital, TaiChung, Taiwan

Background: In 2017, the American Joint Committee on Cancer (AJCC) published the 8th edition of their Cancer Staging Manual (hereafter referred to as the 8th AJCC staging system) for non-small-cell lung cancer (NSCLC). The 8th AJCC staging system adopts new criteria for tumor size, and for determining pTis, pT1a(mi), and pT1a. It incorporates the 2015 WHO classification of lung tumors, including the AIS and MIA concepts. The latter is based on the size of stromal invasion. It is quite challenging for lung pathologists.

Methods: All patients who had undergone surgical resection for pulmonary adenocarcinoma (ADC) at Chung Shan Medical University Hospital between January 2014 and April 2018 were reviewed, and restaged according to the 8th AJCC staging system. The clinical characteristics and survival of patients with tumor stage 0 (pTis), I or II were analyzed.

Results: In total, 376 patients were included. A gross examination revealed that 95.2%, 100%, and 77.5% of patients with pTis, pT1a(mi), and pT1a tumors, respectively, had tumor sizes measuring $\leq$1.0 cm. Moreover, all pTis, pT1a(mi), and pT1a tumors exhibited lepidic, acinar, or papillary patterns histologically. None of the pTis, pT1a(mi), or pT1a tumors recurred during the follow-up period, but pT1b, pT1c, pT2a, and pT2b tumors all had a few tumor recurrences (p<0.0001).

Conclusions: This study demonstrated excellent survival for lung ADC patients with pTis, pT1a(mi), and pT1a tumors. Therefore, staging lung ADC with tumors of $\leq$1 cm as pTis, pT1a(mi), or pT1a may not be essential when the tumors exhibit only lepidic, acinar, or papillary histological patterns.

PP02.18:
Effects of Insurance Type and Distance from the Cancer Center on Outcomes after Robotic-Assisted Pulmonary Lobectomy

Ms. Allison Dumitriu Carcoana[2], Mr. William Doyle[2], Mr. Jose Malavet[2], Ms. Jenna Marek[2], Mr. William West III[2], Ms. Carla Moodie[1], Mr. Joseph Garrett[1], Ms. Jenna Tew[1], Dr. Jobelle Baldonado[1,2], Dr. Jacques Fontaine[1,2], Ms. Kristie Labib[1,2]
[1]Moffitt Cancer Center, Tampa, United States, [2]University of South Florida Health Morsani College of Medicine, Tampa, United States

Background: Patients' insurance type and the distance between their residence and the healthcare provider have been individually correlated with perioperative outcomes, but their combined effects are not well-documented.

Methods: We retrospectively analyzed 725 consecutive patients who underwent RAPL from September 2010 to March 2022 by one surgeon. Patients were divided into six groups based on public, private, or combination insurance and on distance of primary residence ZIP code less than or greater than 160 kilometers from the cancer center. Demographics and perioperative complications and outcomes were analyzed by one-way analysis of variance (ANOVA), Kruskal-Wallis test, or Chi-square analysis. Statistical significance was set at $p \leq 0.05$.

Results: Statistically significant variables are presented in Table 1. There were no significant differences in gender, tumor size, Charlson-Deyo comorbidity index, pulmonary vein bleeding, intraoperative injury (phrenic nerve, laryngeal nerve, bronchus, or diaphragm), overall number of postoperative complications, cerebrovascular accident, myocardial infarction, shock/multisystem organ failure, cardiopulmonary arrest, chyle leak, effusion or emphysema, pneumothorax after chest tube removal, air leak >5 days, hypoxia requiring home oxygen, aspiration, pneumonia, respiratory failure, or in-hospital or 30-day mortality.

Conclusions: Patients with both public insurance and a commute greater than 160 kilometers had the most intraoperative, perioperative, and postoperative complications.

Table 1.

Table 1. Statistically significant differences in patient characteristics, intraoperative complications, perioperative outcomes, and postoperative complications.

Variables	Private <160 km (n = 149)	Public <160 km (n = 112)	Combined <160 km (n = 266)	Private >160 km (n = 53)	Public >160 km (n = 39)	Combined >160 km (n = 106)	p-value
Age* (years)	60.9 ± 9.8	68.9 ± 10	72.9 ± 6.9	58.9 ± 9.9	68.7 ± 9.5	72.8 ± 5.6	<0.001
BMI* (kg/m^2)	28.9 ± 6.7	28 ± 5.3	27.9 ± 5.9	28 ± 5.7	26.1 ± 4.4	26.8 ± 4.9	<0.05
FEV1%*	85.9 ± 16.7	86.2 ± 19.4	92 ± 19.7	89.9 ± 19.9	83.5 ± 21	88.3 ± 21.8	<0.05
Intraoperative Complications							
PA bleeding	3 (2.0%)	2 (1.8%)	6 (6.2%)	0 (0.0%)	4 (10.3%)	2 (1.9%)	<0.05
Perioperative Factors							
EBL** (mL)	150 [75, 125]	150 [100, 300]	100 [50, 200]	100 [50, 250]	200 [100, 375]	100 [50, 250]	<0.001
Skin-to-skin time** (min)	185 [153, 211]	173 [148, 211]	168 [140, 202]	187 [149, 243]	203 [156, 271]	175 [140, 219]	<0.001
Conversion to thoracotomy	8 (5.4%)	9 (8.0%)	8 (3.0%)	5 (9.4%)	7 (18.0%)	3 (2.8%)	<0.05
CT duration** (days)	3 [2, 5]	4 [3, 6]	4 [2, 6]	4 [2, 6]	5 [3, 8]	4 [3, 6]	<0.001
LOS** (days)	4 [3, 6]	5 [3, 7]	4 [3, 6]	4 [3, 8]	5 [4, 8]	5 [3, 7]	<0.001
Postoperative Complications							
New-onset A-Fib***	14 (9.4%)	7 (6.3%)	33 (12.4%)	2 (3.8%)	10 (25.6%)	14 (13.2%)	<0.05
Mucous plug	7 (4.7%)	7 (6.3%)	5 (1.9%)	1 (1.9%)	4 (10.3%)	10 (9.4%)	<0.05

*Mean ± SEM; SEM = standard error of the mean; **Median [Q1, Q3]; Q1, Q3 = first quartile, third quartile; BMI = body mass index; FEV1% = forced expiratory volume in the 1 second as percent of predicted; PA = pulmonary artery; EBL = estimated blood loss; CT = chest tube; LOS = hospital length of stay; A-fib = atrial fibrillation; ***Atrial fibrillation that was not present pre-operatively

PP02.19:
Impact of Preoperative Cardiovascular Comorbidities on Perioperative Outcomes after Robotic-Assisted Pulmonary Lobectomy

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Background: Current literature asserts that cardiovascular diseases are the most prevalent comorbidities observed among patients with lung cancer. We sought to determine effects of cardiovascular comorbidities on perioperative outcomes after robotic-assisted pulmonary lobectomy (RAPL).

Methods: We retrospectively analyzed 719 consecutive patients who underwent RAPL between September 2010 and March 2022 by one surgeon at one institution. Patients were classified into two groups based on presence (Cardiac group, n=275) or absence (Non-cardiac group, n=444) of preoperative cardiac comorbidities. Demographics, smoking history, Charlson-Deyo comorbidity index score, intraoperative and postoperative complications, estimated blood loss (EBL), chest tube duration (CT), hospital length of stay (LOS), and 30-day mortality were analyzed. Variables were compared utilizing Student's t-test, Wilcoxon rank-sum test, and Chi-square or Fisher's exact test, with significance at p≤0.05.

Results: Patients with cardiovascular comorbidities were older (p<0.0001), disproportionately male (p<0.0002), and had longer pack-year histories (p=0.0273). Cardiac patients had greater EBL (p=0.0001), higher incidence of postoperative complications (p=0.0312), longer CT durations (p=0.0402), and prolonged hospital LOS (p=0.0016) compared to Non-Cardiac patients (Table 1).

Conclusion: Patients with cardiac comorbidities demonstrate poorer perioperative outcomes following RAPL. Better understanding of effects of cardiovascular comorbidities in RAPL patients is required to help improve treatment strategies and patient outcomes.

Table 1.

TABLE 1: COMPARATIVE ANALYSIS					
Total # of Cardiac Comorbidities	Number per Patient	n	% (All patients)	% (Cardiac group)	
	One	195	27.1%	70.9%	
	Two	68	9.5%	24.7%	
	Three	10	1.4%	3.6%	
	Four	2	0.3%	0.7%	
	Total	275	38.2%	100%	
Variables			**Cardiac (n=275)**	**Non-Cardiac (n=444)**	**p-value**
Age**, years (range)			71.0 ± 1.1 (37-93)	66.8 ± 1.0 (24-88)	<0.0001*
Sex	Female		123 (44.7%)	275 (61.9%)	<0.0002*
	Male		152 (55.3%)	169 (38.1%)	
BMI**			27.6 ± 0.7	28.1 ± 0.6	0.3398
Smoking History	**Status**	Never/Former	231 (84.0%)	361 (81.3%)	0.3576
		Current	44 (16.0%)	83 (18.7%)	
	Pack-Years**		36.2 ± 3.8	27.2 ± 7.2	0.0273*
Charlson-Deyo Comorbidity Index**			1.08 ± 0.13	0.61 ± 0.10	<0.0001*
Presence of Intraoperative Complications			16 (5.8%)	26 (5.9%)	0.9832
EBL#, mL, Median (Q1, Q3)			150 (100, 250)	100 (50, 200)	0.0001*
Skin-to-Skin Duration#, min, Median (Q1, Q3)			173 (145, 209)	174 (145, 217)	0.7364
Presence of Postoperative Complications			120 (43.6%)	158 (35.6%)	0.0312*
Chest Tube Duration#, Median (Q1, Q3)			4 (3, 6)	3 (2, 6)	0.0402*
Hospital LOS#, days, Median (Q1, Q3)			5 (3, 7)	4 (3, 6)	0.0016*
In-Hospital Mortality			6 (2.2%)	5 (1.1%)	0.2623
30-Day Mortality			8 (2.9%)	5 (1.1%)	0.0812

*statistically significant (p≤0.05); **Student's t-test, mean ± SEM (standard error of mean); #Wilcoxon rank sums test; Q1, Q3 = 1st quartile & 3rd quartile values; CAD = coronary artery disease; MI = myocardial infarction; BMI = body mass index; EBL = estimated blood loss; LOS = length of stay.

PP02.20:
Postoperative Atrial Fibrillation Propensity after Robotic-Assisted Pulmonary Lobectomy by Number of Segments

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Background: Pulmonary lobectomy has been reported to carry a greater risk of postoperative atrial fibrillation (POAF) than segmentectomy. This study aimed to determine whether the number of segments resected during robotic-assisted pulmonary lobectomy (RAPL) correlates with rates of POAF.

Methods: We retrospectively analyzed 720 consecutive patients who underwent RAPL by one surgeon over 11.7 years. Patients were divided into two groups, with Group 1 having had less than 4 pulmonary segments resected (n=311), while Group 2 had 4 or more segments resected (n=409). We analyzed patients' demographics, perioperative complications, hospital length of stay, 30-day mortality, and tumor characteristics. Variables were compared using Fisher's Exact test, Chi-Square, Student's t-test, or Wilcoxon rank-sum test, with significance at p≤0.05.

Results: Only BMI (p=0.020), tumor size (p=0.001), and tumor stage (p=0.002) were found to significantly differ between groups. There was no significant difference in POAF rates (p=0.13) between groups based on number of pulmonary segments resected.

Conclusion: Although pulmonary lobectomy has been reported to have a greater likelihood of POAF compared to segmentectomy, this study found no significant difference in POAF rates when comparing patients based on number of pulmonary segments removed. This finding suggests that other risk factors for POAF warrant further investigation.

Table 1.

Comparison of variables by number of segments resected.

Variables	Less than 4 segments (n=311)	4 or more segments (n=409)	p-value
Body Mass Index (BMI), kg/m^2*	26.7 ± 0.3	27.95 ± 0.3	0.02
Tumor size, cm*	2.5 ± 0.1	3.0 ± 0.1	0.001
Tumor pathologic stage (pStage)			0.002
pStage 1	178 (27.4%)	188 (29.0%)	-
pStage 2	44 (6.8%)	93 (14.3%)	-
pStage 3	57 (8.8%)	89 (13.7%)	-
Estimated blood loss, mL*	150.0 + 30.0	125.0 ± 18.1	0.44
Skin-to-skin duration, min*	170.0 ± 3.6	176.0 ± 3.6	0.48
True postoperative atrial fibrillation	30 (4.2%)	50 (7.0%)	0.27
Chest tube duration, days*	4.0 ± 0.3	4.0 ± 0.3	0.33
Hospital length of stay, days*	4.0 ± 0.3	4.0 ± 0.5	0.63
In-hospital mortality	5 (0.7%)	7 (1.0%)	0.91

*Median ± standard error of mean.

PP02.21:
Impact of the COVID-19 Pandemic on Perioperative Outcomes after Robotic-Assisted Pulmonary Lobectomy

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Background: The COVID-19 pandemic presented patients with changes in healthcare access and practice. We sought to determine how these changes affected perioperative outcomes following robotic-assisted pulmonary lobectomy (RAPL).

Methods: We retrospectively analyzed 720 consecutive patients who underwent RAPL by one surgeon over 140 months. We defined March 1st, 2020, as the pandemic's start and grouped 639 patients as "PreCOVID-19" and 81 patients as "COVID-19-Era" based on surgical date. Demographics, preoperative comorbidities, peri-operative complications, tumor characteristics, nodal status, pathologic stage, chest tube duration, hospital length of stay, and mortality were compared utilizing Student's t-test, Wilcoxon rank-sum test, and Chi-square (or Fisher's exact) test, with significance at $p \leq 0.05$.

Results: COVID-19-Era patients had greater incidences of preoperative atrial fibrillation (p=0.0300), peripheral vascular disease (PVD; p=0.0023), and bleeding disorders (p=0.0333) compared to PreCOVID-19 patients, but COVID-19-Era patients had lower estimated blood loss (EBL; p<0.0001) and greater incidence of effusion or empyema (p=0.0001) postoperatively (Table 1).

Conclusions: COVID-19-Era patients having lower EBL and less new-onset POAF, despite greater incidences of preoperative atrial fibrillation, PVD, and bleeding disorders, demonstrates that RAPL is feasible and safe even during the pandemic. Risk factors for postoperative effusion should be determined to minimize risk of empyema in COVID-19-Era patients.

Table 1.

TABLE 1: COMPARATIVE ANALYSIS				
Variables		Pre-COVID-19 (n=639)	COVID-19-Era (n=81)	*p*-value
Age** (years), (range)		68.5 ± 0.4 (24-93)	67.9 ± 1.3 (29-88)	0.7030
Sex	*Female*	350 (54.8%)	48 (59.3%)	0.4443
	Male	289 (54.2%)	33 (40.7%)	
Preoperative:				
	FEV1%**	88.3 ± 0.8	95.0 ± 2.4	0.0036*
	Atrial Fibrillation	49 (7.7%)	12 (14.8%)	0.0300*
	Peripheral Vascular Disease	28 (4.4%)	11 (13.6%)	0.0023*
	Bleeding Disorder	12 (1.9%)	5 (6.2%)	0.0333*
Charlson-Deyo Comorbidity Index**		0.77 ± 0.04	0.96 ± 0.10	0.0788
Presence of Intraoperative Complications		39 (6.1%)	4 (4.9%)	1.0000
EBL# (mL), Median (Q1, Q3)		150 (75, 250)	50 (25, 110)	<0.0001*
Tumor Size** (cm)		3.2 ± 0.1	3.1 ± 0.2	0.6197
Nodal Status	*0*	397 (68.1%)	53 (68.8%)	0.9913
	1	77 (13.2%)	10 (13.0%)	
	2	109 (18.7%)	14 (18.2%)	
AJCC v8 Pathologic State	*I*	329 (56.0%)	39 (50.6%)	0.6637
	II	125 (21.3%)	19 (24.7%)	
	III	134 (22.8%)	19 (24.7%)	
Presence of Postoperative Complications		319 (50.0%)	48 (60.0%)	0.0919
	New-Onset Atrial Fibrillation	77 (12.1%)	3 (3.8%)	0.0258*
	Effusion or Empyema	13 (2.0%)	18 (22.5%)	<0.0001*
Total Postoperative Complications**		0.94 ± 0.05	1.21 ± 0.16	0.1088
Chest Tube Duration#, Median (Q1, Q3)		4 (2, 6)	3 (2, 6)	0.3105
Hospital LOS# (days), Median (Q1 ,Q3)		4 (3, 7)	4 (3, 6)	0.2350
In-Hospital Mortality		10 (1.6%)	1 (1.2%)	1.0000
30-Day Mortality		10 (1.6%)	3 (4.1%)	0.1412

**Student's t-test; #Wilcoxon rank sums test; *statistically significant (p≤0.05); mean ± SEM (standard error of mean); COVID-19 = coronavirus disease 2019; Q1-Q3 = 1st quartile & 3rd quartile values; AJCC v8 = American Joint Committee on Cancer, 8th edition; FEV = forced expiratory volume in 1 second as percent of predicted; EBL = estimated blood loss; LOS = length of stay

PP02.22:
Effect of Gender on Incidences of Peri-Operative Complications after Robotic-Assisted Video-Thoracoscopic Pulmonary Lobectomy

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Background: Identifying risk factors, such as gender, for certain perioperative complications is important for estimating both patients' total cost of surgery and their long-term health outcomes. This study aimed to investigate whether gender is associated with differences in perioperative outcomes after robotic-assisted pulmonary lobectomy (RAPL).

Methods: We retrospectively analyzed consecutive patients who underwent RAPL over a 140-month period by one surgeon. Occurrences of peri-operative complications were analyzed in 722 study patients, with 322 men and 400 women. Statistically significant ($p \leq 0.05$) differences between the two groups were determined by Chi-square or Fisher's exact analysis.

Results: Proportionately more men had preoperative diabetes mellites (p=0.002), pancreatitis (p=0.020), hyperlipidemia (p=0.010), peripheral vascular disease (p=0.012), atrial fibrillation (p<0.001), other arrhythmias (p<0.001), cardiovascular disease or myocardial infarction (p=0.002), obstructive sleep apnea (p<0.001), and COPD (p=0.009) than women; while proportionately more women had preoperative hypertension (p=0.019) than men. Post-operatively, men have a higher incidence of hypoxia than women (p=0.018).

Conclusions: Men have higher incidences of several pre-operative comorbidities, while women have higher incidence of preoperative hypertension than men. Yet, hypoxia is the only postoperative complication that more men experience than women. Thus, gender does not appear to be associated with increased postoperative complications after RAPL.

Table 1.

Pre-Operative Comorbidity Differences in Men and Women					
		MEN (N = 322)		WOMEN (N = 400)	
Pre-Operative Comorbidities	P-Value	Number of Patients	Percentage of Gender	Number of Patients	Percentage of Gender
Obstructive Sleep Apnea	<0.001	38	11.8%	19	4.8%
COPD	0.009	83	25.8%	71	17.8%
Hypertension	0.019	196	60.9%	210	52.5%
Hyperlipidemia	0.010	3	0.9%	0	0.0%
Periph. Vascular Disease	0.012	25	7.8%	14	3.5%
Atrial Fibrillation	<0.001	45	14.0%	16	4.0%
Other Arrhythmias	<0.001	77	23.9%	56	14.0%
CAD/Previous MI	0.002	68	21.1%	49	12.3%
Diabetes Mellites	0.002	68	21.1%	50	12.5%
Pancreatitis	0.020	12	3.7%	4	1.0%
Post-Operative Complication Differences in Men and Women					
		MEN (N = 322)		WOMEN (N = 400)	
Post-Operative Complications	P-Value	Number of Patients	Percentage of Gender	Number of Patients	Percentage of Gender
Hypoxia	0.018	10	3.1%	3	0.8%

PP02.23:
Effects of Perioperative Potassium Levels on Incidence of Postoperative Complications Following Robotic-Assisted Pulmonary Lobectomy

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Objective: Perioperative potassium abnormalities occur frequently in postsurgical patients. Serum potassium levels have been associated with postoperative outcomes that have increased morbidity and mortality. We sought to determine whether perioperative potassium levels affect perioperative outcomes following robotic-assisted pulmonary lobectomy (RAPL).

