cycle showed an increased concentration of total porphyrins to 310 µg/l, above the upper limit of normal values. There were no other clinical findings characteristic of PCT such as skin lesions or elevation of liver transaminases above baseline levels. Gemcitabine is a pyrimidine analogue of deoxycytidine which has been increasingly used in non-small-cell lung cancer (NSCLC) and pancreas adenocarcinoma. Use of this drug should be avoided, if possible, in patients with porphyria; otherwise, its effects must be carefully monitored.

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Docetaxel and epirubicin plus G-CSF mobilize hematopoietic progenitors in breast cancer

The ideal mobilizing/cytoabusive regimen for patients with cancer enrolled in a high-dose chemotherapy program should be one which contains the drugs most active in producing rapid antitumor effects and which are able to mobilize an adequate amount of peripheral blood progenitor cells (PBPC). In patients with breast cancer, disease-oriented mobilizing strategies allow the administration of full-dose anthracyclines, at present the most active drugs for the polychemotherapy treatment of these patients, and thereby make it possible to avoid the use of myelosuppressive doses of single-agent chemotherapy. We recently found that the combination of cyclophosphamide (600 mg/m²), epirubicin (90 mg/m²) and 5-fluorouracil (500 mg/m²) (CEF) plus granulocyte colony-stimulating factor (G-CSF; 5 µg/kg/d subcutaneously) mobilizes a large amount of peripheral blood progenitor cells (PBPC) ten days after administration of chemotherapy. In fact, CEF + G-CSF, administered as adjuvant chemotherapy in stages II or IIIa previously untreated breast cancer patients, induced recirculation of large quantities of CD34+ cells (Table 1) and of a number of clonable hematopoietic precursors (CFU-GM) comparable to what is observed after the administration of high-dose epirubicin (120 mg/m²) combined with an increased dose of cyclophosphamide (1500 mg/m²) and G-CSF [1] (8000 ± 2000 CFU-GM/ml for CEF + G-CSF and 9100 ± 2500 CFU-GM/ml for epirubicin and increased cyclophosphamide + G-CSF). These results were in accord with those reported by Venturini et al. [2] who reported that the CEF + G-CSF regimen is actually an efficient and reliable mobilizing treatment for high-risk breast cancer. Docetaxel has proved to be very effective in producing clinical responses in breast cancer patients who were chemotherapy-naive or refractory to previous anthracyclines or paclitaxel [3, 4]. Phase I studies have shown that docetaxel can be administered in combination with epirubicin and G-CSF administration allows their maximum tolerable dose to be increased to 85 mg/m² and 120 mg/m², respectively [5]. In this context, we evaluated the ability of the docetaxel (75 mg/m²) and epirubicin (120 mg/m²) combination, administered on the same day and supported with G-CSF (5 µg/kg/d subcutaneously), to mobilize PBPC in previously untreated patients with stage II–IIIa breast cancer. In 15 consecutive patients peripheral CD34+ cells peaked on day 10 on average, reaching the average value of 177/µl. Table 1 shows that, performing a comparable number of leukaphereses, we obtained a similar collection of CD34+ cells per kg in patients treated with CEF + G-CSF (14 x 10⁶/kg on average) and with docetaxel–epirubicin + G-CSF (11 x 10⁶/kg on average), and the peak values of CD34+ cells in the peripheral blood of the two patient series were comparable. These results indicate that an effective regimen such as docetaxel and epirubicin for breast cancer can be exploited successfully to collect large quantities of PBPC which can support one or two subsequent myeloablative or highly myelosuppressive treatments. This result is not unexpected and confirms that a large series of drug combinations produce PBPC mobilization (which can be potentiated by G-CSF administration) as a consequence of transient myelosuppression through an unclear mechanism. However, it is worth noting that a series of 13 patients with metastatic breast cancer, chemotherapy-free for at least 4 months, mobilized an inadequate amount of CD34+ cells (ranging from 0/µl to 30/µl) when treated in our institution with docetaxel alone at the dose of 100 mg/m², irrespective of the administration of G-CSF (G-CSF was administered at the dose of 5 µg/kg/d to 6 patients producing no relevant effects on PBPC mobilization). This suggests that the greater contribution to PBPC mobilization is probably made by epirubicin and that the magnitude of CD34+ cell release into the peripheral blood might be related to its dosage (120 mg/m² in the current study). Hence, changes in the dosage of epirubicin in the above described chemotherapy combination could render this regimen less effective or inadequate for PBPC mobilization and collection in breast cancer patients. Finally, we found that the combination of the very active drugs docetaxel and epirubicin mobilizes a large amount of PBPC in high-risk breast cancer. PBPC can be collected by a single leukapheresis and we were able to rapidly reconstitute hematopoiesis in the same patients after administration of the previously described CEM regimen [6, 7] (7 patients had neutrophils > 500/µl and platelets > 50,000 after a median period of 9 and 10 days after reinfusion, respectively). These findings will contribute to the future planning of intensive polychemotherapy strategies for the treatment of high-risk breast cancer patients.

