Transplantation (EBMT), including adult patients diagnosed with PCNSL who underwent allo-HSCT between 2016 and 2022. **Results:** A total of 31 patients were included, with a median age of 50 years (range: 22–68) at the time of allo-HSCT. The median follow-up period was 1.5 years (95% CI: 0.9–5.8). Males comprised 58% of the cohort, and 61% of patients had a Karnofsky performance status ≥ 90%. The median time from diagnosis to allo-HSCT was 22 months (range: 4–196). Most patients were heavily pretreated, with 54% having received ≥ 3 prior lines of therapy, 12% having received two, and 35% having received one. Prior to allo-HSCT, 57% of patients were in CR, 23% in partial remission (PR), and 20% had active R/R disease. The most frequently used conditioning regimen was a combination of Busulfan, Fludarabine, and Thiotepa (42%). Post-transplant cyclophosphamide was administered in 40% of patients. Total body irradiation (TBI) based conditioning was used in 23% of cases. Donors were predominantly related (48% matched, 26% haploidentical), while 26% were unrelated. The overall survival (OS) rates at 1 and 2 years were 34.9%. Progression-free survival (PFS) at 1 and 2 years was 30.8%. The relapse incidence (RI) was 39.6% in the first year and did not increase in the second year. Non-relapse mortality was 29.7% at 1 and 2 years. Chronic graft-versus-host disease was observed in 24.9% of patients at both 1 and 2 years. The GvHD-free, relapse-free survival (GRFS) rates were 19.9% at 1 and 2 years.
Conclusion: In this large registry-based cohort of patients with PCNSL undergoing allo-HSCT, our findings indicate that allo-HSCT is an effective treatment in a subset of patients. The stable RI beyond one year may suggest a potential for long-term disease control in approximately one third of transplanted patients.

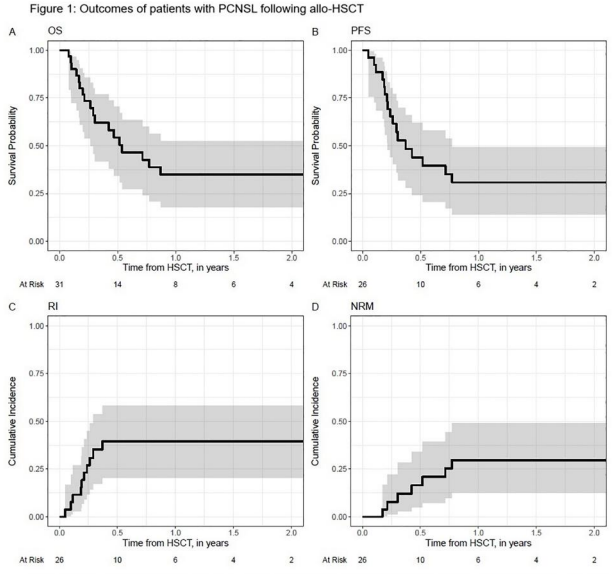

Figure 1 shows the Kaplan-Meier curves for Overall survival (OS) and Progression Free Survival (PFS) and cumulative incidence curves for Relapse (RI) and Non-relapse Mortality (NRM)

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Keywords: cellular therapies; aggressive B-cell non-Hodgkin lymphoma; extranodal non-Hodgkin lymphoma

No potential sources of conflict of interest.

338 | THREE-HOUR INFUSION OF METHOTREXATE AT 3 g/m^2 SIGNIFICANTLY REDUCES CNS RELAPSES AND IMPROVES SURVIVAL IN PATIENTS WITH LARGE B-CELL LYMPHOMAS AND INCREASED CNS RISK

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Background: A few recent studies questioned the effectiveness of high-dose methotrexate (MTX) in preventing CNS relapse in large B-cell lymphomas (LBCL); however, they suffer from biases, such as unbalanced distribution of patients (pts) with high-risk extranodal disease and lack of complete information on MTX dosing schedules and CNS events. We reviewed a large, single-centre cohort of LBCL pts treated with uniform CNS-directed MTX dosing schedule, aiming to demonstrate its favourable effect on CNS recurrence and survival in pts with high CNS risk, as defined by recent consensus criteria (Eyre T, et al., *Lancet Oncol* 2022).
Methods: We reviewed 501 LBCL pts treated from 2002 to 2021, focusing on those who achieved complete metabolic remission (CMR) after upfront RCHOP or similar. Pts at high CNS risk, as defined by our institution's criteria, received 2 (stage I-II) or 3 (advanced stage) doses of MTX (3 g/m^2 over 3 hours, preceded by a fast bolus) after RCHOP. Histological specimens were reviewed, diagnoses updated according to the latest WHO/ICC classifications, and CNS risk reassessed using recent consensus criteria (CNS-IPI ≥ 4, ≥ 3 extranodal sites, or involvement of the testis, kidney, adrenal gland, or breast). MTX's effect on CNS recurrence was assessed using Gray's test, treating other events (systemic recurrence, unrelated death) as competing risks. MTX's impact on PFS and OS was also assessed.
Results: 344 pts in CMR after RCHOP or similar were considered. CNS risk according to recent criteria was low in 231 (66%) pts and high in 113 (33%); MTX was given to 17 (7%) and 49 (43%) pts, respectively. After a median follow-up of 75 months (IQR 54–102), CNS relapse occurred in 13 (4%) pts, always as isolated site: brain (10), meninges (2), and cranial nerves (1). Among low-risk pts, CNS relapse rate was 2% (4/214) without MTX and 0% (0/17) with MTX. In high-risk pts, this rate was 14% (9/64) without MTX and 0% (0/49) with MTX, yielding a 4-year cumulative CNS relapse rate of 18% and 0%, respectively (p = 0.003). The most notable MTX benefit was seen in 62 pts with involvement of testes, kidneys, or adrenal gland, where CNS relapse rate dropped from 23% (7/31) to 0% (0/31) (p = 0.01), and in 66 pts with ≥ 3 extranodal sites, where rate dropped from 13% (5/38) to 0% (0/28) (p = 0.06). MTX also was associated with improved PFS and OS in the 113 high-risk pts (independent in multivariable analysis). In these pts, also event distribution suggested MTX's role in prophylaxis: 8 (12%) unrelated deaths, 13 (20%) systemic relapses, and 9 (14%) CNS relapses occurred in the 64 pts treated without MTX, whereas 4 (8%) unrelated deaths, and 9 (18%) systemic relapses, with no CNS relapses, occurred in the 49 treated with MTX.

