

Multiple myeloma

IS MORE BETTER?

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TRIAL SUMMARY: Consolidation therapy after autologous hematopoietic cell transplant

Stadtmayer EA, Pasquini MC, Blackwell B, et al. Comparison of autologous hematopoietic cell transplant (autoHCT), bortezomib, lenalidomide and dexamethasone (RVD) consolidation with lenalidomide maintenance (ACM), tandem autoHCT with lenalidomide maintenance (TAM) and autoHCT with lenalidomide maintenance (AM) for upfront treatment of patients with multiple myeloma (MM): primary results from the randomized phase 3 trial of the Blood and Marrow Transplant Clinical Trials Network (BMT CTN 0702 – StaMINA Trial). ASH Annual Meeting, San Diego, California, December 3-6, 2016. Abstract LBA-1.

StaMINA is a phase 3 clinical trial of transplant-eligible patients under 71 years of age with symptomatic multiple myeloma (MM). Patients who received at least 2 cycles of induction therapy (according to local standard of care) were randomized 1:1:1 to subsequently receive either ACM (a melphalan

200 mg/m² autologous hematopoietic cell transplant [autoHCT] and 4 cycles of RVD consolidation [lenalidomide, dexamethasone and bortezomib]); TAM (tandem autoHCT); or AM (single autoHCT). All patients received lenalidomide maintenance until progression. The primary outcome of the study was PFS with ancillary secondary endpoints including health-related quality of life.

A total of 758 patients with a median age of 57 were enrolled, and median available followup from randomization was 38 months. Noncompliance rates following the first autoHCT were 12%, 32% and 5% for ACM, TAM and AM, respectively. Estimated probabilities for PFS at 38 months were 57% (95% CI, 50–63%), 56% (95% CI, 49–63%) and 52% (95% CI, 45–59%) for ACM, TAM and AM, respectively (ACM vs TAM p=0.75, ACM vs AM p=0.21, TAM vs AM p=0.37). Corresponding OS probabilities were 86% (95% CI, 80–90%), 82% (95% CI, 76–87%) and 83% (95% CI, 78–88%). Median

OS had not been reached at the time of presentation. Cumulative incidences of disease progression at 38 months were 42%

(95% CI, 36–48%), 42% (95% CI, 35–48%) and 47% (95% CI, 40–54%) for the ACM, TAM and AM arms, respectively.

COMMENTARY: A common management strategy for patients with symptomatic myeloma is to employ continuous multiagent chemotherapy to achieve deeper biochemical and/or molecular responses in the attempt to improve clinical outcomes with a “more is better” approach. In the transplant-eligible setting, the standard of care for these patients is induction therapy with a combination of drugs, including a novel agent, such as bortezomib and/or lenalidomide, followed by a single autoHCT. Further, based on data from large randomized controlled trials, the addition of post-autoHCT therapy with lenalidomide maintenance is commonly employed.^{1,2} In contrast, the clinical utility of post-autoHCT consolidation therapy with either a novel agent or tandem autoHCT prior to maintenance therapy remains controversial.^{3,4}

Patients who fail to achieve very good partial response (VGPR) after first autoHCT benefit from tandem autoHCT, with improvements in PFS and OS.³ Bortezomib-based consolidation therapy has been shown to improve the rates of complete remission and molecular remission following autoHCT, which has translated into improvements in PFS. Additionally, many patients who reach molecular remission have yet to relapse, suggesting that cure may be possible for some patients.^{4,5} However, the majority of consolidation studies were performed in bortezomib-naïve patients, thus, the added benefit of consolidation in patients who received a novel agent as part of their induction therapy remained unknown.⁶ The StaMINA study sought to address this uncertainty by investigating the role of consolidation therapy for transplant-eligible patients with newly diagnosed symptomatic MM.

The StaMINA trial, a Blood and Marrow Transplant Clinical Trials Network study, involved 53 US tertiary care centres between June 2010 and November 2013. At a median followup of 38 months, the investigators estimate a PFS of 57% (ACM), 56% (TAM) and 52% (AM), and OS of 86% (ACM), 82% (TAM) and 83% (AM), without statistical differences between the strategies. Several aspects of the trial results deserve mention. Firstly, there were relatively high rates of noncompliance following the first transplant in the ACM and TAM groups (12% and 32%, respectively) compared to the AM group (5%). However, a per-protocol analysis did not demonstrate any statistical differences between the groups. Further, there were no differences in PFS or OS in patients with high-risk disease as defined by cytogenetic abnormalities or high beta-2 microglobulin. Importantly, the rates of second primary malignancy were similar among all 3 groups (4% to 6%). Unfortunately, no health-related quality-of-life data were presented.

What does this mean for the treating physician? The results of the StaMINA study would suggest that, in the majority of cases, a strategy of novel agent-based induction chemotherapy followed by a single autoHCT and maintenance lenalidomide is safe and effective. Further followup and additional post-hoc subgroup analyses will be necessary to determine whether the results remain firm, or if certain

IN BRIEF

Already known

- Lenalidomide maintenance is commonly employed as maintenance therapy following autologous hematopoietic cell transplant (autoHCT) in patients with myeloma.
- Tandem autoHCT improves progression-free survival (PFS) and overall survival (OS) in patients who do not achieve very good partial response after first autoHCT.
- Consolidation therapy with bortezomib following autoHCT may improve remission rates and PFS, especially in patients who did not receive a novel agent as part of their induction therapy.

What this trial showed

- Preliminary results from the StaMINA trial showed no statistical difference in PFS between patients who, following induction therapy, received consolidation with lenalidomide, dexamethasone and bortezomib; patients who received tandem autoHCT; and patients who received a single autoHCT. All received lenalidomide maintenance.

Next steps

- Wait for health-related quality-of-life data from the StaMINA study.
- Wait for subgroup analysis to see if certain high-risk patients may show benefit from consolidation therapy.
- In most cases, induction, single autoHCT and maintenance lenalidomide appears safe and effective.

subgroups, such as high-risk patients, may benefit from consolidation therapy. For now: more isn't always better; sometimes it's just more.

References

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