9011 ORAL

NGR-hTNF, a vascular targeting agent (VTA), in previously treated patients with malignant pleural mesothelioma (MPM): a phase II study

V. Gregorc[1], G.L. Ceresoli[2], P.A. Zucali[2], F.G. De Braud[3], E. Bajetta[4], A. Santoro[2], M.G. Viganò[1], F. Caligaris Cappio[1], A. Lambiase[5], C. Bordignon[5]. [1]*Istituto Scientifico San Raffaele, Department of Oncology, Milan, Italy;* [2]*Istituto Clinico Humanitas, Department of Oncology, Milan, Italy;* [3]*Istituto Europeo di Oncologia, Clinical Pharmacology and New Drugs Unit, Milan, Italy;* [4]*IRCCS Fondazione Istituto Nazionale dei Tumori, Department of Oncology, Milan, Italy;* [5]*MolMed, Clinical Development, Milan, Italy*

Background: NGR-hTNF is a VTA exploiting a tumor-homing peptide (NGR) that selectively binds an aminopeptidase N overexpressed on tumor blood vessels. In preclinical models, NGR-hTNF has shown antitumor activity even at low doses.
Methods: MPM patients (pts) with radiologically-documented progression after a pemetrexed-based chemotherapy were treated with low-dose NGR-hTNF given intravenously as 1-hour infusion at 0.8 μg/m^2 every 3 weeks (q3w; triweekly cohort). The trial had a 2-stage design with 16 and 27 patients to be enrolled. Primary study aim was progression-free survival (PFS) with restaging performed q6w according to MPM-modified RECIST criteria. Subsequently, an additional 14 pts were treated at 0.8 μg/m^2 on a weekly basis (weekly cohort).
Results: In the triweekly cohort, 43 pts were evaluated over 170 cycles (range, 1−18). Patient characteristics were: median age 64 years (range, 54−80); male/female 27/16; epithelial/nonepithelial histology 34/9; PS 0/1/2 24/10/9; EORTC score good/poor 34/9. Only one grade 3 drug-related toxicity was observed. Main grade 1−2 toxicities were short-lived chills (71%), arising during the first infusions. The median and 3-month PFS were 2.8 months (95% CI, 1.9−3.7) and 43% (95% CI, 28−58), respectively. The disease control rate (DCR) was 44%. One patient (2%) had a partial response lasting 10.0 months and 18 patients (42%) maintained stable disease (SD) for a median time of 4.3 months (range, 2.2−13.7 months). With a median follow-up of 19.6 months, the median and 1-year overall survival (OS) were 11.6 months and 48%, respectively. Median OS in pts who achieved DCR and in those who did not were 13.3 and 8.3 months, respectively. In the weekly cohort, 242 infusions were delivered (range, 4 to 45 cycles) and 5 pts (36%) received ⩾30 weekly cycles. There was no toxicity exacerbation. Seven pts (50%) experienced SD for a median time of 8.1 months (range, 2.4−11.4+). The 6- and 12-month PFS rates were 36% and 19%, respectively. In the overall study population (n = 57), the DCR was 46% (95% CI, 34−59), the median duration of DCR was 4.7 months (95% CI, 4.0−5.3), and the median OS was 13.1 months (95% CI, 9.1−17.1).
Conclusion: NGR-hTNF 0.8 μg/m^2 weekly is well tolerated, showing promising disease control in previously treated MPM patients, and will be further developed in this setting.

