Conclusion: This study demonstrates promising activity and good tolerability of ALIMTA in mesothelioma. Randomized trials that will further define the role of ALIMTA in this disease are ongoing.

67 POSTER DISCUSSION

Gemcitabine plus Carboplatin (Gcarb) versus Cisplatin plus Vinblastine (CV) in Patients (pts) with Stage IIIB and IV Non-Small Cell Lung Cancer (NSCLC)

A.C. Grigorescu[1], I.N. Draghici[1], N. Gutulescu[1], E. Corlan[2]. [1] *Institute of Oncology, Medical Oncology I, Bucharest, Romania;* [2] *National Institute of Pneumophtisiology, Pneumophtisiology, Bucharest, Romania*

Purpose: The combination of Gcarb has demonstrated activity in the treatment of stage III and IV NSCLC. This phase II randomized trial compared the response rate, survival rate, and toxicity of the combination of Gcarb with the combination of CV.

Methods: Chemonaive patients with advanced or metastatic NSCLC were enrolled in the study. Pts were randomized to receive either cisplatin 75 mg/m2 on day 1 plus vinblastine 6 mg/m2 on days 1 and 8 (arm A) or gemcitabine 1000 mg/m2 on days 1 and 8 plus carboplatin 300 mg/m2 on day 1 (arm B). Both regimens were administered on a 21-day course.

Results: A total of 198 patients (99 pts each in arms A and B) were enrolled in the study between July 1997 to November 1999. All pts had an ECOG performance status <2. Patients had a median age of 58.2 years (range, 30 to 78) in arm A and 59.6 years (range, 40 to 78) in arm B. In arm A, there were 15 partial responders (PR), for an overall response rate (ORR) of 15%, compared with 3 complete responders (CR) and 24 PR, for an ORR of 27% ($p < 0.05$), in arm B. Mean survival times were 239 days (95% CI, 214 - 265) in arm A and 349 days (95% CI, 299 ± 390) in arm B. One-year survival rates for arms A and B, respectively, were 9.1% and 20.2%. Percentages of pts with WHO grade (G) 3/4 hematologic and non-hematologic toxicity in arms A/B were leukopenia 0/2, thrombocytopenia 0/2, alopecia 46/33, neurotoxicity 2/1, and asthenia 35/42.

Conclusion: The Gcarb combination showed a good therapeutic response, a benefit in survival, and a similar toxicity profile compared with the CV combination.

Hematological malignancies

68 POSTER DISCUSSION

An allogeneic antitumor effect after hematopoietic stem cell transplantation for colorectal and renal carcinoma

O. Ringden[1], L. Barkholt[1], P. Hentschke[1], P. Wersall[2], P. Pisa[2], M. Uzunel[1], J. Mattsson[1], J. Martola[3], N. Aibiin[3], A. Thorne[4]. [1] *Huddinge University Hospital, Centre for Allogeneic Stem cell Transplantation, Stockholm, Sweden;* [2] *Karolinska Hospital, Dept. of Oncology, Stockholm, Sweden;* [3] *Huddinge University Hospital, Dept. of Radiology, Stockholm, Sweden;* [4] *Huddinge University Hospital, Dept. of Gastroenterology, Stockholm, Sweden*

Purpose: Does allogeneic hematopoietic stem cell transplantation (ASCT) have an anticancer effect in colorectal and renal carcinoma?

Methods: Five patients with colorectal and nine patients with renal adenocarcinoma with metastases underwent ASCT. The donors were HLA-identical siblings for nine patients and HLA-compatible unrelated donors for five patients. Conditioning included Fludarabin 30 mg/m2 for three days in patients with HLA-identical siblings and five days with unrelated donor, followed by 2 Gy total body irradiation. Antithymocyte globulin 4 mg/kg was given to patients with unrelated donors. Peripheral blood stem cells were collected after G-CSF stimulation of all donors. Immunosuppression was by mucophenolate mofetil and cyclosporine. Chimerism was determined using PCR amplification of variable number tandem repeats.

Results: All patients were treated as outpatients. Chimerism showed 100% donor myeloid and T-cells in 7/14 and 2/14 patients at one month after ASCT, respectively. Six patients developed grades II-IV acute GVHD. Two rejected the grafts, one died of renal toxicity, one died of an accident and two died of disease progression. One patient with colon cancer showed an 80% decrease in size of all metastases at two months. He died of pneumonia at four months and autopsy showed necrosis of all metastases with few cancer cells. Another patient with colon carcinoma have shown regression of pleura metastases, but progression of liver metastases. One patient with renal carcinoma died of grade IV acute GVHD. Pulmonary metastases had disappeared at autopsy. Among four renal carcinoma patients who are alive between 4 and 12 months after ASCT, one has shown partial response of metastases, another has shown progression as well as regression of metastases.