Methods: We retrospectively analyzed 722 consecutive patients who underwent RAPL by one surgeon over 140 months. Potassium levels were recorded pre-operatively, immediately following surgery (recovery room), on postoperative day #1, and at lowest and highest potassium levels during the hospital stay. Patients were grouped as having low serum potassium if <4.0 mmol/L or as having high serum potassium if >4.9 mmol/L. Relationships between perioperative potassium levels and postoperative complications were analyzed, with $p \leq 0.05$ as significant.

Results: Statistical analysis between patients who developed abnormal versus normal serum potassium revealed significant differences in postoperative atrial fibrillation, hypotension, hemothorax, pulmonary embolism hypoxia, and total numbers of postoperative complications (Table 1).

Conclusions: Following RAPL, high serum potassium levels was associated with increased postoperative atrial fibrillation, pulmonary embolism, hypotension, and hypoxia, total numbers of postoperative complications, and in-hospital and 30-day mortality. Surgeons should be aware of effects of abnormal potassium levels on postoperative outcomes and should correct potassium levels accordingly to ensure best outcomes.

Table 1: Significant postoperative complications and outcomes based on serum potassium levels.

Variables	PreOp Hypokalemia (n=199)	PreOp Normokalemia (n=498)	PreOp Hyperkalemia (n=21)	p-value
PostOp AFib	26 (13.0%)	89 (17.9%)	12 (57.1%)	0.055*
PostOp PE	0 (0%)	5 (1.0%)	0 (0%)	0.019
Variables	PACU PostOp Hypokalemia (n=298)	PACU PostOp Normokalemia (n=378)	PACU PostOp Hyperkalemia (n=45)	p-value
In-Hospital Mortality	4 (1.3%)	5 (1.3%)	3 (6.7%)	0.043
30-day Mortality	5 (1.7%)	6 (1.6%)	3 (6.7%)	0.047
Variables	POD1 PostOp Hypokalemia (n=199)	POD1 PostOp Normokalemia (n=498)	POD1 PostOp Hyperkalemia (n=21)	p-value
PostOp Hypotension	8 (4.0%)	13 (2.6%)	3 (14.3%)	0.018
PostOp Complications >/=1	87 (43.7%)	269 (54.0%)	13 (61.9%)	0.030
Variables	Hypokalemic Highest K Levels (n=42)	Normokalemic Highest K Levels (n=583)	Hyperkalemic Highest K Levels (n=97)	p-value
PostOp Hypotension	0 (0%)	16 (2.7%)	8 (8.2%)	0.015
PostOp Hypoxia	0 (0%)	7 (1.2%)	6 (6.2%)	0.009
PostOp Complications >/=1	14 (33.3%)	295 (50.6%)	62 (63.9%)	0.003
In-Hospital Mortality	1 (2.4%)	4 (0.6%)	7 (7.2%)	<0.001
30-Day Mortality	1 (2.4%)	6 (1.0%)	7 (7.2%)	0.006

*included by not quite significant; PACU = post-anesthesia care unit; PostOp = postoperative; POD1 = post-operative day 1; AFib = atrial fibrillation; PE = pulmonary embolism.

PP02.24:
Adenocarcinoma In Situ Manifesting as a Part Solid Nodule with High CTR: Radiologic and Pathologic Characteristics

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Background: Adenocarcinoma in situ (AIS) usually presents as a pure ground-glass nodule (GGN) or a part-solid nodule (PSN) with a low consolidation-to-tumor ratio (CTR) on chest computed tomography (CT) images. In patients with suspected AIS, sublobar resection including segmentectomy or wedge resection may be selected. AIS presenting as a PSN with a high CTR is rare and only a few cases have been reported until now.

Methods: We retrospectively reviewed medical records of histologically diagnosed AIS cases (n=3) and invasive adenocarcinoma cases (n=15), manifesting as a PSN with a high CTR of more than 0.5, who underwent surgery at our institution from January 2021 to March 2022.

Results: The AIS group included 2 male cases with a mean age of 62 years, while the invasive adenocarcinoma group included 8 male cases with a mean age of 69 years. The mean tumor diameter was both 2.8 cm (AIS group, range, 1.3-3.5 cm; invasive adenocarcinoma group, 0.9-5.1 cm). The mean CTR in AIS cases and invasive carcinoma cases was 0.59 (range, 0.51-0.64) and 0.73 (range, 0.54-0.85), respectively. The mean maximum standardized uptake value (SUVmax) on positron emission tomography/ computed tomography (PET/CT) was 1.37 (range, 1.1-1.8) and 2.76 (range, 0.7-6.3), respectively. Invasive adenocarcinoma tended to exhibit higher SUVmax than that of AIS, although there was no statistical significance (p=0.31). In the AIS cases, the histopathological examination showed organization and fibrosis in the central portion of the lesion with atypical cells scattering along alveolar septum. The organization was considered to reflect solid part on preoperative CT images.

Conclusion: It is sometimes challenging to distinguish AIS from invasive adenocarcinoma appearing as a PSN, especially with a high CTR. The present study indicates that the SUVmax on PET/CT could be one of the predictors of AIS for patients whose CT revealed a PSN with a high CTR. The accumulation of more cases leading to a more objective assessment is needed.

PP02.25:
Fibroblast Activation Protein Expression in the Alveolar Structures of Patients with Lung Adenocarcinomas

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Background: Lung adenocarcinomas that progress to atypical adenomatous hyperplasia (AAH) and adenocarcinoma in situ (AIS) become invasive. AAH is characterized by the localized proliferation of atypical cells lining the involved alveoli. AIS is characterized by lepidic growth and thickening of the alveolar septa. Some invasive adenocarcinomas have a lepidic component in the peripheral part of the tumors, making them morphologically similar to AIS. Fibroblast activation protein (FAP), a protease expressed on cell membranes, is observed in activated fibroblasts of tumor and fibrotic tissues. FAP expression in cancer-related fibroblasts is associated with disease progression, lymph node metastasis, and poor prognosis in various types of cancers including lung cancer. However, the transition of FAP expression in the progression of lung adenocarcinoma remains unclear.

Methods: Retrieval words, such as "Atypical adenomatous hyperplasia" or "AAH," were searched on our pathological database. A total of 14 lesions in 13 cases were identified. All patients underwent surgical resection for lung cancer at Osaka International Cancer Institute last 2018–2019. Seventeen AIS lesions and 20 invasive adenocarcinoma lesions, with lepidic components, were randomly sampled. A machine learning image analysis was conducted to objectively and quantitatively assess FAP expression in the immunohistochemically stained slides. The percentage of the FAP-positive area was computed.

Results: There were no significant differences among patients with AAH, AIS, and invasive adenocarcinoma in terms of age, sex, smoking status, side and lobe of the lesion, and body mass index. Patients with invasive adenocarcinomas were noted to have elevated preoperative serum carcinoembryonic antigen levels ($p=0.014$). The percentage of FAP-positive areas of patients with AAH, AIS, and invasive adenocarcinomas was 1.69±14%, 6.11±5.3%, and 11.8±7.1%, respectively ($p<0.0001$).

Conclusion: The percentage of the FAP-positive area in patients with lepidic growth tends to increase as the disease progresses. This finding suggests that FAP-positive cells contribute to tumor stroma formation in patients with lung adenocarcinomas.

PP02.26:
Selection of Surgery Focusing on Lymph Node Dissection: Robot-Assisted Surgery or Single Port Thoracoscopic Surgery?

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It is debatable which to choose between robot-assisted surgery (RATS) and single-hole video-assisted thoracoscopic surgery (U-VATS) for lung cancer. The Purpose of this study is to consider the selection of an approach method focusing on lymph node dissection.

We focused on the number of dissected lymph nodes and number of cases that had nodal upstaging of lymph nodes.

We investigated RATS 99 patients (R group) and U-VATS 10 patients (U group) from October 2018 to April 2022 who underwent lobectomy or segmentectomy and ND2a-1 or more for lung cancer. We divided the R group into 4 groups. R1 (1st-25th cases), R2 (26th-50th cases), R3 (51st-75th cases), R4 (76th to 99th cases) and compared with U group.No significant differences were seen between the R group and the U group among the number of dissected lymph nodes(12.6 ± 6.1,14.1 ± 9.1) and nodal upstaging(2/10cases,17/99cases).However, the numbers of dissected lymph node in the R3 and R4 group were significantly higher than those in the R1 and R 2 group (16.5 ± 9.4, 11.6 ± 8.1, $p <0.01$).Also the number of dissected lymph node in the R4 group was significantly higher than that in the U group (21 ± 10.4, 12.6 ± 6.1, $p = 0.02$).

The proficiency level of surgery can be the major reason for selecting the approach method.

 If it can be performed with the same accuracy, you should select U-VATS, which is cheaper and less invasive. In the recent situation, we have been selecting RATS because we think it can be more accurate for lymph node dissection.

We suggest selecting U-VATS for cases that do not require accurate dissection, on the other hand RATS for cases that do so.

PP02.28:
Analysis of PD-L1 Negative Subgroups in Real World Survey (CRIMSON) of Definitive Chemoradiotherapy in Locally Advanced NSCLC

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Background: We are reporting a real-world survey of definitive concurrent chemoradiotherapy (CCRT) for unresectable locally advanced non-small cell lung cancer (NSCLC). PD-L1 negative cases have been reported in clinical trials to not show prolongation of overall survival due to the addition of durvalumab, and treatment strategies for this population are unclear.

Methods: Of the 523 patients who started CCRT in clinical practice from August 1, 2018, to December 31, 2019, at 17 participating institutions, 95 patients with PD-L1 expression negative were evaluated retrospectively.

Results: The patient background includes elderly (over 75 years old)/non-elderly: 30/65 cases, male/female: 69/26 cases, cStage -IIIA / IIIB or more: 42 / 54 cases, PS 0/1: 41 / 54 cases. The median progression-free survival (PFS) was 17.7 months (95% CI: 11.5-24.5 months). In multivariate analysis of PFS, only performance status (PS) was the independent factor associated with PFS, and the with or without durvalumab did not make a significant difference between PFS and OS. (PS, HR: 0.38 (0.21-0.66), P <0.01, durvalumab, HR: 1.06 (0.56-2.16), P=0.86). In the PD-L1 negative subgroup, immune related adversed events (irAE) occurred in 32 (48%) of the 66 patients receiving durvalumab, and Grade 3 or higher in 8 (12%) cases. Late-onset (more than a year later from the initiation date of durvalumab) irAE was one case of pneumonitis (421 days after durvalumab administration) and one case of liver dysfunction (1149 days).

Conclusion: There is no difference in efficacy depending on the with or without of durvalumab in this subgroup, but irAE of Grade 3 or higher and delayed irAE have also appeared. Durvalumab consolidation therapy in this population may not enough to be effective.

PP02.29:
Dynamic Change of Immune Repertoire Profiling in Stage III Non-Small Cell Lung Cancer (NSCLC) Patients During Consolidation Treatment With Immunotherapy

Mr. Dulyathat Anantaya[1], Dr. Narumol Trachu[2], Dr. Nareenart Iemwimangsa[3], Dr. Putthapoom Lumjiaktase[4], Mr. View-Hune Teoh[5], Dr. Songporn Oranratnachai[6], Mrs. Khantong Khiewngam[7], Ms. Nanamon Monnamo[2], Dr. Pimtip Sanvarinda[8], Mrs. Pimpin Incharoen[4], Ms. Angkana Charoenyingwattana[3], Dr. Wasun Chantratita[3], Mrs. Thanyanan Reungwetwattana[1]

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Background: Durvalumab treatment improves survivals in patients with stage III NSCLC. Although, limited reports of both immunological molecular and clinical characteristics as prognostic factors have been found. Here we investigated immune repertoire profiling together with the association of TCR-beta (T cell receptor-beta; TCRb) clonal expansion with treatment response.

Methods: Stage III NSCLC patients whom receiving durvalumab from Ramathibodi Hospital during September 2018 to September 2021 were enrolled. Buffy coats were collected at baseline (before receiving durvalumab) and then every 3-4 months according to the assessment by CT scan until patients developed disease progression or severe adverse events. RNA extraction was performed from buffy coat then NGS was run by the Oncomine TCRb short read assay identifying CDR3 region TCRb polymorphism. Clonal diversity assessment and bioinformatic analysis were complete by using Ion Reporter software per manufacture's instruction (Thermo Fisher Scientific). Clinical status was gathered corresponding TCRb polymorphism changing each timepoint. Convergence TCR frequency and the Shannon diversity were explored in all pooled samples correlated to disease progression status using a Pearson correlation plot vs day in treatment. RStudio software version 2021 build 372 was used for downstream analysis. Significant P-value level was 0.05.

Results: Thirteen patients were included, 50 samples were collected and analyzed. Average day of durvalumab treatment was 284 days. Convergence TCR frequency were higher after receiving durvalumab (R = 0.36) and it was significantly higher in non-progression (non-PD) patients compared to progression (PD) patients (P = 0.011) (Figure1). Increasing of TCR convergence represented T cell specific clonals expansion response to durvalumab treatment in non-PD patients. Shannon diversities were significantly increased in non-PD patients compared to PD patients after durvalumab treatment (P = 0.0002).

Conclusion: Evaluating the TCR-beta repertoire in stage III NSCLC specimens is the potential effective tool for predicting response to durvalumab treatment. Larger cohort is needed.

Keywords: stage III non-small cell lung cancer, stage III NSCLC, TCR polymorphism, immune repertoire, immunotherapy

Image 1.
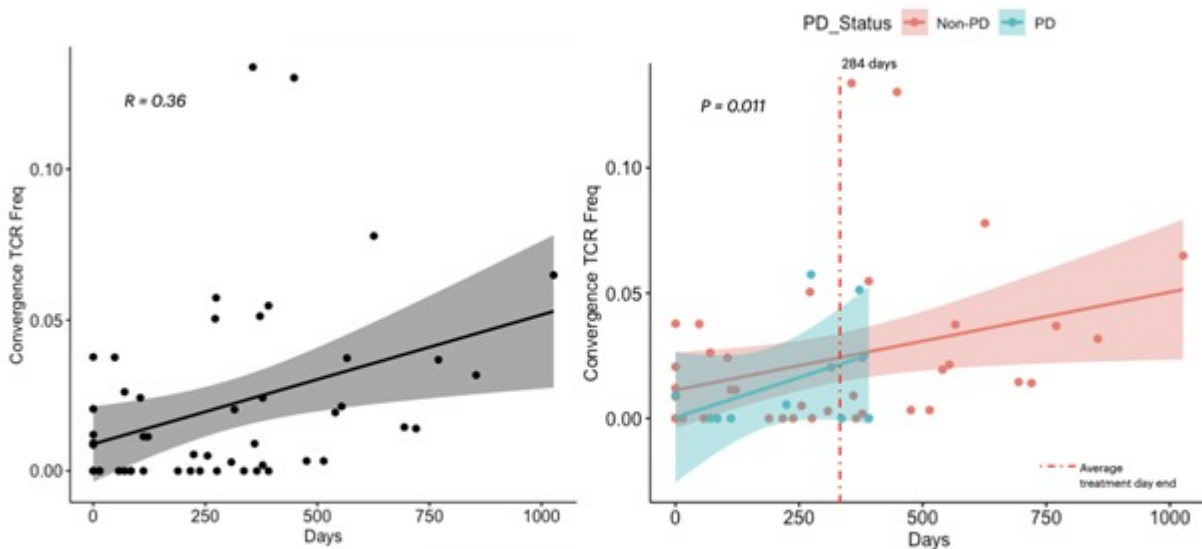
PP02.30:
Normalization of Tumor Marker Value Predicts Better Prognosis in Patients with Unresectable Stage III NSCLC

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Background: The relationship between prognosis and tumor marker (TM) value fluctuation during treatment has only been reported in patients with resectable or stage IV non-small cell lung cancer (NSCLC). This study focused on patients with stage III NSCLC who received chemoradiotherapy (CRT).

Methods: Medical records of patients with CRT for stage III NSCLC at the National Cancer Center Hospital between Jan. 2014 and Dec. 2020 were assessed. We compared TMs (CEA and CYFRA) before and after CRT and evaluated the relationship between TM trends and survival. We excluded patients whose response to CRT was PD or NE. Patients with elevated TM before CRT and experienced reduced levels of all TMs lower than the cutoff value after CRT were defined as the normalized (N) group. Patients whose TM remained higher than the cutoff were defined as the high (H) group.

Results: Overall, 266 patients underwent CRT during the study period. TM fluctuation could be evaluated in 178 patients and the response to CRT was PR or SD in 173 patients. Of these 173 patients, 107 (61.8%) were in the H group, and 66 (38.2%) were in the N group. The ORR, median PFS, and median OS in the H and N groups were 65.4% and 86.4%, 11.3 months and 20.3 months (HR 0.58, 95% CI 0.40-0.87), 53.5 months and not reached (HR 0.73, 95% CI 0.43-1.27), respectively. In the subgroups with/without durvalumab consolidation therapy, median PFS of N groups were 24.5 months and 16.5 months (HR 0.76, 95% CI 0.36-1.64) and those of H groups were 18.6 months and 9.9 months (HR 0.54, 95% CI 0.32-0.89). Multivariate analysis suggested normalized TM, durvalumab, and better response after CRT as statistically significant predictor of better PFS. In the N group, 24 patients experienced disease progression, where 16 patients (67%) had elevated TM levels with a median time of 38.5 days (0-945 days) before recurrence on imaging.

Conclusion: In unresectable stage III NSCLC, patients with normalized TM had better survival. This trend was also experienced irrespective of durvalumab administration, and the effect of durvalumab was more apparent in TM high group than in TM normalized group. However, ability of TM fluctuation was relatively limited because of low evaluability (66.8%) and high incidence of relapses (60%) even in patients whose TM normalized. A better predictive model, such as minimal residual disease (MRD), is warranted.

PP02.31:
MMP3, Fractalkine and MIF are Associated with Clinical Outcomes in Locally Advanced NSCLC Treated with Chemoradiotherapy and Durvalumab

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Background: Immune checkpoint inhibitors (ICIs) target the immune system, the relationship between inflammatory factors and the clinical outcome of ICIs for non small cell lung cancer (NSCLC) has been reported by several theses. Furthermore, chemoradiotherapy induces immunogenic cell death (ICD), and cause the release of damage-associated molecular pattern (DAMPs). DAMPs may enhance the efficacy of ICIs. However, little information has been available with regard to those relationship and kinetics of DAMP levels during the early phase of anticancer therapy in advanced cancer patients.

Methods: This study is a prospective observational study. The study enrolled the patients with locally advanced NSCLC at Kanagawa Cancer Center between August 2019 and July 2021. After enrollment, blood samples were collected from the patients before and after chemoradiotherapy. The patients treated with both chemoradiotherapy and durvalumab were analyzed. The levels of 77 soluble immune mediators (cytokines, chemokines, growth factors, etc.) in plasma were detected with Bio-Plex multi-plex assay. The concentration of high mobility group box-1(HMGB1) and Calreticulin in plasma was measured with ELISA kits.

Results: Sixteen patients were analyzed. Eleven and five patients were non-squamous cell carcinoma and squamous cell carcinoma. PD-L1 status (0%/1-49%/50%/unknown) was 6/2/7/1. 1-year progression free survivors were eleven, and non-1-year progression free survivors were 5. The baseline levels of Fractalkine and Macrophage migration inhibitory factor(MIF) of 1-year progression free survivors were significantly lower than those of non-1-year progression free survivors (p=0.033, 0.022). Furthermore, the increase after chemoradiotherapy of matrix metalloproteinase-3(MMP3), Fractalkine and MIF in 1-year progression free survivors were significantly higher than those of non-1-year progression free survivors (p=0.007, 0.007, 0.034).

