1094 PUBLICATION

Cyclic concomitant chemo-radiotherapy for limited small cell lung cancer

J.-L. Rebischung[1], J.-M. Vannetzel[2], A. Kanoui[2], J. Sauvaget[1]. [1]*Hopital Saint-Joseph, Paris;* [2]*Clinique Hartmann, Neuilly, France*

Among 30 patients with LSCLC, 25 are evaluable for response and survival with a median follow-up of 30 months after CCCR.

Five have been excluded: 1 lost, 1 extensive disease, 3 inadequate histology. It was 6 females, 19 men, median age 59 y. (47–72); 6 with weight loss >10%; LDH level normal 11 cases, < or = 2 N 11 cases, >2 N 3 cases.

Treatment consist in VP16 60 mg/m2/d 1–4; 5FU 600 mg/m2 continuous infusion d 1–4; CDDP 20 mg/m2 d 1–4 with thoracic irradiation 2.5 Gy d 1–4, each 3 weeks for 6 cycles. PCI (24 Gy/8 fr) was used for all patients except one.

17 patients received 6 cycles, 4 only 5 cycles (toxicities) 3 only 4 cycles, 1 only 3 (lung necrosis). Median dose of thoracic irradiation is 55 Gy; 82%, 81% and 83% of planified doses of VP16, 5 FU, CDDP have been delivered. Among 137 cycles, 15 were delayed of 1 week, 2 of 2 weeks. Toxicities were acceptable excepted 1 lethal infection of acute radiation pneumonitis, 1 lung necrosis resected (pTONO), 1 neutropenia Gr 4; 12 Gr 3; 1 thrombopenia Gr 3; 3 infections Gr 4, Gr 3; 2 neuropathies Gr 3. At completion of the treatment 24 CR and 1 PR were noted.

We noted 4 intercurrent deaths, 3 second primaries (2 NSCLC, 1 Breast), 3 local and metastatic progression, 7 metastatic failures. Survival at 1 year is 84%, 2 years 60% with MDS 58 months. MDS of patients with delayed treatment is only 38 m, with 6 failures vs 58 m and 4 failures in the optimal dose intensity treatment group.

1095 PUBLICATION

Treatment intensification with interleukin-3 (IL-3) and granulocyte-macrophage colony-stimulating factor (GM-CSF) in patients with small-cell lung cancer

U. Gatzemeier[1], J. von Pawel[2], R. Tischer-Neuhaus[1], U. Haus[3], L. Färber[3]. [1]*Krankenhaus der LVA Hamburg, Großhansdorf;* [2]*Zentralkrankenhaus Gauting;* [3]*Novartis Pharma GmbH Nürnberg, Germany*

Purpose: Interleukin-3 promotes the survival, proliferation and differentiation of multipotential hematopoietic stem cells. Pilot studies with IL-3 administered to patients with advanced malignancies have shown its effect on platelet counts. The objective of this study was to ameliorate the dose limiting leucopenia and thrombocytopenia with the combination of IL-3 and GM-CSF, allowing dose escalation of Ifosfamide.

Methods: In this phase II dose-escalation study 16 patients with small cell lung cancer (SCLC) received 4 cycles ICE: Carboplatin (300 mg/m^2 day 1), Etoposide (120 mg/m^2 day 1–3) and increasing doses of Ifosfamide as well as IL-3 (5 μg/kg day 4–10) and GM-CSF (5 μg/kg day 11–15).

Results: In the first 5 patients 5.0 g Ifosfamide was tolerated very well. The next cohort was treated with 5.5 g Ifosfamid and 1 episode of neutropenia with ANC < 500 cells/mm^3 for 7 days and 1 episode with thrombocyte count <20.000 cells/mm^3 for 3 days occurred. The next 6 patients receiving 6.0 g Ifosfamide showed more pronounced myelosuppression.

Conclusion: With a combination of IL-3 and GM-CSF a dose escalation of Ifosfamide was possible. But due to its main effect on early megakaryopoiesis in further studies the effect of the combination of G-CSF and IL-3 to mobilize peripheral stem cells will be analyzed.