9012 ORAL

Volumetric helical perfusion CT and FDG-PET/CT as prognostic biomarkers in operable non-small cell lung cancer: correlation with clinico-pathological parameters

Q.S. Ng[1], H. Mandeville[2], W.L. Wong[3], J. Chambers[3], M.M. Burke[4], A. Bell[4], E. Townsend[5], M.I. Saunders[2], P.J. Hoskin[2], V. Goh[3]. [1]*National Cancer Centre, Department of Medical Oncology, Singapore, Singapore;* [2]*Mount Vernon Cancer Centre, Marie Curie Research Wing, Northwood, United Kingdom;* [3]*Mount Vernon Hospital, Paul Strickland Scanner Centre, Northwood, United Kingdom;* [4]*Royal Brompton and Harefield Hospitals, Department of Pathology, Middlesex, United Kingdom;* [5]*Royal Brompton and Harefield Hospitals, Department of Thoracic Surgery, Middlesex, United Kingdom*

Background: Elevated tumor angiogenesis may be associated with poor prognosis in lung cancer. The aim was to investigate the role of volumetric helical perfusion CT and FDG-PET/CT as prognostic biomarkers in patients with operable lung cancer.
Patients and Methods: Following IRB approval and informed consent, 20 prospective patients (14 males 6 females, mean age 64 years) with proven non-small cell lung cancer undergoing curative surgery underwent dynamic contrast enhanced CT in addition to standard pre-operative FDG-PET/CT staging. Multiple dynamic helical CT acquisitions comprising an unenhanced and 8 post contrast breath-hold studies (80 kV, 120 mAs, 2 mm collimation) encompassing the entire tumour were performed following intravenous injection of 108 mls 300 iobitridol; 4 ml/s decreasing bolus injection. Following ROI definition, mean tumor permeability surface area product (PS; ml/100 ml/min), blood volume (BV; ml/100 ml) and blood flow (BF; ml/100 ml/min) were derived on a pixel-by-pixel basis. Tumor SUV_{max} and SUV_{mean} were derived from FDG-PET/CT studies. Correlation was assessed by Spearman rank correlation. Mann-Whitney was used to compare group means. ROC analysis was used to correlate perfusion CT parameters to nodal status.
Results: Mean (±SD) values for PS, BV, BF, SUVmean, and SUVmax were 17.5±12.5, 8.1±3.4, 56.4±18.8, 10.4±5.4, and 17.6±10.1 respectively. PS correlated inversely with SUVmax (r = −0.54, p = 0.050). Tumor size correlated inversely with PS (r = −0.73, p = 0.004), but not with SUVmax (r = 0.47, p = 0.09). PS was significantly lower in squamous cell compared to adenocarcinoma (11.3 vs 17.8; p = 0.043); SUVmax (18.0 vs 12.3, p = 0.043) and SUVmean (12.6 vs 7.5, p = 0.039) were significantly higher. Mean BF was significantly lower in stage I versus II/III tumors (42.2 vs 63.5, p = 0.028), and node negative (N0) versus node positive (N1/2) tumors (44.3 vs 65.1, p = 0.048). ROC analysis for predicting node positivity showed significant AUC of 0.86. Using a BF cut-off of 53.4, sensitivity for predicting node positivity was 71.4% and specificity 100%.
Conclusions: Volumetric helical perfusion CT and FDG-PET/CT correlate with clinico-pathological parameters and show potential as prognostic biomarkers in operable lung cancer.

9013 ORAL

Phase II results of ABT-869 treatment in patients with non small cell lung cancer (NSCLC)

E. Tan[1], G. Goss[2], R.R. Salgia[3], B. Besse[4], D.R. Gandara[5], N. Hanna[6], J.L. Ricker[7], J. Qian[8], D.M. Carlson[7], R. Soo[9]. [1]*National Cancer Centre, Medical Oncology, Singapore, Singapore;* [2]*The Ottawa Hospital Regional Cancer Centre, Division of Medical Oncology, Ottawa ON, Canada;* [3]*University of Chicago Medical Center, Oncology Research Program, Chicago IL, USA;* [4]*Institut Gustave Rousse, Dept of Medicine, Villejuif, France;* [5]*UC Davis Cancer Center, Clinical Research, Sacramento CA, USA;* [6]*Indiana University Cancer Center, School of Medicine, Indianapolis IN, USA;* [7]*Abbott Laboratories, Oncology, Abbott Park IL, USA;* [8]*Abbott Laboratories, Global Statistics & Data Management, Abbott Park IL, USA;* [9]*National University Hospital, Dept. of Haematology-Oncology, Singapore, Singapore*

