public and the medical profession is so low that this in itself will be a major task.

As a practical guide for the present, any family with a history which causes cancer should be referred to a specialist cancer family clinic [5]. In the U.K., such clinics are now available in most regions, attached to clinical genetics departments.

Guidelines for referral might be one close relative with a common 'adult' cancer (breast, colorectal, ovary, etc.) under 40 years; or two close relatives with cancers at any site both under 50 years [6]. The family cancer clinic will extend and confirm the family history, provide advice about the implications for other family members, and recommend screening or preventive measures where appropriate (usually the family will be referred back to their primary doctor for this to be carried out). Genetic testing can be discussed with the family, and blood samples from affected family members stored if testing is not possible now but may become so in the future.

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European Journal of Cancer Vol. 31A, No. 5, pp. 808–809, 1995
Elsevier Science Ltd
Printed in Great Britain
0959–8049/95 $9.50+0.00

Pergamon

0959-8049(95)00096-8

High Dose Therapy and ABMT Rescue in Lymphoma and Solid Tumours

T. Philip

IN ORDER to compare conventional therapy with massive chemotherapy plus autologous bone marrow transplantation (ABMT) in relapsed non-Hodgkin's lymphoma, a randomised multicentre study was initiated by the PARMA group [1, 2]. Between July 1987 and November 1992, 200 consecutive patients from 49 worldwide institutions were included in the study. They all had intermediate or high grade non-Hodgkin's lymphoma with previous complete remission and were entered at time of first or second relapse. Age was between 16 and 60 years. Central nervous system and bone marrow relapses were excluded. Histological proof of relapse was mandatory. After a complete staging, they all received the same rescue protocol i.e. DHAP (Dexamethasone, Cisplatin and Cytarabine) for two consecutives courses at 3–4 weeks interval.

200 patients were entered and 198 were evaluable for response (for 2 patients it was too early for evaluation). 111 patients were in CR (23.2%) or PR (30.8%) after two courses of DHAP (56%). Patients relapsing on therapy had a lower response rate than patients relapsing off therapy. Among these 111 patients, 98 were randomised between four additional courses of DHAP or massive therapy (BEAC: Carmustine, Etoposide, Cytarabine, Cyclophosphamide) and ABMT. Radiotherapy of involved fields was performed after six courses of DHAP in the first arm, and before massive therapy and ABMT in the second one. Reasons for non-randomisation were: 85 non-responders (42.9%) and 13 responders (patients refusal, 3 patients; technical problems, 3 patients; protocol violations, 2 patients; abnormal bone marrow cellularity, 2 patients; hepatic dysfunction, 1 patient; ileum perforation, 1 patient and renal failure, 1 patient).

The main end-point is the failure rate at 2 years (i.e. relapse or death whatever the cause). There was no statistical difference in terms of toxic death rate. The survival of the randomised patients was 50% at 3 years. This second interim analysis showed that initial hypotheses were still valid after 5 years. The study was closed in July 94 and final results will be reported at the EWOC-4 meeting.

Since 1984, the European Bone Marrow Transplantation (EBMT) Registry for solid tumours has collected data from 107 participating institutions of 16 Europeans countries. The total number of registered patients was 105 in 1984, 525 in 1988, 690 in 1989, 1012 in 1990, 1245 in 1991, 1879 in 1992, 2085 in 1993 and 2900 in 1994, with a dramatic increase of registered cases during the last 3 years. Bone marrow transplantation was performed in 70.3% during the 1988–1993 period. Children represent 52.4% of the registered patients and neuroblastoma (56% and 29.9% among all the patients) is still the most frequent diagnosis within the registry. The number of registered cases in adults (46.9%) has recently increased and the ratio paediatric tumours/adults is better balanced than at the beginning of the registry. After neuroblastoma, the main tumours are: breast carcinoma (13.8%), germ cell tumours (12.6%), gliomas (11.9%), soft tissue sarcoma (8.2%) and Ewing's tumours (7%).

Neuroblastoma is the most frequent tumour in this registry (867 patients) and can be analysed according to status at graft.

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Survival was 30% at 5 years for partial response and very good partial response (PR, VGPR), and 33% for patients in complete response (CR) (730 patients treated in consolidation from first line therapy) [3–6].

For testicular cancer, 320 patients were analysed; survival was 43% at 5 years, 27% in the relapse group and 59% in the first line group. For gliomas (345 patients), the survival was 12% at 5 years, 64 patients are children (survival at 5 years: 18%) and 280 are adults (survival at 5 years: 11%).

Among the soft tissue sarcomas (238 patients), 179 patients had rhabdomyosarcomas with a survival at 5 years of 17%; for those with CR (66 patients) the survival was 28%. For Ewing's sarcoma (203 patients), 58 were grafted in CR, 52 in PR and VGPR, and 88 after relapse or progression. Survival was 25% at 5 years for consolidation group and 19% at 5 years in relapse group.

This registry can provide essential data about BMT in solid tumours with large enough samples in each tumour type to analyse efficacy and toxicity of treatments; markers and prognostic factors can also be evaluated by using this large database. Organisation of the registry is cooperative with the data centre in Lyon (Dr Chauvin). The principle secretaries are: Dr Dallorso and Dr Garaventa (Italy) responsible for Wilms' tumours analysis [7], Dr Philip and Dr Ladenstein (France and Austria) for neuroblastoma, Dr Biron (France) for gliomas, Dr Rosti (Italy) for breast carcinoma, Dr Hartmann and Dr Ladenstein (France and Austria) for Ewing's sarcoma, Dr Pico (France) for germ cell tumours, Dr Pinkerton with Dr Koscielniak (England and Germany) for soft tissue sarcoma in children.

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Pergamon

European Journal of Cancer Vol. 31A, No. 5, pp. 809–811, 1995
Elsevier Science Ltd
Printed in Great Britain
0959–8049/95 $9.50+0.00

0959-8049(95)00097-6

High-dose Chemotherapy of Breast Cancer: Current Status and Developmental Strategies

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ACTIVITY OF HIGH-DOSE CHEMOTHERAPY IN METASTATIC BREAST CANCER

IF THE activity of an anticancer treatment can be defined by the rate of response which it produces, high-dose chemotherapy (HDC) with stem cell autografting is the most active treatment currently available for metastatic breast cancer. Complete remission (CR) rates are far in excess of those reported for lower-dose chemotherapy, or for any form of endocrine manipulation [1]. In early studies involving patients with disease which was resistant to prior chemotherapy, HDC produced CR rates of as high as 25% [2]. As most contemporary HDC trials accrue patients who are responding to "conventionally"-dosed chemotherapy, few patients without prior chemotherapy for metastases have been studied in classic phase II trials. In one such study, Peters and colleagues reported a CR rate of 54% among patients who had cancers which were hormone resistant. One quarter of these remissions were durable at or beyond 5 years [3]. These data were supported by a subsequent randomised trial of high-dose versus conventionally-dosed therapy [4], in which CR rates

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