316. Treatment of lung cancer

P2912 Synergistic therapy for NSCLC: Additive preclinical efficacy of interleukin-6 inhibitor madindoline A with crizotinib
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Backgrounds and aims: Crizotinib has also demonstrated the development of secondary mutation, resistance of crizotinib
Acquired drug resistance. Despite secondary mutation, resistance of 
crizotinib may also be influenced by tumor microenvironment. Senescent cells display a senescence-associated secretory phenotype (SASP) involving the production of inflammatory cytokines that alter tumor microenvironment. Here, we analyzed the level of IL-6 and its signaling pathway in NSCLC cells and assessed the efficacy of IL-6 inhibitor madindoline A in combination with crizotinib in vivo.

Methods: We detected senescence, SASP, IL-6/STAT3 and PI3K/AKT/mTOR signaling after crizotinib treatment in the presence or absence of madindoline A. Combined treatment with madindoline A and crizotinib exhibited significant inhibition of tumor growth in NSCLC cell xenografts in nude mice.

Conclusion: IL-6 is essential for the survival of premature senescence NSCLC cells treated with crizotinib. Study of the syngeneic model may be a novel therapeutic option for NSCLC patients with failed BEV treatment.

P2915 Pemetrexed in the first line treatment in non-small cell lung cancer (NSCLC): A multicentre prospective analysis of data from clinical practise of Czech Republic
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Methods: From January 2005 through December 2011. Induction chemotherapy consisted of cisplatin, and etoposide; and concurrent radiotherapy to a mean of 59.3 Gy. Lung resection was performed within 6 weeks of completion of chemoradiation.

Results: Twenty-five patients were submitted to surgery—one, 10 to lobectomies and 5 either to segmentectomies or atypical resections. The overall mortality rate was 2.5% (one died in the lobectomy group). No important morbidity was noted and the overall hospital stay ranged from 7 to 14 days.

Conclusion: Chemoradiation before pulmonary resection in carefully selected patients with surgically resectable stage IIA (N2) non-small cell lung cancer can be performed with low mortality and morbidity and might lead to improved overall and disease-free survival.

P2914 Improved results after preoperative concurrent chemotherapy and high dose radiation therapy in selected cases with stage III N2 lung cancer? Kallipigi Athanassiadis1, Evangelos Bali1, Nectarius Alezopoulous1, Dimitris Liounampus2, Maria-Kalliopi Konstantinidou1, Iakovos Tool1, Irini Mavromati3, Argini Psykh4, Lucilla Comis2, Despina Violaki2, Dimitra Romdougliani1, Ion Bellenis1, 1Thoracic Surgery, 2Pulmonology, 3Oncology, 4Anaesthesiology, 5Pathology, General Hospital “Evangelismos”, Athens, Greece

Objective: Optimal management of stage IIIA-N2 non-small cell lung cancer remains controversial. The use of neoadjuvant chemoradiotherapy can present challenges in the prospective management of patients undergoing lung resec-
tion for non-small cell lung cancer. Preoperative chemoradiotherapy may reduce pulmonary function, and can result in significant fibrosis around key anatomic structures, making dissection difficult and hazardous.

Methods: This is a retrospective study of 40 consecutive patients with T1-3 N2 M0 lung cancer who underwent induction chemoradiation before surgical intervention from January 2005 through December 2011. Induction chemotherapy consisted of cisplatin, and etoposide; and concurrent radiotherapy to a mean of 59.3 Gy. Lung resection was performed within 6 weeks of completion of chemoradiation.

Results: Twenty-five patients were submitted to surgery—one, 10 to lobectomies and 5 either to segmentectomies or atypical resections. The overall mortality rate was 2.5% (one died in the lobectomy group). No important morbidity was noted and the overall hospital stay ranged from 7 to 14 days.

Conclusion: Chemoradiation before pulmonary resection in carefully selected patients with surgically resectable stage IIA (N2) non-small cell lung cancer can be performed with low mortality and morbidity and might lead to improved overall and disease-free survival.

