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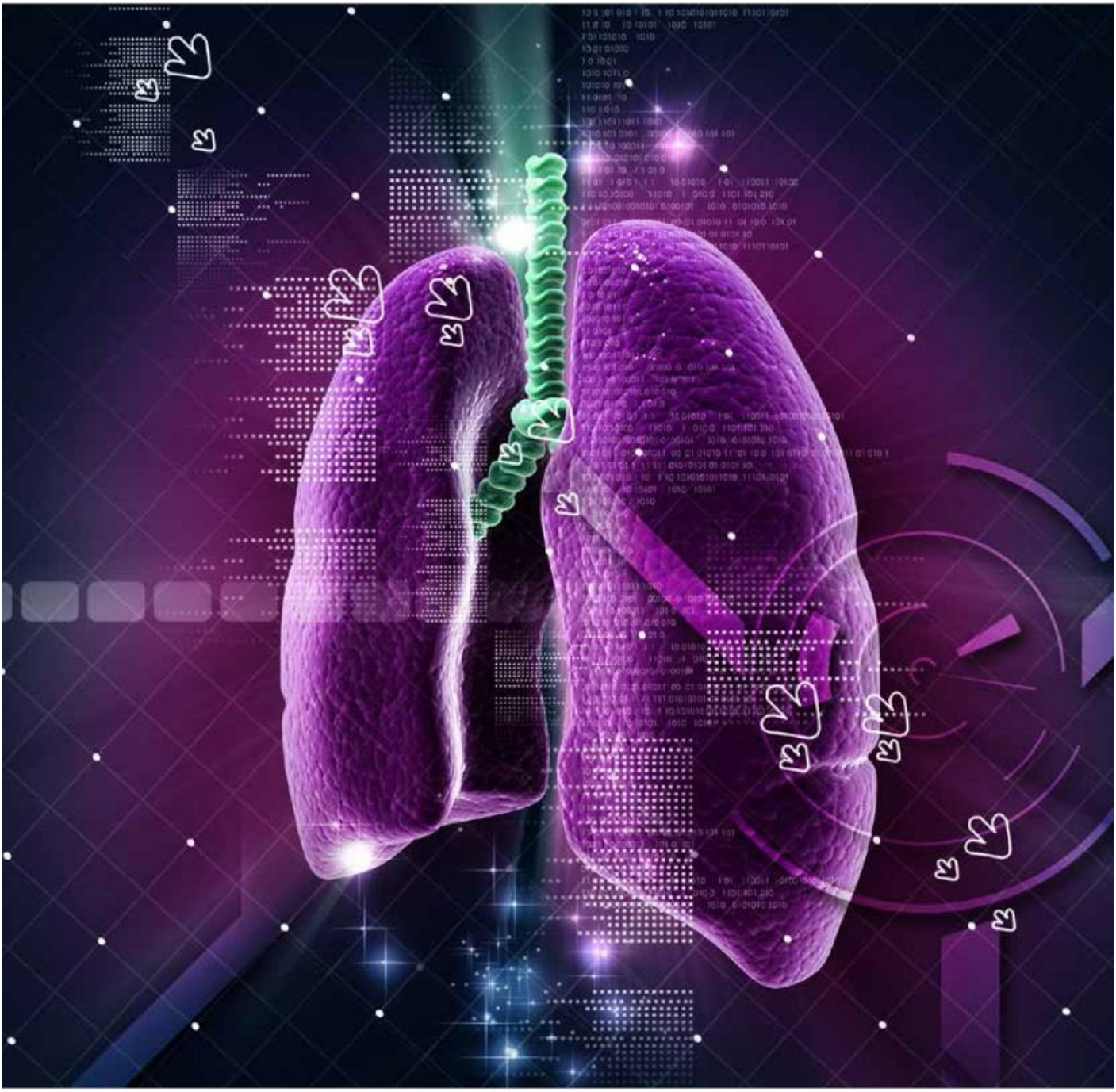
ABSTRACT BOOK



Bio events

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Poster Board #1

Molecular Profiling and Predicting Biomarkers for Immunotherapy

Predictive Biomarkers of Survival for Metastatic Non-Small Cell Lung Carcinoma Patients Treated with Nivolumab – are Pre-Treatment Differential Leukocyte Count and Systemic Inflammation Relevant?