Colorectal cancer II

1096 ORAL

Bolus injection versus short-term infusion of 5-fluorouracil in patients with advanced colorectal cancer: A prospective randomized trial

Å. Berglund[1], A. Jakobsen[2], W. Graf[3], C. Gadeberg[2], P. Hansen[4], M. Kjaer[5], N. Brunsgaard[6], E. Sandberg[7], L. Påhlman[3], B. Glimelius[1]. *For the Nordic Gastrointestinal Tumor Adjuvant Therapy Group;* [1]*Department of Oncology;* [3]*Department of Surgery, Akademiska sjukhuset, Uppsala, Sweden;* [2]*Department of Oncology in Veile;* [4]*Department of Oncology in Århus;* [5]*Department of Oncology in Aalborg;* [6]*Department of Oncology in Odense;* [7]*Department of Oncology in Esbjerg, Denmark*

Purpose: To compare a rapid intravenous 5-FU injection and a short-term 5-FU infusion with respect to objective responses and toxicity in patients with advanced colorectal cancer.

Patients and Methods: Totally 203 patients with advanced colorectal cancer and measurable disease were randomized to bolus 5-FU either as an injection during 2–4 minutes or as a short-term infusion lasting for 10–20 minutes. In both groups, the 5-FU dose was 500 mg/m^2 and Leucovorin 60 mg/m^2 was given 40 minutes after start of 5-FU. Treatment was given on two successive days every other week until progression.

Results: Objective tumour regression was seen in 27/100 (27%) in the injection group and in 13/103 (13%) in the infusion group (P = 0.02). Severe toxicity was rare and did not differ significantly between the groups. Progression-free survival tended to be longer in the injection group (P = 0.07), but overall survival did not differ between the groups.

Conclusion: "Bolus" 5-FU should be administered as a rapid intravenous injection rather than as a short-term infusion since the former rate of administration results in a higher response rate without being more toxic.

1097 ORAL

A prospective randomised trial of protracted venous infusion (PVI) 5-FU with or without mitomycin C (MMC) in advanced colorectal cancer

P. Ross, A. Norman, D. Cunningham, A. Webb, T. Iveson, A. Padhani, A. Massey. *The Department of Medicine and The Gastrointestinal Unit, The Royal Marsden Hospital, London and Surrey, SM2 5PT, UK*

Purpose: We report the results of a prospectively randomised study comparing PVI 5-FU (300 mg/m^2/day for 24 weeks) with or without MMC (10 mg/m^2 IV bolus 6 weekly for 4 courses; 7 mg/m^2 from June 1995) in patients with previously untreated advanced colorectal cancer.

Methods: 200 patients were randomised and analysed for tumour response, survival, toxicity and quality of life (QL).

Results: Overall response rate was 54% (95% confidence interval [CI] 44–64%) with PVI 5-FU + MMC compared to 38% (95% CI 28–48%) with PVI 5-FU alone (p = 0.024). PVI 5-FU + MMC caused more overall haematological toxicity but CTC grades 3/4 was increased only for thrombocytopenia (p = 0.0006). Two patients treated with a cumulative dose of MMC of 40 mg/m^2 developed haemolytic uraemic syndrome (HUS) warranting a reduction in cumulative MMC dose to 28 mg/m^2. No HUS developed in patients treated with MMC to 28 mg/m^2. The median failure free survival was 7.9 months with PVI 5-FU + MMC and 5.4 months with PVI 5-FU alone (p = 0.033). Median overall survival was 14 months with the combination compared to 15 months with PVI 5-FU alone. Global QL scores were better for the PVI 5-FU + MMC at 24 weeks.

Conclusion: We conclude PVI 5-FU + MMC results in improved response and failure free survival, tolerable toxicity and better QL when compared to PVI 5-FU alone. There is no irreversible toxicity with MMC at a cumulative dose of 28 mg/m^2. This regimen should now be evaluated as adjuvant therapy in colorectal cancer.