9108 POSTER

Randomized Phase II Trial of Gemcitabine and Carboplatin (G/C) With or Without Dexamethasone (Dex) Pretreatment in Chemotherapy-naïve Patients (pts) With Advanced Non-small Cell Lung Cancer (NSCLC) − Results of Kyoto Thoracic Oncology Research Group (KTORG) Trial 0501

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Background: G/C is one of the standard regimens for the treatment of advanced NSCLC, but dose reductions in the second cycle were frequently reported due to severe hematological toxicity, especially in terms of thrombocytopenia (Yamamoto, Cancer 2006). Preclinical and early phase clinical studies suggested that Dex pretreatment in combination with G/C reduces the toxicity as well as increases the antitumour activity of G/C (Wang, Clin. Cancer Res. 2004, Rinehart, ASCO Proc 2005).
Materials and Methods: In this prospective, randomized (1:1), open-label, multi-center phase II trial, chemotherapy-naïve pts with advanced stage (IIIB/IV) NSCLC, ECOG PS of 0−1, and adequate organ functions were randomly assigned to receive either G/C (G: 1000 mg/m^2, days 1 and 8, C: AUC 4.5 mg/mL/min, day 1) (Arm A) or G/C + Dex (Arm B) for up to six 21-day cycles. Dex was orally given at the dose of 8 mg/day b.i.d. on days −4, −3, −2, −1 and 0 prior to G/C. The primary endpoint was dose reduction rate (DRR) in the second cycle, which was defined based on the toxicity of the first cycle; Grade 4 neutropenia, Grade 4 thrombocytopenia, febrile neutropenia, Grade 3 or more non-hematological toxicity, and skip of day 8 chemotherapy. Secondary endpoints included deferment rate (DR) of second cycle, objective response rate (ORR), time to progression (TTP), overall survival (OS), safety, and platelet transfusion rate (PTR).
The trial has been registered at UMIN-CTR (www.umin.ac.jp/ctr/index/htm), registration identification number 000000547.
Results: 76 pts were enrolled from July 2006 to Dec. 2009 and 71 pts received at least one cycle of protocol-specified therapy (A 37, B 34). Demographic factors were well balanced. Median number of cycles received in A/B was 3/4. DRR in A/B was 31.0%/32.3% (p = 0.92), whereas DR in A/B was 40.0%/16.1% (p = 0.038). ORR in A/B was 24.3%/23.5% (p = 0.21), and DCR in A/B was 70.3%/82.4% (p = 0.34). Median TTP in A/B was 3.8 months (95% CI, 2.1−4.7) /4.2 months (95% CI, 3.0−5.9)(p = 0.12, log-rank test) and Median OS in A/B was 11.8 months (95% CI, 7.9–18.0)/24.5 months(95% CI, 8.2–28.7)(p = 0.29, log-rank test).
The rates of hematological and non-hematological toxicities were not significantly different between A and B except for that of diarrhea (A/B = 8.1%/29.4%, p = 0.02), but the severity of diarrhea was mild (all Grade 1). The rates of Grade 3 or more neutropenia and thrombocytopenia in A/B were 67.6%/70.6% and 62.2%/55.9%, respectively. PTR in A/B was 13.5% /2.7% (p = 0.061). No treatment-related death was observed in both A and B.
Conclusions: Adding Dex pretreatment to G/C did not reduce DRR but prevented the delay of next cycle. Dex pretretment can be combined with G/C safely with a trend of improved DCR, TTP and OS.

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A Phase II Study of Pemetrexed in Heavily Pretreated Non-squamous Non Small Cell Lung Cancer − HANSHIN Oncology Group 001

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Background: Pemetrexed has shown substantial activity in non-squamous non-small-cell lung cancer (NSqNSCLC) and is one of the current standard agents in second-line settings due to its efficacy and favorable tolerability profile. We conducted phase II study to evaluate the safety and efficacy of pemetrexed in Japanese patients with previously treated, advanced NSqNSCLC.
Patients and Methods: Patients with stage IIIB (wet) or IV NSqNSCLC, performance status (PS) 0 to 2, previous two to five regimens of chemotherapy were enrolled and received pemetrexed (500 mg/m^2 Day 1, every 21 days) until disease progression. The primary endpoint was progression free survival (PFS). The secondary endpoints included overall survival (OS), objective response rate (ORR), disease control rate (DCR), and safety. The trial has been registered at UMIN-CTR (www.umin.ac.jp/ctr/index/htm), registration identification number UMIN000002467.
Results: From August 2009 to May 2010, forty-six patients were enrolled: median age 65 yrs; 52% women; PS 0/1/2 26%/67%/7%; previous treatment regimen 2/3/4/5 48%/26%/24%/2%; EGFR activating mutation positive/wild/unknown 30%/48%/22%. Median duration of follow-up was 9.4 months, with 80% patients progressed and 41% deceased. Median 7 cycles of pemetrexed was administered. Median PFS was 4.2 months (95% CI: 3.0, 6.1). Median OS was not reached. ORR was 8.7% (95% CI: 2.4, 20.8) and DCR was 63.0% (95% CI: 47.5, 76.8) (CR 0%, PR 8.7%, SD 54.3% and PD 28.3%, by investigators). In a total of 129 cycles of therapy, G3/4 neutropenia was observed in 14%/5% cycles, G3/4 anemia in 7%/0% cycles, and G3/4 thrombocytepenia in 4%/0% cycles, respectively. The most common G3−4 non-hematologic adverse events were fatigue (7%) and dyspnea (7%).
Conclusions: Treatment with pemetrexed in previously treated Japanese NSqNSCLC patients is feasible and shows encouraging activity.