Conclusion: Baseline level of Fractalkine and MIF and changes in the levels of MMP3, Fractalkine and MIF after chemoradiotherapy might be associated with clinical outcomes in patients with locally advanced NSCLC treated with chemoradiotherapy and durvalumab. The present results require confirmation in a large-scale prospective study.

PP02.32:
A Phase II Trial of Biweekly Carboplatin and Nab-Paclitaxel with Concurrent Radiotherapy for Patients with Locally Advanced Unresectable Stage III Non-Small Cell Lung Cancer: Long Follow up Survival Data

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Background: Concurrent chemoradiotherapy (CCRT) is the standard treatment for patients with locally advanced non-small cell lung cell cancer (LA-NSCLC). We previously reported the phase II study of biweekly carboplatin (AUC 4) and nab-paclitaxel (nab-PTX) (100 mg/m2) with RT. Here we report the long follow-up survival data of phase II study (UMIN000023802).

Methods: Patients with inoperable stage III NSCLC were treated with carboplatin (AUC 4) and nab-PTX 100 mg/m2 on days 1, 15, and 29. Thoracic radiotherapy was administered from day 1 to a total dose of 60 Gy in 30 fractions. Consolidation chemotherapy after CCRT was 2 cycles of carboplatin (AUC 6) on day 1 and nab-PTX 100 mg/m2 on days 1, 8, and 15.

Results: A total of 28 patients (median age 66 years, male 94%) were enrolled. A median follow-up time was 48 months. Median OS was 4.5 years (95% CI, 1.8–not reached). The rate of 3-year OS and 4-year OS were 57.1% and 53.5%. The rate of 3-year PFS and 4-year PFS were 32.1% and 28.5%, respectively. ICI treatment introduced as post-treatment in 10 of 23 patients (43%) after progressive disease of CRT.

Conclusions: Biweekly carboplatin and nab-PTX with concurrent RT therapy is considered to be reasonable regimen that could expect long-term survival for patients with LA-NSCLC.

PP02.33:
Peripheral Blood Markers Correlate with Pathological Complete Response and Prognosis in Resectable NSCLC Patients Treated with Neoadjuvant Chemoimmunotherapy

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Background: Neoadjuvant chemoimmunotherapy represents an important therapeutic modality for patients with resectable non-small cell lung cancer (NSCLC). Identification of reliable markers predictive of treatment efficacy facilitates patient stratification and optimizes treatment strategy. To date, no peripheral blood markers such as neutrophil-to-lymphocyte (NLR), platelet-to-lymphocyte (PLR) and lymphocyte-to-monocyte (LMR) have been explored to predict clinical outcomes of neoadjuvant chemoimmunotherapy.

Methods: We performed an analysis of retrospectively registered data of patients with resectable NSCLC treated with neoadjuvant chemoimmunotherapy from May 2019 to April 2022 in our institute. Peripheral blood samples of these patients at baseline and before surgery were collected. Data that may affect treatment efficacy were also collected, including age, gender, cumulative smoking exposure, pathological type, PD-L1 tumor proportion score, immune checkpoint inhibitor used, dosage of neoadjuvant therapy and duration from final therapy to surgery. The receiver operating characteristics (ROC) curve was plotted to determine the optimal cut-off values of baseline and preoperative NLR, PLR and LMR. The univariate and multivariate Log-Binomial regression analyses were performed to identify the independent predictors for pathological complete response (pCR) of neoadjuvant chemoimmunotherapy. Disease-free survival (DFS) and overall survival (OS) were calculated and compared using Kaplan-Meier method and log-rank test. The prognostic values of each variable were assessed with univariate and multivariate Cox proportional hazard regression analyses.

Results: A total of 106 patients were included. The median age was 59 years (range, 38-82 years) and 98 (92.4%) patients were men. 42 (39.6%) patients achieved pCR. Higher baseline NLR, higher preoperative NLR, higher preoperative PLR, and lower preoperative LMR were associated with lower incidence of pCR (p= 0.001, 0.011, 0.039, 0.004, respectivey). Multivariate analysis showed higher baseline NLR was an independent predictor for pCR (p= 0.03). After a median follow-up of 9 months (range, 2.5–38.3 months), 8 (7.5%) patients had tumor relapse or progression and 4 (3.8%) patients died. Higher baseline NLR, higher preoperative NLR, and lower preoperative LMR were associated with shorter DFS (p= 0.038, 0.009, 0.021, respectively) and shorter OS (p= 0.017, 0.042, 0.034, respectively). Multivariate analyses showed higher preoperative NLR and lower preoperative LMR were independent predictors for shorter DFS (p= 0.049, 0.027, respectively) and higher baseline NLR was independent predictor for shorter OS (p= 0.045).

Conclusion: In patients with resectable NSCLC treated with neoadjuvant chemoimmunotherapy, higher baseline NLR was associated with lower incidence of pCR and shorter OS and higher preoperative NLR and lower preoperative LMR were associated with shorter DFS.

PP02.34:
Feasibility of Hypo-Fractionated Radiotherapy (55 Gy/20 Fractions) in NACT Unresponsive and Co-Morbid Patients of NSCLC

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Introduction: Concurrent chemoradiation with 60 Gy/30 fractions is the most widely practised schedule in locally advanced NSCLC. However, many centers in the West practise hypo fractionation schedule of various types.

Methods: 25 patients of Stage IIB – IVA NSCLC who had either poor response to induction chemotherapy - stable disease (SD) or local (PD) or were comorbid enough not to tolerate concurrent chemoradiation received 55 Gy/20 fractions RT using VMAT technique from October 2018 – December 2020. Toxicity was studied using RTOG toxicity criteria.

Results: 25 patients (Male – 19, Female – 6) of age 49 – 74 years (mean – 60.76, median – 61 years) having NSCLC (Squamous – 13, Adenocarcinoma – 9, Adenosquamous – 3) of different stages (IIB – 3, IIIA – 9, IIIB – 7, IIIC – 2, IVA – 4) who either had poor response to NACT or were not candidates of CTRT (COPD – 13, PS2 – 16) received 55 Gy/20 fractions RT. After a median follow up of 11 months (range 3 – 13 months), 21 (84%) had a partial response (PR), while 2 (8%) patients each had SD and PD. Acute toxicities included Esophagitis (Grade 2 – 9 cases, Grade 3 – 1 case), Pneumonitis (Grade 2 – 3 cases) while 3 cases had Grade 3 Late Pneumonitis which was significantly associated with V5Gy of lung (p 0.04). Here were only 2 cases of grade 2 skin fibrosis. Median progression free survival (PFS) was 9 months with acceptable quality of life.

Conclusion: 55 Gy/20# schedule is a feasible in select group of patients.

PP02.35:
Locally Advanced Non-Small Cell Lung Carcinoma as a Non-Mucinous Adenocarcinoma in a 15-Year-Old Child: A Rare Presentation

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Background: Lung cancer is amongst the leading cause of cancer death, making up almost 25% of all cancer deaths. Adenocarcinoma accounts for approximately 38-40% of lung cancers; Tobacco use, increasing age, and environmental exposure remain strong risk factors. Mean age of adenocarcinoma is 71 years and this cancer is very rare before 20 years. We present an exceptional case of non-mucinous adenocarcinoma in 15-year-old child without any identifiable risk factors.

Methods (Case report): A previously healthy 15-year-old child presented to the chest OPD with a 3 weeks history of left sided chest pain, progressive dyspnoea, non-productive cough, 4kg weight loss in 3 weeks and loss of appetite. He had no history of previous ATT intake, smoking, tobacco chewing, biomass/factory exposure or family history of cancer. On clinical examination Trachea was shifted towards right side. There was decreased chest movements on left side and dull note present on percussion and decreased breath sounds in left infrascapular, axillary and infra-axillary region. CBC, LFT, RFT, ECG and 2Decho were within normal limits. Chest X ray shows Left sided pleural effusion with tracheal deviation and thoracocentesis further revealed exudative fluid with total protein 3.5g/dl, LDH 200, ADA 23, cell count 975 (N5%, L95%), glucose 40 mg/dl and negative GeneXpert. Repeated pleural fluid cytology were negative for malignant cells and showed lymphocytic predominance leading to presumption of tubercular effusion and ATT was started. A chest tube was placed for further fluid drainage. CECT thorax revealed heterogenous soft tissue density of size 8.8*7.7cm seen in left Para-hilar region with left moderate effusion. USG guided core needle biopsy was done. On HPE it showed features of NSCLC (Non-mucinous type Adenocarcinoma). He is currently started on chemotherapy (Cisplatin plus etoposide) with thoracic radiotherapy.

Results and discussion: In general, about 13% of all lung cancers are SCLC, and 84% are NSCLC. This case brings attention towards younger patients, probably with gene mutations, who develop lung cancer without any known risk factors. Secondly, Increased prevalence of TB can always lead to an early presumptive diagnosis.

Conclusion: We must screen every patient for any associated lung cancer in cases of moderate to massive pleural effusion. Further genetic research and clinical experience are needed in field of lung cancer.

Image 1.
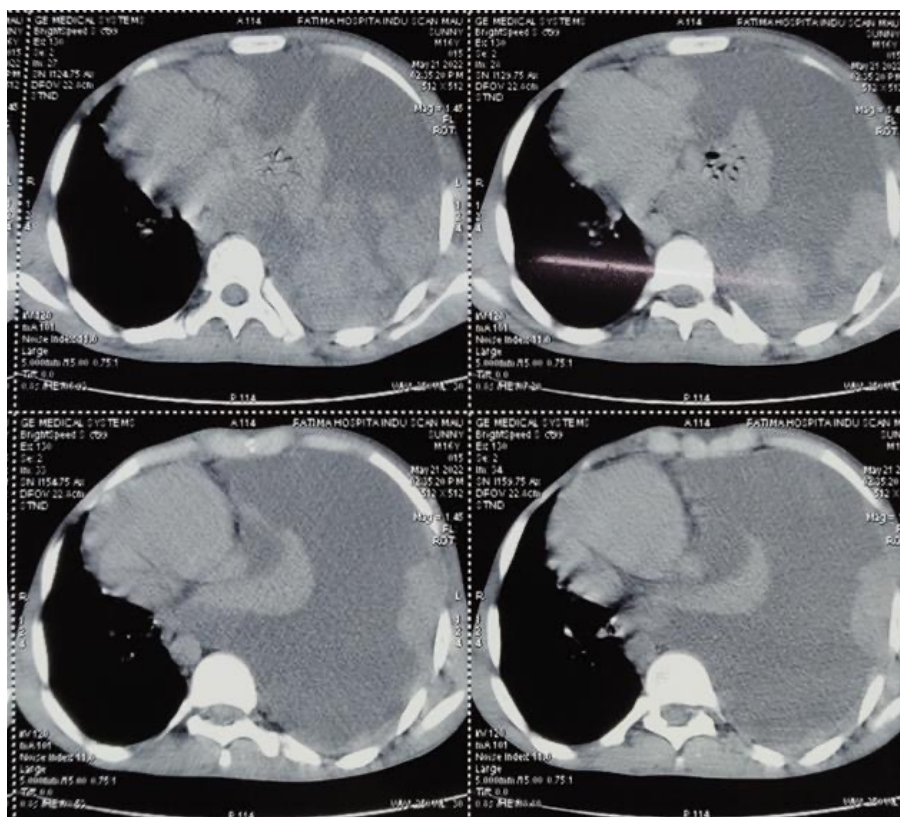
Image 2.

Table 1.
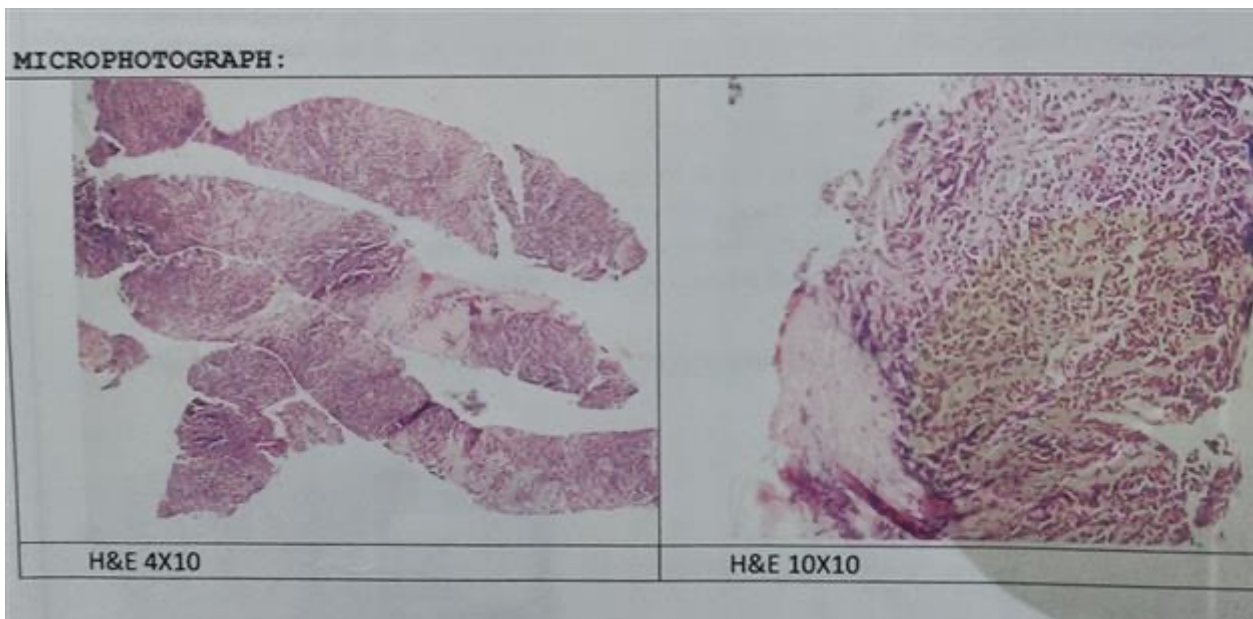
PP02.36:
Pulmonary Carcinosarcoma: A Report Case from Vietnam

Dr. Linh Le Tu[1], Prof Nhung Nguyen Van[1]
[1]National Lung Hospital, Cau giay, Vietnam

Abstract: Pulmonary carcinosarcoma (PCS) is a rare and highly malignant lung neoplasm. These tumors are often composed of epithelial and mesenchymal elements. The incidence of PCS in previous is from 0.1 to 0.3% of all lung malignancies [1], [2]. In general, these neoplasms occur a prevalent of males and smokers, with an average age of 60 years and the important thing is a poor prognosis. Herein, we report a 57-year-old male patient with PCS, who was admitted to our hospital with complaints of cough, chest pain, dyspnea, shortness of breath, and weight loss. The clinical and immunohistochemical (IHC) features of this case are discussed with a review of the literature.

Case study: A 57- year-old male presented to our hospital complaining of chest pain, dry cough, dyspnea, shortness of breath, and weight loss. The patient had a negative history of smoking in the past. The computed tomography (CT) revealed that the pleural effusion was all of the left side, mediastinal lymph node, and loss of the volume in the left lung. Thoracocentesis was performed and detected the malignant fluid but a low cell count was not enough for IHC. However, the histopathology study of the pleural biopsy was carcinosarcoma of the lung. The IHC studies revealed positive stains for sarcomatous components with vimentin, SMA, S100, and adenocarcinoma components with cytokeratin.

Discussion: According to the 2021 WHO classification of lung tumors, the immunohistochemistry of the carcinomatous component is that of the conventional tumors of the same type: TTF1 and napsin A in adenocarcinoma and p40 in squamous carcinoma. Heterologous sarcomatous components can be highlighted by desmin or myogenin for rhabdomyosarcoma or by S100 for chondrosarcoma [3]. In this case report, the patient is stage IV and cannot perform surgery. The choice of regimen involves multidisciplinary consultation meetings and chemotherapy with pemetrexed – cisplatin – bevacizumab is our choice. Pleural effusion reduced by 50% and clinical symptoms improved significantly after 1 month of treatment. The patient was maintained until the end of 6 cycles, assessed for partial response, and then continued for another 6 cycles with pemetrexed.

Conclusion: In summary, the poor prognosis of PSC is primarily due to its biological characteristics and high resistance to classical first-line chemotherapy. However, we have found a treatment regimen that responds well to PCS patients. These results enhance our understanding of PCS and highlight how cancer treatment strategies can be improved.

Image 1.

Fig1: Chest CT showed a left pleural effusion and after 6 cycles of chemotherapy

Image 2.
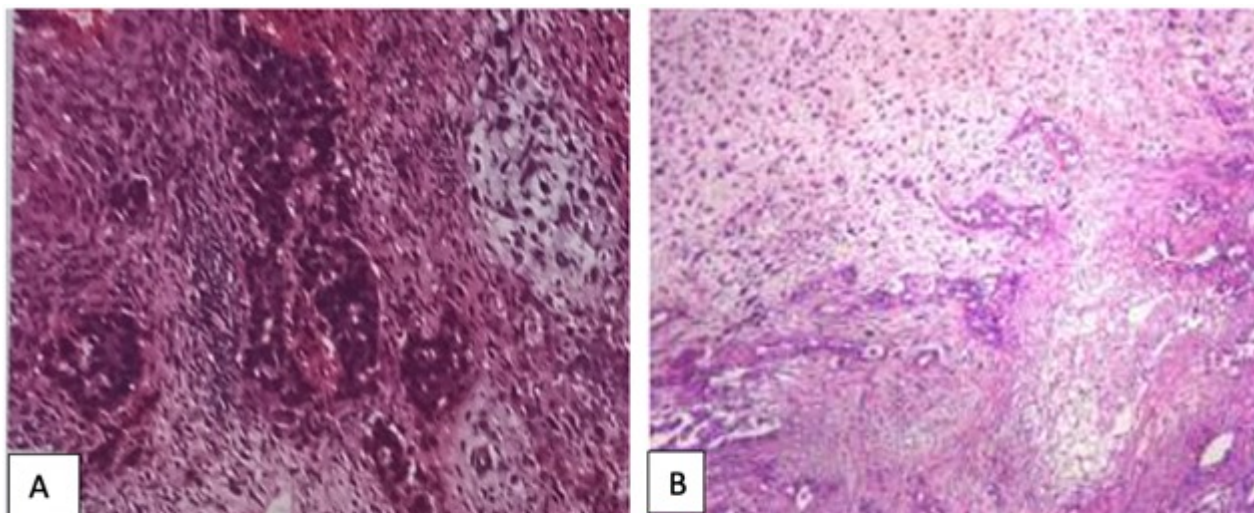
Fig2: A: Poorly differentiated adenocarcinoma alongside an immature matrix-producing cartilaginous focus.
B: Histology of the tumor demonstrating a mixture of well differential adenocarcinoma and heterologous elements of cartilage

PP02.37:
Affected Quality of Life and Burden of Lung Symptoms in Patients with Suspected Lung Cancer: A Prospective Longitudinal Study

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Background: Patients with lung cancer have a significant impact on health-related quality of life (HRQoL) related to the burden of lung symptoms. Measuring HRQoL and symptoms may early recognize arising disease burden and make decisions concerning appropriate treatment.

Objectives: To assess the HRQoL and symptoms in patients suspected of lung cancer since undergoing diagnostic evaluation until 3-month post-cancer treatment.

Methods: A longitudinal cohort study was performed on the newly suspected lung cancer patients. The HRQoL and symptoms were obtained using QLQ-C30 and QLQ-LC13 at the following time points: pre-diagnostic, confirmed-diagnostic, and 3-month post-treatment. Thresholds for clinical importance (TCIs) were used for indicating clinically significant problems or symptoms and repeated measurement of ANOVA was used to assess differences in scores over time.

