



## The 65th ASH Annual Meeting Abstracts

## POSTER ABSTRACTS

## 731.AUTOLOGOUS TRANSPLANTATION: CLINICAL AND EPIDEMIOLOGICAL

**Improving the Utilization and Tolerability of Thiotepa-Based Autologous Stem Cell Transplantation in Primary CNS Lymphoma**

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**Background:** Thiotepa-based autologous stem cell transplantation (ASCT) improves survival in primary central nervous system lymphoma (PCNSL) but up to 30-60% of patients are unable to receive ASCT after MATRix induction, frequently due to treatment-related adverse events. Common conditioning regimens such as thiotepa/BCNU or thiotepa/busulfan/cyclophosphamide have also been associated with risks of pulmonary toxicity or increased transplant-related mortality. Novel strategies to improve the utilization and tolerability of ASCT are therefore needed to maximize the curative potential of this therapy in PCNSL.

**Methods:** This retrospective population-based study included all patients diagnosed with large B-cell lymphoma-type PCNSL who were intended for ASCT in the province of Alberta, Canada between 2011 and 2022. Provincial treatment guidelines recommended an abbreviated, low-intensity induction protocol to reduce toxicity and increase transplantation rates (Figure 1B). Step 1 included 2 cycles of rituximab/high-dose methotrexate (HD-MTX). Step 2 involved 1 cycle of rituximab/high-dose cytarabine (HDAC) for peripheral blood stem cell mobilization. Step 3 consisted of 2 cycles of rituximab/HD-MTX/HDAC and was made optional in July 2018 so that patients with sufficient disease response and performance status following Step 2 could proceed immediately to ASCT. Conditioning consisted of thiotepa 300 mg/m<sup>2</sup> × 2 days and busulfan 3.2mg/kg × 3 days (TT/Bu). Dose reductions of TT/Bu by 10% for every 5 years over the age of 60 were recommended as of May 2021. Progression-free survival (PFS) and overall survival (OS) were determined using the Kaplan-Meier method and compared between groups using the log-rank test.

**Results:** The intention-to-transplant (ITT) cohort included 71 patients with median age 58 years (range 26-72), representing 81% of patients aged 18-60 and 55% of those aged 61-72 who were diagnosed with PCNSL in Alberta during the study period. The proportion of patients aged 61-72 who were treated with ITT increased from 42% before 2018 to 70% afterwards.

Fifty-six (79%) ITT patients proceeded to ASCT while 15 (21%) did not due to poor performance status (n=6), treatment-related adverse events (n=5), or disease progression (n=4). There was 1 (1%) death due to infection-related non-relapse mortality (NRM) during induction. The routine omission of Step 3 starting in 2018 resulted in high transplantation rates at 29/35 (83%) compared to 27/36 (75%) in the preceding era.

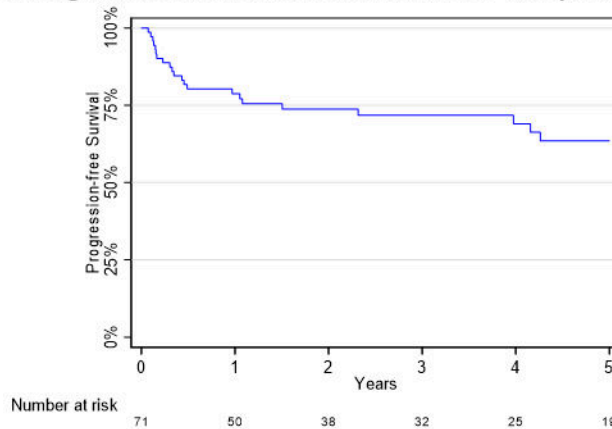
With median follow-up time 3.9 years, the 4-year PFS was 69% (95% CI 56-79%) and OS was 80% (95% CI 67-88%) in the ITT cohort (Figure 1A). For the 56 patients who received ASCT, 4-year PFS was 75% (95% CI 57-86%) and OS was 85% (95% CI 68-93%) from the time of ASCT. There was no significant difference in PFS between patients in complete response (CR)/unconfirmed CR versus partial response (PR) before ASCT (p=0.86); however, 5 patients with progressive disease before ASCT had inferior PFS compared to those with CR/CRu/PR (4-year PFS 40% vs 82%, p=0.0002). Relapse occurred in 8 (14%) patients at median 373 days (range 54-1411) after ASCT, including 7 with CNS relapse and 1 with systemic relapse. No patient in remission after ASCT received whole brain radiation therapy and most recovered without clinically significant neurologic deficits. There were no deaths due to transplant-related mortality. NRM occurred in 2 (4%) patients due to an unrelated cancer and stroke 1.1 and 4.3 years after ASCT, respectively.