Methods: We retrospectively investigated the clinicopathological characteristics of 26 NSCLC patients who had undergone BEV therapy in Saitama Medical University International Medical Center and Saitama Medical University Hospital. The patients had a median age of 64 years (range, 33 to 75 years), and 19 males and current smokers. Epidermal growth factor receptor gene mutations were found in 6 patients (23%). Combined with BEV, each half of 26 patients received the chemotherapeutic regimen of either carboplatin/paclitaxel or carboplatin/pemetrexed. Objective response rate was 54% and disease control rate was 96%, and median progression free survival and overall survival were 100 days and 202 days, respectively. Adverse events included 4% of arthrythemia, 27% of hypertension, 8% of lower gastrointestinal bleeding, 19% of nasal bleeding, and 23% of proteinuria. When Kaplan-Meier survival curves and logrank tests, ther-
apic response influenced neither progression free survival nor overall survival, whereas longer overall survival was observed in NSCLC patients treated with pemetrexed-containing chemorhapy after failure of BEV.

Conclusion: Therapeutic response to BEV does not predict survival benefit of BEV-treated NSCLC patients. Meanwhile, pemetrexed may be a novel therapeutic option for NSCLC patients who have failed BEV treatment.

Poster Discussion
ROOM C6 - 14:45 - 16:45

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in 6.0% and thrombocytopenia in 1.2% pts, but the therapy was finished due to toxicity only in 6 (4.4%) patients. Median OS (95% CI) was 12.5 months (7.5, 17.5). Probability of one-year survival was 52.2%. PFS (95% CI) was 3.9 (3.4, 4.5) and probability of 6-months PFS was 38.9%. The best OS survival (13.5 months) was in pts with adenocarcinoma. We don’t find the differences between groups of pts according smoking (p=0.532), sex (p = 0.696) and PS (p = 0.131).

Conclusions: Patients treated with cisplatin as the first line treatment was well tolerated (only 4.4% of pts finished therapy due to toxicity), with evidence of antitumour activity in adenocarcinomas. The results from clinical practice of Czech Republic are comparable with the results of registration study.

P2916 Non-small cell lung carcinoma-advanced disease (NSCLC-AD): Effectiveness of subsequent therapeutic lines and predictive factors of poor outcome
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Five years observational study (2006-2010) of a cohort of patients with NSCLC-AD (1st line monotherapy excluded). Epidemiology, histology, performance status (PS), therapy, response – disease control (DC) or progression (n-DC), progression free survival (PFS) and overall survival (OS) after each therapy were evaluated. We also tried to assess predictors for DC and OS.

Results: We included 276 patients, 77.9% men, mean age 63.1 years (+/-10.9), most of them smokers (36.6%) with PS 1 (89.1%). The most frequent histology was adenocarcinoma (59.8%). Metastasis in L, 2 or 3 organs was found in 65.2%, 31.2% and 3.6% of the patients. All patients were initially treated with a platinum-based duplex; Pemetrexed or Erlotinib were the most used in 2nd-line setting (53.9% of the patients) and Erlotinib in 3rd (15.6% of the patients). There was a progressive reduction of the DC rate along the three lines: 71.7%, 67.1% and 51.2%. The median PFS and OS for each line were: 1st- 4.53M ± 0.22 and 10.24M ± 0.80, 2nd- 2.47M ± 0.21 and 9.1M ± 0.66, 3rd:- 4.47M ± 0.68 and 10.42M ± 3.35. Prognostic factors were: smoking status (HR 1.54, p-value 0.016), the presence of metastasis=1 organ (HR 1.50, p-value 0.003), PS2 (HR 3.62, p-value<0.001) and n-DC after 1st line (HR 2.71, p-value<0.001). The presence of DC after each line did not predict subsequent DC (HR 0.99, p-value>0.05), but the PFS after 1st line correlates with the following PFS (p-value 0.001).

Conclusions: There is an increase in OS and PFS in the 3rd line, probably reflecting the influence of new biological treatments. Strong predictors for a poor outcome were PS 2 and n-DC after 1st line.

P2917 Prevalence and effectiveness of third-line therapy for advanced non-small cell lung cancer (A-NSCLC)
Catarina Ferreira, Lívia Figueiredo, Fernando Barata. Pulmonology Department, Hospital Geral, Centro Hospitalar e Universitário de Coimbra, Portugal

Background: Systemic chemotherapy is the main option for A-NSCLC. Few patients receive third-line therapy and in this setting little is known about outcomes.