Background: ABT-869, a novel orally active, potent and specific inhibitor of VEGF and PDGF receptor tyrosine kinases, showed single-agent activity in early-phase clinical trials, in a variety of advanced solid-tumor patients (pts) including those with NSCLC.
Materials and Methods: This open-label, multicenter trial assessed antitumor activity and toxicity of ABT-869. Pts, randomized 1:1 to 0.10 mg/kg (Arm A) or 0.25 mg/kg (Arm B), self-administered the daily dose until progressive disease (PD) or intolerable toxicity. Eligibility criteria included locally advanced or metastatic NSCLC; 1 or 2 prior systemic treatment, and ⩾1 measurable lesion (RECIST). Primary endpoint was progression free (PF) rate at 16 wks. Secondary endpoints were objective response rate (ORR), time to progression (TTP), progression free survival (PFS), overall survival (OS). All efficacy results are based on radiographic assessment by the central imaging center (except as noted) and clinical assessment by the investigator. Trial abbreviation: *ABT-869 in subjects with NSCLC*. Trial registry: NCT00716534. Trial status: ongoing; recruiting; sponsored by Abbott Laboratories. ABT-869 is being developed in collaboration with Genentech.
Results: Of 139 pts enrolled from 08/07−10/08, all received prior systemic therapy; 83 (60%) had ⩾2 prior regimens; 17 (12%) had squamous cell carcinoma at screening. Median age was 62y.

Efficacy Results	Arm A n = 65 [95% CI]	Arm B n = 74 [95% CI]
PF rate at 16 wks, %	32.3 [21.2, 45.1]	36.5 [25.6, 48.5]
ORR, %	0	2.7 [0, 9.4]
ORR, % per site	4.6 [1.0, 12.9]	10.8 [4.8, 20.2]
TTP*, m	3.6 [2.1, 4.3]	3.7 [3.1, 5.3]
PFS*, m	3.5 [2.0, 4.3]	3.7 [3.1, 4.9]
OS*, m	10.7 [6.9, –]	8.6 [5.6, 12.8]

ORR per RECIST; − not reached; *Median

The most common AEs were fatigue (45%), hypertension (HT) (37%), anorexia (35%), diarrhea (35%), nausea (33%); rates for HT, diarrhea, proteinuria and hand-foot syndrome were significantly lower in Arm A. The most common AE ⩾Grade 3 (NCI toxicity criteria) was HT (13%). 57% of pts (34% Arm A, 77% Arm B, p < 0.001) had dose interruptions due to AEs and 25% required dose reductions (6% Arm A, 41% Arm B, p < 0.001). The most common reasons for dose interruption included HT (14%), hand-foot syndrome (9%), and proteinuria (7%), which were reversible. 20 pts (10 Arm A, 10 Arm B) remained on study at the time of analysis. 95 pts had

discontinued due to PD (clinical, radiographic or AE related to PD), 16 due to AEs not related to PD, 8 for other reasons.
Conclusions: ABT-869 demonstrates an acceptable safety profile and appears to be active in NSCLC pts.

9014 ORAL

Effect of postoperative adjuvant chemotherapy with UFT on survival in patients with clinical stage IA non-small-cell lung cancer: an exploratory analysis from a meta-analysis of 6 randomized controlled trials

M. Tsuboi[1], C. Hamada[2], M. Ohta[3], S. Fujimura[4], K. Kodama[5], M. Imaizumi[6], H. Wada[7]. *[1]Kanagawa Cancer Center Hospital, Thoracic Surgery, Yokohama, Japan; [2]Tokyo University of Science, Faculty of Engineering, Tokyo, Japan; [3]The Japan Lung Cancer Research Group, Thoracic Surgery, Fukuoka, Japan; [4]Northeast Japan Study Group for Lung Cancer Surgery, Thoracic Surgery, Sendai, Japan; [5]Osaka Lung Cancer Study Group, Thoracic Surgery, Osaka, Japan; [6]Adjuvant Chemotherapy for Lung Cancer Research Group, Thoracic Surgery, Nagoya, Japan; [7]The West Japan Study Group for Lung Cancer Surgery, Thoracic Surgery, Kyoto, Japan*

