Is There a Role for Dose-Intensive Chemotherapy With Stem Cell Rescue in Breast Cancer?

Review Article [1] | December 01, 2002
By Adam M. Brufsky, MD, PhD [2] and Victor G. Vogel, MD, MHS, FACP [3]

During the 1990s, perhaps no other therapy for women with breast cancer was more controversial than high-dose chemotherapy with autologous bone marrow and/or peripheral stem cell support. With encouraging results from late phase I and early phase II trials in the early to mid-1990s, high-dose chemotherapy was promoted by its many enthusiastic proponents as a potentially great leap forward for women with high-risk, node-positive or metastatic disease.

The data from randomized clinical trials presented to date, however, have been mixed. As noted, one randomized trial in metastatic disease was fraudulent.[1] One trial enrolled women with metastatic disease and a complete response to initial standard-dose induction therapy to immediate or delayed high-dose therapy at progression.[4] Immediate consolidation with high-dose therapy produced a better disease-free survival than delayed consolidation but a poorer overall survival. Another study randomized women with metastatic breast cancer and a response to induction therapy to high-dose or standard chemotherapy.[5] This trial demonstrated no difference in disease-free or overall survival between the arms.

Looking Ahead

Williams correctly points out that more long-term follow-up is needed before definitive results can be determined, perhaps through a meta-analysis of completed trials. However, it is likely that the benefit, if any, from high-dose chemotherapy in these studies will be small. In addition, newer agents for the treatment of both metastatic and early-stage disease, such as the aromatase inhibitors, taxanes, and trastuzumab (Herceptin), are gaining widespread clinical acceptance. High-dose
chemotherapy would likely have to prove superior to these newer, less toxic agents to gain acceptance in the therapeutic armamentarium. Williams suggests that the failure of high-dose chemotherapy to improve the outcome of women with breast cancer may be due to residual minimal disease and/or autograft contamination by tumor. These are reasonable hypotheses that deserve clinical investigation. Proof-of-principle trials exploring, for example, high-dose chemotherapy in combination with immunomodulatory strategies[7] such as tumor antigen vaccination or dendritic cell vaccination, are also reasonable and will likely teach us much about the host immune response to minimal residual breast cancer. Whether such studies can be translated into large clinical trials with the potential for altering clinical care remains an open question.

Conclusions
In summary, Williams has provided an excellent brief review of the current state of high-dose chemotherapy for breast cancer. As we await updated analyses of multiple randomized clinical trials, it is clear that high-dose chemotherapy remains an experimental therapy that should be performed only in the context of well-designed clinical trials. While the era of dose intensity (higher dosing) may be closing, randomized trials testing the concept of dose density (more frequent dosing) will soon be presented at national clinical meetings. If such trials prove promising, physicians involved in the treatment of breast cancer may be asking not "how much," but rather, "how fast."

References:


Source URL:
http://www.physicianspractice.com/review-article/there-role-dose-intensive-chemotherapy-stem-cell-rescue-breast-cancer

Links: