1015 PUBLICATION

Cisplatin – gemcitabine – paclitaxel (PGT) in the treatment of advanced non-small-cell lung cancer (NSCLC). A southern Italy cooperative oncology group (SICOG) phase II study

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Purpose: To define the antitumor activity of the PGT combination in chemo-naive NSCLC pts

Patients and Methods: Patients with locally advanced or metastatic NSCLC were considered eligible if they had age ≤ 70 years and ECOG PS 0–2. They received P 50 mg/m^2, T 125 mg/m^2 and G 1,000 mg/m^2 d 1 & 8 q 3 wk.

Results: Since April 1907, 39 patients with stage IIIB (13) or IV (26) disease were enrolled for a total of 135 cycles delivered. ECOG PS was 0–1/2 in 31/8 patients. 38/39 pts were evaluable for response on an intent to treat basis. 2 CRs and 24 PRs have been recorded for a 68% [95% C.I. = 51–82] ORR. Major responses were 10/13 (77%) in IIIB and 16/25 (64%) in stage IV pts. The QoL score improved in 27/38 (71%) pts. At a 7 (range; 1–17)-month median follow-up the MST has not yet been reached, with a 1-year projected survival of 70%. Toxicity was generally manageable. Grade 4 neutropenia and thrombocytopenia were observed in 9 (23%) and 3 (8%) pts, and in 6 cases a packed red blood cell transfusion was required. Severe nonhematological toxicity occurred in 8 pts.

Conclusions: The PGT combination yields very high clinical response and QoL improvement rates in chemo-naive advanced NSCLC pts at a price of a manageable toxicity. A large phase III trial comparing this new regimen to standard combinations is underway.

1016 PUBLICATION

A phase II study of docetaxel (D) and gemcitabine (G) as second-line treatment in patients (pts) with advanced non-small cell lung cancer (NSCLC)

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Background: D and G have demonstrated single agent activity in both chemo-naive and previously treated pts with advanced NSCLC. They share different mechanisms of action. We conducted a phase II trial to evaluable the efficacy and tolerance of the combination as second line treatment in pts with advanced NSCLC. Patients and treatment: Twenty-nine pts with NSCLC (27 male, 2 female) who had progressed or failed first-line chemotherapy were enrolled. Prior chemotherapy was platimum-based with (n = 7) or without (n = 20) docetaxel and docetaxel-vinorelbine (n = 2). Patients received gemcitabine (900 mg/m^2 iv days 1 and 8) and docetaxel (100 mg/m^2 iv; day 8) every 3 weeks. G-CSF (5 ìg/kg, sc) was administered on days 9–18 prophylactically in case of previous grade 3/4 neutropenia. The median age was 63 years (range 27–74); PS (WHO) was 0 (7 pts), 1 (12 pts) and 2 (10 pts). Eight (28%) pts had stage IIIB and 21 (72%) had stage IV disease. Median number of disease sites per pt was 2 (range 1–3).

Results: Twenty-eight pts were evaluable for response and 29 for toxicity. Five (18%, 95% CI: 3.67%–32.04%) pts achieved partial response; 10 (36%) pts had stable disease and 13 (46%) progressed. After a median follow up of 6 months (range 1–19), the median duration of response was 5 months (range 1.5–8), the median TTP 11 months (range 3–16) and the median survival 7 months (range 1–19). The one-year survival rate was 20%. A total of 112 cycles were administered (median 3 cycles/pt). The median administered dose intensity was 100% of the planned dose for both drugs. Ten cycles (9%) were delayed due to toxicity. Neutropenia grade 3/4 occurred in 4 (14%) pts. Two (7%) pts experienced febrile neutropenia. There were no toxic deaths. G-CSF was required in 98 of 112 cycles (87%). Grade 2/3 anemia was observed in 15 (51%) pts, grade 2/3 asthenia in 14 (48) pts and grade 2 neurotoxicity in 3 (10%). Other toxicities were mild.

Conclusions: The D + G combination has tolerable toxicity and modest activity in terms of tumor growth control rate (PR + SD) as salvage treatment in advanced NSCLC.