Results: Of a total of 34 patients with a suspicion of lung cancer, 23 completed the 3-month follow-up. HRQoL measuring by QLQ-C30, the worst scores were detected on all domains except role functioning in a pre-diagnostic period. Most patients were affected by physical functioning (58.8%), symptoms of dyspnea (82.4%), fatigue (64.7%), pain (61.8%), financial difficulties (55.9%), pain (61.8%), and nausea and vomiting (44.1%) after TCIs were applied. Compared with 3-month post-treatment, physical symptoms of fatigue, dyspnea, sleep disturbances, and financial difficulties were worse than those during the pre-diagnostic period ($p < 0.05$). In QLQ-LC13 scoring, the physical symptoms of dyspnea, cough, and pain in the arm and shoulder were the most affected by clinical experiences during the pre-diagnostic period however, they had improved after 3-month treatment initiated ($p < 0.05$).

Conclusion: Measuring a longitudinal HRQoL and symptom score in patients with a suspicion of lung cancer could provide the data on an affected HRQoL and a high burden of lung symptoms before the diagnosis is confirmed and might lead to early management of those symptoms before knowledge of the diagnosis.

Image 1.
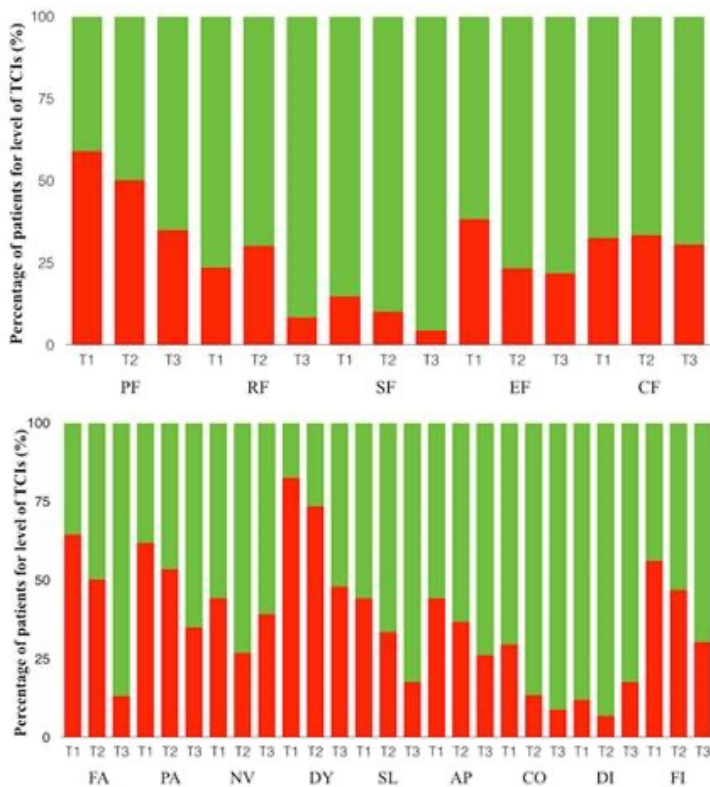
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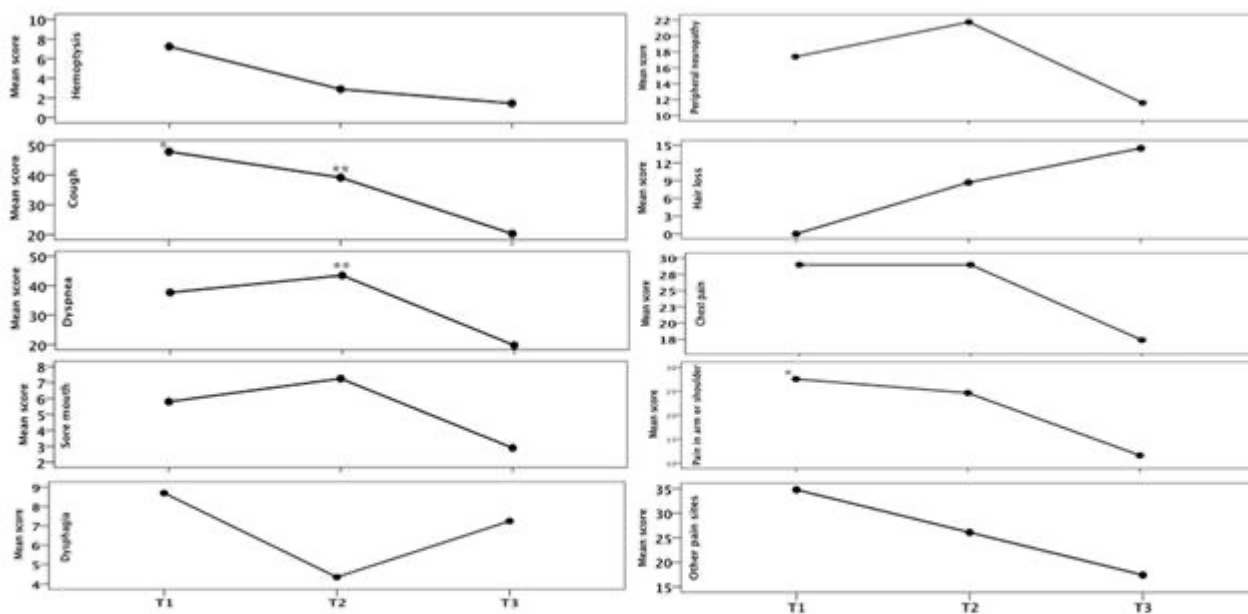
PP02.38:
The Great Survival Benefit from Ma Recipe Therapeutics for Patients with Advanced Lung Cancer: A Retrospective Study

Assoc. Prof. Jiangnan Feng[2], Prof. Dr. Zhenghua Ma[2], Prof. Dr. Hua Wu[3], Prof. Dr. Bixiang Zhang[3], Dr. Dengbing Zhu[2], Dr. Minghai Ma[2], Dr. Chengsheng Yi[2], Prof. Dr. Baoping Yu[4], Prof.Dr. Meiying Gao[3], Ms. Xia Liu[1], Ms. Xue Feng[1], Dr. Xiangfu Li[5], Dr. Yan Yu[1]
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Background: Ma recipe is a Chinese medicine prescription written by Chinese medicine practitioner in the outpatient clinic, in which composed of four kinds of herbs. Ma recipe therapeutics has long been used to treat pleural effusion and ascites. A phenomenon noted that the patients with malignant pleural effusion or malignant ascites reoccurrence were prevented once patients had been treated with Ma recipe therapeutics. On this basis, Ma recipe therapeutics was used as adjuvant or palliative treatment to treat patients with advanced solid tumor in our clinic since 2014.

Methods: Patients with advanced solid tumor were assigned to receive 50 grams of orally administered Ma recipe each day. All treatment-related medical records since 2014 were collected for retrospective analysis. The primary objective was to assess the change of symptoms, the change of tumor target lesion size and survival analysis.

Results: From January 2014 through to May 2022, 88 patients who are no longer eligible for curative treatment were included. A total of 33 patients were admitted with lung cancer among 88 patients. The median patient age was 60.5 years (ranging from 48 to 87 years). The median duration of exposure to MA recipe was 48 months in lung cancer group at the data cut-off point. The symptoms associated with advanced lung cancer such as cancer pain, fatigue, anorexia, pleural effusion was effectively controlled. The clinical effective rate was 100%. The ORR was 29% (PR+CR) and DCR (PR+CR+SD) was 100%. The median PFS-median OS and median DOR had not yet been reached. The 36-month and 48-month survival rates were both 96.5% in lung cancer group. One patient died due to disease progression. Four patients discontinued therapy and follow up information was lost. 28 of the 33 treated patients were still alive and continued to show signs of SD. All surviving patients treated returned to real life.

Conclusions: The Result show that Ma recipe therapeutics has revolutionized the survival of patients with advanced cancer. Ma recipe therapeutics has the potential to become a lifesaving approach for advanced lung cancer and solid tumors.

PP02.41:
Role of Preoperative Inhalation Therapy for Lung Cancer Patients with Chronic Obstructive Pulmonary Disease

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Background: In recent years, there have been increasing opportunities to perform surgery for lung cancer patients with chronic obstructive pulmonary disease (COPD), who have a higher incidence of postoperative complications than those without COPD. On the other hand, few reports regarding the incidence of postoperative complications following perioperative inhalation of a COPD therapeutic agent, such as long-acting muscarinic antagonist (LAMA) or long-acting β2 agonist (LABA), in cases treated with an inhaled corticosteroid (ICS). This study was conducted to investigate the relationship of respiratory function with postoperative complications in patients with COPD given preoperative inhalation.

Methods: When primary lung cancer was diagnosed or suspected [forced expiratory volume in one second (FEV1)/forced vital capacity (FVC) <70%], inhalation of a COPD therapeutic agent was started before surgery, after obtaining informed consent. The functional impact of perioperative inhalation on pulmonary function and postoperative course was evaluated. This study was registered with the University Hospital Medical Information Network Clinical Trial Registry as UMIN000025587 (2017/1/10).

Results: Respiratory function was evaluated before and after inhalation in 68 patients (59 males, 9 females, age 73 ± 5.6 years). Preoperative FEV1 was 2056±542 ml and FEV1/FVC was 63±5.2%, while the inhaled drug was LAMA in seven, LABA in two, LABA/LAMA in 53, ICS/LABA in five, and LABA/LAMA/ICS in one. The inhalation period was less than four weeks in 39 and four weeks or more in 29 cases, while the mean total amount of FEV1 improvement was 191±163 ml (LAMA: 44±122 ml, LABA: 300±170 ml, LABA/LAMA: 199±174 ml, ICS/LABA: 202±39 ml, LABA/LAMA/ICS: 250 ml). There was no significant difference related to inhalation period. The surgical procedure was lobectomy in 59, segmentectomy in five, wedge resection in two, and exploratory thoracotomy in two. All patients were diagnosed with lung cancer, with pathology findings showing adenocarcinoma in 49, squamous cell carcinoma in 13, and others in six, while pathological stage IA, IB, IIA, IIIA, IIIB, and IVA was noted in 41, 12, seven, four, two, and two, respectively. Pulmonary complications were observed in 14 cases. FEV1/FVC before inhalation was not different between patients with or without pulmonary complications, whereas that after inhalation was lower in patients with as compared to without pulmonary complications (61±8.3% vs. 68±6.7%, p=0.02; increase in FEV/FVC: -0.2±5.0% vs. 4.6±5.8%, p=0.01). Surgical procedures, pathology, and stage were not associated with pulmonary complications.

Conclusion: Post-inhalation FEV/FVC as a response to inhaled therapy may be a predictor of postoperative complications

PP02.42:
Clinical Significance of the TTR / RBP Ratio in Patients Undergoing Surgery for Lung Cancer

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Introduction: In recent years, it has been reported that nutritional assessment index and the presence of sarcopenia reflect perioperative outcomes and their prognosis, particularly in digestive surgery. Although the prognostic nutritional index (PNI) is widely used for nutritional assessment, rapid turnover protein has recently been used as a sensitive nutritional assessment protein. This study assesses the impact of these parameters on perioperative outcomes and long-term prognosis.

Methods: This retrospective study included 476 patients who underwent surgery for lung cancer. Representative rapid turnover proteins, retinol-binding protein (RBP) and transthyretin (TTR), were measured preoperatively, and the ratio was defined as the TTR/RBP ratio. The patients were divided according to cutoff values of the TTR/RBP ratio < 7.52, low TTR/RBP ratio group and $\geq$ 7.52, high TTR/RBP ratio group. Clinicopathologic features, including the preoperative state, surgical procedure, and postoperative morbidity and mortality, were compared between the groups.

Results Old age and low PNI correlated significantly with a low TTR/RBP ratio group. Logistic regression analysis demonstrated no relation between high and low TTR/RBP ratio status perioperative outcome. Multivariate analysis revealed that male sex (male : hazard ratio 3.74; 95% confidence interval 1.90–7.35, $p = 0.0001$), age (75<: hazard ratio 2.03; 95% confidence interval 1.22–3.40 $p = 0.0065$), FVC% (FVC<80: hazard ratio 3.17; 95% confidence interval 1.63–6.15, $p = 0.0006$), P-stage (2$\leqq$: hazard ratio 5.87; 95% confidence interval 3.54–9.74 $p < 0.001$) ,and the TTR/RBP ratio (7.53 > hazard ratio 2.03; 95% confidence interval 1.13–3.64, $p = 0.017$) were independently associated with postoperative survival.

Conclusions: A low TTR/RBP ratio was significantly associated with overall survival. The prognostic TTR/RBP ratio may be helpful and reliable as a preoperative assessment of nutritional status in patients with resected NSCLC. Our results may provide some important information for preoperative management.

PP02.43:
Impact of a Multidisciplinary Team Conference on Non-Small cell Lung Cancer Care: Time Barriers and Long-Term Outcomes

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Background: Multiple specialties of physicians are involved in each step and time taken to reach an investigation and management decision in non-small cell lung cancer patients (NSCLC) is potentially prolonged. Delayed timing for each step is effect on long-term outcomes. This study aims to evaluate the impact of a multidisciplinary team conference (MDT) on NSCLC care quality and long-term outcomes.

Methods: This is a retrospective cohort study of resectable NSCLC underwent pulmonary resection at Chiang Mai University hospital, Chiang Mai, Thailand between January 1, 2009, and December 31, 2021. All patients were divided into two groups: non-MDT group and MDT group. The cut point of time between group is March,1 2018 which was the date of MDT initiated. The primary outcome was overall survival (OS) between the two groups. The secondary outcomes were waiting time in each period of investigation and treatment included waiting time for CT-scan, bronchoscopy, pathologic report, and surgery date. Multilevel survival analysis was used to analyze the effect of MDT on the DFS and OS. Each waiting time in each period of investigation and treatment were compared.

Results: There were 856 patients included in this study: 573 in non-MDT and 275 in MDT groups. The proportion of stage I and stage II NSCLC underwent pulmonary resection was higher in MDT groups (72.88 % vs 59.69 %, p<0.001). In Multivariable analysis, patients in MDT groups were more likely to survive longer than those in non-MDT group (adjusted HR 0.2, 95%CI 0.12-0.33). The median waiting time for pathologic report and schedule time for surgery in MDT groups were significant shorter than those in non-MDT group, (7 days vs 13 days, p<0.001) and (15 days vs 25 days) respectively. The median waiting time for bronchoscope in MDT group and non-MDT group was not statistically different. (3 days vs 2.5 days, p=0.288).

Conclusion: Our results demonstrate that the MDT have a survival benefit in NSCLC care. Moreover, the MDT effect on the waiting time for each step of investigation and treatment. Further studies are warranted to support these results.

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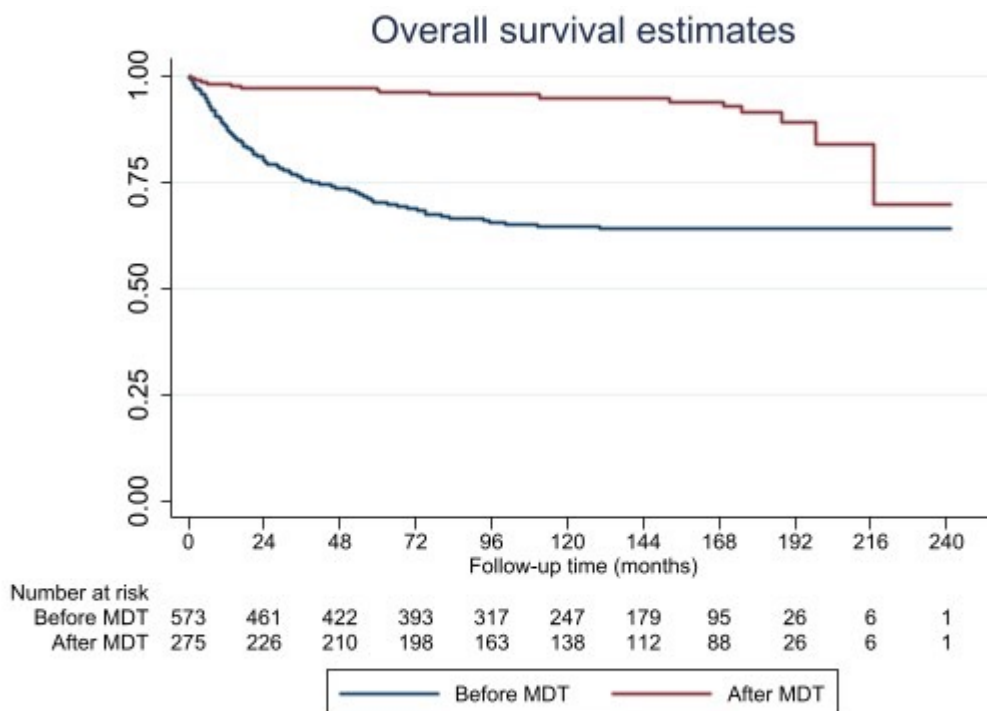
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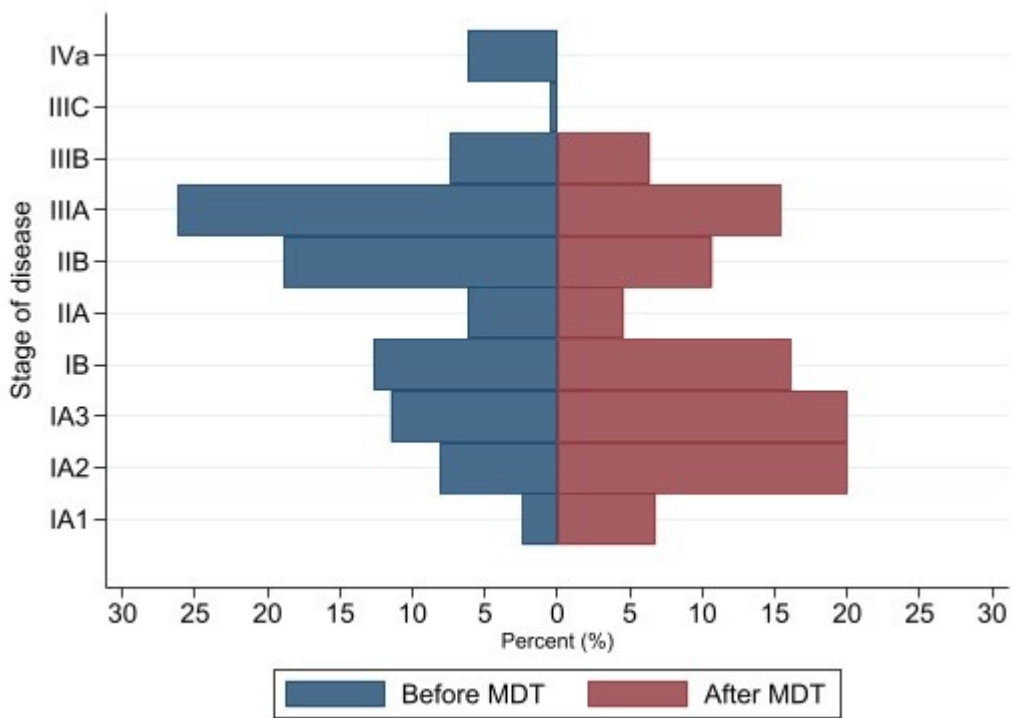
PP02.44:
Relationship Between Worsening Postoperative Dyspnea and Preoperative Respiratory Function

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Background: Radical surgery for lung cancer results in a decrease in lung volume and respiratory function. However, the amount of lung volume lost does not always correspond to the degree of postoperative dyspnea. It is often experienced in practice that dyspnea does not occur despite the loss of lung volume. We examined the relationship between the degree of dyspnea and preoperative respiratory function tests.

Methods: Of the patients who underwent lung cancer surgery at our department from January 2019 to December 2020, we studied 39 patients who were able to be followed postoperatively at our hospital. Patients were divided into two groups: those whose Medical Research Council (MRC) Dyspnea Score decreased (Group D) and those whose MRC Dyspnea Score remained stable (Group S) from 6 months to 1 year postoperatively. Preoperative %VC, %FVC, %FEV, FEV1%, %PEF, and %DLCO' were compared in the two groups.