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Introduction:
Nivolumab (Nivo) improved overall survival (OS) and progression-free survival (PFS) among patients (pts) with metastatic Non-Small Cell Lung Carcinoma (mNSCLC). Peripheral blood/serum biomarkers are attractive due to their accessibility. Modified Glasgow Prognostic Score (mGPS) is an inflammation-based score with prognostic value in lung cancer. We investigated predictive pre-treatment peripheral blood/serum biomarkers among mNSCLC pts treated with Nivo.

Methods:
Data of mNSCLC pts treated with Nivo at Hospital São João, Portugal, were retrospectively collected. Pre-treatment absolute lymphocytes count (ALC), absolute neutrophils count (ANC), absolute eosinophils count (AEC) and neutrophil-lymphocyte ratio (NLR) were dichotomized. mGPS was calculated using pre-treatment albumin and . Survival was estimated with Kaplan-Meier method and curves were compared by log-rank test. Multivariate analysis was performed using Cox proportional hazard model.

Results:
55pts were included. PFS and OS were 5.0 and 9.0 months (mo), respectively. Adverse effects (AE) occurred in 25.5%. AEC≥50/µl was associated with superior OS (11.0 vs 6.0mo, p=0.020) and PFS (7.0 vs 2.0mo, p=0.021). A lower mGPS was associated with superior OS (1: 7.0 vs 2: 4.0 mo, p=0.051) and PFS (p=0.006), (1: 4.0 vs 2: 2.0mo, p=0.006); more than 50% mGPS 0 pts were alive with controlled disease. A trend towards inferior PFS with NLR≥5 and superior PFS and OS with ALC≥1000/µl was noticed, without statistical significance. Other correlated variables (p0.03) were: ECOG, number (nr) metastatic sites, nr previous treatments, time since previous treatment and AE occurrence. Adjusting for ECOG, nr metastatic sites and AE occurrence, mGPS (p=0.021) and AEC (p=0.05) were associated with superior PFS. Concerning OS and adjusting for the same variables, mGPS was close to achieve significance (p=0.064).

Conclusion:
Pre-treatment AEC and mGPS influenced OS and PFS. Although the potential predictive value of pre-treatment differential leukocyte count and systemic inflammation was demonstrated, these results need confirmation in larger and prospective studies.

Poster Board #2

Molecular Profiling and Predicting Biomarkers for Immunotherapy

Induction of Stable Disease with Combination of Immunotherapy plus Chemotherapy in Metastatic Non-Small Cell Lung Cancer: A Case Report

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ABSTRACT of an inhibitory checkpoint that helps protect against autoimmunity by acting as ported a metastatic non-small cell lung cancer (NSCLC) case to received monoclonal Programmed death ligand 1 (PD-L1) is part negative regulators of activated T cells. immunotherapy with nivolumab plus chemotherapy with a stable disease for more than six months. A 46-year-old female with bone metastatic adenocarcinoma of the lung, a history of chronic cough and hemoptysis referred to the Clinic. The computed tomography (CT) scan showed an increased irregular pleural thickness in mediastinal and parietal pleura and liver metastasis. She received erlotinib as the first line treatment and switched to paclitaxel/carboplatin plus bevacizumab and then maintenance therapy. The CT scan showed us better result after nivolumab plus pemetrexed therapy for eight cycles rather than before the policy of treatment. In conclusion, nivolumab-pemetrexed combination therapy can improve survival and reduced progression in metastatic NSCLC patients. But considering to epidermal growth factor receptor mutation and the PD-L1 percentage can be very important in a selected protocol of treatment and improvement of survival of the patient

Poster Board #3

Molecular Profiling and Predicting Biomarkers for Immunotherapy

High Level of EGFR Prevents Apoptosis Induction Mediated by Sulforaphane-Induced Reactive Oxygen Species in Non-Small Cell Lung Cancer Cells