Conclusion: MTX (3 g/m^2 over 3 hs) significantly reduces CNS relapses and improves PFS and OS in LBCL pts with CNS-IPI ≥ 4, ≥ 3 extranodal sites, or involvement of testis, kidney, adrenal gland, or breast who achieve CMR after RCHOP or similar.

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Encore Abstract: EHA 2025

Keywords: aggressive B-cell non-Hodgkin lymphoma; chemotherapy; extranodal non-Hodgkin lymphoma

No potential sources of conflict of interest.

339 | OUTCOMES IN AN INTERNATIONAL MULTICENTRE STUDY OF 600 PATIENTS WITH CNS RELAPSE OF LARGE B CELL LYMPHOMA: COMPARTMENT OF RELAPSE IS PROGNOSTIC

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Background: Secondary central nervous system lymphoma (SCNSL) is a rare disease defined by involvement of the CNS concurrent to or following a diagnosis of systemic large B-cell lymphoma (LBCL). This international multicentre cohort study aimed to determine survival outcomes in patients (pts) with isolated CNS relapse (RI-SCNSL) and synchronous systemic/CNS relapse (RS-SCNSL).

Methods: Pts ≥ 18 years treated 2001–2023 at 35 US, UK and Canadian centres were included. CNS involvement was categorised as: brain parenchyma, spine, leptomeninges, vitreoretinal, or > 1 compartment. The primary outcomes were time-to-CNS event from LBCL diagnosis, and progression-free and overall survival (PFS and OS) from time of CNS involvement.

Results: Six hundred pts were included: 393 RI-SCNSL and 207 RS-SCNSL. Prior systemic LBCL treatment was RCHOP (450; 75%) or REPOCH (82; 14%) in the majority; median age at LBCL diagnosis was 62 (range 53–69); and CNS IPI was 4–6 in 139 (23%). Intrathecal and systemic methotrexate prophylaxis was delivered in 40 (10%) and 44 (11%) RI-SCNSL, and 29 (14%) and 33 (16%) RS-SCNSL respectively. Of RI-SCNSL, involvement of parenchyma (n = 257; 65%), leptomeninges (62; 16%), spine (14; 3.5%), vitreoretinal (11; 2.8%) and > 1 compartment (49; 2.5%) were observed. Of RS-SCNSL, these represented 77 (37%), 77 (37%), 15 (7.2%), 2 (1.0%) and 36 (17%), respectively.

Median time-to-CNS event was 10.3 months (range 6.6–25.6) for RI-SCNSL and 8 months (5.5–16.5) for RS-SCNSL (p = 0.0001). Median PFS and OS were superior for RI-SCNSL (14.7 and 22.6 months) compared to RS-SCNSL (6.8 and 8.2 months, p < 0.0001). Median time-to-CNS event was longer in both RI-SCNSL (p < 0.0001) and RS-SCNSL (p = 0.019) for parenchymal (13.1 and 10.9 months for RI and RS-SCNSL) and vitreoretinal disease (10.8 and 27.1 months for RI and RS-SCNSL) than leptomeningeal disease (6.9 months in both groups). In RI-SCNSL, CNS compartment was prognostic of PFS (p = 0.023), longest for vitreoretinal (median 117.4 months) and shortest for leptomeningeal disease (median 7.6 months). Outcomes were poor irrespective of CNS compartment in RS-SCNSL.

Comparing 139 patients with leptomeningeal to 257 with parenchymal involvement, leptomeningeal disease was enriched for *MYC/BCL2* double-hit status (20% versus 6.3% of parenchymal, p = 0.0002), ≥ 3 extranodal sites at LBCL diagnosis (17% versus 9.3%, p = 0.013), and bone marrow involvement (37% versus 17%, p < 0.0001). Conversely, isolated parenchymal involvement was enriched for a history of testicular LBCL (12% versus 3.6%, p = 0.017).