LACE: An effective conditioning regimen for autologous stem cell transplantation for relapsed or refractory Hodgkin lymphoma

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Background: High dose chemotherapy followed by autologous stem cell transplantation (ASCT) is the preferred treatment for patients with relapsed and primary refractory Hodgkin lymphoma (HL). BEAM (BCNU, etoposide, cytarabine and melphalan) is the most widely used conditioning regimen for ASCT in HL. LACE (Lomustine, cytarabine, etoposide and cyclophosphamide) has been found to be an effective regimen though outcome data is sparse. This study is a single centre retrospective analysis to evaluate outcomes of LACE based conditioning in HL transplants.

Methods: Patients with HL who underwent autologous stem cell transplant with LACE as the conditioning regimen between November 2007 and September 2020 were included in the study. The regimen included lomustine-200 mg/m^2 on d-7, etoposide 1000mg/m^2 on d-7, ara-c 2000 mg/m^2 on d-6, d-5 and cyclophosphamide 1800 mg/m^2 on d-4 to d-2. Regimen related toxicities were graded according to CTCAE Version 4. Response assessment was done using PET-CT at Day 100 and yearly thereafter for next 4 years. Progression free survival (PFS) was defined as time from transplant to progression or death. Overall survival (OS) was defined as time from transplant to death. Data for patients without progression or death was censored at last available follow up. Kaplan–Meier method was used to estimate 5 year PFS and OS.

Results: A total of 96 patients (64 male and 32 female) with HL underwent ASCT with LACE based conditioning. Median age was 21 years (5-54 years). The baseline patient and disease related characteristics are summarised in Table 1. The median number of lines of chemotherapy prior to transplant was 2 (2-4). GDP (66 patients) was the most commonly used salvage chemotherapy. At the time of transplant, 66% were in CR, 29% in partial remission (PR) and 5% had stable or refractory disease. The incidence of grade 3-4 oral mucositis was 10% with a median duration of 5 days. The incidence of grade 3-4 diarrhoea was 11% with median duration of 5 days. 21% patients required TPN and median duration of TPN use was 9 days. Median time to myeloid and platelet engraftment were 10 days and 13

days respectively. At a median follow-up of 71 months (0-147 months), median PFS and OS were not reached. The probability of OS and PFS at 5 years was 68.8% and 59.6% respectively. There were 30 deaths (31.2%) with a transplant related mortality of 5.2%.

Conclusion: This is the largest reported cohort of Hodgkin lymphoma patients transplanted with LACE regimen. LACE is an effective and well tolerated conditioning regimen.

Table 1: Baseline characteristics.

Characteristic	N=96
Age at transplant, years	
Median (range)	21 (05-54)
Gender (%)	
Male	64 (66.7)
Female	32 (33.3)
Histological subtype (%)	
MC	39 (40.6)
NS	34 (35.4)
LR	2 (2.1)
NLPHL	10 (10.4)
Stage at Diagnosis (%)	
Stage I	3 (3.1)
Stage II	23 (24)
Stage III	21 (21.9)
Stage IV	39 (40.6)
Additional radiotherapy after initial chemotherapy	
Yes	53 (55.2)
No	43 (44.8)
Response to initial treatment (%)	
CR	63(65.6)
PR	16 (16.6)
SD	2 (2)
PD	15 (15.6)
Salvage Chemotherapy (%)	
GDP	66 (68.7)
MINE	27 (28.1)
DHAP	06 (6.2)
ICE	04 (4.1)
IGVD/DECA	07 (7.3)
Pre transplant disease status (%)	
CR	63 (65.6)
PR	28 (29.2)
SD	1 (1.0)
PD	4 (4.2)
Number of treatment lines before ASCT (%)	
1	3(3.1)
2	62 (64.6)
3	27 (28.1)
4	4 (4)

Abbreviations: MC, mixed cellularity; NC, nodular sclerosis; LR, Lymphocyte rich; NLPHL, nodular lymphocyte predominant Hodgkin Lymphoma; CR, Complete response; PR, Partial response; SD, Stable disease; PD, Progressive disease