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Allogeneic Hematopoietic Cell Transplantation in the Outpatient Setting

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The article in *Biology of Blood and Marrow Transplantation* by Granot et al. [1] presents a single institution's look at allogeneic hematopoietic cell transplantation (HCT) in the outpatient setting using a nonmyeloablative (NMA) conditioning regimen. The use of fludarabine and low-dose total body irradiation was developed at the Fred Hutchinson Cancer Center to treat patients with hematologic malignancies who could not tolerate higher intensity regimens, either because of age or comorbidities. NMA conditioning regimens are associated with a lower toxicity profile, which could potentially enable a center to perform HCT in an outpatient setting. Subira et al. [2] evaluated a small population of patients undergoing reduced-intensity allogeneic HCT and demonstrated that the median time to conditioning-related toxicities was 16 days post-transplant and that an outpatient approach could have reduced the number of inpatient days from a median of 27 days to 9 days. Performing HCT in the outpatient setting provides several advantages to the patient, including maintaining independence, decreasing the risk of nosocomial infections, and reducing costs. Outpatient HCT also provides advantages to the transplant center, including decreased utilization of resources and financial benefit.

Granot et al. [1] reported their retrospective analysis of data from 1037 patients with advanced hematologic malignancies who underwent allogeneic HCT from related and unrelated donors with an NMA conditioning regimen in an outpatient setting from 1997 to 2017. Patients were managed in the outpatient setting by a group of 6 outpatient teams, consisting of 2 attending physicians, 6 advanced practice providers, 6 nurses, 2 dieticians, 2 clinical pharmacists, 2 schedulers, and a social worker. Facilities were open from 8 a.m. to 10 p.m. 365 days per year. A hospitalist was available after hours. The main reasons for hospitalization included acute graft-versus-host disease, neutropenic fever, infection, regimen-related toxicity, cardiovascular complications, and relapse. The objectives were to evaluate how many patients remained outpatients throughout the entire transplant course, how many experienced at least 1 hospitalization and why, and whether HCT outcome was affected by hospitalization.

Results were similar or favorable compared with those reported from other centers using reduced-intensity conditioning (RIC)/NMA conditioning regimens [3-6]. The 5-year nonrelapse mortality (NRM) was 17% for patients receiving transplants from related donors and 28% for those receiving cells from unrelated donors. Overall NRM was 27% (278 patients) for the entire cohort, and 342 patients died from relapse over the 20-year period. Most patients succumbing to NRM died from complications of graft-versus-host disease (42%).

Of the 1037 patients who underwent NMA HCT in the outpatient setting, 47% were never hospitalized. Twenty-one percent of related recipients and 35% of unrelated recipients has a single hospital admission, whereas 19% of unrelated recipients and 29% of unrelated recipients had more than 1 admission. Sixty-six percent of all admissions occurred within the first 20 days after HCT. Median duration of hospitals stay for both groups was 6 days. Five-year NRM was significantly higher among patients who had at least 1 hospital admission before day 100 compared with those who remained outpatient through day 100 (26% versus 13%, $P < .0001$).

Outpatient HCT is not a novel idea but until recently has predominantly been reserved for autologous stem cell transplant, particularly in myeloma patients [7,8]. Several centers have published their data regarding outpatient allogeneic HCT using RIC/NMA and myeloablative conditioning regimens and have demonstrated safety and feasibility [3,9,10]. The present data from Fred Hutchinson Cancer Center corroborates that. There are clear benefits to outpatient HCT in this setting.

Therefore the question remains, why aren't more centers performing RIC/NMA conditioning allogeneic HCT as outpatients? For most institutions, outpatient HCT is not feasible. Many institutions cannot develop the needed infrastructure required to carry out HCT in the outpatient setting. Fred Hutchinson Cancer Center has facilities that are open from 8 a.m. to 10 p.m. 365 days a year and has 6 outpatient teams, each staffed with several providers to help care for patients.

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Extending clinic hours and nighttime coverage are difficult obstacles for institutions already dealing with shortages of nurses and other personnel.

What about costs related to transplant in the outpatient setting? The outpatient approach to transplant should decrease hospital admission–related expenses. Guru Murthy et al. [9] demonstrated cost savings within the first 100 days of transplant when comparing outpatient RIC allogeneic HCT with their inpatient cohort (median total charges, $247,334 versus $339,621, respectively). Although overall expenses are decreased by outpatient transplant, specific cost savings for institutions and patients may be more difficult to demonstrate.

Over nearly 20 years, the Fred Hutchinson Cancer Center has demonstrated that NMA allogeneic HCTs can be safely performed in the outpatient setting. Perhaps demonstrating the cost benefit of outpatient HCT to go along with the noted clinical benefit would spur institutions to be more inclined to allocate resources, such as extended hours and increased staffing, to accommodate the need to perform transplants in the outpatient setting. Centers may be more inclined to create an improved outpatient system to handle the workload that inevitably comes with trying to keep our patients out of the hospital.

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