Fifteen Year Follow up of Relapsed/Refractory Patients with Hodgkin Lymphoma Treated with Autologous Hematopoietic Stem Cell Transplantation

Sabree Abedrabbo, MD; Harrah Chiang, DO; Jacob Bitran, MD; Tulio Rodriguez, MD; Leonard Klein, MD

1Hematology and Oncology, Advocate Lutheran General Hospital, Advocate Health Care, Park Ridge, IL; 2Internal Medicine, Advocate Lutheran General Hospital, Advocate Health Care, Park Ridge, IL; 3Hematology and Oncology, City of Hope, Chicago, IL; 4Oncology, Chicago, IL

Problem
Relapsed Hodgkin Lymphoma is treated with high-dose chemotherapy with autologous stem cell transplantation (ASCT). There are a number of studies previously that have reported 3-year and 5-year disease free (DFS) and overall survival (OS) in patients of this population. There, however, has been no reported studies over a 15-year follow up.

Objectives
There are 36 patients with relapsed/refractory Hodgkin Lymphoma that have been treated with ASCT and followed for 15-year DFS and OS. Comparisons were made between a preparative regimen of carmustine, etoposide, melphalan (CEM) vs. BCNU, etoposide, cytarabine, and melphalan (BEAM) and complications associated were documented.

Background
Classical Hodgkin lymphoma is a monoclonal lymphoid neoplasm classified by presence of Reed-Sternberg cells. Approximately 10% of all lymphoma cases are diagnosed in the United States and are associated with high cure rates of up to 80%. However, despite novel agents of first line therapy, many patient relapse and require additional treatment including conditioning regimens with ASCT. Cure rates in these with these methods are 60-70% in relapsed disease, and 30% in refractory disease.

Post-transplant maintenance therapy has shown to improve outcomes in the high-risk patient population. Phase 3 AETHERA trial demonstrates that consolidation after transplant with 1-year brentuximab vedotin improves progression free survival.

Recognizing and managing long-term complications of these therapies are also vital steps in improving outcomes in the patients.

Methods
Retrospective cohort studies were conducted on 36 patients at Advocate Lutheran General Hospital from 1992 to 2022.

Age and Gender
Median age of 41 years (range 21-70) with 19 males and 17 females with median Eastern Cooperative Oncology Group (ECOG) status of 1 (range 0-1).

Apheresis and CD34+ Collection
Apheresis commenced when the CD34 count as determined by flow cytometry was equal to or greater than 20 cells per microliter. Apheresis was performed at least a 6 L exchange initially on a COBE Spectra and since 2000 on a Spectra Optia. A minimum of 2x10^6 CD34+ cells/kg were collected and cryopreserved.

Conditioning Regimens
The preparative regimens used were carmustine (BCNU), etoposide, and melphalan (CEM) (5) and starting from 2006 to present BCNU, etoposide, cytarabine, and melphalan (BEAM) (6). Since 2018, brentuximab (Br) was added to BEAM as post-transplant consolidation therapy in 13 patients.

Supportive Care
Following the completion of the conditioning regimen and infusion of the CD34+ collection product, all patients received prophylactic antibiotics that started on day -1 that included vancomycin, oral ciprofloxacin or levofloxacin, and oral fluconazole. Filgrastim 5 micrograms/kg was started on day 0 until 2012 when the protocol was changed to be administered on day +5 and continued until hematologic recovery.

Results
From 1992 to 2023, 36 patients with relapsed Hodgkin’s lymphoma were treated with AH SCT. Of the 36 patients, fifteen (41.7%) of which were treated with CEM and 21 (58.3%) were treated with BEAM. In 2018, brentuximab was included in the BEAM regimen as a post-transplant consolidation therapy for 13 (36.1%) of the 21 patients (61.9%).

Of the 15 patients treated with CEM, 9 (60%) achieved a complete response
Of the 20 patients treated with BEAM, 16 (80%) achieved a CR.

The median time to hematologic recovery was 12 days (range 8-21 days).

The 15-year disease free survival (DFS) - 55%.

The 15-year overall survival (OS) 61%.

Treatment/Long term Complications
Staphylococcus epidermidis sepsis in three patients, two treated with CEM and one treated with BEAM. Three patients developed Escherichia coli sepsis, two treated with CEM and one treated with BEAM. One patient treated with CEM developed an esophageal perforation that led to death. Long-term complications of high dose therapy included cardiomyopathy (6 patients), ischemic heart disease, liposarcoma, breast cancer stage III, and peripheral neuropathy that occurred in one patient each.

Conclusions
The results reported herein are similar to outcomes previously reported with the exception being that we are reporting 15 year DFS and OS as opposed to 10 year survival. Our outcome of a 15 year DFS of 54% is encouraging. Of the long term complications that our cohort of patients experienced included heart disease, cardiomyopathy, breast cancer, and liposarcoma. Whether these long-term effects are a consequence of high dose chemotherapy are not entirely clear. Interestingly, we have not observed secondary treatment related leukemia or myelodysplasia. Overall this data is encouraging and with the incorporation of novel agents can be improved upon.

References