Objectives: Evaluate demographics, histology, performance status (PS), sites of metastasis, toxicity, progression-free survival (PFS) and overall survival (OS) in patients with A-NSCLC treated with third-line therapy.

Methods: We reviewed 5 years of clinical practice (Jan 2006 - Dec 2010): 676 patients with A-NSCLC were diagnosed and 330 received systemic chemotherapy. Of these, 44 completed 3 lines.

Results: 73% male, mean age 61.8y ± (9.4). Smoking status: 36% non-smokers, 36% former-smokers and 28% active smokers. Histology: 66% adenocarcinomas, 27% squamous cell carcinomas, 5% large cell carcinomas and 2% NSCLC-NOS. Initially all patients had PS 0-1. Main sites of metastases: lung (80%) and bone (43%), with 34% of patients with ≥ 2 metastatic foci. First-line platinum-based duplex: 50% achieved an objective response, 30% had stable disease; PFS 6-7M. Second-line setting (docetaxel/pemetrexed/erlotinib): partial response (PR) 30%, stable disease (SD) 52%, PFS 5-7M. Third-line (erlotinib/pemetrexed): PR 14%, SD 36%, PFS 4-7M. Hematological toxicity: 18% in 1st-line, 16% in 2nd-line and 14% in 3rd-line. OS was 24.05M.

Conclusions: Third-line therapy was used in 6.5% of the patients. 1st-line platinum-based chemotherapy with new-generation agents like pemetrexed and erlotinib in escalation therapy was well tolerated. The tested erythropoietic agents increased the Hb level in anemic patients with LC. In our study epoetin alpha was better in terms of efficacy and safety than epoetin beta.

P2919 The management of chemotherapy-induced anaemia in patients with lung cancer (LC): A comparative study of erythropoietic agents
Angelica Totiu1, Christelle Clément-Duchêne1, Pierre Vaillant1, Pauline Barber2, Decedal Totiu3, Yves Martinet1, Pulmonary Diseases, CHU Brugeois, Nancy, France,2 Pharmacy, CHU Brugeois, Nancy, France,3 Public Health, CHU Brugeois, Nancy, France.

Chemotherapy-induced anaemia is a frequent complication of LC platinum-based chemotherapies (CT) particularly impair erythropoietin production. One option for the management of this anaemia is the administration of recombinant human erythropoietin (RHE) which stimulates red blood cell (RBC) production.

We compared the efficacy and safety of two types of RHE: epoetin alpha (Eprex) and epoetin beta (Neoreccrom) in anemic patients with LC. Thirty eight patients (mean age 62 ± 11y) were treated: 14 patients receiving CT for a LC (stage III and IV) with anemia (hemoglobin level<11g/dl) were included: 14 patients in group 1 treated by Eprex 40000U/week and 19 patients in group 2 treated by Neoreccrom 30000U/week for 6 weeks. A hematopoietic response was defined as an increase in hemoglobin concentration ≥2g/dl or hemoglobin (Hb) concentration ≥12g/dl in the absence of a RBC transfusion. The mean Hb levels at baseline were identical: 10 g/dl in group 1 and 9.8 g/dl in group 2. Each group was divided into two subgroups (transfused and non-transfused). 15.8% of patients in the first group required a RBC transfusion versus 36.8% in the second group (p=0.026). The mean changes in hemoglobin level during treatment in non-transfused patients were 0.83 g/dl for group 1 (p=0.003) and 0.31 g/dl for group 2 (p=0.13) without statistical difference among groups (p=0.08). While 12.5% patients in group 1 had a significant hematopoietic response, none was observed in group 2. Two patients in group 2 developed thrombotic events.

The tested erythropoietic agents increased the Hb level in anemic patients with LC. In our study epoetin alpha was better in terms of efficacy and safety than epoetin beta.

P2920 Docetaxel-related peripheral neuropathy is a dose-dependent event; a retrospective study in a Greek population with NSCLC
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Introduction: Neurotoxicity is the most important non-hematologic toxicity of taxanes. It presents as peripheral neuropathy with tingling, numbness and pain with a "glove and stocking" distribution and influences the daily activities of patients treated with taxanes.

