

of the tumor region on the pre-treatment CT scan. The AUC of the ROC curve of the final model on the validation set was 0.77 (95% CI, 0.69–0.85).

Conclusion: Our results indicate that meaningful and reliable image traits extracted from the pre-treatment CT scan can predict patient outcome after treatment. The prediction of two year survival with our approach may be an important tool for the analyst in oncology to extract informative CT image traits that may assist them in the decision of treatment choice, allowing them with the possibility of treatment individualization.

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POSTER

8473T>C COX-2 polymorphism and susceptibility for lung cancer: a strategy for individualised chemoprevention

A. Pereira¹, P. Machado¹, A. Araújo², A. Coelho¹, A.L. Teixeira¹, R. Medeiros¹. ¹I.P.O., Molecular Oncology Group, Porto, Portugal; ²I.P.O., Medical Oncology Department, Porto, Portugal

Background: Lung cancer (LC) presents a major health problem in the world, being the most common cause of death from cancer in 2002. Cyclooxygenase-2 (COX-2), normally undetected in physiological conditions, is promptly triggered under inflammatory and tumor promotion settings, contributing to key steps of carcinogenesis. Up-regulation of COX-2 is believed to be an early event in lung carcinogenesis. It is known to be induced by cigarette smoke condensate *in vitro* and by the tobacco-specific carcinogen nitrosamine 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) in mice. Furthermore, several epidemiological studies point to a lung cancer chemopreventive effect of non-steroidal anti-inflammatory drugs (NSAIDs), known to suppress COXs enzymes. The 8473T>C COX-2 polymorphism in an AU-rich elements region (3'UTR) might contribute to cancer development by influencing COX-2 mRNA stability. The aim of our study was to assess the influence of this polymorphism in the development of LC.

Material and Methods: This case-control study gathered 1069 individuals: 718 healthy individuals and 351 patients with histopathologically confirmed lung cancer, from the Northern region of Portugal. The 8473T>C COX-2 polymorphism genotypes were determined by Real-Time PCR allelic discrimination technique.

Results: We found no statistically significant differences in the distribution of the 8473T>C polymorphism genotypes between LC cases and controls ($P=0.122$). However, in a stratified analysis by histological type and gender we observed an increased risk for epidermoid non-small cell lung cancer (OR = 1.47; 95% CI: 1.00–2.15) and more interesting, males C allele carriers revealed had an higher susceptibility for epidermoid non-small cell lung cancer (OR = 1.55; 95% CI: 1.03–2.33).

Conclusion: The 8473T>C COX-2 polymorphism appears to modulate the genetic susceptibility for epidermoid non-small cell lung cancer, especially in males. This genetic profiling based higher-risk group definition may help shift the balance between and benefits for the use of COX-2 inhibitors in chemoprevention that is currently hampered by the adverse gastrointestinal and cardiovascular side effects.

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POSTER

Cyclin D1 and Non-Small cell lung cancer – a role of CCND1 gene variants in lung carcinogenesis

R. Catarino¹, A. Coelho¹, A. Araújo², A. Nogueira¹, M. Gomes¹, A. Nogueira¹, R. Medeiros¹. ¹Portuguese Institute of Oncology, Molecular Oncology, Porto, Portugal; ²Portuguese Institute of Oncology, Medical Oncology, Porto, Portugal

Background: In most industrialised countries, lung cancer is the main cause of cancer death and has a poor prognosis. Non-small cell lung carcinoma (NSCLC) accounts for approximately 75% of cases. Experimental evidence suggests that lung cancer development and progression can be linked to an increased proliferation rate. Cyclin D1 (CCND1) has been described as having a pivotal role in the carcinogenesis of lung carcinoma. CCND1 is a key regulator of the G1/S phase of the cell cycle and its altered activity is associated with the development of several human cancers.

Patients and Methods: We analysed the A870G CCND1 polymorphism by PCR-RFLP in genomic DNA isolated from peripheral blood of 1535 individuals including, 297 cases of NSCLC and 1238 healthy individuals. Statistical analysis was performed using the computer software SPSS for Windows (version 13.0). Chi-square analysis was used to compare categorical variables and a 5% level of significance was used in the analysis. The odds ratio (OR) and its 95% confidence interval (CI) were calculated as a measurement of the association between CCND1 genotypes and cancer risk. Logistic regression analysis was used to calculate the adjusted OR (aOR) and 95% CI for the influence of CCND1 genotypes in the risk of cancer.

Results: Our results demonstrate that patients carrying the GG CCND1 genotype present an increased risk for the development of NSCLC (OR = 1.57, 95% CI 1.17–2.10, $P=0.003$). This genetic susceptibility was even more evident when considering the epidermoid histological type (OR = 1.84, 95% CI 1.30–4.07, $P=0.005$). Multivariate logistic regression analysis adjusted by gender, age and tobacco smoke confirmed this association, indicating that individuals carrying two G-alleles present an increased risk of 2.7-fold for the development of lung cancer (aOR = 2.68; 95% CI 1.54–4.69; $P=0.001$).

