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POSTER ABSTRACTS

731.AUTOLOGOUS TRANSPLANTATION: CLINICAL AND EPIDEMIOLOGICAL

Total Body Irradiation Versus Chemotherapy-Only Conditioning in Autologous Hematopoietic Stem Cell Transplantation for Large B-Cell Lymphoma

Maryam Ebadi, MD[1], Xinyi Fan[2], Gary Schoch[2], Ted Gooley, PhD[2], Armin Rashidi, MDPhD[3], Stephen D Smith, MD[4], Mazyar Shadman, MD MPH[3], Leona Holmberg, MDPhD[4], Chaitra S Ujjani, MD[4], Christina Poh, MD[4], Vikram Raghunathan, MD[4], Naveed Ali, MBBS[5], Phuong T Vo, MD[4], Shivaprasad Manjappa, MDMBBS,MPH[4], Manoj Menon, MD[4], Ryan C Lynch, MD[4], Carrie I Ho, MD[4], Brian G Till[3], Ralph Ermoian, MD[1], Ajay K Gopal, MD[4], Yolanda D Tseng, MD[1]

[1] Department of Radiation Oncology, University of Washington and Fred Hutch Cancer Center, Seattle, WA
[2] Clinical Research Division, Fred Hutch Cancer Center, Seattle, WA
[3] Fred Hutchinson Cancer Center, Seattle, WA
[4] Clinical Research Division, Fred Hutch Cancer Center; and Division of Oncology, University of Washington, Seattle, WA
[5] Clinical Research Division, Fred Hutchinson Cancer Center, Seattle, WA

Introduction

Recent data suggest that compared with high-dose chemotherapy conditioning and autologous stem cell transplant (ASCT), CD19-chimeric antigen receptor (CAR) T-cell therapy as second-line therapy improves outcomes in patients with primary refractory or early relapsed large B-cell lymphoma (LBCL). However, more than half of patients will not attain a long-term remission with CAR T-cell therapy, and may subsequently be considered for ASCT, indicating an unmet need for alternative therapies including strategies to improve ASCT outcomes. Given that LBCL is radioresponsive, we evaluated whether total body irradiation (TBI)-based conditioning may improve outcomes compared to chemotherapy-only conditioning among LBCL patients who underwent peripheral blood ASCT at our institution.

Methods

We reviewed the records of adults with relapsed/refractory LBCL who underwent ASCT at Fred Hutch Cancer Center between 2012-2021. LBCL was categorized as de novo DLBCL, transformed DLBCL, and double-hit lymphoma (DHL). Patients with primary CNS lymphoma were excluded. Given that TBI is generally reserved for younger patients ($\leq$ 60 years), we excluded patients in the chemo-only group older than the oldest patient in the TBI group (58.7 years) to reduce the bias due to age differences. The hazards for failure for progression-free survival (PFS) and for overall mortality (OM) were compared between TBI-based and chemo-only groups using Cox regression with adjustment for clinically important variables including age, sex, histology, LDH at ASCT, conditioning type, PET positivity at the time of ASCT and year of ASCT. LDH at ASCT, age and year of ASCT were modeled as continuous linear variables.

Results

Among 225 patients, we excluded 121 patients in the chemo-only group who were older than 58.7 years, leaving 104 patients for the analysis (**Table 1**). A total of 48 (46%) patients received TBI-based and 56 (54%) received chemo-only conditioning. All patients in the TBI group received 12 Gy in 6-8 fractions. Most patients (n=46, 82.14%) in the chemo-only group received BEAM conditioning. Patients receiving TBI-based conditioning had more adverse features including male sex (72.9% vs 58.9%), DHL histology (31.3% vs 7.1%), and PET-positive disease at the time of ASCT (39.6% vs 23.2%). With a median follow-up of 51.2 months (range 1.3-134.2) among survivors, point estimates of PFS at 2 and 5 years were 74.3% and 66.3%, respectively among TBI patients and 68.5% and 64.0%, respectively among the chemo-only patients (**Figure 1**). Time to engraftment was similar between the groups. On multivariable analysis, compared to chemo-only conditioning, TBI was not associated with improved PFS (TBI vs chemo-only: HR 1.02, 95%CI 0.45-2.31, P=0.96) or OS (HR 0.85, 95%CI 0.37-1.98, P=0.7). Predictors of worse PFS were PET positivity at the time of ASCT (HR 3.39, 95%CI 1.61-7.17, P $<$ 0.01) and higher LDH (HR 1.0011, 95%CI 1.0002-1.0020, P=0.02). Similarly, both PET positivity (HR 3.12, 95%CI 1.47-6.63, P$<$0.01) and higher LDH (HR 1.0013, 95%CI 1.0003-1.0022, P $<$0.01) were associated with worse OS. Age, sex, histology and year of ASCT were not significant.

Conclusions

Despite worse prognostic factors, TBI-based conditioning yielded similar outcomes compared to chemo-only conditioning for patients with relapsed/refractory LBCL undergoing ASCT. These results confirm prior findings from a registry-based study. Although a proportion of patients may achieve a long-term remission with ASCT, other strategies are needed to improve ASCT outcomes.