Results: There were 22 male and 17 female patients with a median age of 73 years. Preoperative tumor localization was right upper lobe in 15 cases, right middle lobe in 2 cases, right lower lobe in 5 cases, left upper lobe in 13 cases, and left lower lobe in 4 cases. The surgical approach was Video-assisted thoracoscopic surgery in 27 cases, robot-assisted thoracoscopic surgery in 7 cases, and open thoracotomy in 5 cases. Lobectomy was used in 29 cases and segmental resection in 10 cases. Of Group D, MRC score decreased from 0 to 1 in 15 cases and from 1 to 2 in 5 cases. Group S had 18 cases with MRC score 0 and 2 cases with MRC 1. Comparing preoperative respiratory function between Group D and Group S, preoperative %PEF in Group D was $79.15 \pm 13.78\%$, which was significantly lower than that in Group S, $94.84 \pm 16.54\%$ ($p = 0.0045$). Other parameters such as %VC, %FVC, %FEV1, FEV1% and %DLCO' in Group D and Group S were $99.29 \pm 12.94\%$ vs. $105.39 \pm 12.175\%$ ($p=0.22$), $102.75 \pm 14.91\%$ vs. $110.40 \pm 14.93\%$ ($p=0.11$), $97.72 \pm 16.89\%$ vs. $100.54 \pm 16.20\%$ ($p=0.68$), $76.04 \pm 10.86\%$ vs. $73.82 \pm 9.12\%$ ($p=0.47$), $137.12 \pm 54.04\%$ vs. $116.22 \pm 30.00\%$ ($p=0.33$), with no significant differences.

Conclusion: Patients with lower MRC scores tend to have lower preoperative %PEF. Preoperative %PEF may be predictive of postoperative respiratory status.

PP02.45:
An Investigation on Inflammatory and Oncological Biomarkers in Lung Cancer Diagnosis: A Data-Driven Approach

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Background: Due to the lack of established non-invasive diagnostic biomarkers, a delay exists in the diagnostic trajectory for faster directed examination (e.g., tissue biopsy) of suspected lung cancer (LC) patients. The aim of this study was to explore the association between inflammatory and cancer-associated plasma proteins and to discover potential biomarkers for the early diagnosis of LC.

Methods: Patients referred for suspected LC and later diagnosed with primary LC (PLC), other cancer, and no cancer (NC) were included in this study. Before the clinical investigation of cancer, demographic information and plasma samples were collected, and diagnostic information of cancer was later retrieved from medical records. Relative quantification of 92 plasma proteins were carried out by proximity extension assay (PEA). In the cohort of 252 patients with available plasma samples, 173 (54% female) were diagnosed with PLC, 23 (43% female) were diagnosed with other cancer, and 56 (38% female) had NC. Patients with PLC were further grouped based on histology, of which 125 had adenocarcinoma (ADC), 32 had squamous cell carcinoma (SCC) and 16 had small-cell LC (SCLC). Patients in each group of ADC, SCC, and SCLC were further grouped into early (stage I, II, and IIIA) and advanced (stage IIIB and IV) stages. Patients' protein profiles with different histology and stage of LC were assessed by several machine-learning approaches considering the confounder-effect (age, gender, smoking, and pulmonary disease status).

Results: In the investigated patients cohort, the optimal linear combination of 4 proteins (TRAIL, CD8A, HO1, and CD83 with AUROC 0.70 and Youdin index 35.20) classify ADC, 3 proteins (MMP12, TRAIL, and VEGFA with AUROC 0.75 and Youdin index 40.20) classify SCC and 5 proteins (MMP12, CD8A, IL8, PGF and IL12 with AUROC 0.89 and Youdin index 69.60) classify SCLC against NC patients respectively. Also, a panel of 8 proteins (MMP12, GZMB, CCL23, GZMA, CD8A, CD83, CSF1, and TIE2) demonstrate a higher diagnostic ability for the early stage of LC (AUROC 0.74 and Youdin index 34.80), as well as for advanced stage of LC (AUROC 0.81 and Youdin index 54.00) also.

Conclusions: Several pre-treatment plasma proteins, particularly when used in combination, may be able to differentiate LC from NC patients and serve as potential pre-diagnostic biomarkers for identifying patients with ADC, SCC, and SCLC. Additionally, several proteins in combination may potentially be utilized for predicting the early stages of LC.

PP02.46:
Sublobar Resection Might Be Effective Option for Lung Cancer Patients on Dialysis

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Background: In recent years, advances in dialysis technology have improved prognosis, and lung cancer patients with hemodialysis (HD) are increasing due to the aging of the population. Surgery in HD patients is often associated with many risks, including delayed wound healing, easy infection, easy bleeding, and cardiovascular complications. Reports of dialysis-associated lung cancer are increasing, especially in the Asian country, but there are no reports that have examined the difficulties and prognosis of each procedure. The 5-year overall survival was 26 to 58% in the previously reported paper, and the overall natural survival of dialysis patients was about 60%.

Methods: From 2008 to 2018, among 1643 patients who underwent pulmonary resection for primary lung cancer in our institute. Fifteen lung cancer surgeries were performed on patients undergoing HD for chronic renal failure. Their clinicopathological characteristics and clinical information were reviewed retrospectively. We aimed to achieve dry weight the day before and from the day after surgery and set DW lower if necessary. Nafamostat mesylate is used for HD to reduce the risk of posterior bleeding.

Results: Among 15 patients, 14 cases of clinical-stage 0-I, 6 of which underwent sublobar resection. Six (40%) of these 15 patients suffered postoperative complications, defined as Clavien-Dindo classification grade $\geq$ 2. The number of 90-day mortality in the patients was 0, and the 5-year overall survival rate and recurrence-free survival rate of the patients were 80.0% and 66.7%, respectively. There was no significant difference in prognosis between lobectomy and sublobar resection.

Conclusions: In this study, the overall five-year survival rate was 80.0%, which was better than previously reported papers and the overall natural survival of dialysis patients. Surgical complications can be tolerated in patients with lung cancer complicated by dialysis if appropriate operable cases are selected, and strict perioperative management is performed. Sublobar resection might be a good option for selected lung cancer patients on HD.

PP02.47:
Two Cases of Sarcomatoid Mesothelioma from Mesothelioma In Situ

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Background: The attention and chance of diagnosis to mesothelioma in situ has been increasing, but the progression or prognosis are still unclear. It is becoming clear that there are variations in mesothelioma in situ clinically, pathologically or genetically. Some problems such as how to follow-up or choose treatment intervention can be difficult even for experts. It is necessary to clarify which factors correlates prognosis, which may lead to solve these problems.

Methods and results: We experienced two cases of sarcomatoid mesothelioma progressing from mesothelioma in situ. Both cases men in their 70's with occupational asbestos exposure and smoking habit. The first clinical sign were pleural effusion in both cases. Both cases had the diagnosis of mesothelioma in situ by pleural biopsy. Both patients select careful follow-up, but follow-up images showed tumor formation. Surprisingly, re-biopsy revealed progression to sarcomatoid mesothelioma, with intervals from the first biopsy were 25 and 9 months, respectively. Interestingly, both cases had same genomic abnormalities, which MTAP loss and CDKN2A homozygous deletion.

Conclusion: MTAP loss and/or CDKN2A homozygous deletion in MIS may be aggressive features. Treatment or careful follow-up are necessary for mesothelioma in situ, especially for this type of genetic abnormalities. Re-biopsy of invasive lesion after diagnosis of mesothelioma in situ is also desired.

Image 1.
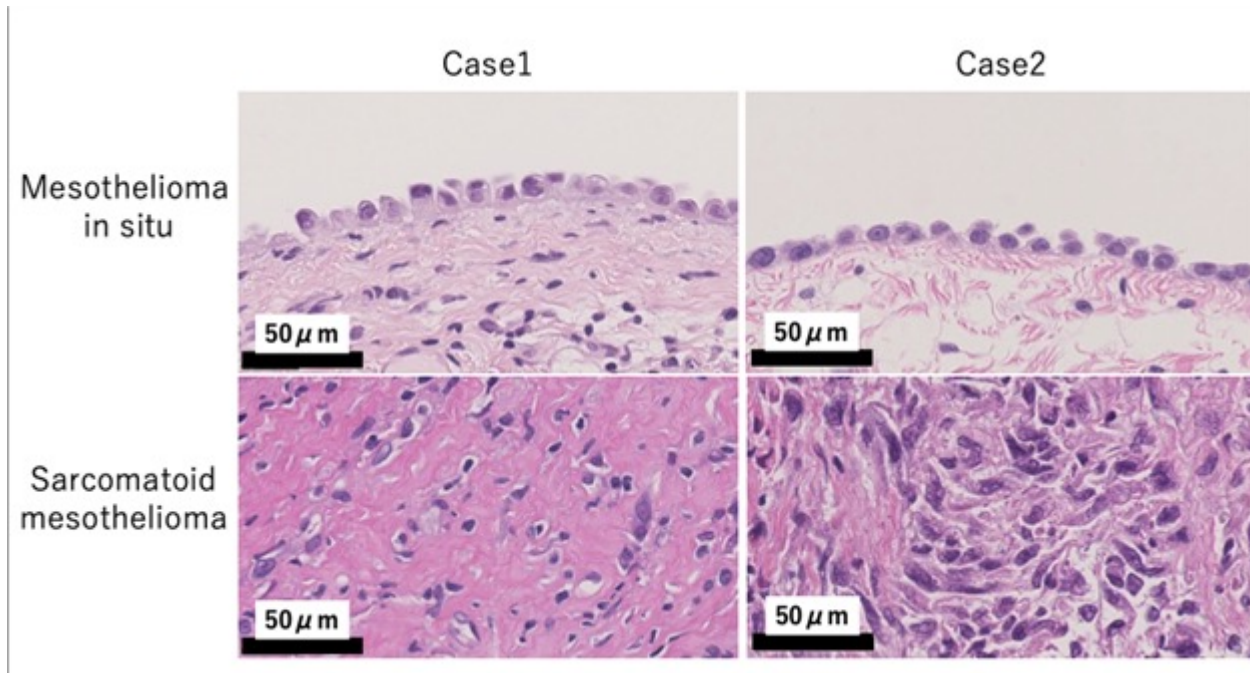
PP02.48:
Semi-Rigid Thoracoscopy using Small Forceps; a Promising Diagnostic Method for Malignant Pleural Mesothelioma

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Background: Due to the histological diversity of malignant pleural mesothelioma(MPM), there are many difficulties in diagnosis through biopsy. Full-thickness pleural biopsy using VATS or rigid medical thoracoscopy is preferred because diagnosis of MPM is possible only after obtaining tissue of an appropriate depth. Semi-rigid thoracoscopy is a new diagnostic modality, but its usefulness in MPM diagnosis is unknown. Biopsy using small forceps is not performed because it is difficult to obtain a full-thickness specimen. Despite of these limitations, there were several cases diagnosed with a semi-rigid medical thoracoscopy with small forceps. Therefore, we introduce our cases and discuss about clinical usefulness of semi-rigid medical thoracoscopy with small forceps in diagnosis of MPM.

Method: From January 2015 to May 2022, patients diagnosed with VATS pleural biopsy and semi-rigid thoracoscopy with small forceps among patients diagnosed with MPM at Incheon St. Mary's Hospital were included. In the case of semi-rigid thoracoscopy, local anesthesia was performed, and the results of frozen section were confirmed by pathologist while performing semi-rigid thoracoscopy.

Result: From January 2015 to May 2022, a total of 14 patients were diagnosed with MPM, and 5 patients (35.7%) were diagnosed with VATS pleural biopsy, and a semi-rigid thoracoscopy 6 patients (42.9%) were diagnosed as with small force, 2 patients (14.3%) were diagnosed as PCNB, and 1 patient (7.1%) was undiagnosed. A total of 8 patients were diagnosed with a semi-rigid thoracoscopy with small forceps. Among them, 6 patients were diagnosed with MPM.

Conclusion: The diagnostic value of semi-rigid thoracoscopy with small forceps performed in our hospital was considerable. Semi-rigid thoracoscopy with small forceps has fewer complications, does not require general anesthesia, and shortened length of hospital day. It is worthy of a study with a larger patient population.

PP02.49:
Paraneoplastic Neurological Syndrome in Small Cell Lung Cancer

Dr. Takayo Ota[1], Dr. Masaaki Terashima[2], Dr. Kaoru Matsui[1], Dr. Yukihiro Hamada[1], Dr. Shuichi Ueno[1], Dr. Masaaki Kobayashi[1], Dr. Yumiko Nishide[1], Dr. Kazuya Saito[1], Dr. Yusaku Yoshida[1], Dr. Naoko Tada[1], Dr. Noriyuki Masuda[1], Dr. Masahiro Fukuoka[1]

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Background: Paraneoplastic neurological syndrome (PNS) is a rare type of neurological disorder associated with tumors that demonstrate a wide variety of clinical symptoms. Immunological responses affecting the nervous system are characterized by an autoantibody, which is cross-reactive against tumors and neuronal systems. The most common cancer associated with PNS is small cell lung cancer (SCLC). This abstract includes one PNS case presented at the 18th Annual Meeting of the Japanese Society of Medical Oncology in 2021.

Methods: Patients with SCLC at our institute from December 2019 to November 2021 were enrolled in this retrospective study.

Results: A total of 73 patients were included in this study. Of the 73 patients, 5 patients were diagnosed with PNS. Three patients were limited disease (LD) and two patients were extensive disease (ED). The presented cases of symptoms and autoantibodies in cerebrospinal fluid (CSF) or in serum were (i) loss of consciousness, anti-GABAB receptor, (ii) cerebellar ataxia, anti-AMPH, anti-Ri, and anti-GAD65, (iii) intentional tremor, anti-CV2, (iv) blindness, recoverin, and anti-SOX1, (v) vertigo, anti-GAD65. Case 1 was diagnosed with PNS when the tumor became progressive disease after a first-line chemotherapy, and all other cases were diagnosed because of preceding neurological symptoms. Steroid pulse therapy (1g/day for 3 days) was administered for 4 patients ((i)-(iii), (v)), however, it was not effective except case 1. Because of severe symptoms, all 3 patients with LD-SCLC were not able to be treated with concurrent chemoradiotherapy (CCRT) as a first-line therapy. After the symptoms relieved, only for case 5, CCRT was performed. Chemotherapy for SCLC was effective for all patients, except for case 4. Over time, chemotherapy was resistant to PNS and none of them complete recovered.

Conclusion: We described PNS cases in SCLC. Suspecting neurological symptoms in SCLC guided us to diagnose PNS. Direct treatment of SCLC might be more effective than indirect treatment as immuno-suppressive agents.

PP02.50:
A Real-World Study on the Efficacy and Safety of PD-L1 inhibitor Plus Platinum-Etoposide Chemotherapy in Patients with Extensive Stage SCLC: A Prospective Observational Study

Dr. Kenji Morimoto[1], Dr. Tadaaki Yamada[1], Dr. Takayuki Takeda[2], Dr. Shinsuke Shiotsu[3], Dr. Koji Date[4], Dr. Taishi Harada[5], Dr. Nobuyo Tamiya[6], Dr. Yusuke Chihara[7], Dr. Yoshizumi Takemura[8], Dr. Takahiro Yamada[9], Dr. Hibiki Kanda[10], Dr. Akihiro Yoshimura[1], Dr. Masahiro Iwasaku[1], Dr. Shinsaku Tokuda[1], Dr. Young Hak Kim[1], Dr. Koichi Takayama[1]

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Background: The efficacy and safety of programmed death ligand-1 (PD-L1) inhibitor plus platinum-etoposide chemotherapy for patients with extensive stage small-cell lung cancer (ES-SCLC), with real-world evidence, stratified based on age and performance status (PS), have not been fully investigated.

Methods: This multicenter prospective study enrolled patients with ES-SCLC who received PD-L1 inhibitor plus platinum-etoposide chemotherapy between September 2019 and October 2021 (UMIN: 000044048).

Results: Forty-five patients with ES-SCLC received PD-L1 inhibitor plus platinum-etoposide chemotherapy, including eighteen elderly ($\geq$75 years old) patients and six patients with a PS of 2. Multivariate analysis indicated that a PS of 2 was a significant independent prognostic factor for progression-free survival (PFS) and overall survival (OS) (p=0.008 and p=0.001, respectively). Of patients with PS 2 at the initial phase, those achieved PS improvement during treatment had significantly longer PFS and OS than those who did not (p=0.02 and p=0.02, respectively). The incidence of treatment discontinuation due to adverse events (AEs) was significantly higher in the elderly patients than in the non-elderly patients (p=0.03).

Conclusion: This real-world prospective study found that PD-L1 inhibitor plus platinum-etoposide chemotherapy had limited efficacy in ES-SCLC patients with a PS of 2, except for cases with improvement of PS during treatment. Owing to the emergence of AEs and treatment discontinuation, this treatment should be administered with caution in elderly patients with ES-SCLC.

PP02.51:
Life Expectancy after Discontinuation of Chemotherapy in Patients with Small Cell Lung Cancer

Dr. Kazushi Yoshida[1], Dr. Yoshitaka Seki[1], Dr. Yuri Baba[1], Dr. Wakako Shinohara[1], Dr. Chiaki Hosoda[1], Dr. Akihoro Ichikawa[1], Dr. Yusuke Kurita[1], Dr. Kenji Kobayashi[1], Dr. Kazuyoshi Kuwano[2]
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Background: Small cell lung cancer (SCLC) is a subtype of lung cancer with a very poor prognosis, resulting in rapid disease progression. Although the prognosis has improved in recent years with the advent of immune checkpoint inhibitors, the prognosis still disastrous. Since most of the large clinical trials have focused on the therapeutic effect, there are few reports on the prognosis after discontinuation of chemotherapy. This study was conducted to investigate the prognosis after standard treatment with chemotherapy.

Method: We retrospectively examined the prognosis and life history of 34 patients who were diagnosed as SCLC at the Jikei University Katsushika Medical Center from January 2018 to December 2020. Survival time from the date of the change of treatment plan without further chemotherapy by the physician was examined. The protocol for this research project has been approved by a suitably constituted ethics committee of our institution, where the work was undertaken under the provisions of the Declaration of Helsinki.

Results: Median age was 74 years (Range: 54-84), 6 females and 28 males, and stage at diagnosis was 2 patients with limited-stage and 32 patients with extensive-stage. Performance status at diagnosis was 0-2 in 30 patients and 3-4 in 4 patients. Twenty patients were introduced to home visitation care. The median overall survival from the date of diagnosis and discontinuation of chemotherapy decision was 9.2 months (0.2-37.6 months), 1.3 months (0.1-9.8 months), respectively.

Conclusion: The prognosis of patients with SCLC after discontinuation of chemotherapy was quite poor. Physicians need to tailor the advance care plan, taking into short life expectancy.

PP02.52:
Clinical Profile, Prognostic Factors, and Treatment Outcomes in Patients of Thymoma: a Decade of Experience from a Single Centre

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Background: Thymomas are the commonest tumor of the anterior mediastinum. Treatment recommendations involve multidisciplinary management with surgery holding the cornerstone of treatment while radiotherapy and chemotherapy are added as an adjunct to surgery or for palliation. The present study aims to explore the clinical presentation and effect of various prognostic factors on the survival of thymoma patients.

Methods: A retrospective analysis of 44 patients enrolled between January 2010 to December 2020 was carried out. Patient related and treatment related factors including staging, surgery details, radiotherapy and chemotherapy were analyzed. Data was analyzed using SPSS 25.0. Survival curves were calculated using Kaplan-Meier method.

