

When Do You Send the Troops In? The W5 of Transplantation in Myeloma

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Autologous stem cell transplantation remains the standard of care in multiple myeloma for eligible patients. However, must all eligible patients be exposed to the risks and complications of high-dose therapy?

A Monday Spotlight Session was dedicated to teasing out the critical details of stem cell transplantation in myeloma. Drs. Sundar Jagannath and Vincent Rajkumar discussed the role of transplant in this rapidly evolving field. They reminded us that it remains the standard of care, but not for all patients. The issue of early vs. delayed transplant was raised — evidence is emerging that there may not be a difference in overall survival if a patient is delayed until progression, but that stem cells should be collected early in the course of their disease.

The second question raised was single vs. tandem transplant. The five trials that have been designed to answer this question were reviewed — it appears that tandem transplant results in an improved event-free survival, but subgroup analysis may lead us to believe that not all patients may benefit from this strategy. Close review of the IFM data has revealed that tandem transplant is most effective in patients whose response was <90 percent after first transplant, although it was superior overall to single transplant.

Another key to appropriately deciding on transplant is the need to stratify patients into high and standard-risk categories. The method adopted by the Mayo Clinic classifies high-risk patients who have the following features: FISH del 17p-, t(4;14) t(14;16); cytogenetic del 13, cytogenetic hypodiploidy; and PCLI >3%. Standard-risk patients would be defined as all others, including hyperdiploid, t(11;14), and t(6;14). Although exact regimens for high- and standard-risk patients have not been validated, it is clear that these groups of patients respond differently, and risk-adapted therapies will be the future of transplantation in these patients.

Some patients are clear candidates for allogeneic stem cell transplant. Although this is feasible in only a small minority of patients with myeloma, it may confer long-term survival in young patients with high-risk disease such as adverse cytogenetic abnormalities and rapidly relapsing disease. Furthermore, more patients may be eligible for “mini” allogeneic transplants, as they minimize the risks of transplant and maximize graft-versus-myeloma effect.

What do we do after transplant? Should patients be observed, or should they undergo maintenance therapy? The recently published maintenance trial by the French IFM group was reviewed. Although used in the post-tandem transplant setting, which may not be applicable to all centers, the evidence for maintenance therapy with thalidomide was encouraging. This was balanced, of course, by its risks and complications.

Do we really have to use high-dose therapy at all? With the dawn of novel agents like thalidomide, bortezomib, and lenalidomide, should all patients still be considered for transplant? These controversies were discussed at length during the session. Although only further trials will provide the evidence required to change the standard of care, it is clear that the transplant approach is not for all. Certain groups were identified who may not be best served with transplant. Furthermore, conditioning regimens are also changing, with greater incorporation of novel agents.

Participation during this session was extensive and productive. Although stem cell transplant is still important for treatment of myeloma, the future of the high-dose therapy is unclear — we will have to continue to re-evaluate its use in this disease.