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.

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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.