Trends in Autologous Stem Cell Transplantation for Newly Diagnosed Multiple Myeloma: Lessons for Resource-Challenged Regions

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Swan et al report the trends in autologous hematopoietic stem cell transplantation (ASCT) for newly diagnosed multiple myeloma over the past three decades in the European Society for Blood and Marrow Transplantation (EBMT) centers.[1] The stem cell utilization rates (STUR) of ASCT for myeloma have shown a rising trend for most resource-rich regions (13 to 24% in Northern America and 15 to 22% in Europe).[2] However, we would like to focus on the trends in treatment-related mortality (TRM) that has important lessons for resource-challenged regions. The TRM rates from ASCT reported in the EBMT centers show a downward trend over the past three decades from approximately 5 to 1%.[1] The same in the US centers is down from approximately 3 to less than 1%.[3,4] Trends in increasing STUR parallel decreasing TRM for ASCT in multiple myeloma. ASCT is the standard of care in the treatment paradigm of eligible myeloma patients.[5,6] Undoubtedly, there is a progression-free survival (PFS) benefit to multiple myeloma patients with ASCT as reported in meta-analysis; however, no overall survival benefit was observed.[7,8] The data on PFS benefits are drawn from landmark randomized controlled studies in resource-rich countries. With the current standard dose therapy (SDT) comparator (VRD-bortezomib-lenalidomide-dexamethasone), this median PFS benefit has narrowed to just 14 months (50 vs. 36 months).[9] There is no reason to believe the benefits would be different in other parts of the world. However, what level of TRM justifies this narrow PFS benefit needs to be addressed.

The STUR have not gone up proportionately in the rest of the resource-challenged regions (1.8–4%).[2] The common reasons for these are financial limitations, patient perception, and cultural bias.[10] This is despite Indian patients with myeloma being younger and having a high-risk disease at onset.[11] The ASCT TRM in most Indian centers is still high (2–7.2%).[12] Possible reasons for this include the frailty of Indian patients at the time of ASCT with increased toxicity from ASCT and center experience.[13] A systematic review and meta-analysis done in the era of such high TRM in the resource-rich settings[14] found that the odds ratio of TRM was three times with upfront ASCT compared with SDT (~2%). The calculated number needed for treatment harm from upfront ASCT was 26. This number was high enough to question the benefit of ASCT in favor of alternative treatment options. It took the resource-rich settings more than two decades to decrease the TRM to just approximately 1%, which brings the number needed for treatment harm to more than 100, justifying frontline use of ASCT in all eligible patients. As centers expand their ASCT numbers, their TRM rates will naturally decrease with experience and better supportive care.[1,14] Until then, centers in resource-challenged settings should periodically audit their TRM from SDT and ASCT and make an informed decision by discussing the pros and cons of upfront ASCT in consultation with their patients. Without a substantial survival benefit, even quality of life benefit will help guide the patient's decisions until the TRM rates are down to 1% or lower.[10]

Conflicts of Interest
None declared.

References

1 Swan D, Hayden PJ, Eikema DJ, et al. Trends in autologous stem cell transplantation for newly diagnosed multiple myeloma: Changing demographics and outcomes in European Society for Blood and Marrow Transplantation centres from 1995 to 2019. Br J Haematol 2022;197(01):82–96

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2 Cowan AJ, Baldomero H, Atsuta Y, et al. The global state of hematopoietic cell transplantation for multiple myeloma: an analysis of the worldwide network of blood and marrow transplantation database and the global burden of disease study. Biol Blood Marrow Transplant 2020;26(12):2372–2377
3 Barlogie B, Kyle RA, Anderson KC, et al. Standard chemotherapy compared with high-dose chemoradiotherapy for multiple myeloma: final results of phase III US Intergroup Trial S9321. J Clin Oncol 2006;24(06):929–936
4 Gertz MA, Buadi FK, Hayman SR, et al. Safety outcomes for autologous stem cell transplant in multiple myeloma. Mayo Clin Proc 2018;93(01):56–58
5 Dimopoulos MA, Moreau P, Terpos E, et al; EHA Guidelines Committee. Electronic address: guidelines@ehaweb.org; ESMO Guidelines Committee. Electronic address: clinicalguidelines@esmo.org. Multiple myeloma: EHA-ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†. Ann Oncol 2021;32(03):309–322
6 Dhakal B, Shah N, Kansagra A, et al. ASTCT Clinical Practice recommendations for transplant and cellular therapies in multiple myeloma. Transplant Cell Ther 2022;28(06):284–293
7 Jain T, Sonbol MB, Firwana B, et al. High-dose chemotherapy with early autologous stem cell transplantation compared to standard dose chemotherapy or delayed transplantation in patients with newly diagnosed multiple myeloma: a systematic review and meta-analysis. Biol Blood Marrow Transplant 2019;25(02): 239–247
8 Dhakal B, Szabo A, Chhabra S, et al. Autologous transplantation for newly diagnosed multiple myeloma in the era of novel agent induction: a systematic review and meta-analysis. JAMA Oncol 2018;4(03):343–350
9 Attal M, Lauwers-Cances V, Hulin C, et al; IFM 2009 Study. Lenalidomide, bortezomib, and dexamethasone with transplantation for myeloma. N Engl J Med 2017;376(14):1311–1320
10 Asrar MM, Lad DP, Bansal D, et al. Health-related quality of life in transplant eligible multiple myeloma patients with or without early ASCT in the real-world setting. Leuk Lymphoma 2021;62 (13):3271–3277
11 Yanamandra U, Saini N, Chauhan P, et al. AYA-myeloma: real-world, single-center experience over last 5 years. J Adolesc Young Adult Oncol 2018;7(01):120–124
12 Yanamandra U, Malhotra P. Stem cell transplantation in multiple myeloma: very much alive and kicking. Indian J Hematol Blood Transfus 2019;35(02):205–207
13 Nampoothiri RV, Kasudhan KS, Patil AN, et al. Impact of frailty, melphalan pharmacokinetics, and pharmacogenetics on outcomes post autologous hematopoietic cell transplantation for multiple myeloma. Bone Marrow Transplant 2019;54(12): 2088–2095
14 Koreth J, Cutler CS, Djulbegovic B, et al. High-dose therapy with single autologous transplantation versus chemotherapy for newly diagnosed multiple myeloma: a systematic review and meta-analysis of randomized controlled trials. Biol Blood Marrow Transplant 2007;13(02):183–196