Among 27 patients >60 years old treated with ITT, 17 (63%) proceeded to ASCT, including 6 who received dose reductions of TT/Bu. The transplantation rate in this age group increased from 45% to 75% following the routine omission of Step 3. All 17 transplanted patients remain alive and in remission with median follow-up 2.5 years.

**Conclusion:** In this real-world study of 71 patients with PCNSL, an abbreviated, low-intensity induction protocol resulted in high transplantation rates (~80%) and favorable long-term outcomes with 4-year OS 80%. Notably, TT/Bu conditioning achieved a low incidence of relapse with no transplant-related mortality observed, including among patients >60 years old. These data demonstrate that de-escalated induction therapy can result in improved rates of successful ASCT, thereby optimizing the outcomes of PCNSL.

**Disclosures Puckrin:** Kite: Honoraria; Beigene: Honoraria; Incyte: Honoraria. **Owen:** F. Hoffmann-La Roche Ltd, AbbVie, AstraZeneca, Beigene, Merck, Incyte, Seattle Genetics, Novartis: Honoraria. **Street:** Seattle Genetics: Honoraria; Recordati: Honoraria; Kyowa Kirin: Honoraria. **Perry:** Beigene: Honoraria; Novartis: Honoraria; Seattle Genetics: Honoraria; Sobi: Honoraria; Incyte: Honoraria. **Shafey:** AstraZeneca: Honoraria; Roche: Honoraria. **Stewart:** Amgen: Honoraria; Celgene: Honoraria; Gilead: Honoraria; Sandoz: Honoraria; Janssen: Honoraria; Novartis: Honoraria; Abbvie: Honoraria; AstraZeneca: Honoraria; Roche: Honoraria; Teva: Honoraria.

**Figure 1A: Progression-free survival of the intention-to-transplant PCNSL cohort**



**Figure 1B: Alberta PCNSL transplant-eligible treatment protocol**

Week	Step 1				*Step 2			**Step 3		Step 4	
	1	2	3	4	5	6	7	8	9	10	12-14
Rituximab 375mg/m <sup>2</sup> IV d0, then 1400mg sc d4 & 14 high-dose methotrexate 3.5 g/m <sup>2</sup> d1&15 procarbazine 100 mg/m <sup>2</sup> d1-7	x		x								
rituximab 1400mg sc d1 cytarabine 3 g/m <sup>2</sup> x d1&2 G-CSF 5-10 µg/kg d8-13 Apheresis ~d14 or 15					x						
Rituximab 1400mg sc d0 high-dose methotrexate 3.5 g/m <sup>2</sup> d1 cytarabine 2 g/m <sup>2</sup> twice daily days 2-3 all q21d for 2 cycles					x						
thiotepa 300 mg/m <sup>2</sup> IV days -6,-5 busulfan 3.2 mg/kg IV days -4 to -2, ASCT day 0									x		x

\* Step 2 may begin either week 4 or 5 depending upon patient status and apheresis scheduling  
 \*\*Step 3 may be omitted in patients who have achieved some response and are physically fit to proceed directly to ASCT on week 9.

**Figure 1**

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