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More equal access and improved treatment for multiple myeloma

INVITERT KOMMENTAR

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First-line treatment for younger patients with newly diagnosed multiple myeloma has proven highly effective, but there are expectations of, and scope for, further improvement.

High-dose chemotherapy with autologous stem cell transplantation (HD-ASCT) has been a mainstay of first-line treatment for younger patients with multiple myeloma since the early 1990s. In this edition of the Journal of the Norwegian Medical Association, Nørgaard et al. publish retrospective data covering the period 2008–2020, which demonstrate improved median survival from 5.1–7.3 years in the period 2005–2010 to 9.5 years in the study period (1). Patients were followed until 2022, and the data confirm that HD-ASCT is a safe and efficacious treatment up to the age of 75 in carefully selected patients.

During the study period, there were significant regional differences in the choice of induction and consolidation therapy, which may have impacted long-term prognosis. Centres using bortezomib, lenalidomide and dexamethasone for induction, and where the highest proportion of patients also received consolidation and maintenance therapy, had the longest median progression-free and overall survival.

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In the absence of comparative studies, three treatment options were considered equivalent in the national treatment programme between 2016 and 2020. From autumn 2020 to 2024, most younger patients with newly diagnosed multiple myeloma in Norway were included in the REMNANT study (2). In the study, all patients received bortezomib, lenalidomide and dexamethasone for induction and consolidation, which is now the preferred regimen in the Norwegian treatment programme for multiple myeloma (3).

This is not to suggest that there is no room for improvement. The addition of the CD38 antibody daratumumab has been investigated in the prospective, randomised PERSEUS trial (4). After a median follow-up of 47.5 months, progression-free survival was 84.3 % in patients receiving daratumumab, compared with 67.7 % in those receiving only bortezomib, lenalidomide or dexamethasone. Corresponding response data have been reported for the CD38 antibody isatuximab, although with a shorter observation period (5). There is no reason to believe there are clinically meaningful differences in efficacy between the different CD38 antibodies.

Adjunctive treatment with a CD38 antibody is now recommended in European guidelines as first-line treatment prior to HD-ASCT (6). The treatment has already been introduced in Sweden, and in Norway it is currently under evaluation by the Decision Forum (a governmental body responsible for approving new diagnostic and treatment methods in Norway) (7). For patients ineligible for HD-ASCT due to age or comorbidity, however, the combination has already been introduced as first-line treatment. This is considered paradoxical by clinicians treating multiple myeloma, as younger patients derive at least as much benefit from this treatment as elderly patients.

Another question concerns the role of HD-ASCT in multiple myeloma treatment as more effective therapies for relapsed patients become available and as future research enables better patient selection.

The absence of measurable residual disease in bone marrow aspirates, known as MRD negativity, indicates a very deep treatment response and is associated with significantly longer progression-free survival (8). The MIDAS trial demonstrated that patients achieving MRD negativity after induction therapy had comparable responses following HD-ASCT or consolidation therapy (9). If these results hold over time, this may be an indication that it is safe to omit HD-ASCT in selected patients.

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There is also anticipation regarding whether HD-ASCT may eventually be replaced by newer treatments, such as chimeric antigen receptor (CAR) T-cell therapy or CD3 bispecific antibodies. Numerous prospective studies are ongoing.

Treatment for multiple myeloma is specialised, costly and lengthy, but patients live longer and have a better quality of life than before. Despite these advances, most patients with multiple myeloma still ultimately die from the disease (10). HD-ASCT remains effective, safe and cost-effective, and will continue to be a central component of first-line treatment for younger patients for many years to come.

New, more effective medications usually provide the greatest benefit when administered early in the treatment course. It is therefore crucial to confirm results from randomised trials in real-world patient populations, as Nørgaard et al. have done. Systematic and robust evaluation requires high-quality registries, exemplified by the Myeloma Registry of Central Norway, which should serve as a model for the rest of the country. The authorities will hopefully support this work going forward.

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