Aim: To record peripheral neuropathy in relation with the dosage of docetaxel in NSCLC.

Method: We retrospectively studied 700 consecutive files of patients from the archive of the oncology unit of our institution in treatment from December 2006 until May 2008. Election criteria includes patients with NSCLC, PS 0-2, any stage, treated with docetaxel in any combination. We evaluated peripheral neuropathy with CTCAE v3.0

Results: We found 105 patients,84 males(80%),21 females(20%), median age 62.94(49.29, smokers 95(90.5%), median dose of docetaxel 74.42±7.88mg/m², median aggregate dose 426.17±202.9mg, dose intensity 3.6±1.2g/m²/week, median treatment duration 12.6±7.9weeks. Peripheral neuropathy presented in 28 (26.7%) patients, mild or moderate gravity, mainly sensory neuropathy in 75%, after 2.64±1.68 cycles. The group of patients who received docetaxel >80mg/m² presented neuropathy at 37.5% versus 21.9%(p=0.09). The group with dose intensity ≥37.5mg/m²/week presented neuropathy at 47.1% versus 16.9%(p=0.001). In the group of aggregate load dose ≥600 mg, 51.6% presented neuropathy versus 16.4% with <600 mg(p=0.001). Neurohypathy was a reversible adverse event in 25 of 28 patients.

Conclusion: Peripheral neuropathy is a dose-dependent adverse event that increases with the accumulation and the dose intensity of docetaxel. Symptoms usually resolve after treatment or by decreasing the dosage.

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Tumor-infiltrating lymphocytes (TIL) were isolated from tumor tissue by culturing for 3 weeks. Lymph node mononuclear cells (LNMC) were obtained from TDLN and cultured in 3 ways: medium alone (LN neg), stimulated once by XAGE-1b (LN XAGE) or p53 (LN p53). For peripheral blood mononuclear cells (PBMC), TIL and the 3 LNMC cultures were analyzed for antigen-specificity by a 4-day proliferation assay and in supernatants taken at day 2 cytokine release was determined.

In 1 out of 6 patients, XAGE-1b induced proliferation in LN XAGE and IFNγ release in LN XAGE and TIL. In another patient, XAGE-1b induced proliferation in PBMC and LN neg, but no IFNγ release. In 3 out of 6 patients, a p53-induced proliferation was observed in LN p53, which was accompanied by IFNγ release in 2 patients. In one patient, p53 induced TNF-α release in TIL.

These preliminary data show T-cell immunity to XAGE-1b and p53 in lung adenocarcinoma indicating that these antigens are potential targets for immunotherapy. More patients are needed to define strength, breadth and phenotype of this antigen-specific response and its relation with antigen expression in the primary tumor.

Poster Discussion  Room C6 - 14:45 - 16:45

MONDAY, SEPTEMBER 3RD 2012

P2921 Is skin toxicity a predictive or prognostic factor in EGFR-inhibition as treatment of advanced NSCLC?  Stefan Röddiger1, Cornelia Groβ-Sanchen1, Gerald Schmid-Bindert1, Thomas Wibmer1, Kathrin Stoiber1, Joanna Blam1, Wolfgang Rothbauer1, Christian Schumann1, 1Department of Internal Medicine, Pneumology, University of Ulm Medical Center, Ulm, Germany; 2Medical Faculty Mannheim, University Medical Center, Mannheim, Germany

Targeted therapy addressing the Epidermal Growth Factor Receptor (EGFR) is available for the treatment of advanced NSCLC in our clinic with the Tyrosine Kinase Inhibitors Gefitinib and Erlotinib as well as the Monoclonal Antibody Cetuximab within the Gemtux Trial. We analysed clinical markers especially skin toxicity to find predictive and prognostic factors in this therapeutic setting. Between March 2003 and December 2008 we began TKI therapy in 81 patients and between August 2006 and April 2011 cetuximab therapy in 51 patients (induction chemotherapy and cetuximab maintenance after four cycles). Median age was 66 years and median treatment duration 3 months, patients with treatment less than six weeks were not considered. We found a median Time to Progression (TTP) of 3.5 months and Overall Survival (OS) for a start of therapy of 7.5 months. In the subgroup of patients who developed no or mild skin toxicity TTP was 2.0 month, whereas patients who developed a skin toxicity above grade 1 had a TTP of 4.5 months (p = 0.002, HR = 0.48). Difference in OS in these two subgroups was 6.0 and 14.9 month respectively (p = 0.025, HR = 0.64). Age, gender, histology and smoking status showed less strong correlations.

