

High-Dose Chemotherapy: Changes in Approaches and Applications

The concept that higher doses of available cytotoxic antitumor drugs would alter outcomes of treatment of many types of cancer drove the early practice and trials of high-dose chemotherapy with bone marrow or stem-cell salvage. Benefit was seen in patients with a variety of hematologic malignancies, and several phase I and II trials provided encouraging results in other diseases, including breast cancer. Over time, much was learned about improving the support and care of patients treated with high-dose therapy, and the concept of turning the graft-vs-host problems into a beneficial graft-vs-tumor-effect paradigm followed. Coincident with these developments, some relatively large-scale phase III comparative studies matured, allowing clinicians to better place these aggressive treatment approaches in context.

Clearly, much more is needed to be learned about hematopoietic stem cells and where they fit in hematopoiesis. Dr. Clayton Smith addresses this topic in the lead article of this issue and also explores the tantalizing concept of stem-cell plasticity: whether hematopoietic and other stem cells can generate other tissues. We will hear of and learn much more about this important field of research.

One of the difficulties that clinicians had in evaluating the appropriate place of high-dose therapy in

clinical practice was the paucity of reliable and objective information on the balance between “good” vs “harm” from the reported clinical trials. In order to begin to get some sense of these clinically relevant parameters in the increasingly popular “mini-transplants” (nonmyeloablative allogeneic stem-cell transplantation) for hematologic malignancies, Dr. Benjamin Djulbegovic and coworkers present an elegant exposition of currently available published studies of this approach. Formal reviews such as this are key for developing evidence-based guidelines.

Investigators in European countries are sometimes better able to perform clinical studies than in the United States, in part because they can encourage rapid accrual of patients into difficult and often low-accruing trials. The French PEGASE group was formed to study high-dose chemotherapy for breast cancer in large groups. At one time, their protocols included 80% of all the women who received high-dose chemotherapy for breast cancer in France! Dr. Roché et al describe their outcome data for various stages of disease and report some encouraging results in disease-free survival that unfortunately have not so far translated into long-term survival benefit.

As Lance Anderson so eloquently demonstrates, cisplatin-based chemotherapy for germ tumors has

been one of oncology’s major success stories. Not all patients are cured, however, and Dr. DeGiorgi and coauthors trace the history of high-dose chemotherapy used to salvage these “resistant” patients and describe the development of the current active clinical trials for these “poor-risk” patients.

Moving away from oncology, modern drug development has provided benefit to an increasing number of patients with rheumatic autoimmune disease. Nevertheless, some patients continue to experience severe morbidity for these diseases. Drs. van Laar and Tyndall review for us the information available on the novel trials of intense immunosuppression and stem-cell transplantation for selected groups of these patients.

Also in this issue, we include a listing of the “10 best” recent articles on high-dose chemotherapy, a listing of selected clinical protocols in the field, the second part of the review on catheter-related infections, and an intriguing new look at financial costs incurred in cancer clinical trials.

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