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First-Line Modified Schedule of Gemcitabine With a Lower Dose Than Standard in Elderly or PS 2 Patients With Advanced Non-Small Cell Lung Cancer

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Background: Monochemotherapy with gemcitabine (Gem) is often the treatment of choice in elderly or poor performance status (PS) patients with advanced non-small cell lung cancer (NSCLC). Our study was aimed to assess the efficacy and tolerability of a modified schedule of Gem using a lower dose than standard.
Patients and Methods: From May 2009 through December 2010, fifty patients (43 males and 7 females with a median age of 76 years ranging from 64 to 85) with advanced NSCLC (stage IIIB 34.0% and IV 66.0%) were enrolled. Histology was: squamous 39.6%, adenocarcinoma 31.2%, large cell 6.2%, undifferentiated 4.2%, undetermined 18.8%. Only eight patients (16.0%) had a WHO PS 0 whereas nineteen (38.0%) were PS 1 and eleven (46.0%) PS 2. All patients received first-line chemotherapy with 6 cycles of Gem 1000 mg/sq on days 1 and 8 every 4 weeks.
Results: At the time of analysis 35 patients were evaluable for response. Partial response (PR) was achieved in 7 patients (20.0%), stable disease >12 weeks (SD) in 16 (45.7%) whereas 12 had progressive disease (34.3%). Importantly, the clinical benefit rate (PR + SD) was 65.7%. Tumour markers (CEA and NSE) were high in 28 patients with a reduction in their values observed in 11 of them (39.3%). Both pain and PS improved in 6 patients (17.1%) whereas 19 (54.2%) had an improvement in pain with no worsening of PS. We observed only grade 2 WHO haematological toxicities including anemia, leucopenia, neutropenia and trombocytopenia. Not-neutropenic fever occurred in 4 patients (11.4%). Overall, we did not observe any not-haematological treatment-related event.
Conclusions: Our data show that a modified schedule of Gem with a lower dose intensity than standard may be beneficial in terms of both disease control and tolerability when employed in elderly or PS 2 patients with advanced NSCLC.

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Biweekly Docetaxel-Cisplatin in Chemonaive Patients With Advanced Epidermoid Carcinoma of the Lung − a Phase II Study of Galician Lung Cancer Group

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Background: Non-small cell lung cancer (NSCLC) represents a 80% all lung cancer. A third of the patients have metastatic disease when they are diagnosed. Standar treatment in patients with good performance status is a combination of two drugs, one of them containing platinum. We conducted a multicenter study in advanced stage squamous NSCLC to evaluate the efficacy of first-line biweekly docetaxel-cisplatin.
Materials and Methods: Patients with advanced NSCLC and epidermoid histology received biweekly docetaxel (50 mg/m^2 days 1, 14) and cisplatin (50 mg/m^2 days 1, 14) every 28 days (DC) with restaging after 3 and 4 cycles. The primary end point was to evaluate the overall response rate and the secondary were the progression-free survival and median overall survival.
Results: Forty-five patients were accrued from six centers across Galicia. Overall response rates were 45.9%, all them had a partial response. Median overall survival was 12.6 months (95% confidence interval, 10 to 15.2); progression-free survival was 4.7 months (95% confidence interval, 3.9 to 5.5). The treatment was well tolerated, with the most common treatment-related side effects being grade 1 anemia (48.8%), asthenia (32.5%), nausea (30.2%) and anorexia (27.91%). Grade 3 and/or 4 toxic reactions were neutropenia (20.9%, 11.6% with fever), diarrhea (4.6%), mucositis and neuropathy (2.3% both).
Conclusions: Biweekly docetaxel-cisplatin show favorable toxicity profiles and activity in patients with advanced stage squamous NSCLC.

9100 POSTER

Erlotinib in Previously Treated NSCLC − a Critical Appraisal Based on Monoinstitutional Experience