9110 POSTER

Long-term Chemotherapy for Advanced NSCLC

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Background: Survival in patients with advanced non-small-cell lung cancer (NSCLC) has substantially improved. Long-term chemotherapy with epidermal growth factor tyrosine kinase inhibitors (EGFR-TKIs) and other agents has been associated with long survival.
Materials and Methods: Of 360 patients who received first-line chemotherapy between January 1, 2004 and December 31, 2007, 185 subsequently received additional outpatient chemotherapy and 175 underwent inpatient chemotherapy only. Of the 185 patients, 147(79.5%), 96 (51.9%), and 60 (32.4%) received second-line, third-line, and fourth-line chemotherapy, respectively. We retrospectively examined the associations between overall survival (OS) and clinical variables in patients with advanced NSCLC who received at least one dose or course of outpatient chemotherapy in our institution.
Results: Patients who received outpatient chemotherapy had significantly longer median OS (22.3 months) than did those undergoing inpatient chemotherapy only (7.6 months; P < 0.0001). In univariate analysis of the 185 patients, sex, performance status (PS), smoking status, stage, best response to first-line chemotherapy, use of docetaxel, and EGFR-TKIs were significantly associated with OS (P values: 0.0019, 0.0066, 0.0001, 0.0231, 0.0011, 0.0250, and 0.0023, respectively). In multivariate analysis, PS, stage, best response to first-line chemotherapy, and use of docetaxel were significantly associated with OS (P values: 0.0272, 0.0028, 0.0030, and 0.0376, respectively). Survival was significantly longer among patients who responded to docetaxel and/or EGFR-TKIs. Long-term chemotherapy did not increase cumulative hospitalization.
Conclusions: In patients with advanced NSCLC, an effective long-term chemotherapy regimen might prolong survival in responders to first-line chemotherapy.

9111 POSTER

Survival in Patients With Non-small Cell Lung Cancer Which is Clinically Acquired Resistance to Gefitinib: Natural History Since Progression

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Background: Most of patients with tyrosine kinase inhibitors (TKIs)-sensitive non-small cell lung cancer (NSCLC) eventually develop acquired resistance to TKIs. And it remains uncertain what would affect survivals of TKI-sensitive patients since progression while on TKIs.

Materials and Methods: We retrospectively reviewed 81 advanced NSCLC patients who experienced disease progression following tumour response and durable (⩾ 6 months) disease stabilization from first-line or second-line gefitinib. Post-progression survival (PPS) and characteristics were investigated and compared in patients who resumed TKIs (n = 16) and who did not resume (n = 65).
Results: Most of patients were female never-smokers with adenocarcinoma. Median overall PPS was 10.3 months (95% CI; 7.458–13.142). Age, gender, smoking history, histology, ECOG performance status (PS) at the start of gefitinib, initial stage and platinum-based chemotherapy (PBC) after gefitinib were not significant predictors for PPS. Using pemetrexed after gefitinib showed significantly longer PPS (18.5 vs 8.6 months, HR = 0.45, p = 0.008). Resuming gefitinib had a trend to lengthen the PPS but, lost its significance by multivariate analysis (27.4 vs 8.8 months, HR = 0.53; p = 0.095).

Table: Response to resumed TKIs

Response	Gefitinib resumed (n = 11)	Erlotinib resumed (n = 5)
PR	3	1
SD	5	2
PD	3	2

Conclusions: In NSCLC patients who assumed to have clinically acquired resistance to TKIs had relatively long PPS. Resuming TKIs or using pemetrexed after PD on gefitinib could improve the PPS.

