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Cisplatin-gemcitabine-vinorelbine (PGV) vs cisplatin-vinorelbine (PV) vs cisplatin-gemcitabine (PG) in advanced non-small cell lung cancer (NSCLC). Interim analysis of a SICOG phase III trial

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Purpose: To compare the impact on survival and QoL of the PGV regimen with that of PG and PV.

Patients and Methods: NSCLC pts with locally advanced or metastatic disease aged ≤70 years and with ECOG PS ≤1 were randomized to receive PGV (P 50 mg/m^2 + G 1,000 mg/m^2 + V 25 mg/m^2 on d 1 & 8 q 3 wk) or PG (P 100 mg/m^2 d 1 + G 1,000 mg/m^2 d 1, 8, 15 q 4 wk) or PV (P 120 mg/m^2 d 1 & 29 + V 30 mg/m^2/wk). An interim analysis had been planned after 60 pts per arm had been enrolled, according to the Schaid's optimal two-stage design for survival comparisons.

Results: The survival data of 199 NSCLC (PGV = 69, PG = 63, PV = 67) randomized from March 1997 and February 1999 were analysed by an independent monitoring board. Stage was IIIB or IV in 70 and 129 pts, respectively. At a 15 (range; 1–23)-month median potential follow-up, MST was: PGV = 50 wks, PG = 47 wks, PV = 34 wks. The observed difference in the risk of death between the PV and PGV arm met the early stopping rule criteria ($p < 0.01$).

Conclusions: The PGV treatment is associated with a significantly better survival outcome when compared with the PV combination. The accrual still continues in the PGV e PG arms until the planned final sample size of 120 pts per Arm.

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A multicenter randomized trial of paclitaxel (175 mg/m^2) plus carboplatin (6AUC) versus paclitaxel (225 mg/m^2) plus carboplatin (6AUC) in advanced non-small cell lung cancer (NSCLC)

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Paclitaxel (P) and Carboplatin (C) has become a widely used combination in NSCLC due to phase II reports of high tolerability, efficacy and easier outpatient administration. Purpose of our present prospective study was to evaluate the dose-response relationship of P. Since July 1996, 198 patients with non-operable NSCLC and measurable disease without previous chemotherapy entered the trial. Ninety nine (Group A) were randomized to receive P 175 mg/m^2 in 3 h infusion plus C dosed to an area under the concentration-time curve of 6 every 3 weeks and 99 (Group B) to receive the same regimen with P increased to 225 mg/m^2. Patients in both groups were well-matched with baseline disease characteristics. In group A with 90 evaluable pts response rate was 25.6% (6CR, 17PR) whereas in group B with 88 evaluable pts response rate was 31.8% (3CR, 25PR) P = 0.733. Median time to progression favored the high dose P (4.3 mts versus 6.4 mts, P = 0.044). The median survival was 9.5 mts for group A versus 11.4 mts for group B (P = 0.16). The 1-year survival was 37% for group A and 44% for group B (P = 0.35). The best prognostic factor for 1 year survival was the response rate ($P < 0.0001$). With a relative dose intensity of P = 0.94 in both groups, neurotoxicity (P = 0.025) and leucopenia (P = 0.038) were more pronounced in group B pts. No toxic death was noticed. In conclusion, higher dose P prolongs the median time to progression but causes more neurotoxicity and leucopenia.

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Randomized study of taxotere (TAX) versus best supportive care (BSC) in non-small cell lung cancer (NSCLC) patients previously treated with platinum-based chemotherapy

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Study objectives were to assess the impact of TAX on survival, response and quality of life (QoL) in NSCLC pts previously treated with platinum-based chemotherapy. Pts were randomized to TAX (100 mg/m^2 49 pts; 75 mg/m^2 55 pts) or BSC (100 pts). The baseline demographics were balanced across the arms (TAX, BSC respectively). Median age – (61, 63); Male – (69%, 65%); ECOG PS < 2 -(76%, 75%); Stage IV – (84%, 81%); more than one prior chemotherapy – (26%, 24%); best response to prior platinum therapy as PD – (18%, 20%). The ORR was 7.6% (duration 24–26 wks). TAX pts had a longer median survival (7.2 mo. TAX vs. 4.9 mo. BSC) and statistically significantly better TTP compared to BSC patients ($p < 0.05$). Patients treated with TAX at 75 mg/m^2 had the best overall survival ($p < 0.05$). Febrile neutropenia and grade 3/4 related infections occurred in 12% and 6% of pts (3 deaths – all TAX 100 mg/m^2). The incidence of non-hematologic grade 3/4 or severe adverse events were comparable across the two arms. A QoL analysis of the first 100 patients (TAX 100 mg/m^2 vs. BSC) showed significantly better QoL assessments (pain and fatigue) with TAX. QoL analysis of the whole study is not complete. In advanced NSCLC pts in whom prior chemotherapy has failed, TAX improves survival, TTP and disease-related symptoms.

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Paclitaxel-cisplatin-etoposide (TEP) versus cisplatin-etoposide (EP) as first line treatment in small cell lung cancer (SCLC): A preliminary analysis of a multicenter randomized phase III trial

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Background: Previous phase I-II studies suggest that paclitaxel (T) can be added safely to the cisplatin (P)-etoposide (E) combination and this may improve the effectiveness of the regimen in SCLC. We conducted a phase III study to compare the activity and tolerability of the two regimens in previously untreated SCLC patients.

Patients and Treatment: 138 chemotherapy-naive SCLC patients have been enrolled into the study. Treatment consisted of either Arm-A(TEP): T 175 mg/m^2 IV over 3 hrs on day-1 and P 80 mg/m^2 IV on day-2 and E 80 mg/m^2/d IV on days 2–4 with prophylactic G-CSF 5 mcg/kg/d SC on days 5–15 for all pts or Arm-B(EP): P 80 mg/m^2 IV on day-1 and E 120 mg/m^2/d IV on days 2–4 with G-CSF support only for pts developing neutropenia. In both arms, cycles were repeated every 4 weeks.

Results: 62 pts from Arm-A and 64 pts from Arm-B have been analysed with 44/60 and 56/63 pts evaluable for response/toxicity in each arm, respectively. CR(%) + PR(%): 4(9%) + 21(48%) for Arm-A and 2(4%) + 23(41%) for Arm-B; duration of response and median survival was 5 and 11 months for Arm-A versus 3 and 10 months for Arm-B; one-year survival was 42% for Arm-A and 31% for Arm-B. There is no statistically significant difference (p = NS) in any of the above comparisons between the two arms. A total of 486 cycles of treatment have been administered (232 Arm-A; 254 Arm-B) with a median of 3 and 4 cycles/pt, respectively. Toxicity (WHO criteria) was (Arm-A/Arm-B): grade 3/4 neutropenia 24 pts (40%)/26 pts (41%), grade 3/4 thrombocytopenia 10 pts (16%)/4 pts (7%), grade 3/4 diarrhea 5 pts (8%)/1 pt (2%), grade 2/3 neurotoxicity 7 pts (11%)/2 pts (4%), grade 3/4 asthenia 6 pts (10%)/2 pts (4%). Febrile neutropenia occurred in 15 cycles (6.5%) of arm-A versus 9 (3.5%) of arm-B. There were 7 toxic deaths in the TEP arm versus 0 in the EP arm (p = 0.005).

Conclusion: From our preliminary data it seems that the two regimens have comparable activity as first line treatment in SCLC although the TEP arm is more toxic than the EP arm. Based on these results and for safety reasons further accrual onto the study has been terminated.