Should ASCT be a frontline option for Waldenstrom's macroglobulinemia? [NO]

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High dose therapy (HDT) and auto transplant are feasible as frontline therapy in Waldenström's disease but whether or not this strategy can significantly improve EFS and OS only relies from retrospective studies or from a registry that have concerned subgroups of young responder patients.

Assuming that HDT and auto-transplant may actually be proposed to selected young patients, the induction and mobilization chemo steps should use Rituximab, at least as in vivo purging technique. In contrast, it should avoid nucleoside analogs (and probably also Bendamustin) because of their well-known detrimental effects on stem cell collection. Rituximab plus cytoxan based regimen is the main option for which we have some data, the combination of Rituximab and Bortezomib needing to be further explored. We have even less data regarding the HDT regimen, particularly whether or not it should include a total body irradiation. This may impact not only the immediate toxicity of the procedure but also the occurrence of long-term complications, particularly the risk of secondary malignancy.

In any case, evidence is still lacking that any HDT strategy can produce a superior outcome as compared to standard dose regimens. In the EBMT registry, which analysed HDT-treated young selected patients in good response after a first line treatment, estimated PFS and OS at 5 years were 51.5% and 77%, respectively (Kyriakou et al., J.C.O.,2010). The corresponding values for the conventionally first line treated older patients in the prospective SWOG study (Dhodapkar et al, Blood, 2001 & 2009) were quite similar, being 49% and 62% respectively.

Another point that argues against HDT frontline is that it exposes the patient to a risk of sustained impairment in his/her bone marrow capacities, which could compromise the chance of delivering at relapse some of the major drug class, particularly nucleoside analogs and bendamustin.

Accordingly, in those young patients with symptomatic WM who may be candidates for HDT and auto-transplant, this treatment should not be a front-line therapeutic option, but may be eventually considered as a rescue treatment, in case of resistance or at relapse.