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Sulforaphane (SFN) has been shown to induce production of reactive oxygen species (ROS) and to inhibit epidermal growth factor receptor (EGFR) mediated signaling in non-small cell lung cancer (NSCLC). NSCLC cells harboring constitutive active EGFR mutations are more sensitive to the SFN treatment than cells with wild-type EGFR, yet it is not known if the NSCLC cells with high expression level of EGFR may be more resistant or sensitive to the SFN treatment. In this work, we employed a set of cell lines, CL1-0 and CL1-5, which have the same genetic background but different levels of EGFR expression, to examine the effects of high EGFR level in the sensitivity to SFN. Here, we present evidence that cells with high-level EGFR (CL1-5) are more resistant to SFN treatment than the CL1-0 cells. Treatment of SFN produced similar increase of ROS and induced an arrest of cell population at S-phase which was accompanied with the induction of γH2AX, a DNA damage response marker, in both cells. However, induction of apoptosis by SFN was only observed in CL1-0 cells, but not in CL1-5 cells. Pretreatment with N-acetyl-L-cysteine (NAC) prevented the apoptosis induction in CL1-0 cells and the SFN-induced production of γH2AX in both CL1-0 and CL1-5 cells. shRNA mediated knock-down of EGFR in CL1-5 cells rendered the cells susceptible to SFN-induced apoptosis. These results suggest that high level of EGFR expression prevented the apoptosis induction by SFN-induced ROS in NSCLC cells, which may account for the increased resistance to SFN in these cells. Despite of this, we presented evidence that SFN could inhibit tumor growth of NSCLC with high-level of EGFR expression in vivo.

Poster Board #4

Molecular Profiling and Predicting Biomarkers for Immunotherapy

Inter-Tumor Heterogeneity of PD-L1 Expression in Non-Small Cell Lung Cancer

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Background:
Following to approval of Pembrolizumab for patients with advanced NSCLC, PD-L1 IHC 22C3 pharmDx (Dako) was adopted as a companion diagnostic test. However heterogeneity of immunohistochemistry has been one of clinical issues in a few years.

Objective:
We aimed to make a proof of inter-tumor heterogeneity of immunohistochemistry.

Methods:
Between December 1, 2014 and May 7, 2018, total 517 patients with NSCLC underwent surgical resection at our hospital. We excluded all patients with no informed consent, with no lymph node metastasis, with chemotherapy/radiotherapy before surgery and with never enough volume of material for genetic testing. Finally 34 formalin-fixed paraffin-embedded primary tumors with paired metastatic lymph nodes were available in this study. After PD-L1 immunohistochemistry 22C3 pharmDx (Dako) staining, we determined Tumor Proportion Score (TPS) on each slide, making three subgroups as follows; No Expression (TPS: 1%), Low Expression (TPS: 1-49%) and High Expression (TPS: ≥50%).

Results:
Average age of 34 patients was 66.8 years old and there were 9 females (26.5%), 9 never smokers (26.5%), 26 adenocarcinomas (76.5%) and 11 tumors with EGFR mutation. The number of cases in No Expression, Low Expression and High Expression were 7 (20.6%), 21 (61.8%) and 6 (17.6%) in primary tumor, meanwhile 16 (47.1%), 14 (41.2%) and 4 (11.8%) in metastatic lymph node, respectively. The concordant rate was 32.4% between TPS subgroups in primary tumor and that in metastatic lymph node.

Conclusion:
Our result demonstrated apparent discrepancy between PD-L1 IHC 22C3 expression in primary tumor and that in paired metastatic lymph node.

Poster Board #5

Molecular Profiling and Predicting Biomarkers for Immunotherapy

Circulating Tumor DNA Signature to Predict Response to Immunotherapy in Non-Small Cell Lung Cancer (NSCLC)

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Background:
Immunotherapy become a backbone in NSCLC therapy for all patients. Tissue based biomarkers such as PD-L1 expression, tumor mutation burden (TMB), genomic alterations in EGFR/ALK/ROS1 and KRAS/TP53/STK11 mutations, all competing for limited tissue biopsy samples, are able to predict response (or lack thereof) to therapy. Therefore, we investigated whether these biomarkers can be detected from a non-invasive plasma sample. Challenges of assessment of TMB with cell-free DNA next-generation sequencing (NGS) include the limited size of liquid biopsy gene panels and the fact that low shedding of tumor DNA into circulation may fail to detect hypermutated tumors.