Table 1 Mobilization and collection of PBPC.

<table>
<thead>
<tr>
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<th>CEF + G-CSF (n = 15)</th>
<th>Docetaxel + epirubicin + G-CSF (n = 15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD34 cells/µl (peak)</td>
<td>257±200 (14±10³/kg)</td>
<td>177±168 (11±10³/kg)</td>
</tr>
<tr>
<td>Apheresis number</td>
<td>1.07±1 (1-2)</td>
<td>1±1 (1-1)</td>
</tr>
<tr>
<td>Collected CD34 cells x10³/kg</td>
<td>14±13 (4-40)</td>
<td>11.3±11 (4-22)</td>
</tr>
</tbody>
</table>

* Comparisons were made by Mann–Whitney U nonparametric test.

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The section on the conservative management of CML has significantly improved and continues to evolve. The use of interferon-α, which can now be combined with cytarabine, has transformed the conservative management of CML. Allogeneic bone marrow transplantation, which remains the only curative treatment modality of CML, has also witnessed major developments, with the use of peripheral blood stem cells and of alternative donors, and with the introduction of adoptive immunotherapy and, quite recently, of mini-transplants. Our current understanding of the biology of CML and of BCR-ABL is providing a rational approach for the development of novel therapeutic approaches. The book edited by Moshe Talpaz and Hagop Kantarjian reviews the various aspects of the current management of CML and is very timely.

Following a general introductory part, the book is divided in four sections: chemotherapy and interferons, bone marrow transplantation, detection of minimal residual disease (MRD), and developmental therapies. The section on the conservative management of CML is the most comprehensive one. The clinical trials of the German, Italian, French and Australian cooperative groups on interferon-α therapy are presented in individual chapters. The experience of the French and Australian groups on the combination of interferon-α with cytarabine is discussed in depth. In comparison to the information provided in the first part, I must admit that I found the section on bone marrow transplantation relatively disappointing. Although the two reviews on allogeneic bone marrow transplantation are excellent, recent developments in this field, such as adoptive immunotherapy or autologous bone marrow transplantation, are only discussed too briefly. The section on the detection of MRD is also quite extensive and complements very well the clinical sections. Current approaches used for monitoring MRD with conventional cytogenetics, FISH and quantitative PCR, are presented in three individual chapters. The section on developmental therapies is nice to read and will help readers understand the basis of current innovative approaches in CML. In particular, there are excellent and timely contributions on the use of antisense therapy by Alan Gewirtz and on ABL protein kinase inhibitors by Brian Druker. Other novel drugs, such as homoharringtonine, are briefly presented in the introductory chapter.

In addition, this book contains several chapters, which will render it very useful for clinicians involved in the care of patients of CML and related myeloproliferative disorders. The practical aspects of interferon-α therapy, which can be difficult to manage in individual patients, are discussed specifically in a separate chapter by the team of Dr O'Brien. Moreover, there are chapters on two rare chronic leukemias: BCR-ABL negative CML and chronic myelomonocytic leukemia, which are rarely covered and are reviewed in detail.

In summary, this clinically-oriented book provides an excellent overview of the current medical management of CML at the turn of the century. It also provides information to understand the basis of some of the novel therapeutic modalities, which will reach clinical trials in the near future. Although this volume will be of more interest to physicians involved in the conservative management of CML, it can be highly recommended to all physicians dealing with CML.