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Background: Erlotinib is a potent inhibitor of epidermal growth factor receptor tyrosin-kinanase activity approved in the EU and in the USA for the treatment of non small-cell lung cancer (NSCLC) in patients with stage IIIB or IV who had received one or more prior chemotherapy regimens. The registration study BR.21 (NEJM 2005, 14, 353, 123) showed to prolong significantly overall survival (OS) and progression free survival (PFS) in Erlotinib arm. In 2005 AIFA (Italian Agency on Drugs) has activated a web-based national registry of oncology drugs (RFOM) as an appraisal on new drugs introduced into the Italian market. Oncologists are required to subscribe all patients in treatment completing patient's data and recording in follow-up toxicity, variations in dosage and final outcomes. The analysis of polled records achieved in this way may be used for effectiveness estimates.
OS and Time to Progression (TTP) may be achieved from clinical practice as a valuable indicator of effectiveness through retrospective observational analysis. The aim of the study is to assess Median OS and TTP in clinical practice compared to outcome values obtained from the registration study of Erlotinib in NSCLC.
Materials and Methods: An independent Drug Evaluation Unit of the Istituto Oncologico Veneto collected data from the registers and the patient's charts to establish the real clinical impact of the drug. The follow up duration was 39 months, from December 2006 to February 2011. Every patient was checked for *length of treatment, toxicity and outcomes*. The data of EGFR mutation and EGFR FISH positive had not been done for all patients because they are not mandatory for RFOM. For the efficacy/effectiveness comparison assessment we used registration RCT outcome measures: OS, PFS with Kaplan–Meier estimates. The multivariate regression analysis was performed to detect potential associations between the baseline characteristics of the patients and the effect of Erlotinib.
Results: A total of 131 patients treated with Erlotinib were reviewed (median age = 69 years, M = 79, F = 52). More than 50% of patients had received two or more prior chemotherapy regimens. Median TTP and OS were 2 and 3.6 months, respectively compared to Erlotinib arm of the BR.21 study with PFS 2.2 months and OS 6.7 months. There was no significant difference in OS based on age groups ($\geqslant$70 and <70). The disease control rate was 18% (RP = 4, SD = 20) and the median duration of the response was 7.6 months. Only one patient discontinued the treatment due to toxic effects.
Conclusions: The results of our retrospective observational study have showed that for patients with two or more prior chemotherapy regimens and with no selection for EGRF mutation/amplification, it is not recommended the use of Erlotinib for the treatment of NSCLC.

9101 POSTER

Pre-planned Subgroup Analyses From the Phase III, Randomised, Placebo-controlled, Parallel-group Study of Gefitinib (G) as Maintenance Therapy in Patients (pts) With Locally Advanced or Metastatic Non-small-cell Lung Cancer (NSCLC) (INFORM; C-TONG 0804)

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Background: The phase III, randomised, placebo (P)-controlled, parallel-group INFORM study (NCT00770588) investigated the efficacy, safety and tolerability of G *v* P as maintenance therapy in pts with locally advanced/metastatic NSCLC following standard first-line platinum-based chemotherapy (CT).

Materials and Methods: Pts (⩾18 years, stage IIIB/IV NSCLC, WHO PS 0−2, completed 4 cycles of first-line platinum-based doublet CT without progression/unacceptable toxicity) were randomised 1:1 to G 250 mg/day or P 3−6 weeks post-CT. Progression-free survival (PFS; primary endpoint; intent-to-treat population) was assessed: Cox proportional hazards adjusted for histology (adenocarcinoma *v* non-adenocarcinoma), smoking status (never-smoker *v* smoker), EGFR mutation status (positive [M+] *v* negative [M-] *v* unknown), best response to first-line CT (complete response [CR]/partial response [PR] *v* stable disease [SD]). PFS subgroup analyses defined by: primary PFS analysis covariates, type of CT (taxane *v* non-taxane), gender, disease stage at screening (IIIB *v* IV). A global treatment by covariate interaction (5% significance level) assessed consistency across subgroups. Secondary endpoints included objective response rate (ORR), disease control rate (DCR), overall survival (OS).
Results: 296 pts (n = 148 G, n = 148 P) were randomised (27 centres in China; 26 September 2008−10 August 2009; PFS data cutoff 24 January 2011). Median duration of follow-up: 16.8 months. Demography was balanced between treatments: 54.1% never-smokers, 70.6% adenocarcinoma, 40.9% female. For PFS G *v* P: HR = 0.42; 95% CI 0.32–0.54; p < 0.0001; median PFS 4.8 *v* 2.6 months. A generally consistent treatment effect was observed across all subgroups (interaction p = 0.4256). ORR and DCR significantly favoured G *v* P; median OS 18.7 *v* 16.9 months.

Subgroup	N		PFS	
	G	P	HR	95% CI
Adenocarcinoma	105	104	0.33	0.24–0.46
Non-adenocarcinoma	43	44	0.72	0.46–1.14
Never smoker	79	81	0.36	0.25–0.51
Smoker	69	67	0.52	0.35–0.75
CR/PR	58	51	0.44	0.29–0.66
SD	90	97	0.40	0.29–0.56
Male	83	92	0.49	0.35–0.69
Female	65	56	0.34	0.22–0.50
Taxane	60	66	0.41	0.28–0.61
Non-taxane	88	82	0.43	0.31–0.61
Stage IIIB	42	32	0.46	0.28–0.77
Stage IV	106	115	0.41	0.30–0.55
EGFR M+	15	17	0.16	0.07–0.40
EGFR M-	32	31	0.64	0.38–1.07
EGFR M unknown	101	100	0.43	0.31–0.58

Conclusions: PFS was significantly longer with G *v* P as maintenance therapy in pts with locally advanced/metastatic NSCLC, with generally consistent benefit observed across all subgroups. ORR and DCR significantly favoured G; there was no significant difference between treatments for OS.

