alternative approach between ART discontinuation and toxicity due to HAART administration.

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Role and limits of salvage chemotherapy in breast cancer patients treated with high-dose chemotherapy

High-dose chemotherapy (HDC) with autologous peripheral blood progenitor cell support for breast cancer has been widely investigated in phase III clinical trials [1]. The majority of transplanted patients relapse, but the most appropriate treatment for them has not yet been established. In the literature, there are few data regarding salvage chemotherapy after HDC. Martin et al. used a combination of methotrexate, oral tegafur plus uracil and leucovorin to treat 24 patients with metastatic breast cancer who had relapsed after HDC [2]. The response rate was 38%, including one patient who achieved a complete response, while median progression-free survival and overall survival (OS) were 6 and 9 months, respectively. Zambelli et al. published data on salvage treatment with a 4-day infusion of fluorouracil plus vinorelbine in 48 heavily pretreated metastatic breast cancer patients (14 of 48 relapsed after HDC) [3]. The authors reported an overall response rate of 50%, with a median duration of response of 9 months and a median survival of 16 months. In our single institutional trial, with 32 metastatic breast cancer patients treated with epirubicin and/or paclitaxel at relapse after HDC, we obtained an overall response rate of 57%, with a median time to progression and a median survival of 7 and 27.5 months, respectively [4]. The main reported toxicity was a World Health Organization (WHO) grade 3–4 neutropenia observed in 25% of patients. The patients who relapsed again after this salvage treatment underwent another line of chemotherapy with infusional fluorouracil and vinorelbine, obtaining an overall response rate of 23%, including one complete response, with a median time to progression of 8 months and a median OS of 16.5 months [5].

The role of a second course of HDC as salvage treatment was investigated by Bearman et al. in 26 metastatic breast cancer patients [6]. The authors concluded that second transplants as salvage treatment are generally well tolerated, but their efficacy is modest. Recently, Rodenhuis et al. published the largest randomised trial comparing HDC with standard dose chemotherapy, conducted in the adjuvant setting [7]. In this trial 885 patients were randomised to receive (post-operatively) five cycles of 5-fluorouracil 500 mg/m², epirubicin 90 mg/m², cyclophosphamide 500 mg/m²; q21 (FEC) or four cycles of FEC followed by HDC. The 5-year relapse-free survival rates were 59% in the conventional-dose group and 65% in the high-dose group (in the group with ≥10 positive nodes, the relapse-free survival rates were 51% and 61% in the conventional-dose and HDC groups, respectively), while at a median follow-up of 57 months there was no significant difference in OS between the two groups. In this study, the influence on survival of subsequent treatments was not investigated; however, considering that at relapse all patients underwent similar regimens, the results in terms of survival were equivalent in the two patient groups.

How then should patients who relapse after HDC be treated? As with patients pretreated with standard-dose chemotherapy, the
goals of chemotherapy in HDC patients are to obtain maximum control of symptoms, to prevent serious complications and to increase survival with an acceptable side-effect profile. The problem of toxicity has been particularly emphasised in HDC-pretreated patients. However, from the reported review of clinical trials and from our own experience, it seems that previous HDC does not significantly modify tolerability of subsequent chemotherapy. Even if most transplanted patients have already received anthracycline–taxane-containing regimens, several drugs in combination or as single agents are currently available for this purpose, including docetaxel (in patients pretreated with paclitaxel), fluorouracil, gemcitabine, vinorelbine, mitomycin c and novel oral therapies (capcitabine, vinorelbine).

Finally, patients who have failed a previous transplant would be ideal candidates for novel approaches, such as use of new agents, molecular targeted therapy, antiangiogenetic factors and gene therapy.

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Can the ISO9000 quality assessment be applied to the practice of medical oncology?

Increased safety in drug administration and continuous monitoring of the quality of clinical and research process is necessary in medical oncology, but to our knowledge no medical oncology unit in Europe has yet planned or achieved certification. In Europe, the quality accreditation system is mainly provided through ISO 9001/2000 VISION. From February 2002 to November 2002, we addressed a program to develop a management framework for the implementation of a specific quality system to retain effective management control according to ISO 9000 rules.

The Quality Management System (QMS) includes three accreditation components—besides improvement objectives—namely diagnosis and care for in-patients and out-patients, chemotherapy preparation and administration, and scientific planning.

The main improvement objectives were: reduction in the waiting time for chemotherapy administration to outpatients; decrease in the risk of errors in the administration of chemotherapy; improvement in the implementation and running of phase II–III trials; and increase in patient satisfaction. Counselling for the implementation of the quality system was provided by OPT s.r.l. directional consulting, whose activity was sponsored by a pharmaceutical company.

The QSM is guaranteed by assessment inspections, periodic meetings on quality, and corrective actions on non-conformity procedures.

Two site visits were made, with an external audit to check on other possible non-conformities of our quality system. The third-party registrar (Certiguality) assessed that our system was compliant with the ISO requests for the three above-mentioned aspects, which was followed by the Certification of the Medical Oncology Unit on 17 December 2002.

In conclusion, certification of a medical oncology unit is a goal that should be pursued to improve not only the level of clinical activity, but also the whole process of design, implementation and running of clinical trials. However, this can not be achieved without the investment of additional resources.

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