Patients who develop skin toxicity during EGFR inhibiting therapy show a prolonged TTP and OS. To what extend skin toxicity is rather a prognostic or, is yet unclear. Further prospective studies should differentiate the predictive and prognostic value of skin toxicity. There is also a need to identify biomarkers that correlate to the development of skin toxicity and thus could predict a favorable therapeutic course of these costly targeted agents.

P2922 Anti-cancer therapy and monitoring plasma concentration of carboplatin in lung cancer patients receiving hemodialysis Yasumasa Sunaga1, Ryo Oka2, Shinya Sakata1, Sho Saeki1, Ji-ichiro Sasaki1, Kazuhiko Nishi2, Tetsunobu Hamada1, Hideyuki Saito1, Hirotsugu Kohergi1, 1Department of Respiratory Medicine, Kumamoto University Hospital, Kumamoto, Japan; 2Department of Respiratory Medicine, Kumamoto Saisinhon National Hospital, Kumamoto, Japan

To investigate the pharmacokinetics of carboplatin (CBDCA) in lung cancer who were receiving hemodialysis (HD), we measured plasma concentrations of platinum by inductively coupled plasma mass spectrometer. We sampled bloods from two patients at the starting of HD one hour after the finishing administration of CBDCA, and at the end of HD. Patient 1, a 78 year-old man with SCLC, was treated with CBDCA(250mg/m²) and etoposide(100mg/m²) and received HD at day 1, 3, 8. Patients 2, 71 year-old man with NSCLC, was treated with CBDCA(200mg/m², day1) and paclitaxel (180mg/m², day 7). received HD at day 1, 2, 3, 4, 5, 8, and he was treated with same doses of the drugs at day 28 as the second course and received HD at s.c. day 1(day28), 2, 3, 5, 8. Plasma concentrations of platinum before HD were 6.76 to 8.16 g/ml. Mean reduction rate of plasma platinum concentrations (after hemodialysis/before hemodialysis) was 16.4±6.1%, suggesting highly effective clearance of CBDCA by hemodialysis. From 3 days after the administration of CBDCA, plasma concentrations of platinum at the end of HD were higher than those at the starting of the next HD. Thus, we speculated that CBDCA is stored in the tissues and then backflow to blood depending on the plasma concentration of platinum. In Patient 1, partial response and adverse events of grade 3 neutropenia and grade 4 thrombocytopenia were observed. In Patient 2, progressive disease and grade 4 neutropenia was observed. We conclude that in patients with lung cancer receiving HD, monitoring of plasma concentrations of platinum is valuable to get effective plasma concentrations of CBDCA or CDDP and to avoid severe adverse effects.

P2923 XAGE-1b and p53: Potential targets for immunotherapy of non-small cell lung cancer (NSCLC) Mehrdad Talebian-Yarad1, Nikki M. Loof1, Jouke T. Annema1, Cornelis J. Meelis1, Pieter S. Hiemstra1, Marij J.P. Weiters2, Jaap Oostendorp3, Sjoerd H. van der Burgt2, 1Pulmonology, Leiden University Medical Center, Leiden, Zuid-Holland, Netherlands; 2Clinical Oncology, Leiden University Medical Center, Leiden, Zuid-Holland, Netherlands; 3Department of Immunology and Blood Transfusion, Leiden University Medical Center, Leiden, Zuid-Holland, Netherlands; 4Clinical Pharmacy and Toxicology, Leiden University Medical Center, Leiden, Zuid-Holland, Netherlands

