W15: The EBMT/ECWM/IWMF consensus project on the role of autologous and allogeneic stem cell transplantation in Waldenstrom's Macroglobulinemia

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In an era of major advances in the management of Waldenstrom's Macroglobulinemia (WM), defining the role and timing of autologous (ASCT) and allogeneic stem cell transplantation (alloSCT) is a major challenge. In the absence of evidence-based data, the RAND-modified Delphi consensus procedure was adopted by a panel of international experts. Eighteen pre-defined statements were scored individually and anonymously by each participant, using a 7-point scale (1-3: disagree, 4: neither agree nor disagree, 5-7: agree). Consensus in favour or against of the statement was reached if 80% of the rankings fell in the same group and was reached or not after two rounds of rating.

Consensus was reached on the following statements: 1. ASCT is not an appropriate treatment option as part of the 1st-line therapy in patients responding ($\geq$partial response – PR-) to induction therapy); 2. ASCT is an appropriate treatment option following $\geq$2 relapses in high-risk patients with chemo-sensitive disease; 3. Choice of 1st-line therapy should avoid the use of stem cell toxic agents in transplant eligible patients; 4. ASCT is not an appropriate treatment option in patients responding and tolerating B-cell receptor inhibitors (BCRi); 5. AlloSCT could be considered for patients with relapse after ASCT; 6. AlloSCT should be considered in patients with high-risk ISSWM in $\geq$3rd relapses provided they have received immunochemotherapy and BCRi; 7. AlloSCT should be considered in patients with

relapsed/refractory WM to immuno-chemotherapy and resistant to BCRi; 8. If BCRi are available, allo-SCT should not be considered in BCRi-naïve patients; and 9. Treatment decisions for SCT should preferentially be based on the clinical course rather than on ISSWM or on biological/genetic factors.

In contrast, consensus was not reached on: 1. ASCT is an appropriate treatment option in patients who require ≥1 line of therapy to achieve a PR; 2. ASCT is an appropriate treatment option in patients with chemo-sensitive relapse with a response duration <12m; 3. ASCT is not an appropriate treatment option in patients who have not received BRCi, if available; 4. ASCT should not be offered to patients with chemo-resistant WM; 5. Storage of autologous stem cells for future use should be considered in patients <60 years; 6. AlloSCT could be considered instead of ASCT in patients <60 years with relapsed high-risk ISSWM disease responding to salvage therapy; 7. AlloSCT could be considered in patients in 2nd relapse; 8. AlloSCT should be considered instead of ASCT in patients with relapsed/refractory WM with p53 abnormalities/other adverse mutations; and 9. AlloSCT should be only considered in patients with WM responding to salvage treatment.

Consensus methods provide valuable tools to define indications for SCT especially in rare disorders. The impact on the quality and duration of response of new combination therapies and BCRi is undoubted and the place of SCT is debatable. There was agreement on not offering SCT to patients who have not received BCRi, provided they are available. ASCT remains a possible treatment option in patients with chemo-sensitive high-risk WM following ≥2 relapses. AlloSCT could be considered in high-risk (ISSWM in ≥3 relapses.