Background: The Seventh Edition of the TNM Classification of Malignant Tumors in non-small-cell lung cancer (NSCLC) proposes a more detailed classification of primary tumor diameter. Clinical stage IA T1 disease is subdivided into 2 groups: T1a disease (tumor diameter, $\leqslant$2 cm) and T1b disease (tumor diameter, >2 to $\leqslant$3 cm). Tegafur-uracil (UFT) improves survival in patients with clinical stage I NSCLC. But whether it is effective in patients with T1 disease (clinical stage IA) remains controversial.
Methods: Data from a 2005 UFT meta-analysis, which was beased on 6 randomized controlled studies of UFT (West Japan Study Group for Lung Cancer Surgery [WJSG] second trial, WJSG fourth trial, Northeast Japan Study Group for Lung Cancer Surgery trial, Osaka Lung Cancer Study Group [OLCSG], Adjuvant Chemotherapy for Lung Cancer Study Group [ACTLC], and JLCRG), were reanalyzed to evaluate the effectiveness of UFT according to T1a and T1b tumors as proposed by the new TNM classification in patients who had T1 tumors with no lymph-node metastasis. In all 6 studies, patients were randomly assigned to receive either surgery alone or surgery followed by UFT monotherapy and were followed up for at least 5 years.
Results: Data from 1354 patients were analyzed: 699 (51.6%) had T1a tumors and 655 (48.4%) had T1b tumors. In the surgery alone group, survival rates at 5 years were 85% in patients with T1a tumors and 81% in those with T1b tumors after surgery alone and 87% in patients with T1a tumors and 87% in those with T1b tumors after surgery followed by adjuvant treatment with UFT. In patients with T1b tumors the survival rate was significantly higher in the UFT group than in the surgery alone group (hazard ratio[HR] = 0.61; 95% confidence interval [CI], 0.43 to 0.86; log-rank p = 0.005). Subgroup analyses of our data showed no evidence of an interaction between the effectiveness of postoperative UFT and age, sex, or histologic type. However, the proportion of patients with adenocarcinoma (89.9%) was far higher than that of patients with squamous-cell carcinoma (9.5%).
Conclusions: Our study showed that postoperative adjuvant chemotherapy with UFT was effective for T1b tumors (tumor diameter, >2 to $\leqslant$3 cm) among patients with stage IA NSCLC, even though further studies in patients with squamous-cell carcinoma were required. UFT can be used as standard postoperative adjuvant chemotherapy not only for stage IB, but also stage IA (T1b) NSCLC.

Poster presentations (Wed, 23 Sep, 09:00−12:00)
Lung cancer

9015 POSTER

Phase II study of the combination of docetaxel and S-1 in patients with refractory or relapsed advanced non-small cell lung cancer

Y. Oki[1], T. Hirose[1], T. Yamaoka[1], T. Shirai[1], K. Okuda[1], T. Sugiyama[1], S. Kusumoto[1], T. Ohnishi[1], T. Ohmori[2], M. Adachi[1]. *[1]Showa University School of Medicine, Division of Respiratory and Allergy Department of Internal Medicine, Tokyo, Japan; [2]Showa University School of Medicine, Institute of Molecular Oncology, Tokyo, Japan*