Conclusion: ASCT after minimal conditioning was well tolerated. 7/14 patients are alive after 4-12 months. Partial tumor regression (>50%) was seen in two patients with colorectal and two patients with renal carcinoma.

69 POSTER DISCUSSION

High activity rhenium-186 HEDP with peripheral blood stem cell support -a novel approach to hormone refractory prostate cancer metastatic to bone

J.M. O'Sullivan[1], V.R. McCready[2], J. Treleaven[3], A.R. Norman[4], G. Flux[2], G. Cook[2], J. Gadd[5], A. Horwich[1], R.A. Huddart[1], D. Dearnaley[1]. [1] *Institute of Cancer Research/Royal Marsden Hospital, Department of Radiotherapy, Sutton, UK;* [2] *Institute of Cancer Research/Royal Marsden Hospital, Department of Nuclear Medicine/Physics, Sutton, UK;* [3] *Institute of Cancer Research/Royal Marsden Hospital, Department of Haematology, Sutton, UK;* [4] *Institute of Cancer Research/Royal Marsden Hospital, Department of Computing and Information, Sutton, UK;* [5] *Institute of Cancer Research/Royal Marsden Hospital, Bob Champion Research Unit, Sutton, UK*

Purpose: The radioisotope Rhenium-186 HEDP has been used successfully for many years in the palliation of pain from bone metastases, with thrombocytopenia as the dose limiting toxicity. In this study we have tested the feasibility of escalating activities of Rhenium-186 HEDP by using peripheral blood stem cell support in a phase I trial. We hypothesise that by increasing the administered activity it will be possible to increase the ionising radiation dose to individual metastases allowing potential ablation of small lesions, reduction in new lesion formation, and improved disease free survival.

Methods: Twenty patients with hormone refractory prostate cancer metastatic to bone, minimal soft tissue metastases, and rising PSA, each received one treatment of intra-venous Rhenium-186 HEDP. Stem cells were returned 14 days post isotope treatment. A starting activity of 2500MBq was chosen following previous work by ourselves showing unacceptable toxicity without stem cell support at 3000MBq. We have now reached activities of 5000MBq, initially with increments of 250MBq and subsequently 500MBq when low toxicity rates were seen.

Results: All patients tolerated the treatment and stem cell transplant well. There was no incidence of grade III platelet toxicity (<50 x 109/l). Three patients (15%) had grade III leucopenia (1-2 x 109/l). A trend towards lower nadir platelet levels was seen with activities of Rhenium-186 above 3500MBq (p=0.1). Each patient had a total of 4 days spent in hospital for radioprotection purposes with all other procedures performed on an outpatient basis. As yet we have not found the maximum tolerated activity. Actuarial survival figures are encouraging compared to the literature with a median survival of 9.8 months at a median follow up of 7.5 months (range 2-36). PSA responses were seen in 60% of patients with a non statistically significant trend towards better response above 3500MBq (p=0.37).

Conclusions: Activities up to 5000MBq of Rhenium-186 HEDP can be administered with peripheral blood stem cell support with minimal toxicity. The potential exists for higher doses of ionising radiation to be delivered to individual metastases. We plan to continue phase I until the maximum tolerated activity is reached and then proceed to a Phase II evaluation of response.

70 POSTER DISCUSSION

Induction of differentiation of human chronic myeloid leukemia cells by synthetic 6 base phosphodiester oligonucleotides

M.C. Filion, B. Filion, S. Reader, S. Ménard, N.C. Phillips. *Bioniche Therapeutics, R & D, Montreal, Canada*

Purpose: A series of synthetic 6 base non-antisense phosphodiester oligonucleotides with either GpA, GpC, GpG or GpT dinucleotides motifs within specific sequence contexts has been identified as a potent inducer of apoptosis in a wide range of cancer cells, including acute lymphocytic leukemia cells. In this study, we have evaluated the activity of these oligonucleotides on a human chronic myeloid leukemia (CML) cell line.

Methods: K562 cells, derived from the leukemic cells of a CML patient in blastic crisis, were incubated for 48 h with different concentrations (2.5 to 100 μg/ml) of oligonucleotides with either GpA (BT 99-45) or GpT (BT 99-25) dinucleotides motifs within specific sequence contexts. Cellular division was monitored using a Coulter Counter. Apoptosis was evaluated