1017 PUBLICATION

Phase II study of Docetaxel and Cisplatin in a circadian timing as first line chemotherapy (CT) in advanced non small cell lung cancer (NSCLC)

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Introduction: The combination of Docetaxel and Cisplatin used in a time unspecified fashion as first line CT in NSCLC produced 21–45% resonses with a median survival time of 8–12 month. Animal data showed improved efficacy and reduced toxicity if both agents were given in a circadian timing.

Methods: Based on these data the combination of Docetaxel and Cisplatin was investigated in the following time specified fashion: Docetaxel 75 mg/m" i.v. over 1 hour at 9 a.m. followed 7 hours later (4 p.m.) by 75 mg/m" Cisplatin i.v. over 30 minutes together with i.v. hydration. Cycles were repeated every 3 weeks. Steroids were given before and after Docetaxel. Patient characteristics: 63 pts. have received 240 cycles. 63 pts. are evaluable for toxicity and 56 pts. are evaluable for tumor response. M/F ratio: 49/14, median age 64 (43–75) years, median WHO performance status 1 (0–2).

Results: Neutropenia NCI-CTC grade 4 occurred in 10% of pts. and grade 3/4 in 19% of pts. Other toxicities of NCI-CTC grade 3/4 (platelets, anemia, diarrhea, stomatitis and vomiting) occurred in <5% of pts. No other toxicities of grade 3/4 were observed.

Response: In 56 pts. 27 (48%) PR [95% Confidence interval 35–62%], confirmed by CT-Scan, were achieved.

Conclusion: Present results indicate that Docetaxel/Cisplatin, given in a circadian timing, produces comparable response rates but significantly less NCI-CTC grade 4 and grade 3/4 Neutropenia than this combination in similar dosages in a time unspecified fashion does.

1018 PUBLICATION

Preoperative treatment with cisplatin-gemcitabine in locally advanced nsclc: Survival, toxicity and salvage surgery

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Purpose: To assess efficacy, toxicity and salvage surgery in patients with unresectable locally-advanced NSCLC treated with Cisplatin-Gemcitabine.

Methods: Between September-97 and October-98, 24 patients with unresectable NSCLC were included. Patients with pleural effussion and superior vena cava syndrome were excluded. Mean age: 55.5 years (43–69); 23 males and 1 female. Histology: 11 squamous cell, 10 adenocarcinoma and 3 undifferentiated carcinoma. Stages: 17 IIIA (clinical N2) and 7 IIIB. Treatment schedule: Cisplatin 100 mg/m^2 day 1 and Gemcitabine 1200 mg/m^2 days 1 and 8, every 21 days, to a maximum of 6 cycles, in an out-patient setting. Surgical salvage was evaluated after 3rd and 6th cycles with CT scan.

Results: 117 cycles were administered; mean: 4.8 (1–6). Hematological toxicity: neutropenia III, 3 episodes (ep) and anemia III, 1 ep. Extra-hematological toxicity: fatigue III, 10 ep. emesis III, 4 ep. and emesis IV, 1 ep. There was 1 toxic death because of pancytopenia. Overall response rate: 65%; 14 partial response (61%) and 1 complete response (4%). Stable disease, 3 (13%) and progressive disease, 5 (22%). Salvage surgery was performed in 7 patients (30%), with 5 pathologic partial response and 2 pathologic complete response. In 3 patients exploratory thoracotomy, without resection due to vena cava infiltration. Of the 7 patients resected, 4 are free of disease after 20.5, 13, 12.5 and 7 months. Median survival has not been reached. Actuarial survival at 18 months is 75%.

Conclusions: Cisplatin-Gemcitabine is an effective scheme of chemotherapy with high response rate, being possible salvage surgery. Toxicity is mild and manageable. Initial results are encouraging, but long term follow up will allow the impact of this aproach on overall survival.

1019 PUBLICATION

Photodynamic therapy in bronchial carcinoma

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Purpose: Retrospective evaluation of patients with bronchial carcinoma treated by photodynamic therapy (PDT).