Background: Docetaxel is a standard treatment for recurrent non-small cell lung cancer (NSCLC). S-1 is an oral agent active against lung cancer which consists of tegafur (a prodrug of cytotoxic 5-fluorouracil), 5-chloro-2,4-dihydroxypyridine, and potassium oxonate in a molar ratio of 1:0.4:1. Preclinical studies have shown that the combination of docetaxel and S-1 has synergistic cytotoxicity against human cancer cell lines in vitro. However, no trials have evaluated the combination of docetaxel and S-1 in patients with refractory or relapsed NSCLC. The aim of the present phase II study was to assess the antitumor activity and toxicity of this regimen in patients with refractory or relapsed NSCLC.
Material and Methods: Patients with refractory or relapsed advanced stage IIIA/IIIB/IV NSCLC were eligible if they had a performance status of 0 to 2, were 80 years or younger, and had adequate organ function. Patients were treated with 35 mg/m^2 of docetaxel on days 1 and 15 and with 80 mg/m^2 of S-1 for 14 consecutive days every 4 weeks.
Results: From October 2006 through March 2009, 47 patients (37 men and 10 women; median age, 65 years; age range, 43 to 79 years) were enrolled. The most common histologic type was adenocarcinoma. The overall response rate was 17% (95% CI, 7.6% to 30.5%). The median survival time after treatment was 9 months (range, 1 to 22 months). The median time to progression was 4 months (range, 1 to 11 months). Grade 3 to 4 hematologic toxicities included neutropenia in 49.0% of patients, thrombocytopenia in 2.1%, and anemia in 21.3%. Grade 3 to 5 nonhematologic toxicities included infection in 25.6% of patients, diarrhea in 12.8%, and nausea in 4.2%. The 2 treatment-related deaths were due to diarrhea and dehydration.
Conclusions: This combination chemotherapy is effective for refractory or relapsed advanced NSCLC.

9016 POSTER

Nutritional assessment on hospitalised lung cancer patients

M. Harikiopoulou[1], P. Heras[1], A. Hatzopoulos[1], K. Kritikos[1]. *[1]Hellenic Medical Society for the Study of Psychosomatic Problems, Hellenic Medical Society for the Study of Psychosomatic Problems, Athens, Greece*

The aim of this study was to assess the nutritional status of hospitalized advanced lung cancer patients in Greece and identify factors related to their nutritional status.
Patients and Methods: Participants were adult lung cancer patients (N = 91) from three medical centers in Greece. Patients' nutritional status, symptom severity, performance status, and dietary intake were assessed by the Mini-Nutritional Assessment (MNA), Symptom Severity Scale, Karnofsky's Performance Scale, and 3-day dietary record, respectively.
Results: All 91 subjects completed the MNA. Every five patients were also asked to record their dietary for 3 days. In total, there were 30 subjects completed the 3-day dietary record. Based on MNA cutoff points, 92.3% of subjects were either malnoutrished or at risk for malnutrition. Overall symptom severity, body mass index, performance status, hemoglobin level, significantly predicted nutritional status. Cancer patients had low overall caloric intakes, particularly fat intake. Future studies should expand the sample size and add outpatient sites.

9017 POSTER

Sleep disturbances and depression in patients with lung cancer

E. Mihail[1], P. Heras[1], A. Hatzopoulos[1], K. Kritikos[1], M. Mantzioros[1], M. Hera[1]. *[1]Hellenic Medical Society for the Study of Psychosomatic Problems, Hellenic Medical Society for the Study of Psychosomatic Problems, Athens, Greece*

Aim of this study is to estimate the degree of sleep disturbances, as well the possible contributing factors in patients with lung cancer.
Patients and Method: 41 patients concluded in our study. 9 were female and 31 male with mean age of 51 (range: 29−74). These patients underwent to a clinical psychiatric interview according to the diagnostic criteria of ICD-10. The degree of sleep disturbances during the month prior to patients evaluation was assessed through the Athens Insomnia Scale (AIS) and psychopathology was assessed through the Montgomery Asberg Depression Rating Scale (MADRS).
Results: There was a strong correlation between the score of the AIS and that of the MADRS for a?? 41 patients (r: 0.40, p < 0.01). 13 of our patients complained of insomnia. These patients scored higher on the MADRS, than the ones without sleep difficulties (z: −3.032, p = 0.002).
Conclusion: The results of our study suggest that sleep disturbance (insomnia) in patients with lung cancer is a probable indicator of depression. Furthermore, these data suggest that insomnia in these patients is one of the factors mediating the association between depression and impairment in their functioning.