

relapse, 8/16 were localized at diagnosis and received HDC as a consolidation after treatment of a metastatic relapse. Prior to HDC, conventional treatments consisted of chemotherapy for all the patients (pts), surgery of the primary tumor (12/16), surgery of the metastases (4/16), radiotherapy on the primary tumor (10/16). At the time of HDC, CR or GPR of the primary tumor was obtained in 13 and 3 pts, respectively. CR, GPR and PR of the metastases were observed in 10, 5 and 1 pt, respectively. Toxicity was severe but acceptable: 1 toxic death occurred (cerebral hemorrhage). The mean durations of neutropenia and thrombopenia were 10 days (d) (SD = 5 d) and 39 d (SD = 20 d), respectively. Overall survival at 5 years post SCT was 70% and DFS was 55%. All the 6 metastatic pts grafted in first intention are alive with NED with a median follow up (FU) of 21 m (range 13–33 m), the 2 metastatic pts grafted after a metastatic relapse died 12 and 22 m post SCT. Among the pts with initially localized tumors, 5 are alive with NED with a median FU of 36 m post SCT (range 15–59 m), 1 is alive with disease, 1 is dead of PD and 1 of toxic death. In conclusion, the HDC with Busulfan and Melphalan was toxic but feasible. Prognosis of these children with metastatic disease compares very favorably with historic controls.

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ORAL

HIGH-DOSE CHEMOTHERAPY (HDC) WITH STEMCELL RESCUE FOR PATIENTS WITH METASTATIC EWING'S SARCOMA

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Metastatic Ewing's sarcoma has generally a fatal outcome. Patients with bone metastases cannot be cured by conventional treatment and only 10% of patients with pulmonary disease have a considerable disease-free survival (DFS). From 1990 six patients with metastatic Ewing's sarcoma have been treated in Leiden Univ. Hospital with HDC, followed by either bone marrow and/or peripheral stemcell rescue (SCR). Three of them suffered from recurrent Ewing's sarcoma, the other three had metastases at primary presentation.

Pat. characteristics: 5× male, one female. Mean age: 23 yrs. Localisation of primary tumor: rib 1×, vertebra 1×, scapula 2×, pelvis 2×. Metastases: bone 2×, lung 4×, lhn 2×. Induction treatment: VP16-Ifosfamide 4×, CDDP 2×. HDC: VP-16, Melphalan, Carboplatin 4×, VP-16-Melphalan 2×. TBI 1×. Four patients got 2 cycles of HDC; bone lesions were irradiated. Results: mean PFS 9+ months (3–20+). Overall survival: 12+ months (6–26+).

Conclusion: HDC with bone marrow and/or peripheral SCR is still an experimental treatment. Although toxicity is substantial some patients do have a relative long DFS.

1203

ORAL

EXTRAOSSEOUS EWING'S SARCOMA AND PRIMITIVE NEUROECTODERMAL TUMOR. A PLEA FOR MULTIDISCIPLINARY APPROACH

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Ewing's sarcomas (ES) and primitive neuroectodermal tumors (PNET) are both rare small round cell tumors. ES may arise in the soft tissues and is then referred to as extra-osseous Ewing's sarcoma (EOES). Both ES/EOES and PNET have a specific chromosome translocation resulting from reciprocal exchange of material between chromosomes 11 and 22, suggesting an identical cytogenetic event, as evidence that these two tumors are related entities on a common pathway of differentiation. This does not mean that the clinical course and treatment response of PNET and ES are the same. Data on PNET and EOES are rare. From most retrospective studies it is suggested that the prognosis of patients with ES is determined by local control of primary site and early suppression of clinical overt or hidden distant metastases. Where local therapy alone resulted in a 5-year survival of 10% only, the introduction of adjuvant chemotherapy in the last two decades has improved longterm survival to more than 50%. We present our clinical experience with PNET (11×) and EOES (17×) in 28 adolescents and adults, with specific details on the results of different treatment strategies. Two of the 8 patients, primarily metastasized, that started with chemotherapy, followed by various forms of local treatment, are still in complete remission for more than two years. In non-metastasized disease, a combined modality therapy was also the most successful treatment strategy. Single modality treatment (3 patients) resulted in relapse in all, where salvage surgery and radiotherapy could render one patient only into NED for more than 9 years now. Multimodality treatment (chemotherapy, surgery and radiotherapy) alike the Ewing's Sarcoma CESS and EICESS protocol, resulted NED in 6/10 patients, where surgery upfront resulted in NED in 3/7 patients. Also in our data survival among PNET patients was worse than in EOES (36% vs 47%). The overall disease free 5 year survival of EOES and PNET in this study is 41% (12/28 patients), with response to treatment in 25 patients (21 CR, 4 PR). Multidisciplinary treatment seems essential in improving treatment results in these rare tumours. The optimal chemotherapy schedule and timing of local therapies is still to be assessed.

Supportive care

1204

ORAL

PREVENTING NAUSEA AND VOMITING DURING DAYS 2-7 FOLLOWING HIGH DOSE CISPLATIN CHEMOTHERAPY (HDCCP)

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The combination of dexamethasone (D) and granisetron (G), a selective 5HT₃ receptor antagonist, has greatly reduced the incidence of emesis and nausea in the first 24 hours after HDCCP (≥50 mg/m²). How best to control emesis after this time remains a key problem in patient management. Our double-blind multicentre trial addressed the issue by determining whether the addition of G to D enhanced the efficacy of D alone in controlling emesis beyond 24 hours. Prior to chemotherapy, 434

randomized patients (pts) received G 3 mg IV and D 10 mg IV and G 1 mg PO at +6 and +12 hours. Beginning day 2, 218 pts received G 1 mg PO and D 8 mg PO bid for 6 days (group (gp) 1) and 216 pts received D 8 mg PO bid for 6 days (gp 2). Pts completed a self report diary daily in which the number of emetic episodes were recorded. A 100 mm visual analogue scale (VAS) was used to assess nausea severity. An intent to treat analysis on all evaluable pts was performed. Baseline characteristics were similar for both groups. The proportion of pts who did not vomit in the first 24 hours was 47% in gp 1 and 44% in gp 2. Over the 7 day period the proportion of pts who had no emesis, no rescue medication and who completed the diary was 38% in gp 1 and 35% in gp 2, a difference of 3% ($P = 0.532$; 95% CI -6% to 12%). The proportion of pts with nausea severity scores ≤5 mm for the complete 7 day period was 28% in gp 1 and 25% in gp 2, a difference of 3% (95% CI, -6% to 11%). We conclude that the effectiveness of D is not augmented by the addition of G and D is as effective as the combination of D and G during days 2-7 following HDCCP.