Conclusions: In conclusion, our results may be important in the definition of a biological predictive profile for the development of NSCLC within our population. Furthermore, the knowledge of the mechanisms involved in NSCLC carcinogenesis may help to identify targets for the development of chemoprevention or therapeutic strategies.

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POSTER

Impact of zoledronic acid on follow-up duration in lung cancer patients with bone metastasis in a US managed care plan

S. Kaura¹, S. Thayer². ¹Novartis Pharmaceuticals Corporation, Health Economics Oncology, USA; ²i3 Innovus, Health Economics and Outcomes Research, San Francisco, USA

Background: For lung cancer patients with bone metastasis, skeletal complications including fractures are common and cause considerable morbidity, reduce quality of life, and reduce survival. This study was designed to assess the impact of zoledronic acid (ZOL), an intravenous bisphosphonate (IVBP), in patients with solid tumor cancers, including lung cancer.

Methods: A claims-based analysis using commercial and Medicare Advantage data from over 45 US managed care plans was used to evaluate the relation between treatment persistency and follow-up duration in patients treated with ZOL, compared with those who were not (non-IVBP). A secondary analysis assessing the effect of time to treatment with ZOL will also be conducted. Persistency was defined as the absence of a >45 day gap between ZOL treatments. Index date was set at bone metastasis or first ZOL fill. Age 18+ with a lung cancer and a bone metastasis diagnosis between 01/01/01 and 12/31/06, continuous enrollment in the health plan for 6 months pre-index, with no evidence of bone metastasis or IVBP in the pre-index period was required. Patients were followed until disenrollment (including mortality) or end of study (12/31/07). ANOVA tests were used to compare follow-up duration, a proxy for survival, between ZOL persistency groups.

Results: The study sample included 10,513 lung cancer patients; 1,729 in the ZOL cohort and 8,784 in the non-IVBP cohort. Mean age was 62.4 years (± 11.24) and 59.0% of patients were male. 78.5% of patients were commercial enrollees. Mean Charlson was 4.67 (± 2.95). Treatment persistency groups included in the analysis were 31–90 days ($N=475$), 91–180 days ($N=239$), 181–365 days ($N=133$), ≥ 366 days ($N=44$). Persistent use of ZOL was associated with longer follow-up duration. There was a statistically significant difference ($p < 0.001$) in the unadjusted mean follow-up duration for the non-IVBP cohort, 216 days (± 304), compared with 236 (± 233 ; 31–90 days persistency group); 330 (± 259 ; 91–180 days); 425 (± 237 ; 181–365 days); and 729 days (± 418 ; ≥ 366 days).

Conclusions: This study showed that in cancer patients with lung cancer and bone metastasis, patients with longer periods of persistence with ZOL achieved the better outcomes in terms of longer follow-up duration in the health plans.

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POSTER

The value of day 8 blood count in treatment decisions when using oral vinorelbine in non-small cell lung cancer (NSCLC) patients

A. Faria¹, J.S. Myerson¹, M. Puglisi¹, N. Starling¹, S. Ashley¹, S. Popat², M.E.R. O'Brien¹. ¹Royal Marsden Hospital, Medical Oncology, Sutton, United Kingdom; ²Royal Marsden Hospital, Medical Oncology, London, United Kingdom

Background: Chemotherapy regimens most used in our NSCLC patients are intravenous (IV) cisplatin/carboplatin and IV/oral vinorelbine on day (d) 1 and oral vinorelbine on d8, 3 weekly, and oral vinorelbine monotherapy on d1 and d8 for elderly or performance status (PS) 2 patients. As per local policy, d8 oral vinorelbine is only given after clinical and full blood count (FBC) review. This is inconvenient for patients and also results in considerable clinical time spent. We aimed retrospectively review the relevance of FBC result in d8 vinorelbine therapeutic decision making.

Material and Methods: This audit was approved by our Audit Committee. We reviewed the clinical files of the last 100 NSCLC patients treated with vinorelbine and each patient's first two courses were identified. Episodes where d8 vinorelbine was omitted, delayed, or given with dose reduction, and reasons for these actions were recorded.

Results: 91 patients (48 males, 43 females) were evaluable. Median age was 66 yrs. 70% had PS of 0 or 1, 27% PS 2, and 3% PS 3. The total number of courses recorded was 170 (107 carboplatin and vinorelbine, 42 cisplatin and vinorelbine, and 21 vinorelbine alone). D8 vinorelbine was not administered as planned in 23 courses (14%). In 20 (12%) courses, d8 vinorelbine was omitted, delayed in 2, and given with dose reduction in 1. Low FBC was the reason for d8 vinorelbine omission in only 1 course; a patient with PS 2 treated with vinorelbine monotherapy.