Method:
In this retrospective study, data was collected from NSCLC patients treated in multiple medical centers in Israel between 2014 and 2017. We used NGS on cell-free circulating tumor DNA (ctDNA) to evaluate whether mutational burden and specific genomic alterations influence the response to immunotherapy in these patients. Response to immunotherapy was defined by a cutoff of four months of progression free survival (PFS).

Results:
Overall, 336 NSCLC patients underwent NGS on ctDNA. Of these 336 patients, 192 (57%) were females and 144 (43%) were males. The average age (range) was 64 (23-103) years. Clinical treatment information is currently available for 117 patients, of whom 50 (43%) received immune check-point inhibitors; complete data was examined for 27 patients. One patient was treated with immunotherapy in first line, 18 patients received immunotherapy in second line and 8 patients received immunotherapy in third line or more. Thirteen patients were considered as responders and 14 patients as progressors. cfDNA signature will be further presented based on a 73-gene cfDNA NGS panel that adjusts for the degree of tumor shedding.

Conclusion:
ctDNA collection was feasible in 336 patients, amongst which 27 were treated with immunotherapy. Application of multifactorial mutational load approach to this pilot advanced NSCLC cohort is promising as it integrates TMB and prediction of immunotherapy response.

Poster Board #6

Early Detection of Lung Cancer (Update & Biomarkers)

Radiological and Clinical Findings of Pulmonary Mucinous Adenocarcinoma; Experience in Japan

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Background:
Pulmonary mucinous adenocarcinoma (PMA), a rare variant form of pulmonary adenocarcinoma, is radiologically characterized by pneumonic consolidation, ground-glass opacity (GGO) and nodule. The true diagnosis sometimes delays especially in consolidation type that resembles infectious or organizing pneumonia.

Objective:
The purpose of this study is to summarize radiological and clinical findings of our consecutive cases with PMA and to determine how to manage PMA patients for early diagnosis.

Methods:
This study involved 53 consecutive cases with pathologically proven PMA between 2011 and 2018 at IbarakiHigashi National Hospital. We retrospectively analysed their clinical courses and radiological and pathological findings. In this study, we defined PMA as primary lung cancer that pathologically had goblet cell or tumor cell producing mucin. We classified those patients into two groups, based on the high-resolution CT findings as follows: group A (pneumonic type, N=15), in which the shadow represented consolidations that mimic pneumonia, and group B (GGO or nodular type, N=38).

Results:
Seventy-three percent of those cases, especially patients in group A (86%), were predominantly located in the lower lobes. Most of group A cases tended to have more respiratory symptoms. Three cases were misdiagnosed as infectious pneumonia and 2 cases were done as organizing pneumonia and treated with corticosteroids. Eighty percent of the type A patients and 23% of the type B patients were accurately diagnosed by flexible bronchoscopy. Normal body temperature and serum CRP could serve to distinguish from pneumonia, whereas CEA or CYFRA did not in this study. Curative surgical resections were undertook in 40% of the group A patients and 86% of the group B.

Conclusion:
This study suggests that the cases, showing non-resolving pneumonia in lower lobe even after treatment with antibiotic or corticosteroid, should be actively examined by bronchoscopy for early detection and curative treatment of PMA.

Poster Board #7

Early Detection of Lung Cancer (Update & Biomarkers)

Can Liquid Biopsies be used to Identify Lung Cancer Biomarkers?

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Background:
With the increasing and fast development of molecular medicine, we can aspire to carry out treatments directed to the sickness of each patient, and with this practice the idealized precision medicine.

Objective:
Its objectives are not only survival and response rates, but also best quality of life with lowest toxicity, with more cost-effective choices for each single patient.

Method:
Defining the complete genomic picture of all cancerous lesions, in the near future, is a major goal in Oncology that will benefit everyone. The further and recent use of liquid biopsies, processed by next generation sequencing , as a method to determine specific genetic mutations, has obtained clinical utility and validity in the metastatic scenario, with a predictive value.

