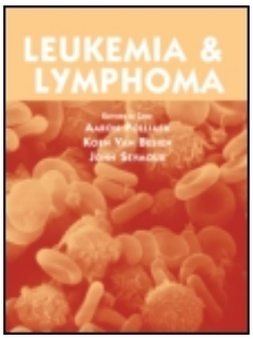

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COMMENTARY

Stem cell transplant: an effective salvage therapy for multiple myeloma

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In this issue of *Leukemia and Lymphoma*, Fenk and colleagues describe the use of a second stem cell transplant for salvage therapy of multiple myeloma in 55 patients. Treatment-related mortality with this technique was 5%. Event-free and overall survival, respectively, were 14 and 52 months. A response duration of more than 12 months after the first stem cell transplant predicted for a superior outcome following a second stem cell transplant, with event-free and overall survivals of 15 months and of 41 months in patients whose first response duration was 1–2 years, and an overall survival of 78 months when the response to the first transplant was greater than 2 years [1].

What makes this unique is that these patients' stem cells were not collected proximate to the second stem cell transplant but were collected and cryopreserved prior to the first stem cell transplant. The apheresis product was split and was maintained in cryopreservation until needed for salvage therapy. There are data that autografts can safely be stored for at least 5 years in 5% dimethylsulfoxide (DMSO) without impacting engraftment [2]. This concept of collecting stem cells for a subsequent 'rainy day' autologous harvest has been developed by consensus in Australia. A panel agreed that sufficient stem cells should be harvested after induction therapy to accommodate two autologous stem cell transplants. The second dose of stem cells could be used in tandem transplant but was considered acceptable to be given as a second transplant after salvage therapy [3]. The group from the Royal Marsden Hospital reported on the outcome of 83 patients who received a second course of high-dose therapy after relapse. Eligibility for the second stem cell transplant did not require a response to salvage chemotherapy. Two groups of patients with highly significant differences in survival could be identified. Patients with a relapse-free survival of < 18 months after the first stem cell transplant had a median survival of < 6 months. However, those with a relapse-free survival after the first stem cell transplant of > 18 months had a median survival approaching 3 years. This suggested that the use of previously collected stem cells for a second transplant can produce good therapeutic outcomes [4].

Treatment-related mortality with a second stem cell transplant is greater than following a first transplant. This may be a consequence of the poorer performance status and greater age when patients come to a second stem cell transplant. In a case series of 25 patients who had a second stem cell transplant at relapse, elevation of the serum creatinine following conditioning occurred in 36%, and treatment-related mortality was 8% [5]. At the University of Pennsylvania, 41 patients had received a salvage autologous stem cell transplant with an overall response rate of 55% and a treatment-related mortality of 7%. Median overall survival was 20 months, and time to progression after initial autologous stem cell transplant at greater or less than 12 months predicted outcome. At Mayo Clinic, we have performed 149 salvage stem cell transplants for patients using previously cryopreserved stem cells. In the Mayo cohort, the median survival from the date of the second stem cell transplant was 35.9 months (interquartile range 11.4–61.5 months). In a

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multivariable analysis, the duration of response to the first transplant was significant ($p < 0.0001$) in predicting survival following a second transplant.

There are a number of limitations of the study by Fenk *et al*. This was not an intent-to-treat analysis. We have no idea how many patients failed to mobilize sufficient stem cells for two transplants and therefore could not be considered for salvage transplant. This is an important selection bias. Their patients had a median age of only 51 years, which is one of the youngest stem cell cohorts reported. Obviously, patients eligible for a second stem cell transplant need to have preserved organ function, and again, this introduces selection bias.

With these limitations kept in mind, however, and with the increasing cost of novel agent-based regimens for relapsed multiple myeloma, considering a second stem cell transplant as a salvage regimen can be cost effective, with low morbidity, and capable of providing durable benefit. Second stem cell transplant using cryopreserved stem cells collected within 6 months of diagnosis is a viable alternative for managing this complex disease [1].

Potential conflict of interest: A disclosure form provided by the author is available with the full text of this article at www.informahealthcare.com/lal.

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