9112 POSTER

AVAPERL1 (MO22089) − Interim Safety of Maintenance (mtc) Bevacizumab (bev) + Pemetrexed (pem) in Patients (pts) With Advanced Non-squamous Non-small Cell Lung Cancer (nsNSCLC) After First-line (1L) Bev-cisplatin (cis)-pem Treatment (Tx)

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Background: 1L bev-based Tx followed by mtc bev offers clinical benefit over chemotherapy alone, as do either 1L cis-pem or mtc pem. AVAPERL1 investigates whether continuing pem with bev offers additional benefit over bev alone after 1L bev-cis-pem. AVAPERL1 is fully enrolled; follow-up is ongoing.
Materials and Methods: Eligible pts with advanced, metastatic or recurrent nsNSCLC who achieve CR/PR/SD after 4 cycles of bev-cis-pem were randomized to receive bev or bev+pem until disease progression or unacceptable toxicity. Adverse events (AEs) were graded by NCI CTC v.3.0 (MedDRA coding).
Results: As of 11Feb11, 373 pts who received ⩾1 dose of any study drug were included in the safety analysis. Baseline characteristics were reported at ESMO 2010 (Barlesi, 430P). 244 pts (59%) initiated mtc Tx. Median follow-up, 7.6 months. *Safety population*: Overall AEs are shown in Table 1. The most common grade (G)⩾3 AEs with onset in 1L or mtc are neutropenia (8%), fatigue/asthenia (4%) and anemia, dyspnea, hypertension (HTN) and pulmonary embolism (PE) (3% each). The most common SAEs with onset in 1L or mtc are pneumonia and PE (3% each), and diarrhea, nausea, neutropenia and renal failure (2% each). *Mtc phase*: More pts treated with bev+pem (90%) reported AEs with onset in mtc than those treated with bev (79%). The most common (⩾10%) AEs in the bev+pem arm are fatigue/asthenia and HTN (22% each), nausea (20%), constipation, cough and dyspnea (12% each), anorexia (11%), and diarrhea (10%) and those in the bev arm are HTN (17%), fatigue/asthenia (12%) and cough (10%). The number of G ⩾ 3 AEs with onset in mtc was greater in the bev+pem arm (56 events, 33% pts) than in the bev arm (30 events, 18% pts), with the most common being neutropenia (4%) in the bev+pem arm, and PE (3%) in the bev arm. The number of SAEs with onset in mtc was greater in the bev+pem arm (33 events, 20% pts) than in the bev arm (15 events, 13% pts), with the most common being pneumonia and TIA (2% each) in the bev+pem arm, and PE and general deterioration (2% each) in the bev arm.
Conclusions: 1L bev-cis-pem was tolerable. More G⩾3 AEs and SAEs with onset in mtc were reported in pts treated with bev+pem than bev and this increased toxicity may be attributable to pem.

Table 1

	Safety population, N = 373	Bev mtc, n = 119	Bev+pem mtc, n = 125
Any G AE			
n	3450	1105	1500
% pts	95	96	97
G⩾3 AE			
n	349	76	106
% pts	53	40	47
SAE			
n	218	35	70
% pts	39	23	36
% pts with AE by phase			
1L	88	84	89
Mtc	55	79	90
% pts with AE by intensity			
G1/2	85/77	92/81	90/83
G3/4	45/9	36/5	43/6
G5	6	3	4

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Total Direct and Segmented Medical Cost-of-Care for Stage IV (Adv) Non-Small Cell Lung Cancer (NSCLC) in a Private Insurance Population

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Background: New treatments for stage IV (adv) NSCLC have emerged this past decade. The direct medical cost-of-care for adv NSCLC has not recently been studied. Our primary objective was to characterize the direct cost of adv NSCLC from 2000−9. We also want to determine cost segmented by time in the disease course (diagnosis, active treatment, end-of-life), cost impact of new therapies, and cost trend from 2000−9.
Methods: This PharMetrics claims database study uses a retrospective cohort study design. Diagnosed NSCLC patients ⩾20 years were included. Small cell lung cancer was excluded. Sub analyses include division into disease segments and time periods representative of changes in therapy available throughout the study period. The study period was divided into the “pre” (2000−2), “transition” (2003−5), and “current” (2006−9) periods to account for the change from standard chemotherapy to the introduction of pemetrexed, TKIs, and the biologics.
Results: The study sample contains 5,847 eligible patients. Over the study period the mean total cost of care was $162,134 per patient (patients receiving ⩾ 5 months of therapy; n = 432), while the mean per patient per month (pppm) cost was $10,284 (med [median] $7,696; SD $12,295). Diagnosis cost was $9,162 pppm (med $6,978; SD $8,328). Active mean treatment cost was $10,141 pppm (med $7,807; SD $10,435) and end-of-life mean cost was $18,033 pppm (med $12,301; SD $19,370). Pemetrexed (5%), TKIs (6%), and biologic agents (5%) accounted for 16% of the active treatment segment. In total, they accounted for 4% of overall cost. Cost of “pre” was $8,662 pppm (med $6,747; SD $8,747), “transition” was $10,578 pppm (med $7,722; SD $13,716), and “current” was $10,141 pppm (med $7,731; SD $11,186).
Conclusions: The mean total direct cost of care for advanced NSCLC was over $160,000 per patient or $10,284 pppm. The most costly segment was end-of-life at $18,033 pppm. The newer agents (pemetrexed, TKIs, and biologics) represent only a modest portion of the active treatment cost, which was a mean of $10,141 pppm, but represented only a very small portion of total cost. The “current” time period retained similar costs as the “transition” period.