Conclusion:
Further clinical trials need to be performed in surgical cases, so that specific gene mutations can be used as biomarkers, to evaluate residual disease, stratify risk of relapse (prognostic value) and identify the patients that will need adjuvant treatment besides the classical staging system.

Keywords: Precision Medicine, Circulating Tumor DNA, Liquid Biopsies, Biomarkers.
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Poster Board #8

Radiotherapy

Oral Administration of Herbal Medicines for Treating Radiation Pneumonitis in Lung Cancer Patients: Protocol for a Systematic Review and Meta-Analysis

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Introduction:
Thoracic radiotherapy in lung cancer can induce lung injury in acute phase, called radiation pneumonitis (RP), but there are no specific treatments except oral corticosteroid. Therefore, many clinical trials using herbal medicine have been implemented for RP treatment. In present study, the objective is to evaluate the effectiveness and safety of herbal medicine for RP treatment in lung cancer patients.

Methods and Analysis:
In present study, we will use the following databases; 3 English medical databases (MEDLINE (PubMed), EMBASE and The Cochrane Central Register of Controlled Trials (CENTRAL)), 5 Korean Medical Databases (Korean Studies Information, Research information Service System, KoreaMed, DBPIA, National Digital Science Library) and 2 Chinese Medical Databases (the China National Knowledge Database (CNKI) and WanFang Database). 2 reviewers will screen the searched studies independently, determine suitability for inclusion and perform data extraction. When adequate, the data will be extracted from studies for meta-analysis using a fixed or random effects model. The risk of bias will be assessed according to the Cochrane Risk of Bias tool.

Results:
This study will evaluate the effectiveness and safety of herbal medicine for RP. The primary outcome will be effective rate and secondary outcome will include clinical symptoms, treatment periods, the Karnofsky performance status score, Pulmonary function test, CXR or CT, the blood tests such as cytokines, thymus dependent lymphocytes (T Lymphocytes), natural killer cell (NK cell), and adverse events.

Conclusion:
Clinicians and patients may find out the therapeutic efficacy of herbal medicine for RP through this review. It can be helpful to decide the use of herbal medicines for RP occurred after radiotherapy in lung cancer patients.

Poster Board #9

Tissue Analysis in the Era of Precision Cancer Care

Large Pericardial Effusion in Lung Cancer Patients: New Considerations in the Era of Advanced Molecular Diagnosis

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Introduction:
Significant pericardial effusion in lung cancer is associated with poor prognosis, yet successful therapeutic intervention may improve quality of life and prolong survival. The appropriate surveillience and management of pericardial effusion in lung cancer (LC) is not yet clearly defined.

Methods:
We documented all cases of patients with lung adenocarcinoma who were admitted to the cardiology or cardiothoracic surgery departments due to large (>500 mL) pericardial effusion, in Beilinson Hospital, between the years 2014-2017. We then assigned a control group randomly chosen from all patients with lung adenocarcinoma lung cancer who visited the thoracic cancer department in Beilinson Hospital in 2016.

Results:
Twenty- six patients with a large pericardial effusion were included in the study group; fifty- two patients were included in the control group. The mean age was 57.6 (median 59, range 20-80) in the study group versus 68.9 (69, 50-91) in the control group. Women constituted fifty-seven percent (15/26) of the study group, versus 30% (16/52) of the control group. Active or past heavy smokers constituted 53% (14/26) versus 65% (34/52) of study and control groups, respectively.
Thirteen (50%) patients in the study group had an EGFR/ ALK mutation harboring tumor (EGFR 9, ALK 4), versus only 27% (EGFR 12, ALK 2) in the control group.
Sixteen patients had gone through pericardiocentesis as the initial procedure of choice for the management of the pericardial effusion; in ten, recurrence of the effusion results in the creation of pericardial window in the cardiothoracic surgery unit. In seven patients, pericardial window was chosen as the initial procedure.
Twenty (76%) of pericardial effusions were diagnosed as malignant by fluid cytology. Nine (45%) of patients with malignant pericardial effusion had EGFR/ALK mutation-harboring tumor.

Conclusion:
The percentage of patients with EGFR/ ALK mutation harboring tumors was higher in the study group compared with control group. These findings might indicated that detection of driver mutations in LC has to stipulate active surveillance for pericardial effusion.