Disclosures Rashidi: *Seres Therapeutics, Ltd.:* Consultancy. **Smith:** *BeiGene:* Membership on an entity's Board of Directors or advisory committees; *ADC Therapeutics, AstraZeneca, Ayala (spouse), Bayer, BeiGene, Bristol Myers Squibb (spouse), De Novo Biopharma, Enterome, Genentech, Inc., Ignyta (spouse), Incyte Corporation, Kymera Therapeutics, Merck Sharp and Dohme Corp., MorphoSys, Nanjing Pharmaceu:* Research Funding; *ADC Therapeutics, AstraZeneca, BeiGene, Epizyme, Karyopharm, KITE pharma, Incyte, Numab Therapeutics AG, Abbvie, Coherus Biosciences, advisory board (spouse) Genentech, Inc.:* Consultancy. **Shadman:** *MorphoSys/Incyte:* Consultancy, Research Funding; *BeiGene:* Consultancy, Research Funding; *Bristol Myers Squibb:* Consultancy, Research Funding; *Vincerx:* Research Funding; *Genentech:* Consultancy, Research Funding; *ADC therapeutics:* Consultancy; *Fate Therapeutics:* Consultancy; *Regeneron:* Consultancy; *TG Therapeutics:* Research Funding; *Mustang Bio:* Consultancy, Research Funding; *AstraZeneca:* Consultancy, Research Funding; *Pharmacyclics:* Consultancy, Research Funding; *AbbVie:* Consultancy, Research Funding; *Genmab:* Consultancy, Research Funding; *Kite, a Gilead Company:* Consultancy; *Eli Lilly:* Consultancy; *Janssen:* Consultancy; *MEI Pharma:* Consultancy. **Ujjani:** *Genentech:* Consultancy, Honoraria; *Atara:* Consultancy; *Beigene:* Consultancy, Honoraria; *Abbvie:* Consultancy, Honoraria, Research Funding; *Pharmacyclics:* Consultancy, Honoraria, Research Funding; *Janssen:* Consultancy, Honoraria; *Lilly:* Consultancy, Honoraria, Research Funding; *Epizyme:* Consultancy; *Astrazeneca:* Consultancy, Honoraria, Research Funding; *Kite, a Gilead Company:* Consultancy, Other: Travel expenses , Research Funding; *PCYC:* Research Funding. **Poh:** *Seattle Genetics:* Consultancy; *BeiGene:* Consultancy; *Acrotech:* Consultancy; *Incyte:* Research Funding. **Lynch:** *TG Therapeutics:* Research Funding; *Bayer:* Research Funding; *Incyte:* Research Funding; *Cyteir:* Research Funding; *Genentech:* Research Funding; *Rapt:* Research Funding; *Seagen Inc.:* Research Funding; *Cancer Study Group:* Consultancy; *SeaGen:* Consultancy; *Foresight Diagnostics:* Consultancy; *Abbvie:* Consultancy; *Merck:* Research Funding. **Till:** *Mustang Bio:* Consultancy, Patents & Royalties, Research Funding; *BMS/Juno Therapeutics:* Research Funding; *Proteios Technology:* Consultancy, Current holder of *stock options* in a privately-held company. **Gopal:** *Compliment Corporation:* Current holder of *stock options* in a privately-held company; *Merck, I-Mab bio, IgM Bio, Takeda, Gilead, Astra-Zeneca, Agios, Janssen, BMS, SeaGen, Teva, Genmab:* Research Funding; *Incyte, Kite, Morphosys/Incyte, ADCT, Acrotech, Merck, Karyopharm, Servier, Beigene, Cellectar, Janssen, SeaGen, Epizyme, I-Mab bio, Gilead, Genentech, Lilly, Caribou, Fresenius-Kabi:* Consultancy.

Table 1. Patient characteristics

	All patients (n = 104)	TBI-based (n = 48)	Chemo only (n = 56)
Transplant age			
Median (range)	51.2 (20.2-58.7)	51 (20.2-58.7)	51.9 (24.3-58.5)
Sex			
Female	36 (34.6%)	13 (27.1%)	23 (41.1%)
Male	68 (65.4%)	35 (72.9%)	33 (58.9%)
Histology			
DLBCL	65 (62.5%)	21 (43.8%)	44 (78.6%)
Transformed DLBCL	20 (19.2%)	12 (25%)	8 (14.3%)
Double hit lymphoma	19 (18.3%)	15 (31.3%)	4 (7.1%)
LDH prior to ASCT			
Median (range)	156 (88-2380)	156 (91-2380)	155 (88-1510)
PET score prior to ASCT			
Positive (Deauville 4-5)	32 (30.8%)	19 (39.6%)	13 (23.2%)
Negative (Deauville 1-3)	67 (64.4%)	25 (52.1%)	42 (75%)
NA	5 (4.8%)	4 (8.3%)	1 (1.8%)
Days to engraftment, median(range)			
ANC>500	13 (9-24)	13 (10-24)	13 (9-21)
Platelets>20,000	12 (9-34)	12 (9-34)	12 (9-26)
Platelets>50,000	14 (10-57)	14 (10-28)	14 (10-57)

Figure 1. KM curves for progression free survival among younger patients

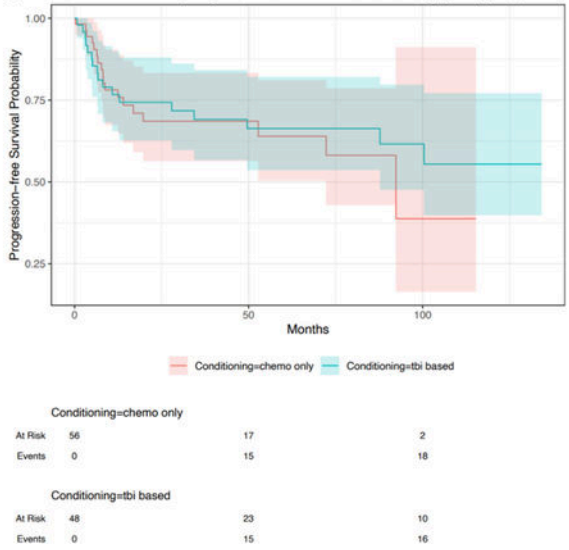

Figure 1

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