



# 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.<sup>1</sup> 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).<sup>2</sup> 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%.<sup>1</sup> The same in the US centers is down from approximately 3 to less than 1%.<sup>3,4</sup> 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.<sup>5,6</sup> 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.<sup>7,8</sup> 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).<sup>9</sup> 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%).<sup>2</sup> The common reasons for these are financial limitations, patient perception, and cultural bias.<sup>10</sup> This is despite Indian patients with myeloma being younger and having a high-risk disease at onset.<sup>11</sup> The ASCT TRM in most Indian centers

is still high (2–7.2%).<sup>12</sup> Possible reasons for this include the frailty of Indian patients at the time of ASCT with increased toxicity from ASCT and center experience.<sup>13</sup> A systematic review and meta-analysis done in the era of such high TRM in the resource-rich settings<sup>14</sup> 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.<sup>1,14</sup> 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.<sup>10</sup>

## Conflicts of Interest

None declared.

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