Conclusions: D8 vinorelbine administration can generally be safely led by clinical assessment alone in patients receiving combination treatment. We will still assess FBC on d8 in patients receiving single agent vinorelbine. This will save NHS resources and improve patient comfort.

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POSTER

Intravenous Topotecan in patients with advanced non-small cell lung cancer pre-treated with platinum and taxanes: Results of a phase II study

E. Esteban¹, G. Crespo¹, J.P. Berros¹, M. Sanmamed¹, C. Muriel¹, P. Blay¹, N. Villanueva¹, P. Jimenez¹, M. Luque¹, A.J. Lacave¹. ¹Hospital Central de Asturias, Oncology, Oviedo, Spain

Background: Topotecan, a semi-synthetic camptothecin analogue with topoisomerase I interaction has shown to be an active agent in the treatment of advanced refractory lung cancer and ovarian cancer. In this report, experience with this drug is described when used as a single agent in patients with advanced NSCLC refractory to chemotherapy regimens containing at least platinum and taxanes.

Methods: Patients with NSCLC refractory to previous chemotherapy including platinum and taxanes in first and/or subsequent lines of treatment and KI = 60% were eligible for the study. Topotecan was given at a dose of 1.25 mg/m² i.v. daily for five days, repeated every 21 days until progression disease or intolerable toxicity occurred. Efficacy and toxicity were assessed following OMS criteria. The Simon two-stage design and the Kaplan-Meier method were applied to estimate activity and progression free survival (PFS) respectively.

Results: Thirty four patients were included showing the following features: median age of 52 years (range 43–69) and karnofsky PS of 70 (50–80), 26 were male and 8 female. Twenty-one (63%) pts had adenocarcinoma, ten (25%) squamous cell and three (12%) undifferentiated carcinoma. The median number of disease sites and prior regimens received were two in both cases. After 64 cycles administered, patients received a median of 2 cycles of treatment (1–9). All patients except one were considered evaluable for toxicity, with the recording of five episodes of (15%) nausea/vomiting grade 1–2 and two (6%) of asthenia grade 1. Four (12%) patients developed anaemia grade 2–3 and neutropenia grade 1. Three additional patients (9%) had neutropenia grade 2 and one (3%) grade V. Among 32 evaluable patients for activity, one (3%) showed partial response, nine (27%) stable disease and 23 (70%) progression disease. Median PFS was 52 days (12–210).

Conclusion: Intravenous topotecan at that dose and schedule of administration has little activity in terms of response rate in third line of advanced NSCLC. The role and utility of chemotherapy in this setting warrants further investigation and confirmation through comparative studies.

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POSTER

Phase II study of the combination chemotherapy with weekly carboplatin and gemcitabine in advanced non-small cell lung cancer

K. Mori¹, Y. Kamiyama¹, H. Kasai¹, T. Kodama¹. ¹Tochigi Cancer Center, Thoracic Diseases, Utsunomiya, Japan

Background: The efficacy and safety of combination chemotherapy with weekly carboplatin (CBDCA) and gemcitabine (GEM) was evaluated as a protocol for first-line chemotherapy with advanced non-small cell lung cancer (NSCLC).

Methods: Eligible patients were the measurable NSCLC with the treatment of previously untreated patients. Patients were treated with a regimen consisting of GEM 1000 mg/m² and CBDCA AUC 2 on day 1 and day 8 at every 3 weeks.

Results: A total of 46 patients (pts) (Male/Female, 30/16 pts; median age 67 years [27–75]; Performance Status 0/1/2, 22/21/3 pts) were enrolled. Twelve patients (26%) had initial stage III disease and 34 patients (76%) had stage IV disease. The histological subtypes were adenocarcinoma (78%) and squamous cell carcinoma (15%). Fourteen patients (30%) achieved a partial response. The median number of treatment cycles was 3 (range 1–12). The time to progressive disease was 19.4 weeks and the median survival was 46.3 weeks. The one-year survival rate was 46.9%. The major toxicity was hematotoxicity and occurred grade 3 or 4 neutropenia (58.7%), thrombocytopenia (45.7%). One patient of grade 3

general fatigue were shown, and grade 2 nausea (17.4%), rash (8.7%), fever (6.5%), vomiting (6.5%), general fatigue (6.5%), constipation (2.7%) were occurred. None of other severe toxicities were appeared.

