Advanced CTCL: Include HSCT as an Option

BY SARAH DIGIULIO

Hematopoietic stem cell transplant (HSCT) should be included as an option for patients with advanced cutaneous T-cell lymphoma—specifically mycosis fungoides and Sézary syndrome. That is the message from Christiane Querfeld, MD, PhD, Director of the Cutaneous Lymphoma Program and Assistant Professor of Dermatology and Dermatopathology at City of Hope Cancer Center & Beckman Research Institute and lead author of a recent review article on the topic.

As she explains in the article (***Dermatologic Clinics 2015;33:807-818***), because there is no cure and none of the standard regimens or investigational regimens have shown a sustained response to treatment, allogeneic transplant has the potential to cure patients with these diseases.

She and her colleagues (first coauthors are Pooja Virmani, MBBS, MD, and Jasmine Zain, MD) review the current data, which has to date been minimal, on conditioning regimens, treatment-related complications, and outcomes for such patients who do undergo HSCT.

The article concludes that for patients with advanced-stage mycosis fungoides (stages IIB to IV) with relapsed or refractory disease or for aggressive CTCL subtypes such as Sézary syndrome, allogeneic HSCT has been shown to result in complete clearance of skin lesions, blood involvement, and other evidence of disease, with some patients achieving long-term remission.

No Clear Guidelines

But, a big challenge for using HSCT for these patients is that there are no clear guidelines to select appropriate patients for stem cell transplant, Querfeld added in an email message.

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The authors also note that the use of genetic profiling and gene sequencing is likely to allow better prognostic characterization of these tumors and may allow better selection of patients who require transplant for disease control. In addition, dedicated transplant protocols should be developed in multicenter trials to address the needs of these patients with CTCL with improved conditioning regimens and supportive care measures. The increasing number of targeted agents for CTCL, HDAC, and checkpoint inhibitors in particular, should be incorporated into transplant protocols—either in conditioning regimens or as maintenance strategies, the team said.

More Key Conclusions

Other conclusions:

- There is no consensus about the degree of remission needed before transplant for a successful outcome;
- Both related and unrelated matched donors have been used, and there are now supporting data using cord blood as a source of stem cells;
- Although there is still no consensus on conditioning regimens, remissions have been achieved using reduced-intensity approaches, even in patients with advanced and refractory disease, indicating that intense conditioning may not be required for response;
- Total skin electron-beam therapy before transplant may be associated with improved skin control;
- Relapses still occur after allogeneic transplants, but have been treated successfully with adjustments of immunesuppression, donor lymphocyte infusion, or skin-directed treatments; and
- The use of allogeneic stem cell transplant is associated with a higher incidence of complications, including graft-versus-host disease, infections, and death.

MYELOMA

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A Phase II study in newly diagnosed elderly multiple myeloma patients is now comparing ixazomib plus dexamethasone or ixazomib in three-drug combinations with dexamethasone plus cyclophosphamide, bendamustine or thalidomide, he said.

In conclusion, Palumbo said: "Use a three-drug combination for fit patients, such as induction with bortezomib-cyclophosphamide-dexamethasone or bortezomib-melphalan-prednisone or bortezomib-lenalidomide-dexamethasone for nine to 12 cycles, followed by maintenance with lenalidomide-bortezomib for two years or until disease progression. In frail patients, use induction with two drugs followed by maintenance, such as lenalidomide-dexamethasone, then lenalidomide, bortezomib-dexamethasone, then bortezomib or thalidomide-dexamethasone, and then thalidomide.

'Induction, then Consolidation'

"We have learned from the transplant setting to give induction then consolidation," he continued. "For induction, use two drugs, such as an IMiD or proteasome inhibitor plus dexamethasone for four cycles to reduce toxicities. For consolidation, use three drugs, such as a proteasome inhibitor and dexamethasone plus cyclophosphamide or an IMiD for six to nine cycles to improve efficacy. For maintenance, use a proteasome inhibitor or an IMiD to prolong remission."

If patients are in a grey zone, "use two drugs, not three drugs. Most toxicity occurs during the first few courses of therapy. Use two drugs for three or four courses, and if this is tolerated but not effective enough, add in a third drug," said Palumbo, stressing that maintenance is a must for all patients.

The key, he said, is gentle induction, consolidation, and then maintenance. Continuous therapy in low doses helps keep patients on therapy for the required time, he noted.

Coleman agreed that the standard of care in young, fit myeloma patients is three drugs. "In the U.S., we use proteasome inhibitors, IMiDs, and steroids. The EVOLUTION trial showed that bortezomib plus cytotoxic therapy is almost as good.

"Among community oncologists, bortezomib-lenalidomide-dexamethasone is the most common combination," he continued. "Carfilzomib-lenalidomide-dexamethasone seems to do much better, but there are toxicity issues, such as cardiorespiratory problems, which have to do with the amount of fluid given." He said he believes that given properly, the carfilzomib combination "probably is superior."

Coleman said he thinks that daratumumab should be able to be readily adapted into community practice. "I have seen great responses with daratumumab, which works by itself and in combinations."

FDA Approval

Daratumumab received FDA approval less than a month after the conclusion of the meeting—approved for intravenous infusion for patients who have received at least three prior therapies. The approval is the first for a monoclonal antibody for multiple myeloma.

Cycling Inhibitors

Cycling inhibitors, such as ibrutinib, may also be applicable to myeloma patients. "Right now, the dosage is high, but data suggest that these drugs will work," he said. They appear to work on stromal cells and may interfere with myeloma cell adhesion.

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