Results: The median age of the presentation was 50 years (range, 17-74years). Male to female ratio was 1.75. Myasthenia gravis was present in only 7 patients (15.9%). As per Masaoka staging, 23 patients had early stage (stage I/II) while 21 patients had advanced stage (III/IV). Surgery was done in 26 patients: R0 in 21, R1 in 2 and R2 in 3 patients, respectively. In total, 39 patients (88.63%) received radiotherapy – adjuvant radiotherapy in 22, definitive in 8 and palliative radiotherapy in 9 patients, respectively. Definitive radiotherapy was given in unresectable patients. Chemotherapy was given in 10 patients (22.7%). Recurrences were seen in 17 patients (38.63%) with 7 local and 14 distant recurrences. Among distant recurrences, lung was the commonest site (n=8). Median follow up was 45.5 months (range, 7-141 months). The 3-year overall survival (OS) and progression free survival (PFS) were 71.8% and 45.7% respectively. Median OS could not be reached, while median PFS was 95 months. On univariate analysis, early Masaoka stage (I/II), surgical resection and extent of resection (R0) were associated with improved OS and PFS. Though radiotherapy did not significantly impact OS and PFS, it improved the local control.

Conclusion: Surgery remains the mainstay of treatment paradigm. Adjuvant radiotherapy improves local control. Masaoka stage and surgical resection are independent prognostic factors for survival. The present study supports the role of multidisciplinary team approach for the management of these patients.

PP02.53:
Neuro-Cognitive Effect of WB-PCI in LS-SCLC

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Background: Small-cell lung cancer (SCLC) is an aggressive type of cancer associated with poor prognosis due to rapid growth and early distant metastasis, especially brain metastasis. Patients with limited stage (LS) achieve a median survival of 18 months and a 5-year survival rate of 15%. Several studies have shown prophylactic cranial irradiation (PCI) to be an independent prognostic factor. Whole brain (WB) PCI 30 Gy/10 fractions has impact on neuro-cognitive function. Present study was designed to measure the impact of WB-PCI on neuro-cognitive function.

Methods: 10 patients of LS-SCLC were administered WB-PCI in 2021. All patients received 30 Gy/10 fractions. Baseline neuro-cognitive function was measured before administering WB-PCI and final neuro-cognitive function was measured after median follow up of 12 months. Neuro-cognitive function was assessed by Montreal Cognitive Assessment (MoCA).

Results: All patients are alive with some degree of deterioration of neuro-cognitive function/score compared to baseline measurement. Mean pre-treatment MoCA score was 27/30 and mean post-treatment MoCA score was 25/30. None of the patients developed any brain metastasis at last follow up.

Conclusions: WB-PCI is effective in reducing symptomatic brain metastasis in LS-SCLC, however, affects neuro-cognitive function in short term. Longer follow up is needed to know the impact in long term.

PP02.54:
Experience in the Treatment of Patients with Advanced Thymic Cancer

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Background: Thymic cancer is a rare type of aggressive malignant disease with an incident rate of 0.15 per 100,000 persons. Because of its scarce nature, treatment strategies have not been established yet. Generally, response to cytotoxic chemotherapy for thymic cancer is poor. In Japan, lenvatinib, a multiple kinase inhibitor, was approved for unresectable thymic cancer in 2021. In this research, we examined the treatment strategies, safety, and efficacy of cytotoxic chemotherapy and lenvatinib for unresectable and post-operative recurrent thymic cancer in our institute.

Methods: We retrospectively analyzed treatment data of unresectable and post-operative recurrent patients with thymic cancer.

Results: Among eight patients, six of them were female and two were male. Median age was 66 years old (range, 51-82). Six of them had squamous histology, one had basaloid cell carcinoma and one had combined large cell neuroendocrine carcinoma. Six of them had ECOG-PS 0 to 1, and two had ECOG-PS 2. Six patients received cytotoxic chemotherapy (CBDCA+PTX for 4, CBDCA+nab-PTX for 1, CDDP+VP-16 for 1), and two received lenvatinib for first-line treatment. Two started CBDCA+PTX for first-line treatment after the approval of lenvatinib in order to avoid the risk of cardiovascular-related adverse events. Lenvatinib was administered to three patients for later-line treatment.
At the time of submission of this abstract, three died due to the progression of the disease. Response to first-line treatment was observed in four patients in cytotoxic chemotherapy group, and one in lenvatinib. Two of the four patients who received lenvatinib for later-line showed partial response.
All patients who took lenvatinib experienced grade 2 or 3 adverse events (thrombocytopenia 2, hypertension 2, fatigue 1, appetite loss 1, hand-foot syndrome 1). Temporal cessation followed by dose reduction of lenvatinib was required in all these cases. No case of treatment-related death was observed in this research.

Conclusion: REMORA, a single-arm phase 2 trial, showed the activity and safety of lenvatinib for previously treated thymic cancer. Currently, in Japan, lenvatinib is regarded as one of the standard care for advanced or post-operative recurrent thymic cancer. However, its safety and efficacy for previously untreated advanced and post-operative cases with thymic cancer have not been proved yet. In our retrospective research, adverse events of all cases, including first-line patients, were managed well and treatment of lenvatinib was tolerable by adequate dose reduction and management for adverse events. Further accumulation of data is warranted.

PV01.01:
Individualized Prediction of Survival Benefit from Postoperative Radiotherapy for Patients with Malignant Pleural Mesothelioma

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Background: The role of postoperative radiotherapy (PORT) in malignant pleural mesothelioma (MPM) remains controversial and the eighth edition staging scheme for MPM has not been fully verified. We aimed to develop an individualized prediction model for identifying optimal candidates for PORT among MPM patients who received surgery plus chemotherapy and externally validate the performance of the new TNM staging scheme.

Methods: Detailed characteristics of MPM patients during 2004-2015 were retrieved from SEER registries. Propensity score matching (PSM) was conducted to reduce disparities of baseline characteristics between the PORT group and no-PORT group. A novel nomogram was constructed based on independent prognosticators identified by multivariate Cox regression model. The discriminatory performance and degree of calibration were evaluated. We stratified patients into different risk groups according to nomogram total scores, and estimated the survival benefit of PORT in different subgroups in order to identify the optimal candidates.

Results: We identified 596 MPM patients, among which 190 patients (31.9%) received PORT. PORT conferred significant survival benefit in the unmatched population (P=0.025), while there was no significant survival difference favoring PORT in the matched population (P=0.192). The prognostic performance of the new TNM staging scheme was far from perfect. A novel nomogram was constructed based on clinicopathological factors, including age, sex, histology, and N stage. The discriminatory power of the novel nomogram outperformed that of conventional TNM staging system. Based on cut-point analyses, patients risk subgroups were stratified as follows: high risk (score>252), intermediate risk (96<score<241), and low risk (score<84). Subgroup analyses indicated that PORT was beneficial for high risk group (P=0.003) rather than low risk group (P=0.965) and intermediate risk group (P=0.661).

Conclusion: We established a novel predictive model which could make individualized prediction of survival benefit of PORT for MPM and could compensate for weakness in TNM staging system

Image 1.
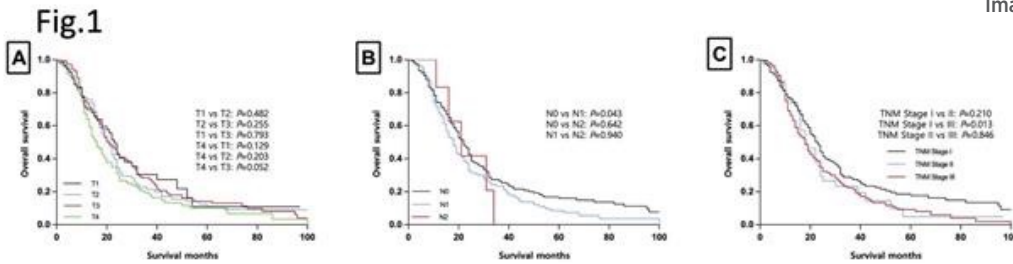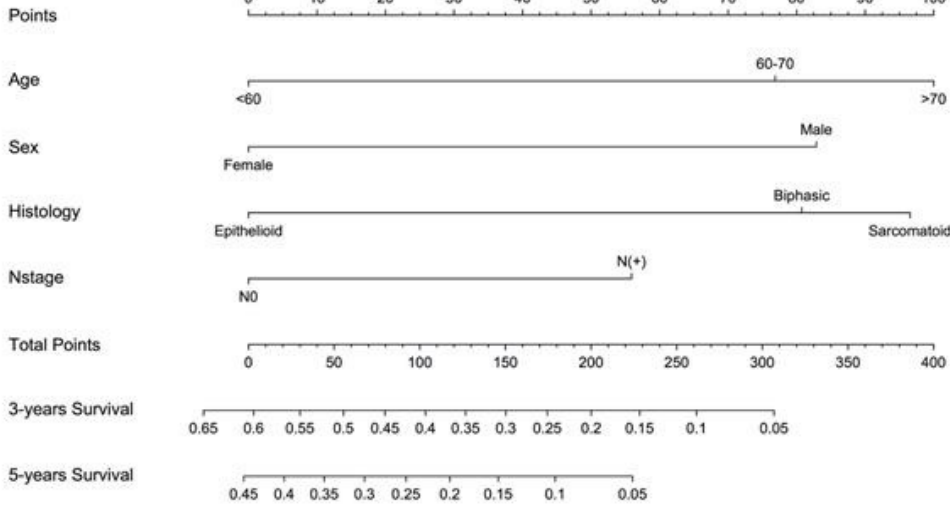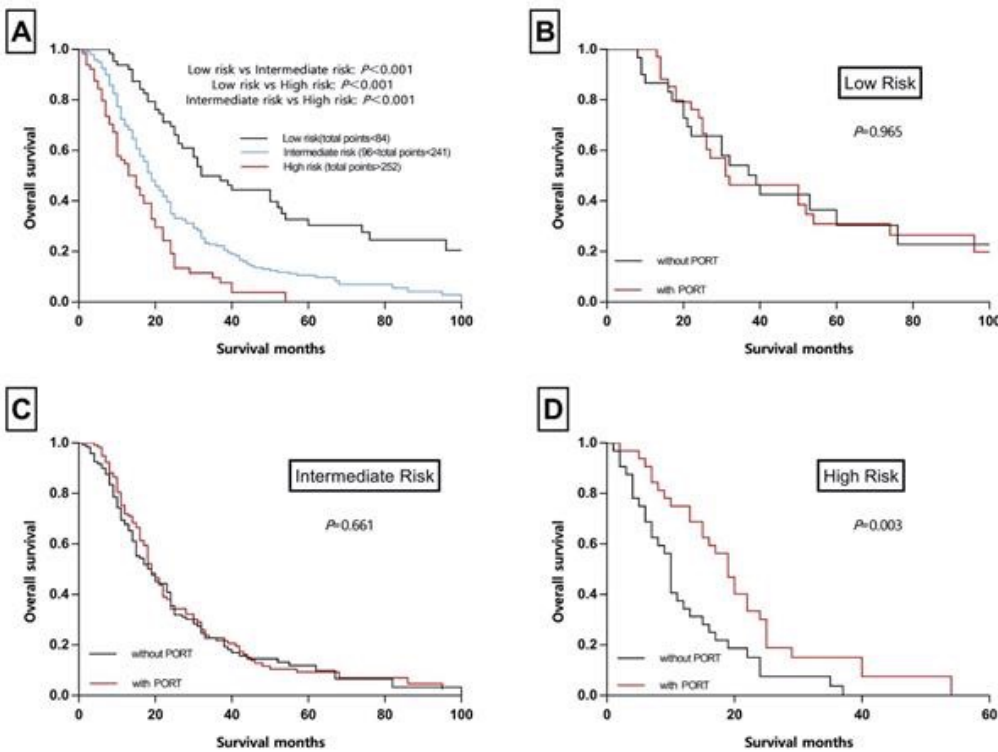
Fig 1. Survival curves of overall survival according to (A) T descriptors, (B) N descriptors, and (C) TNM stage.
Fig 2. Constructed nomogram for predicting overall survival and benefit of postoperative radiotherapy in stage I-III malignant pleural mesothelioma.
Fig 3. Survival curves of overall survival according to (A) risk subgroups, (B) treatment modality in low risk subgroup, (C) treatment modality in intermediate risk subgroup, and (D) treatment modality in high risk subgroup.

PV01.02:
Experience of Cyto-reductive Surgery and Intra-Operation Adjuvant Therapy for Malignant Pleural Mesothelioma at a Single Center in Taiwan

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Background: Background: The study aimed to determine outcomes and overall survival (OS) in patients undergoing cytoreductive surgery and intra-operation adjuvant therapy (heated intrapleural chemotherapy or photodynamic therapy) for malignant pleural mesothelioma at a single center in Taiwan.

Methods: This was a retrospective review of patients that underwent cytoreductive surgery and intra-operation adjuvant therapy for MPM from April 2003 to December 2021.

Results: A total of 17 patients with MPM underwent the operation. There was one surgical mortality due to intra-operative uncontrolled bleeding. Median OS was 20.0 months. Subtype analysis according to the histology of epithelioid, biphasic, and sarcomatoid types was 29.7%, 11%, and 7.6% respectively.

Conclusion: This is the first report for a single center in Taiwan devoted to lung-sparing decortication/pleurectomy with intra-operation adjuvant therapy for malignant pleural mesothelioma. Although this is a rare disease and we are not a high volume center, the survival rate is comparable with the global survival rate those received operations. We provide a treatment choice for Taiwan's malignant pleural mesothelioma patients.

PV01.03: A Phase I Trial of the HER2 TKI, BI 1810631, in Patients with Advanced Solid Tumors with HER2 Aberrations

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Background: HER2 mutations are present in 2–4% of NSCLC tumours; of these ~50% occur in the tyrosine kinase domain (TKD) of the gene, the majority of which are exon 20 insertion (ex20ins) mutations. There is an unmet need for effective TKIs against *HER2* mutations in solid tumors, particularly in NSCLC. BI 1810631 is a HER2 selective TKI that covalently binds to both wild-type and mutated HER2 receptors, including ex20ins, whilst sparing EGFR signaling; preclinical data suggest good tolerability and efficacy. This Phase Ia/Ib, open-label, non-randomized study aims to determine the safety, maximum tolerated dose (MTD), pharmacokinetics (PK), pharmacodynamics and preliminary efficacy of BI 1810631 in patients with HER2 aberration-positive solid tumors (NCT04886804).

Methods: ~96 pts from 5–7 sites in the US, Netherlands, Japan, and China will be recruited. Phase Ia: pts will receive escalating doses of BI 1810631 BID (~36 pts) or QD (~30 pts). Starting dose: 15 mg BID; QD schedule will begin after one dose level above estimated therapeutic dose of BI 1810631 is determined safe by the Dose Escalation Committee (expected starting dose: 60 mg). BI 1810631 dose escalation will continue until MTD/recommended phase II dose for each schedule is determined, as well as a preferred Phase Ib schedule. In Phase Ib, an initial 30 patients with *HER2* TKD mutation-positive, pre-treated NSCLC will be enrolled, with possible inclusion of additional cohorts in the future.

Overall patient inclusion criteria: ≥18 years old; histologically/cytologically confirmed HER2 aberration-positive advanced/unresectable/metastatic solid tumor refractory/not suitable for standard therapy; exhausted treatment options; measurable/evaluable lesions (per RECIST v1.1); ECOG PS ≤1. Phase Ib criteria: *HER2* TKD mutation-positive NSCLC; received ≥1 line of platinum-based combination chemotherapy in the advanced/metastatic setting.

Primary endpoints: MTD based on number of dose-limiting toxicities (DLTs)/number of patients with DLTs (Phase Ia); objective response (Phase Ib). Secondary endpoints: number of patients with DLTs throughout entire treatment period and PK parameters (Ph Ia/Ib); duration of response, disease control, duration of disease control and PFS (Phase Ib). The trial is actively recruiting with 13 patients treated to date. Dose escalation data, MTD, safety and preliminary efficacy data will be presented at the meeting

PV01.04:
Clinical Trials During Covid Pandemic - The Show Must Go On

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Background: The covid pandemic and the ensuing measures to control pandemic have had long lasting implications on the mankind. In the pandemic, cancer patients were fighting twin simultaneous battles of cancer and covid. Clinical trial participation is the best way to treat the cancers. However, even in the best of times, clinical trial participation in developing countries is difficult. During the pandemic, especially, in view of stringent measures like lockdown, travel restrictions, it became further difficult for patients to actively enroll in the clinical trials.

Aim: To audit the clinical trial conduct of lung cancer patients during the pandemic years from March 2020 to Dec 2021 at a tertiary cancer institute in Northern India.

Methods: A retrospective audit was done to analyze the number of clinical trials, active number of patients, recruitment patterns during covid, special toxicity profile due to covid during the period of March 2020 to Dec 2021.

Results: A total of 47 patients participated in phase III and IV clinical trials. The number of active Lung cancer clinical trials was 8. The male to female ratio was 1.13, the median age was 56. The active recruitment decreased during the initial covid peak in April-June 2020. However, there was no subsequent decline in patient accrual in the subsequent months even during the second and third waves. The incidence of Covid infection during trial was 8%. There were no covid related deaths in the trial patients. 90 % of patients received covid vaccination.

Conclusions: The results depict that while initially there was a decline in enrollment of patients in clinical trials, subsequently there was a phase of learning and adaptation, and patients could be safely recruited in the clinical trials. There were no unexpected SAE or complications due to covid. The current pandemic has taught us that cancer care, covid and clinical trials for betterment of patients should go hand in hand.

PV01.05:
Efficacy of Immunotherapy in Second-Line Treatment of KRAS Mutated Patients with Non-Small Cell Lung Cancer - Data from Daily Practice

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Background: The efficacy of immunotherapy in pre-treated NSCLC was documented in patients without abnormalities in EGFR and ALK genes. The next-generation sequencing (NGS) allows for the identification multiple other abnormalities- mutations in the KRAS gene are the most common. We aimed to confirm the benefits for immunotherapy in this group of patients.

Methods: This study was a retrospective analysis of pts treated in the routine practice in Poland. NGS was performed using MiniSeq (Illumina). The sequencing data were processed using Archer Analysis (v6.2.1) software. The median of progression-free (PFS) and overall survival (OS) were estimated using the Kaplan-Meier method. The log-rank test was used for comparisons. Analyses were performed with SASS v.27.0 software.

Results: A total of 96 patients were qualified to nivolumab or atezolizumab treatment after procedure NGS. The following molecular abnormailities were identified : KRAS – 24 patients (25% of patients), RET – 2 cases, BRAF V600E, MAPK, CTNNB1 and MET – 1 case, no of patients had EGFR or ALK alterations. Among KRAS mutated patients mutation G12C was the most common (54%). Median PFS and OS were 2 months (95% CI: 1.5-2.5) and 10 months (95% CI: 6.47-13.53) for overall population. In the group of KRAS mutated patients, ORR was observed in 12% patients, SD and PD- accordingly- in 25% and 54% patients. No differences were observed in terms of mPFS between KRAS mutated and KRAS WT patients. A trend towards longer OS was observed in KRAS mutated patients. The data are presented in the Table 1.

Conclusion: Immunotherapy in second-line NSCLC allows for benefit regardless of KRAS gene mutation status. The treatment sequence, including sotorasib or adagrasib, is still discussed. NGS is a valuable method to identify a variety of molecular abnormalities in patients with NSCLC in daily practice.

Table 1.

	KRAS(-) (n=72)	KRAS(+) (n=24)	p
Progression free survival			
Median months (95% CI)	2 (1.16-2.84)	2 (1.43-2.57)	p=0.825
Overall survival			
Median months (95% CI)	9 (2.35-15.65)	12 (8.53-15.47)	p=0.882

PV01.06:
The Value of Next-Generation Sequencing in the Differential Diagnosis of Mediastinal Tumor. Case Report

Dr. Magdalena Knetki-Wróblewska[1], Dr Marta Olszyna-Serementa[1], Dr Andrzej Tysarowski[2], Prof. Dariusz M. Kowalski[1], Prof. Małgorzata Szołkowska[3]
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Introduction: NUT is a rare tumor for which there may be diagnostic uncertainties. The case of a patient with a diagnosis, which has been confirmed by NGS testing, is described.