Conclusion: Weekly chemotherapy with CBDCA plus GEM is effective and is acceptable for the first line treatment of advanced NSCLC

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POSTER

Myelotoxicity of oral Topotecan in relation to treatment duration: Phase I study

G. Stathopoulos¹, A. Ardavanis², P. Papakotoulas³, G. Papadopoulos⁴, D. Antoniou⁵, A. Athanasiadis⁵, D. Trafalis⁵, J. Koutantos⁵, M. Vaslamatzis⁵, A. Rapti⁵. ¹Errikos Dunant Hospital, A' Oncology Clinic, Athens, Greece; ²Saint Savas Hosp., Oncology Dept., Athens, Greece; ³Theagenion Hosp., Oncology Dept., Salonika, Greece; ⁴Errikos Dunant Hosp., B' Oncology Clinic, Athens, Greece; ⁵Errikos Dunant Hosp., A' Oncology Clinic, Athens, Greece

Background: Topotecan intravenously administered has a place in Small Cell Lung cancer and ovarian cancer in pretreated patients. Oral Topotecan has been recently brought into clinical practice and has been suggested to be given for 5 days continuously at a dose of 2.3 mg/m² every 3 weeks. The published data showed a quite common myelotoxicity. The aim of the present trial is to define the daily dose and treatment duration that permits safe toxicity.

Material and Methods: Twenty eight patients were included, 25 males and 3 females. The median age was 60 years (46–77). In 26 patients the diagnosis was small cell lung cancer and in 2 patients ovarian cancer. All patients were treated before by 1 or more lines of chemotherapy. 14 patients were treated for 1–3 cycles with oral Hycamptin at a dose 2.3 mg/m² for 5-days, planned to be repeated every 3 weeks. In 7 patients the same dosage of Topotecan was given for 4 days. 7 patients had 3 days treatment's duration and 2 more patients were included in the 3 days duration, after unacceptable toxicity from the group of 5 or 4 days treatment.

Results: Nine patients from the 5-days treatment group presented serious myelotoxicity of Grade III and IV (64.28%). Myelotoxicity included neutropenia (Grade IV: 42.85%), thrombocytopenia of Grade II–III in 8 patients (57.14%) and anemia Grade II–III in 7 patients (50%). 4 patients treated for 4 days had neutropenia of grade III–IV (57.14%) and half of those thrombocytopenia. 4 patients out of 9 with 3 days of treatment had grade III and IV neutropenia (44.4%). The grade IV neutropenia was 22.2%. Several patients had dose reduction by 25% or shortened treatment duration from 5 days to 4 days, or from 4 days to 3. Two treatment related deaths were seen in the 5-days group and one in the 4-days group. It is worth to be mentioned that nearly one-third of the patients were previously heavily treated. Granulocyte growth factor was applied in over 60% of the patients.

Conclusion: The safe duration of treatment with oral Topotecan seems to be not longer than 3-days at a dose of 2.3 mg/m².

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POSTER

Antitumour activity of pemetrexed (Pem) and carboplatin in elderly patients in IIb and IV stages of non small cell lung cancer (NSCLC): a multicenter phase II study

R. Gervais¹, G. Robinet², C. Clement-Duchene³, F. Denis⁴, C. El Koury⁵, P. Martin⁶, A. Thureau-Vaury⁷, N. Chouaki⁷, N. Bourayou⁷, J.F. Morere⁸. ¹Centre François Baclesse, Medical Oncology, Caen, France; ²Hôpital Morvan, Pneumology, Brest, France; ³Hôpital Brabois, Pneumology, Nancy, France; ⁴Clinique Victor Hugo, Medical Oncology, Le Mans, France; ⁵Centre Catherine De Sienne, Medical Oncology, Nantes, France; ⁶Centre Bourgogne, Medical Oncology, Lille, France; ⁷Eli Lilly, Medical Oncology, Suresnes, France; ⁸Hôpital Avicennes, Medical Oncology, Bobigny, France

Background: Pemetrexed activity is synergistic with both carboplatin and cisplatin in chemo-naïve NSCLC patients. Two phase II Pem plus carboplatin trials have confirmed the doublet's activity in NSCLC and response rates were 31% and 24% (Scagliotti and al 2003, Zinner and al 2005). In elderly patients who are currently excluded from trials, age can impair physiologic processes and reduces the therapeutic index of drugs. In addition, because of renal toxicity related to cisplatin, carboplatin is a good alternative in this population suggesting a balanced benefit/risk profile when combined with Pem.

Materials and Methods: Sixty-two elderly patients (≥ 70 years) with measurable stage IIb not amenable to radiotherapy/IV NSCLC, without brain metastases, received at least one dose of chemotherapy. Pem 500 mg/m² over 10 min on day 1 with folic acid and vitamin B12 supplementation followed by carboplatin AUC 5 on the same day were given every 21 days for 6 cycles. Primary endpoint was objective response rate.