985 POSTER DISCUSSION 2*

Phase II trial of mta (LY231514) in patients (PTS) with non-small cell lung cancer (NSCLC) who relapsed after previous platinum or non-platinum chemotherapy

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Purpose: While new chemotherapeutic agents for NSCLC have emerged in the recent past, there remains a critical need for agents which are also active in the second-line setting. This study was designed to evaluate the activity of MTA (multitargeted antifolate), in the treatment of NSCLC pts who relapsed following front-line therapy. MTA inhibits multilple folate-dependent enzymes and has shown promising activity in a wide range of tumor types.

Methods: Pts with Stage IIIb or IV NSCLC who had relapsed during or within 3 months of prior therapy were entered into two cohorts, depending on whether their prior therapy did (PT) or did not contain platinum (NP) (i.e. mitomycin, docetaxel, paclitaxel, vinorelbine, and/or gemcitabine). All pts received MTA 500 mg/m^2 every 21 days with prophylactic dexamethasone.

Results: 67 pts have been enrolled, with 43 evaluable for response. Pts received a median of 2 cycles of therapy (range 1–7), with 6% and 3% of cycles delayed or reduced, respectively. In the PT arm, there have been 3 partial responses (PRs) in 23 evaluable pts, for an overall response rate (RR) of 13%. The NP arm has included 1 complete and 5 PRs in 20 evaluable pts, for a RR of 30%. Grade 3/4 toxicity (as % of cycles) includes Hgb: 6/1, WBC: 19/3, ANC: 14/9, platelets: 3/4, bilirubin: 2/0, elevated transaminases: 3/0, and infection: 1/2, respectively. One pt discontinued due to drug-related pneumonia. Four on-study deaths are thought not to be drug-related.

Conclusion: MTA has activity in the second-line treatment of NSCLC, and appears to be non-cross resistant with a variety of front-line agents

986 POSTER DISCUSSION 2*

Docetaxel plus cisplatin versus docetaxel plus gemcitabine chemotherapy in advanced non-small cell lung cancer: A preliminary analysis of a multicenter randomized phase II trial

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Background: Docetaxel/CDDP (D/C) and docetaxel/gemcitabine (D/G) are active and well tolerated chemotherapy regimens for the treatment of patients with advanced non-small-cell lung cancer (NSCLC). A phase II randomized trial was conducted in order to compare the efficacy and toxicity of these regimens.

Patients: 315 chemotherapy-naive patients with stage IIIB and IV NSCLC were enrolled onto the study. Patients were treated with either Arm A: docetaxel (100 mg/m^2; day 1) and CDDP (80 mg/m^2; day 2) or with Arm B: gemcitabine (1100 mg/m^2; days 1 and 8) and docetaxel (100 mg/m^2; day 8); rhG-CSF (150 mcg/m^2 s.c.) was given in arm A (day 3–9) and in arm B (day 9–15). Both regimens were repeated every 3 weeks.

Results: Arm A (D/C): [No of pts treated/evaluated: 152/132, CR (%) + PR (%): 3 (2.3% + 39 (30%), overall response rate (95%CI): 32% (24–40), SD (%)/PD (%): 42 (32%)/48 (36%), duration of response (months): 5, time to progression (months) 8, median survival (months): 10, 1-year survival (%): 42%]. Arm B (D/G): [No of pts treated/evaluated: 144/114, CR (%) + PR (%): 1 (0.9%) + 38 (33%), overall response rate (95% CI): 34% (25–43), SD (%)/PD (%): 37 (32%)/38 (33%), duration to response (months): 4, time to progression (months): 8, median survival (months): 9, 1-year survival (%): 38%]. The probability of response to the docetaxel/CDDP was significantly higher (p = 0.03) in patients with a non-adenocarcinoma whilst the opposite was observed in patients with an adenocarcinoma (p = 0.002). A total of 1161 cycles were administered (Arm A = 595; Arm B = 566) with a median of 3 and 4 cycles/patient, respectively. Toxicity by WHO criteria (Arm A/Arm B) was: grade 3/4 anemia 9 pts (6%)/6 pts (4%); grade 3/4 neutropenia 50 pts (33%)/31 pts (22%); grade 3/4 thrombocytopenia 4 pts (3%)/7 pts (5%); febrile neutropenia 24 pts (16%)/20 pts (14%); grade 3/4 diarrhea 18 pts/4 pts (p = 0.00296); grade 3/4 fatigue 45 pts (30%)/49 pts (33%); grade 2/4 neurotoxicity 10 pts (7%)/6 pts (4%).