Case Report: 32-year-old female patient of Caucasian race, a smoker, without comorbidities had undergone diagnostic tests due to cough, chest pain and increasing dyspnea. CT scan showed the right lung tumor mass with a mediastinal infiltration, 82x65 mm, and mediastinal lymph nodes involvement, CS IIIB (Fig.1) Intermediate bronchus tissue samples were obtained during bronchoscopy. Microscopic analysis (Fig 2.) revealed poorly differentiated epithelioid neoplasm composed of nests of small cells with scant cytoplasm, relatively large nuclei and distinct, eosinophilic nucleoli (inset) (A). In immunohistochemical tests the cells were weakly positive for cytokeratin (B) and almost completely negative for p40 (C). Immunohistochemical reaction with NUT antibody revealed diffuse but weak nuclear reaction (D). Based on the immunoprofile of neoplastic cells, which was rather unusual for NUT carcinoma the diagnosis of NUT variant carcinoma was suggested. Genetic analysis revealed NUTM1 gene fusion (NSD3[7]-NUTM1[3]) confirming the histopathological suggestion. No other molecular genetic abnormalities were found. The diagnosis of NUT-variant carcinoma was established. The patient started immediate treatment – concurrent chemoradiotherapy based on cisplatin 75mg/m2 and docetaxel 75mg/m2 with good response (PR according to RECIST 1.1) and significant improvement of the patient's symptoms. Total dose of 60 Gy in 30 fractions was planned, 6 MeV X-rays, 4D-IGRT. Despite a good response to treatment, further follow-up revealed disseminated disease and the patient died 6 months after diagnosis.

Conclusions: NUT-variant carcinoma is a tumor associated with poor prognosis. Molecular diagnostics carried out using NGS can help to make a precise diagnosis. There is a need for clinical trials to identify more effective therapies.

Image 1.
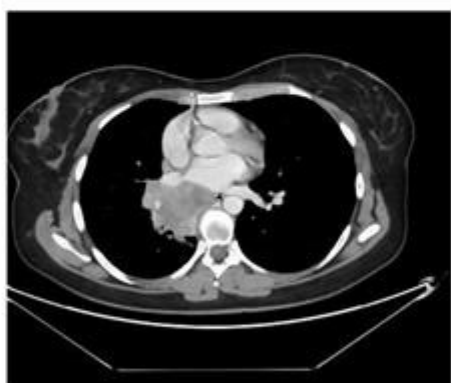
Fig 1. CT scan before diagnosis

Image 2.
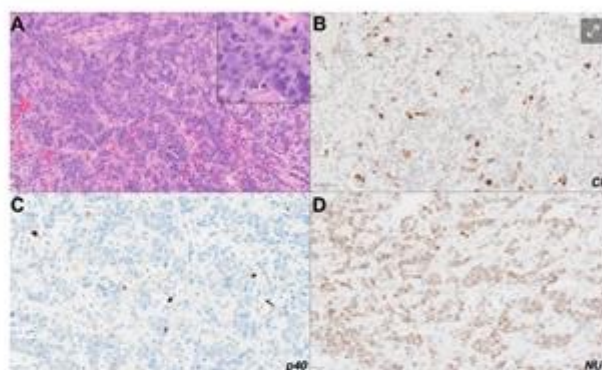
Fig.2 Histopathology of NUT-variant carcinoma

PV01.07:
Predictors of Psychological Distress in Informal Caregivers of Patients after Surgical Treatment of Early-Stage Lung Cancer

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Background: Informal caregivers of lung cancer patients often suffered from psychological distress, such as depression, anxiety, and stress. Caregivers with a high level of psychological distress are at great risk of increased caregiver burden and low quality of life. Current literature has primarily focused on investigating the psychological distress of informal caregivers of patients with advanced lung cancer. Studies for caregivers of postoperative patients with early-stage Non-Small Cell Lung Cancer (NSCLC) are limited. This study aims to examine the predictive factors of psychological distress for informal caregivers of patients with early stage NSCLC after surgical treatment.

Methods: A cross-sectional study was carried out in a university-affiliated hospital in Changsha, China. Informal caregivers of patients with early-stage NSCLC and postsurgical treatment were invited to participate in this study. Psychological distress was evaluated using the Hospital Anxiety and Depression Scale (HADS). Structured questionnaires were administered to obtain caregivers' sociodemographic information, coping style, social support, and caregiver burden. Stepwise multivariate linear regression was employed to identify factors affecting caregivers' psychological distress

Results: A total of 385 caregivers were included in this study. The mean age was 56.1 Å} 10.5 years for patients and 45.2 Å} 12.4 years for caregivers. Most of patients (83.4%) had stage I lung adenocarcinoma. Caregivers were mostly married (89.6%) and living with the patient (66.2%). Most caregivers were spouses (48.1%) or children (38.2%) of the patients. The average HADS score of caregivers was 14.10 Å} 5.09. Over half of participants (57.7%) experienced psychological distress. Caregiver burden (r = 0.140, p = 0.006), active coping (r = -0.105, p = 0.040), and social support (r = -0.143, p = 0.005) were significantly associated with caregivers' psychological distress. The multivariate linear regression analysis showed that perceived financial hardship (β = 0.169, p = 0.001), caregivers' social support (β = -0.106, p = 0.035), and caregiver burden (β = 0.101, p = 0.047) were significant predictors of caregivers' psychological distress..

Conclusions: Over half of caregivers of postoperative patients with NSCLC experienced psychological distress. Lower caregivers' social support, higher perceived financial hardship, and higher caregiver burden were significant predictors of higher psychological distress. This study highlights the need to offer emotional support to informal caregivers of patients with earlystage NSCLC.

PV01.08:
Liquid Biopsy-Based Fragmentomic Assay for Malignancy Classification of Radiographically Highly Suspicious Lung Nodules

Siwei Wang[1], Ming Li[1], Feng Jiang[1,] Min Wu[2], Wenda Yin[1], Jingyuan Zhang[3], Hongyu Zhu[1], Fanchen Meng[1], Hua Bao[3], Yang Shao[3], Prof Jie Wang[4,5], Lin Xu[1,6], Assoc. Prof. Rong Yin[1,6]

[1]Department of Thoracic Surgery, Jiangsu Key Laboratory of Molecular and Translational Cancer Research, Jiangsu Cancer Hospital & Nanjing Medical University Affiliated Cancer Hospital & Jiangsu Institute of Cancer Research, 21009, Nanjing, PR China., Nanjing, PR China, [2]Geneseeq Research Institute, Nanjing Geneseeq Technology Inc., 210032, Nanjing, PR China., Nanjing, PR China, [3]Department of Pathology, Jiangsu Cancer Hospital & Nanjing Medical University Affiliated Cancer Hospital & Jiangsu Institute of Cancer Research, 21009, Nanjing, PR China., Nanjing, PR China, [4]Department of Science and Technology, Jiangsu Cancer Hospital & Nanjing Medical University Affiliated Cancer Hospital & Jiangsu Institute of Cancer Research, 21009, Nanjing, PR China., Nanjing, PR China, [5]Biobank of Lung Cancer, Jiangsu Biobank of Clinical Resources, 21009, Nanjing, PR China., Nanjing, PR China, [6]Collaborative Innovation Center for Cancer Personalized Medicine, Nanjing Medical University, 211116, Nanjing, PR China., Nanjing, PR China

Background: Screening by low-dose computed tomography (LDCT) has been proven effective to reduce 20%-39% lung cancer-specific mortality. However, around 15%-35% of surgically resected lung nodules that were initially evaluated of high risk with careful radiographic and clinical judgements were eventually confirmed pathologically benign. There is an unmet need of a non-invasive method for malignancy classification in radiographically highly suspicious lung nodules.

Methods: We recruited 307 patients with high-risk lung nodules identified by LDCT who received surgical resections as standard of care. 247 were later pathologically confirmed malignant and 60 benign. We collected a plasma sample from each patient before the surgery and performed low-depth (5X) whole-genome sequencing (ldWGS). We constructed an ensembled classifier model for nodule malignancy that incorporated cell-free DNA (cfDNA) fragmentomic data from ldWGS and radiomic data from LDCT. We then validated the model in an independent validation cohort.

Results: With cfDNA fragmentomic features including fragment size ratios, nucleosome protection patterns, breakpoint motif compositions, copy number variations, and neomer reads, our model accurately distinguished benign and malignant nodules in both the study and validation cohorts (AUC = 0.95 and 0.93, respectively). Radiomic features in the model alone reached AUC of 0.79. Further combining fragmentomics and radiomics, our model achieved AUC of 0.97, yielding 93% sensitivity at 90% specificity.

Conclusions: cfDNA fragmentomics could provide an efficient non-invasive tool to distinguish malignancies and radiographically high-risk but pathologically benign lung nodules to which surgical resections were recommended by standard management.

Image 1.
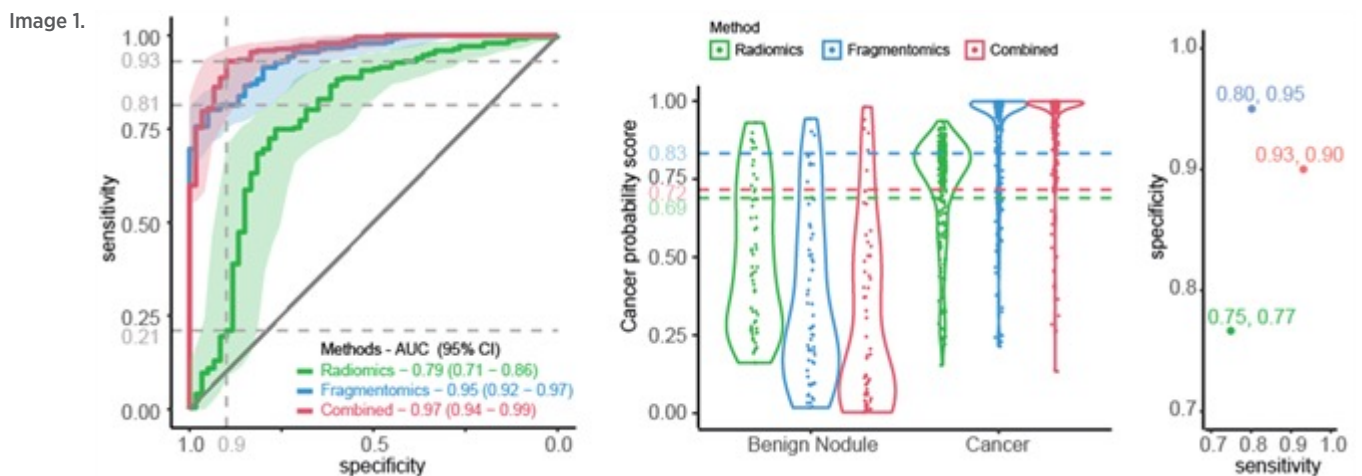
PV01.09:
Electronic Cigarettes Use and 'Dual-Use' among the Youth in 75 Countries- Estimates from Global Youth Tobacco Surveys (2014-2019)

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Background: Estimates of EC use are seldom reported for middle-income countries. We report country-level prevalence of awareness about and electronic cigarette use, and 'dual use' and its associations with age, sex and country income and e-cigarette regulatory status.

Methods: We analyzed data from the most recent Global Youth Tobacco Surveys done on nationally representative samples of school-going youth aged 13-15 years in 75 countries. The weighted prevalence of 'awareness' (heard about EC), 'ever EC use' (even tried a few puffs), 'current EC use' (during the last 30 days), and 'dual use' (EC use and cigarette smoking during the last 30 days) were estimated.

Results: A total of 264, 940 (male= 128,581, female=135909) youth was analyzed. Overall pooled estimates of awareness 'ever use', current use', and 'dual use' were 56.7% (95% CI 55.2,58.2), 20.2%, (95% CI 55.2, 58.2), 10.9% (95% CI 19.2, 21.3) and 4.6% (95% CI 4.1, 5.1) respectively. Awareness was >80% in 13 countries mostly from Europe, Poland being the highest 95.8% (95% CI 94.8, 96.6). In seven countries, a third to half the youth had ever used EC, the highest of 55.1% (95% CI 51.3, 58.9) was in Italy. In 30 countries, the prevalence of current use was >10%, highest was 35.1% [95% CI 32.4, 38.0] in Guam. Youth from Europe (74.6% and 34.5%) and HIC (83.6% and 39.4%) had the highest EC awareness and ever EC use. Ever EC, current EC, and dual-use among boys was more than 2-fold (28.5% vs. 11.8%), 3-fold (1.6% vs. 5.6%), and 5-fold higher (7.6% vs. 1.6%) than girls respectively. Awareness was moderately and positively correlated with ever use (r=0.731, (95%CI 0.566 to 0.839, p<0.001) and current use (r=0.333, 95% CI: 0.089 to 0.540, p=0.009). Higher age, being a boy, current cigarette smoker, from a high-income country, and having stricter EC regulations had higher odds of being a current EC user. Youth from a country with high income and restrictive policies had 1.7 times (aOR 1.7, 95% CI 1.5, 1.9) and 1.4 times (aOR 1.4, 95% CI 1.2, 1.16) higher odds of being current EC users.

Conclusion: Awareness, EC use, and dual-use varied across the countries. EC and dual-use are higher among boys and children aged 11 years and below, Eastern Mediterranean and upper-middle-income countries. Global surveillance of youth EC use should be expanded to more countries to assist in EC regulation policy drafting.

PV01.10:
Modulating EGFR TKI Resistance by Dosage and Timing

Mr. Jo Monsen[1]
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When the EGFR pathway first became an avenue for diagnosis and treatment it was a paradigm change for how NSCLC patients were treated.

Now two decades later EGFR TKIs are still used and have a remarkable initial response rate in EGFR+ lung adenocarcinomas.

However resistance to treatment remains a clinical relevant limitation of their long term success, this is true for all generations of EGFR TKIs.

In cell lines EGFR TKI resistance is duplicated in a matter of weeks, by continuous exposure to EGFR TKIs.

A clinical trial (Costa et. al. 2016) and case reports (Monsen, 2021) have shown the tolerability and safety of long term pulsed Afatinib.

In addition it is well established that pulsed and higher doses of selected EGFR TKIs can control and prevent brain metastasis, a common site of resistance and reason for treatment failure due to lack of effective blood brain barrier penetration of all EGFR TKIs at regular doses.

As a patient advocate I urge the scientific and clinical community to probe the feasibility and efficacy of once weekly doses of second and third generation EGFR TKIs, both in vitro and in vivo experiments are needed. A real obstacle so far has been to find an industry sponsor for relevant research and trials. Government bodies and NGOs have a critical role in securing funding as the potential to increase PFS and OS of standard treatments need to be explored.

Given the long term efficacy, safety and tolerability records of pulsed Afatinib at a doses of 240 mg and 280 mg once weekly, 240 mg seems like a viable dose for a clinical trial setting (even a somewhat lower dose could be relevant to study). This could also be verified in cell lines and in mouse models where time to resistance is the main outcome. Currently one patient has been taking 240 mg Afatinib once weekly since August 2019, and is approaching 5 years OS after EGFR+ L858R NSCLC stage IV diagnosis).

PV01.11:
Unique Molecular Properties of East Asian EGFR-Mutant Non-Small Cell Lung Cancer Patients at Early and Advanced Stages: K-MASTER Project

Assoc. Prof. Yoon Ji Choi[1,2], Dayoung Yoon[15,16], Ju Won Kim[1,2], Ah Reum Lim[1,2], Jae Sook Sung[2], Hee-Joon Chung[2], Professor Byoung Chul Cho[3], Eun Joo Kang[4], Jung Sun Kim[5], Taekyu Lim[6], Hye Sook Kim[7], Yu Jung Kim[8], Mi Sun Ahn[9], Young Saing Kim[10], Ji Hyun Park[11], Seungtaek Lim[12], Sung Shim Cho[13], Jang Ho Cho[14], Sang Won Shin[1], Yeul Hong Kim[1,2], Jason K. Sa[15]
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The remarkable clinical success of small molecule receptor tyrosine kinase inhibitors (TKIs) against EGFR-mutant subgroups of non-small cell lung cancer (NSCLC) has facilitated the transition to an oncogene-driven molecular classification paradigm. However, recent studies have shown that co-occurring genomic alterations such as TP53 and STK11 are major determinants of diverse clinical responses. Furthermore, propagation of NSCLC at various progression stages manifested dynamic molecular and clinical characteristics.

The present study aimed to identify the unique molecular properties of EGFR-mutant NSCLC at early and advanced stages in Korean patients from the K-MASTER project.

Our study included 197 NSCLC patients with EGFR mutations who were enrolled in the K-MASTER screening program between June 2017 and July 2021. Among them, 122 patients had localized disease, whereas 75 patients were diagnosed with metastatic or recurrent disease. Mutational analysis was performed on all tumor tissue specimens, using previously established and validated K-MASTER NGS panels.

The most common co-occurring genetic variants with EGFR in early stage of NSCLC composed of TP53(44%), PIK3CA (12%), KMT2A (12%), BCR (11%), and SLX4 (10%), and in advanced stages, TP53 (37%), followed by LRP1B (17%), ATM (13%), ATRX (13%), MSH6 (13%), and MTOR (13%) (Figure 1A). For early-stage NSCLC patients, mutations in JAK2 and ERBB2 demonstrated the most robust differences, whereas MTOR, ATRX, and LRP1B mutations were highly predominant in advanced-stage tumors (Figure 1B, 1D). Next, we analyzed the molecular correlations between different stages of NSCLC with distinct mutational signatures. While, Signature 1 (age) was highly dominant in the advanced stage tumors, both Signature 24 (exposure to aflatoxin) and 15 (defective DNA mismatch repair) were mainly observed in the early stage (Figure 1C). Interestingly, mutational signature 4, which is associated with smoking and frequently observed in NSCLC patients, did not demonstrate a strong correlation with EGFR mutations, whereas Signature 3 (DNA double-strand break) was actively observed in tumors harboring EGFR L858R mutation (Figure 2D).

Collectively, a broader understanding of the co-occurring genetic alterations in EGFR-mutant NSCLC could facilitate a transition from the current single carcinogenic driver model to a more complex molecular diversity model. Future studies will improve the prediction of clinical response in EGFR-mutant NSCLC patients and identify the potential mechanism of action behind therapeutic resistance in advanced tumors.

PV01.12:
Comparison of Adjuvant Osimertinib, 1st TKIs, Chemo-TKI, Immunotherapy and Chemotherapy for Resected EGFR-Mutant NSCLC – an Updated Network Meta-Analysis of 3300 Patients

Dr. Guang-Ling Jie[1], Miss Hong-Lian Lu[1], Miss Si-Yang Maggie Liu[1], Dr. Si-Yang Liu[1], Dr. Jia-Tao Zhang[1], Dr. Zhi-Hong Chen[1], Dr. Song-Rong Wang[1], Dr. Hong-Xia Tian[1], Dr. Song Dong[1], Dr. Ri-Qiang Liao[1], Dr. Wen-Zhao Zhong[1], Dr. Xue-Ning Yang[1], Dr. YI-LONG WU1[2]

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Background: Multiple adjuvant treatment strategies are available for resected epidermal growth factor receptor (EGFR)-mutant non-small cell lung cancer (NSCLC), but questions regarding the survival benefit and safety profile among these strategies remain unsolved. This abstract has previously been presented at ESMO Asia 2020.

Method: : A network meta-analysis was performed to compare the efficacy and safety of targeted therapy, immunotherapy, and chemotherapy for resected EGFR-mutant NSCLC. Electronic databases including PubMed, EMBASE and Web of Science were searched using relevant keywords. Randomized controlled trials comparing two adjuvant treatments for resected EGFR-mutant NSCLC patients were included. The primary endpoint was disease-free survival (DFS), and secondary endpoints were overall survival (OS) and grade ≥3 adverse events (AEs).