Induction of immune responses specifically against tumor-associated antigens by vaccination is a promising approach for cancer immunotherapy. XAGE-1b is a cancer-testis antigen that is aberrantly expressed in lung adenocarcinoma. p53 is a tumor suppressor protein that is over-expressed in NSCLC. We investigated local (primary tumor, tumor draining lymph node (TDLN)) and systemic (peripheral blood) immune responses against XAGE-1b and p53 in lung adenocarcinoma. Tissue and blood samples from 6 lung adenocarcinoma patients were obtained, Background: The Tumorzentrum Berlin (TZB) amalgamates the clinical data of lung cancer pts. in order to improve pt. care by means of joint quality assurance. Aims: To evaluate the effect of changing therapeutic concepts on survival times in pts. with newly diagnosed NSCLC stage II/III from 2000 to 2008. Methods: In this retrospective case study, the pooled data of the TZB of pts. with newly diagnosed lung cancer during 2000 and 2008 were analyzed. Pts. were divided into three 3-year groups (G1: 2000-2, G2: 2003-5 and G3: 2006-8). Kaplan-Meier survival analysis could not demonstrate significant differences between the two groups (p=0.05).

Conclusions: There was no survival benefit for the Radical Lymphadenectomy. Although in some reports a systematic mediastinal lymphadenectomy is recommended for correct staging, a pulmonary resection with non-performance of radical lymphadenectomy the radical systematic lymphadenectomy, the radical systematic lymphadenectomy (RLA) associated with a pulmonary resection for lung cancer RLA remains controversial. Our objective is to investigate the impact of radical lymphadenectomy compared to the sampling on the overall survival for elderly lung cancer patients and assess whether the non-performance of an RLA could be justified in the surgical treatment for this group.

Material: We analysed the records of 60 patients aged 75 years and older (41 males, 19 females) who underwent surgery for non-small-cell lung cancer. They were divided into two groups, according to the type of mediastinal lymphadenectomy: the radical systematic lymphadenectomy, the radical systematic lymphadenectomy (RLA) associated with a pulmonary resection for lung cancer RLA has no protective effect on mortality; the hazard ratio for the RLA group in comparison to the SNL group was 0.93 in the multivariate analysis. The 3-year survival for the SNL group, was marginally better than that of the RLA group. There was no significant difference in the overall survival between the two groups (p=0.05).

P2924 Elderly lung cancer patients profit from radical mediastinal lymphadenectomy? Kallioni Athanassiadi1, Vassiliki Karameri2, Irini Mavromati2, Ilias Samiotis1, Maria-Kalliopi Konstantinidou1, Despina Violidaki1, Dimitra Riga1, Dimitris Lioumpas1, Dimitra Rondogianni1, Ion Bellenis1, 1Thoracic Surgery, Evangelik Hospital “Evangeliou”, Athens, Greece; 2Anasthesiology, General Hospital “Evangeliou”, Athens, Greece; 3Pathology, General Hospital “Evangeliou”, Athens, Greece

Objective: The therapeutic impact of a radical mediastinal lymphadenectomy (RML) associated with a pulmonary resection for lung cancer is still unclear. Further prospective studies should differentiate the predictive and prognostic value of skin toxicity. There is also a need to identify biomarkers that correlate to the development of skin toxicity and thus could predict a favorable therapeutic course of these costly targeted agents.
Lung cancer patients frequently present with advanced stage. HDReB has always been used as a palliative treatment option in end-stage disease, and has not yet been thought of as a first-step therapeutic approach of a multimodality treatment strategy. We strongly feel that HDReB could be the method of choice in carefully selected patients with endobronchial obstruction, prior to other treatments.

Aim: HDReB could be used as a first-step, introductory treatment in selected patients with inoperable obstructive endobronchial carcinoma of the lungs.

Methods: A catheter is placed through bronchoscopy in the obstructed lumen. HDReB is delivered in two sessions separated by one week. Bronchoscopy is performed 3 times per week. Pulmonary function tests are performed before and after HDReB monthly. Evaluation of quality of life is assessed with the Saint George Respiratory Questionnaire. Obstruction score is also evaluated before and after treatment.