9102 POSTER

A Phase II Study of Biweekly Irinotecan and Cisplatin for Patients With Extensive Stage Disease Small Cell Lung Cancer

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Background: An irinotecan and cisplatin (IP) combination is one of active regimen used in treatment of extensive stage disease (ED) small cell lung cancer (SCLC). However, a 4-week cycle of irinotecan treatment can result in significant myelosuppression and diarrhea. Therefore, the present study was conducted to evaluate the efficacy and safety of biweekly IP in patients with ED SCLC.
Methods: Patients with previously untreated ED SCLC received intravenous irinotecan at a dose of 60 mg/m^2 and cisplatin at a dose of 30 mg/m^2 on days 1 and 15 every 4 weeks.
Results: Thirty-five patients were enrolled in this study. Three complete responses and 23 partial responses were confirmed, giving an overall response rate of 74.3%. After a median follow-up of 15.1 months, the median time to progression and overall survival were 7.7 months and 12.2 months, respectively. Grade 3/4 neutropenia occurred in seven patients and grade 3 febrile neutropenia was observed in one patient. Grade 3 diarrhea occurred in two patients.
Conclusions: The combination chemotherapy of biweekly IP was found to be well tolerated and effective in patients with ED SCLC. Further evaluation of the combination of IP at the dose and schedule in this study is warranted in ED SCLC patients.

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Phase II Trial of NGR-hTNF and Doxorubicin in Relapsed Small Cell Lung Cancer (SCLC)

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Background: NGR-hTNF is a selective vascular targeting agent, which is able to improve the intratumoral doxorubicin penetration by normalizing tumour vasculature and decreasing interstitial fluid pressure. A phase I trial previously selected NGR-hTNF 0.8 μg/m^2 + doxorubicin 75 mg/m^2 for further testing.
Methods: SCLC patients relapsing after a platinum-based regimen received every 3 weeks NGR-hTNF until progressive disease (PD), while doxorubicin dose was capped at 550 mg/m^2. The trial had 2-stage design with a total of 27 patients to be accrued. Progression-free survival (PFS) was the primary study aim.
Results: Twenty-eight patients (median age: 63 years; M/F: 19/9; PS 0/1−2: 13/15) were recruited. Prior treatment lines ranged from 1 to 3. Median treatment-free interval from last line was 2.8 months (95% CI, 1.0−3.9), with 16 patients being platinum resistant (pl-R; PD ⩽ 3 months) and 12 patients platinum sensitive (pl-S; PD >3 months). Baseline neutrophil-to-lymphocyte ratio (NLR), an index of systemic host immune response to tumour, was ⩽ or > the median value of 4 in 18 and 10 patients, respectively. Overall, 114 cycles were given (median 3; range 1−10) and 13 patients (46%) received ⩾4 cycles. NGR-hTNF did not increase doxorubicin related toxicity. No grade 3−4 toxicities related to NGR-hTNF were noted, while grade 1−2 events were transient chills (61%). The median PFS time was 3.2 months (95% CI 2.6−3.8). Six partial responses (PR; 22%) and 9 stable diseases (SD; 33%) were observed for an overall disease control rate of 55% (95% CI 35−74). Patients who experienced PR or SD had median PFS times of 6.3 and 4.1 months, respectively. With median follow-up of 19.3 months, the 6-month and 1-year overall survival (OS) rates were 49% and 34%, respectively. By subset analyses, response rates were 19% and 27%, median PFS times were 2.7 and 4.1 months, and 1-year OS rates were 27% and 42% for pl-R and pl-S patients, respectively. For patients pretreated with two or more regimens (n = 8), median PFS was 4.1 months and 1-year OS rate was 44%. By univariate Cox analyses, both PFS and OS did not correlate with age, gender, PS and platinum sensitivity, while only NLR was associated with OS (HR = 0.30). The 1-year OS rates in patients with baseline NLR below or above the median value were 48% and 10%, respectively (p = 0.01).
Conclusion: Further development of NGR-hTNF plus doxorubicin in platinum resistant or sensitive SCLC is of interest.

9104 POSTER

Weekly Divided Carboplatin Combined With Irinotecan in Patients With Small Cell Lung Cancer

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Background: Systemic chemotherapy is mainstay of treatment in patients with small cell lung cancer(SCLC). However, adverse effects of chemotherapeutic agents, especially platinum-based, causes neutropenia, infection, sepsis, and even death. Weekly devided platinum-based chemotherapy in concurrent chemo-radiation of non-small cell lung cancer is acceptable regimen. We tested feasibility of devided platinum-based chemotherapy in SCLC without concurrent radiation.
Material and Methods: Patients with chemotherapy-naive SCLC received carboplatin 2 AUC combined with irinotecan (60 mg/m^2) at day 1, 8, and 15 every 4 weeks for 4 cycles at out-patient department. The primary end point was evaluation of over all response rate, and secondary end points were treatment related serious adverse events and discontinuation of chemotherapy due to side effects.
Results: Twenty-one (16 extensive stage and 5 limited stage) patients were enrolled. Complete response, partial response, stable disease, and progressive disease were 2(9.5%), 16(76.2%), 1(4.8%), and 2(9.5%), respectively. Serious adverse events were happened 5 times in 2 patients, 1 patient stopped chemotherapy due to side effects.
Conclusions: Weekly divided carboplatin combined with irinotecan was feasible regimen in never treated SCLC patients.