Conclusions: These preliminary results seem to indicate that the docetaxel/CDDP and the docetaxel/gemcitabine regimens have a comparable activity and toxicity profile in patients with advanced NSCLC.

*Poster Discussion 2 will be held on Thursday 16 September 1999

987 POSTER DISCUSSION 2*

Gemcitabine + vinorelbine (GV) vs vinorelbine (V) alone in elderly or frail non-small cell lung cancer (NSCLC) patients. Interim analysis of a SICOG phase III trial

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Purpose: To compare the impact on survival and QoL of the GV regimen with that of V alone.

Patients and Methods: NSCLC pts with locally advanced or metastatic disease aged between 71 and 80 years with ECOG PS ≤ 2 or younger with PS = 2, were randomized to receive GV (G 1,200 mg/m^2 + V 30 mg/m^2 d 1 & 8 q 3 wk) or V (30 mg/m^2 d 1 & 8 q3wk) alone. A final sample size of 120 pts for each arm had been chosen. An interim analysis had been planned after that 60 pts per arm had been enrolled.

Results: The survival data of 138 randomized pts (GV = 70 and V = 68) were analysed. 103 pts were elderly (>70) and 35 were younger with poor PS. At a 13 (range; 1–19)-month median potential follow-up, the observed MSTs were: GV = 25 wks and V = 23 wks. If only the 103 elderly pts are taken into account, the MSTs were slightly shorter (GV = 23 wks and V = 18 wks). At the present analysis the observed difference in the risk of death between the two arms was not statistically significant.

Conclusions: These data suggest that either GV or V alone do not represent an effective treatment for both elderly and frail NSCLC pts, since the MSTs in both arms were not substantially longer than that recently reported with the best supportive care alone (21 weeks) in elderly pts. A further analysis will be performed after 120 elderly pts have been enrolled.

Other Participant Investigators: Comella P, Di Rienzo G, Cioffi R, Natale M, Bilancia D, Micillo E, Pusceddu G, Contu A, Filippelli G.

988 POSTER DISCUSSION 2*

Chemotherapy (CT) and twice daily radio-chemotherapy (HA RT/CT) *versus* chemotherapy (CT) alone before surgery in stage III non small cell lung cancer (NSCLC): Analysis of toxicity of a randomized trial

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In 10/95 a multicenter randomized phase III study was started to evaluate the contribution of preoperative radiochemotherapy on tumor downstaging and survival in locally advanced NSCLC. After mediastinoscopy and stratification according to stage and institution pts. were randomized to *(Arm A)* 3 cycles PE (cisplatin 55 mg/m^2 (d1 + 4)/etoposide 100 mg/m^2 (d1 – 4)), followed by hyperfractionated accelerated RT (HA RT, 45 Gy; 2 × 1.5 Gy/d) with concurrent CT (carboplatin 100 mg/m^2, vindesin 3 mg, d 1, 8, 15) and surgery (if no or R1/2 – resection additional HA RT 24 Gy) *versus (Arm B)* 3 cycles PE followed by surgery and postop. RT (54 Gy or (if no or R1/2 resection) 68.4 Gy, 1 × 1.8 Gy/d). Study endpoints are survival, resectability and toxicity. Of 234 pts. entered up to 10/98 (IIIA/IIIB 69/132), 186 are evaluable for toxicity. Toxicity (WHO 3, 4) to PE was 19%, 9%, 9% leukocytopenia, 2%, 3%, 2% thrombocytopenia without treatment related deaths (TRD). Esophagitis and pneumonitis rates were 31% and 3% after HA RT/CT and 6% and 9% after RT. TRD (pneumonitis) occurred in 3 cases (Ann B). Overall response rate to induction was 55%. 104/162 pts were considered for surgery. So fare, R0-resection rate is 79% (IIIA:87%, IIIB:73%), TRD occurred in 7 pts. As toxicities are acceptable and response- and resection rates are good, the trial will be continued to 350 randomized pts. (Supported by "Deutsche Krebshilfe")

989 POSTER DISCUSSION 2*

Cisplatin (CDDP) and irinotecan (CPT-11) versus CDDP and vindesine (VDS) in advanced (stage IIIB and stage IV) non-small cell lung cancer (NSCLC). A multicenter phase III study

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CDDP and CPT-11 combination is an active regimen against advanced