Results: Six patients with previously untreated, inoperable NSCLC associated with endobronchial obstruction, were treated with HDReB as an introductory treatment of a multimodality therapeutic approach. We found significant improvement on symptoms (cough, dyspnea, hemoptysis) and intraluminal reduction of the obstruction.

Conclusions: HDReB is a low-cost, semi-invasive, and well-tolerated method that has been applied with a limited palliative purpose, whilst it could provide an improved performance status and partial disease regression by early enough, giving the patient the opportunity of a better outcome of treatment, overall.

P2928
Non-small cell lung cancer – Advanced disease: Barriers to inclusion in clinical trials and its impact on survival
Claudia Laras dos Santos, Lúcia Fernandes, Ines Sanches, Filipa Cruz e Costa, Fernando Barata. Pulmonology Department, Centro Hospitalar Universitário de Coimbra, CHC, Coimbra, Portugal

Introduction: Inclusion in clinical trials allows patients to submit to innovative therapies and a meta-analysis showed that this may be associated with increased rates of survival.

Aims: Identify reasons that hindered the inclusion of patients in clinical trials of first-line therapy; Compare overall survival (OS) and progression-free survival (PFS) between groups of included and excluded patients.

Methods: This study was conducted over 36 months in a central hospital. Patients with well defined histology and candidates to chemotherapy were considered eligible for clinical trials. Reasons for non inclusion have been detailed. OS and PFS were compared.

Results: We identified 199 eligible patients, mean age 64.9±10.7 years, 75.9% males, 61.8% with non-squamous cell carcinoma. From these 22.1% were included in trials. Among those not included 18.7% had performance status ( Zubrod ) 2 and 66.5% had other exclusion criteria, mainly heart disease (22.3%), respiratory disease (21.4%), brain metastases (15.5%) or second malignancy (15.5%). About 15% of patients refused to be involved in trials. Patients who had performance status 0/1 (N = 170), there was no statistically significant difference in analysis of OS or PFS between those included in trials and the excluded, whether by criteria (Cox Regression: OS p=0.705/PFS p=0.807) or by refusal (Cox Regression: OS p=0.465; PFS=0.900).

Conclusion: Liberalization of exclusion criteria and recognition of causes that lead to refusal are possible determinants of increased participation in clinical trials.

P2929
Intratumoral injection of plasmid-encoded flagellin inhibits growth of NSCLC-cells in murine lung cancer model
Marek Jankowski1, Zbigniew Wanda2, Robert Lenartowski1, Olga Haus1, Piotr Kopinski1. 1Gene Therapy, Nicolaus Copernicus University, Bydgoszcz, Poland; 2Clinical Genetics, Nicolaus Copernicus University, Bydgoszcz, Poland; 1Gene Therapy, Nicolaus Copernicus University, Torun, Poland

Lack of progress in the treatment of NSCLC urges to look for experimental therapeutic methods, such as gene therapy. Currently used therapeutic vectors can cause adverse effects, or have a limited potential to transduce cells. The aim of this work was 1) to construct a vector suited for gene therapy allowing for selective transduction of only tumor cells 2) to assess therapeutic potential of Salmonella flagellin (FiC).

Engineered plasmid vector was obtained by PCR synthesis. For the purpose of tumor-specific transcriptional activity it was necessary to design a two-step promoter unit system based on telomerase minimal promoter.

Influence of FiC on NSCLC cells was assessed by measuring proliferation of transfected cells and by phenotyping of maturation markers on DCs incubated with
A549 cells. NSCLC tumors in mice were injected with empty or FltC-coding vector. Tumor growth and survival of the mice were analyzed. FltC-transfected A549 cells had significantly lower proliferative potential. Such cells enhanced maturation of MoDC as suggested by higher expression of CD80 and CD83. NSCLC-inoculated mice administered with a vector containing FltC gene had a significantly longer survival time (p<0.002) and slower tumor growth (p<0.01) comparing to the control group. Designed two-step promoter unit allows for efficient and tumor-selective expression of therapeutic gene. Results suggest that NSCLC transduction with FltC gene may inhibit its proliferation in vitro and tumor growth in vivo and increase survival rate. Due to ambiguous results obtained in co-culture of transfected A549 and DC antitumor properties of FltC other than induction of DC maturation need to be considered.