Results: Thirteen eligible trials involving 3300 patients and six treatment strategies were included. All EGFR-TKIs-based adjuvant therapies, including osimertinib (hazard ratio=0.23, 95% confidence interval: 0.16-0.33), chemotherapy followed by first-generation EGFR-TKI (Chemo-TKI; 0.34, 0.16-0.69) and first-generation EGFR-TKIs (1st EGFR-TKI; 0.62, 0.52-0.74), can provide significant DFS benefits compared with chemotherapy for EGFR-mutant NSCLC patients. DFS favored EGFR-TKIs-based adjuvant therapy when compared with immunotherapy. Adjuvant immunotherapy did not improve DFS when compared with chemotherapy (0.98, 0.64-1.50). In patients who were treated with adjuvant 1st EGFR-TKI, previous chemotherapy did not improve the DFS (0.54, 0.26-1.14) and OS (0.83, 0.15-4.52) benefit. In addition, no OS improvements were identified when comparing all the EGFR-TKI-based treatment with chemotherapy. Osimertinib showed the fewest toxic effects, whereas Chemo-TKI caused the most toxicity. In subgroup analysis, patients with EGFR exon 19 deletion, stage III disease, and adenocarcinoma can benefit more from adjuvant EGFR-TKIs therapy.

Conclusions: EGFR-TKIs-based adjuvant therapies can provide a significant DFS benefit compared with immunotherapy or chemotherapy for resected EGFR-mutant NSCLC, especially osimertinib. Adjuvant immunotherapy failed to show a DFS benefit versus chemotherapy. Adjuvant EGFR-TKIs could be an important treatment option for resected early-stage EGFR-mutant NSCLC, regardless of previous chemotherapy.

Image 1.
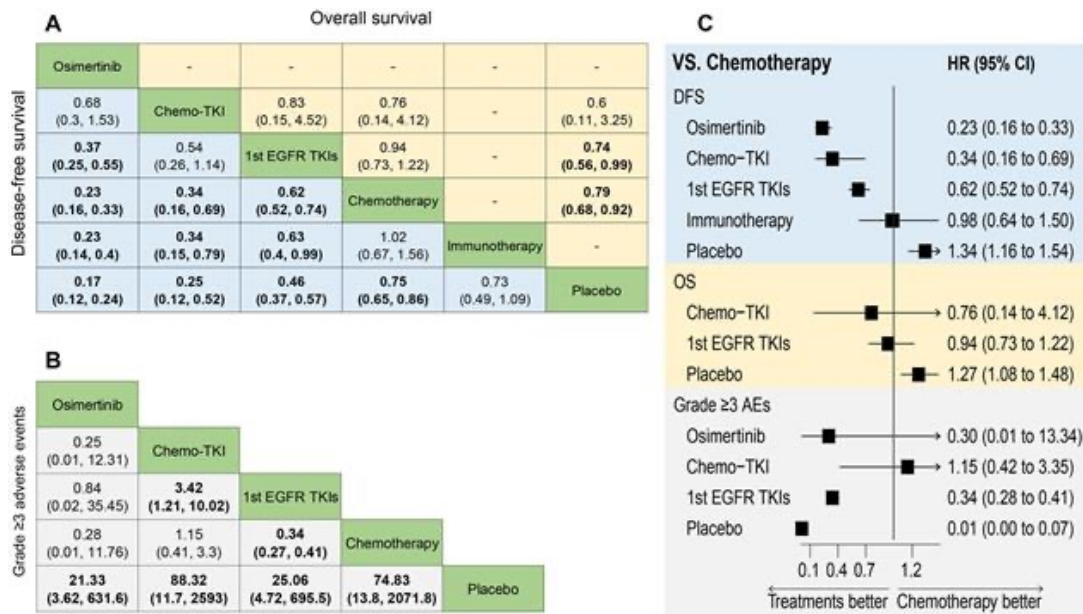
Figure 1: Pooled estimates of the network meta-analysis for resected epidermal growth factor receptor-mutant non-small cell lung cancer.
Pooled hazard ratio and 95% confidence interval for disease-free survival and overall survival (A) as well as pooled odds ratio for grade ≥3 adverse events (B).
Forest plot of individual agents versus chemotherapy on disease-free survival, overall survival, and grade ≥3 adverse events (C).

Image 1.

Figure 1A. Median PFS (months)
Nicotinamide : 12.7 (95% CI 10.4~18.3)
Placebo : 10.9 (95% CI 9.0~13.2)
Log–rank p=0.2

Figure 1B. Median OS (months)
Nicotinamide : 31.0 (95% CI 25.2~45.2)
Placebo : 29.4 (95% CI 20.3~35.6)
Log–rank p=0.2
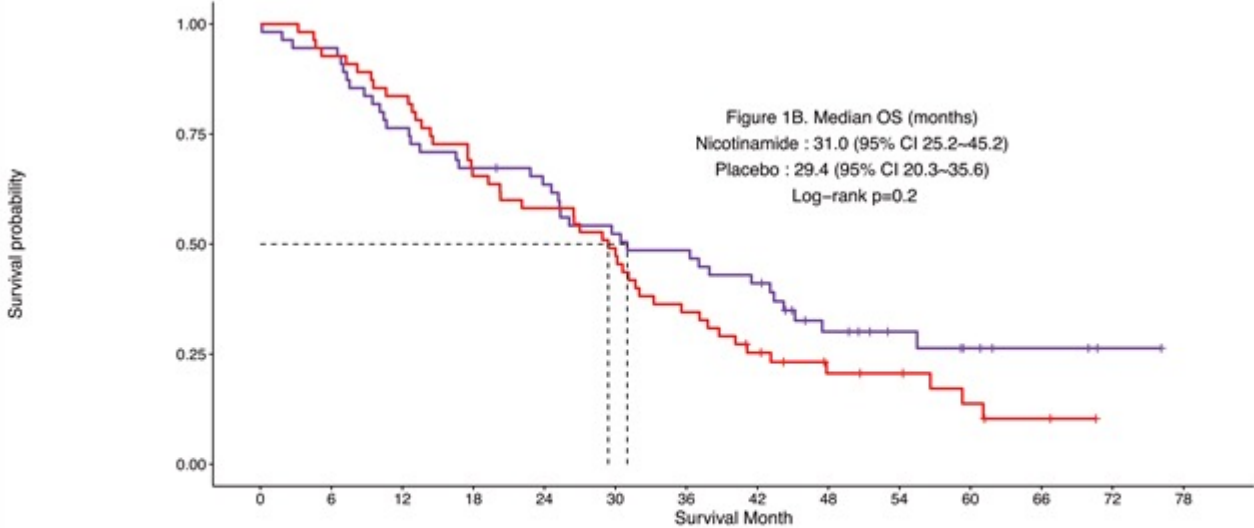
PV01.13:
Hippocampal Avoidance Whole Brain Radiotherapy with Simultaneous Integrated Boost – An Alternative to Stereotactic Radiosurgery?

Dr. Jai Prakash Agarwal[1], Dr. Anil Tibdewal[1], Dr Amani Bhogadi[1], Dr. Naveen Mummudi[1], Mr Ritesh Mhatre[2], Dr Rajesh Kinhikar[2], Dr Vijay Patil[3], Dr Vanita Noronha[3], Dr. Kumar Prabhash[3], Dr. Nivedita Chakrabarty[4], Dr. Trupti Pai[5], Dr. Amit Janu[4]
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Background: Stereotactic radiosurgery (SRS) for limited brain metastases (BM) has higher local control (LC), and better neurocognitive function (NCF) preservation but poorer intracranial control. Hippocampal avoidance whole-brain radiotherapy (HA-WBRT) with simultaneous integrated boost (SIB) could provide similar LC and NCF preservation and higher intracranial control rates.

Methods: A total of 36 patients with 83 metastatic lesions who received HA-WBRT-SIB from Nov 2017 – to April 2022 were included in this study. Hippocampus (HC) was contoured as per the RTOG 0933 protocol. The WBRT target volume was defined as brain parenchyma excluding the HA region. HA-WBRT-SIB plans were made with volumetric modulated arc radiotherapy and the intracranial response was assessed with MRI at every 3-month interval for the first year. Intracranial progression-free survival (icPFS) was calculated from the radiotherapy starting date till intracranial progression or death, whichever is earlier. Overall Survival was calculated from radiotherapy starting date till the date of death.

Results: The median age was 57 years (range, 29-78 years). Fourteen patients had a single BM lesion, 2 lesions (n-7), 3 lesions (n-5), and 4 lesions(n-10). Eight underwent surgical excision for at least one BM lesion. Twenty-eight patients had a synchronous presentation, 11 had EGFR activating mutations, 8 had ALK rearrangement, and 2 had ROS mutations. The median GPA score was 2.5. The median WBRT and SIB doses delivered were 30Gy and 50Gy in 10 fractions, respectively. The median of maximum, mean, and D100% received by the right HC were 15.4Gy, 9.4Gy, and 7.6Gy, respectively. For left HC, the same doses were 15.5Gy, 9.5Gy, and 7.5Gy, respectively. With a median follow-up of 19.5 months (IQR, 5.4-21.0 months), 82 lesions (98.7%) were locally controlled. Thirty-one patients had intracranial control and 5 patients developed intracranial failure but none within the hippocampal avoidance region. The median and 2-year icPFS were 20.4 months (95% CI, 18.4 -22.5) and 44.4%, respectively. The median and 2-year OS were 24.8 months (95% CI, 17 – 32.6) and 50%, respectively. Nine patients developed radiation necrosis after a median time of 12.6 months but none had $\geq$ grade 3 radiation necrosis.

Conclusion: HA-WBRT with simultaneous integrated boost for limited BM is a feasible, safe, and acceptable alternative to SRS and provides excellent local and intracranial control and should be explored in future randomized controlled trials.

PV01.14:
A Long Term Follow-Up of Papillary Thyroid Carcinoma Arising in Mature Cystic Mediastinal Teratoma

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Introduction: We reviewed the patient's database and analysed a 4-year follow-up case of papillary thyroid carcinoma arising in mature cystic mediastinal teratoma by considering chest CT scan and thyroid CT scan, bronchoscopy, pulmonary function, tumour marker (AFP and B-HCG) and thyroid hormones.

Case Report: In 08/2018, a 36-year-old female presented to our academic hospital in Riau province of Indonesia with complaints intermittent episodes of right chest pain, shortness of breath and cough. Chest CT scan revealed a rounded-well defined enhacement inhomogen solid mass containing fat and calcification in mediastinal anterior. Lobectomy of the right upper and middle lobe with total excision of the tumor was performed. Histopathology examination revealed papillary thyroid carcinoma arising in mature cystic teratoma. The patient underwent extensive evaluation of the thyroid gland with CT scan which revealed no evidence of a mass. The patient was remained asymptomatic and no further need for chemotherapy. The patient has been in long term follow-up at our hospital, we observed tumour markers level (AFP and B-HCG), chest and thyroid CT-Scan, bronchoscopy and also pulmonary function test and no sign of disease relapse or further treatment related to complication.

Discussion: Mature teratomas, which represent approximately 60% to 70% of mediastinal germ cell tumors, are usually well-differentiated and benign. Complete surgical removal of the primary tumour is an essential component of treatment for the majority of patients with teratoma. We report this case of a patient because such a long time follow up of papillary thyroid carcinoma arising in mature cystic mediastinal teratoma is uncommon and needs to be reported. Multidisciplinary management has been crucial in this case because of the presence of concomitant diseases and consequently, differential diagnosis challenges.

Image 1.

Image 2.

Table 1.

Table 2.
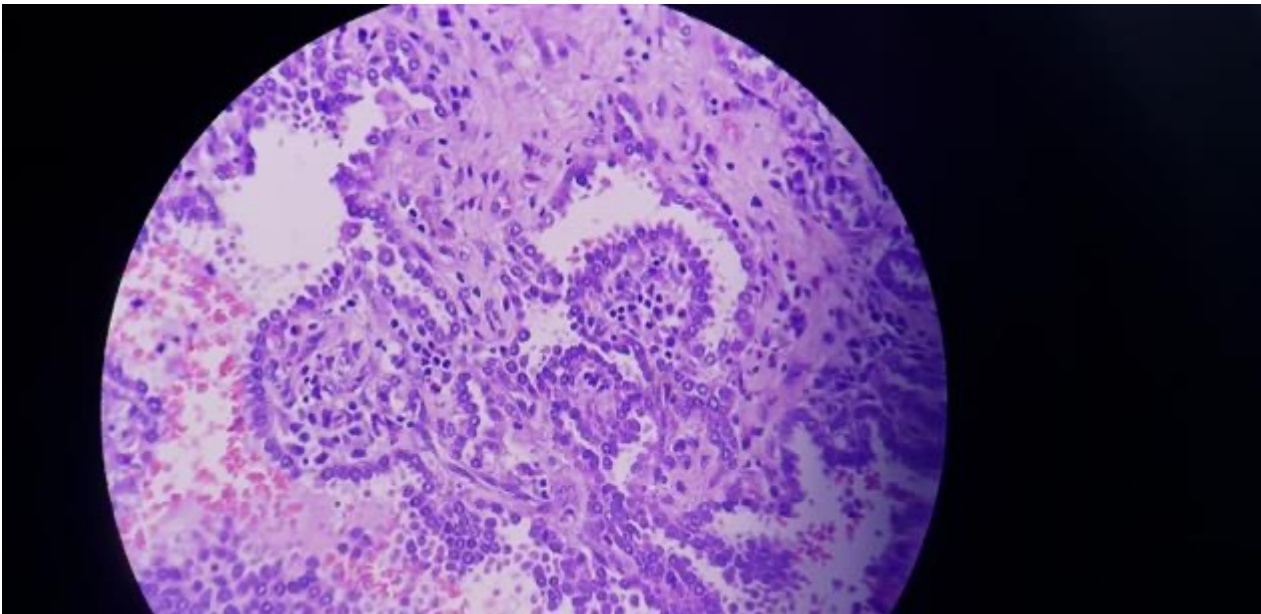
PV01.15:
Randomized Double-Blind Placebo-Controlled Trial of Nicotinamide and EGFR-TKIs for EGFR-Mutated Lung Adenocarcinoma

Prof. Young-chul Kim[1], Prof. In-Jae Oh[1], Prof. Cheol-Kyu Park[1], Prof. Hyung-Joo Oh[1], Prof. Il Yeong Park[2], Prof. Suk-Chul Bae[3]

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Runt-related gene 3 (RUNX3) inactivation by promoter hypermethylation correlates with poor clinical outcome and occurs in 70% of lung adenocarcinomas. Nicotinamide, a well-known sirtuin inhibitor, re-activates the epigenetically silenced tumor suppressor RUNX3 in cancer cells. We examined whether the addition of nicotinamide to epidermal growth factor receptor tyrosine kinase inhibitors (EGFR-TKIs) increases the survival of patients with stage IV lung cancer with EGFR mutations (exon 19 deletion or L858R). This abstract was presented as an ePoster at WCLC 2020.

From 2015 to 2018, a total of 110 consecutive patients were randomized into nicotinamide (1g/day, n=55) or placebo (n=55) groups, stratified by EGFR mutation status, ECOG PS, and type of TKIs. Nicotinamide or placebo was administered upto 2 years. The mean age was 68.5 years, and 63.6% were female and 76.4% were never-smokers. Gefitinib was used in 59.1% of patients and erlotinib in the remaining 40.9%, resulting in an objective response of 56.0%. The number of adverse events, such as skin rash, mucositis, and diarrhea, was not significantly different between the two groups.

After a median follow up duration of 54.3 months, the median PFS of the nicotinamide group was 12.7 months (95% confidence interval: 10.4~18.3) whereas that of the placebo group was 10.9 months (9.0~13.2) (Log-rank p=0.2, Fig 1A). After a median follow up of 58.4 months, the median OS of the nicotinamide group was 31.0 months (25.2~45.2) whereas that of the placebo group was 29.4 months (20.3~35.6) (p=0.2, Fig 1B).

After progression, the EGFR T790M mutation was found in 44 (40.0%) of patients using re-biopsy or plasma DNA samples, and third generation EGFR TKIs were used in 42 (38.2%) subjects, without a significant difference between the two groups.
In conclusion, PFS and OS were numerically longer when EGFR TKIs were used in combination with nicotinamide than TKIs alone. (NCT02416739)

PV01.15:
Treatment Outcomes of Surgery and SBRT for Early Lung Cancer

Assistant Professor Chi Young Kim[1], Assistant Professor Beong Ki Kim[2], Assistant Professor Eun Hye Lee[1], Associate Professor Eun Young Kim[1], Professor Yoon Soo Chang[1]

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Background: The optimal treatment of early stage lung cancer who can tolerate surgery, lobectomy and systematic mediastinal lymph node dissection or sampling is still the standard treatment. While for patients with poor lung function or medically inoperable patients are considered as the preferred treatment method for inoperable patients with early lung cancer. However, the efficacy of the stereotactic body radiotherapy(SBRT) and surgery remains controversial.The aim of this study was to compare overall survival and outcomes of surgical resection and SBRT.

Methods: We systematically reviewed studies from PubMed, Embase, and Corchrane Library up to march 30, 2022. Data for analysis mainly included overall survival (OS) and disease-free survival (DFS), which were obtained directly from the results or calculated from the Kaplan–Meier survival curve.

Results: Total of 10,813 early lung cancer who received wedge resection or SBRT were included. The results showed that patients receiving wedge resection had a significantly better OS (HR = 1.19, 95% CI = [1.05-1.36], P = 0.007) than those with SBRT, but no significant difference of DFS was observed. There was no significant heterogeneity during our analysis, but there may be potential publication bias among these studies.

Conclusions: Our meta analysis showed that early lung cancer with surgical resection had superior OS than those treated with SBRT. However, more prospective clinical trials should be well-designed to evaluate the optimal treatment modality of early stage lung cancer.

PV01.16:
Pilot Study for Early Diagnosis of Lung Cancer in a Public Hospital in Northeast Brazil

Professor Carlos De Araújo[1], Radiologist Ingrid Mendonça Pires Ferreira[1], Student Ytallo Oliveira Barros[1], Student Paulo Roberto Nóbrega Costa[1], Student Eliane Nadine Tavares de Carvalho[1], Co-author Ana Carolina Zimmermann[1]
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Lung cancer is currently the world's highest mortality and incidence. According to information from the National Cancer Institute (INCA), it is the cancer with the highest mortality in Brazil, accounting for 27,931 in 2017, being only the fourth in incidence. The Institute estimates 31,270 new cases for the year 2019. A good prognosis is directly related to treatment in the early stages of the disease. However, according to INCA, only about 16% of cases in 2016 were reported in early stages, which reduces the chances of treatment and cure.

The scientific literature is abundant demonstrating the effectiveness of early diagnosis in reducing lung cancer mortality, since the seminal paper published in the New England Journal of Medicine, demonstrated the effectiveness of screening using low-radiation computed tomography in patients with high smoking habits for the early diagnosis of lung cancer. In Brazil, the implementation of a national public health plan for screening and early diagnosis is extremely difficult due to the lack of public resources for this purpose. In addition to the situation in Brazil, the State of Rio Grande Norte (RN), where it accounts for less than 1% of the Brazilian GDP. Highlighting our poverty. As an alternative way of showing our epidemiological reality, Brazil is considered an endemic area for tuberculosis, we designed a project to screen patients admitted to the University Hospital in Natal, the capital of RN.

Thus, the main objective of the present study is to diagnose lung cancer early in a sample of a population at risk consisting of patients hospitalized at the Onofre Lopes University Hospital during the study period, aged between 55 and 75 years, who are "heavy smokers" " - that is, who have a smoking history (calculated from the number of cigarettes consumed daily and the time of smoking) greater than or equal to 30 packs/year - or who have had the same smoking profile and have stopped smoking less than of 15 years.

With the described action, it is expected to reduce the lung cancer mortality rate in our country from the early detection of cancer and the possibility of a surgical treatment at a stage in which the disease can be cured. We also hope to demonstrate the effectiveness of screening and early diagnosis in a population of a poor state in Brazil. In this way, hopefully, we could have the implementation of a national public policy in Brazil.

Image 1.

Image 2.

Abstract Author Index

L

M

N

O

P

Q

R

S

X

Y

Z