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POSTER ABSTRACTS

627.AGGRESSIVE LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

Real-World Experience with RTOG 0227 Induction for First Line Therapy of Primary CNS Lymphoma (PCNSL)

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Introduction

PCNSL is an aggressive and rare subtype of extranodal non-Hodgkin Lymphoma affecting the brain, spinal cord, cerebrospinal fluid (CSF), leptomeninges and/or vitreoretinal components. While there have been trials comparing outcomes of consolidation treatment with whole brain radiation therapy (WBRT) versus (vs) autologous hematopoietic cell transplantation (auto-HCT) following different induction regimens in PCNSL, the optimal induction regimen to pair with these forms of consolidation remains controversial. Our group adopted a modified version of the RTOG 0227 induction as our standard PCNSL induction in 2017. This regimen includes 5 cycles of Methotrexate (MTX) at 3.5 g/m ^{2} and Rituximab (R) at 375-500 mg/m ^{2}, and Temozolomide (TMZ) on cycles 2 and 4. Based on the published phase 2 trial of 53 patients (pts), the regimen is significantly less toxic than more aggressive induction regimens such as MATRiX, especially in older pts or those with comorbidities. We evaluated our real-world outcomes in PCNSL pts treated with RTOG 0227 induction followed by consolidation with either WBRT/TMZ or auto-HCT, at a single academic university hospital.

Methods

We identified newly diagnosed PCNSL pts treated at a single academic university hospital between 2017 and 2023. Electronic medical records were retrospectively reviewed to collect data including demographics, clinicopathological features, treatment details, response rates, long-term follow up, disease recurrence, and survival. The IELSG prognostic index tool was used for risk assessment. All pts received induction regimen consisting of R (dose between 375- 500 mg/m ^{2}) and 3.5 g/m ^{2} of MTX with leucovorin on weeks 1, 3, 5, 7 and 9 along with TMZ daily for 5 days on weeks 4 and 8, followed by consolidation with either WBRT/TMZ or auto-HCT. In WBRT cohort, maintenance TMZ was given at 200mg/m ^{2} daily for 5 days every 28 days, for total of 10 cycles, and dose was reduced if side effects developed. Objective response rate (ORR) and complete response rate (CRR) after induction chemotherapy were calculated. Overall survival (OS) and progression free survival (PFS) at 2 years were estimated with the Kaplan-Meir method (using GraphPad Prism 9.3.1) and compared between the WBRT and auto-HCT cohorts, using the log-rank test.

Results

A total of 29 PCNSL pts were included in the study. Patient and disease characteristics for the entire cohort, as well as pts treated with WBRT vs auto-HCT consolidation, are shown on the Table. On average (avg), pts received 4 cycles of MTX and 8 cycles of TMZ. Nine (31%) pts developed acute kidney injury and 1 (3.4%) developed transaminitis from MTX. The avg total cumulative TMZ dose was 5913 mg/m ^{2} and 8 (27.5%) pts required TMZ dose reduction. Treatment related mortality (TRM) following induction was 0%. Eight (27.5%) pts had complete response, 19 (65.5%) had partial response, 1 (3.5%) had stable disease and 1 (3.5%) had disease progression. ORR was 93.1% and CRR was 27.5%. Eighteen (62%) pts received WBRT/TMZ consolidation, while 11 (38%) received auto-HCT consolidation. Median dose of WBRT administered was 36 Gy (23.4 to 36 Gy). Thirteen (72.2%) pts received 36 Gy in 30 fractions (fx) of 1.2 Gy BID, 4 (22.2%) pts received 23.4 Gy in 13 fx of 1.8 Gy OD, and 1 (5.5%) pt received 30.6 Gy in 17 fx of 1.8 Gy OD. Most common conditioning regimen prior to auto-HCT was carmustine/thiotepa (BCNU/TT). With a median follow up of 36 months, 4 (22.2%) pts in WBRT cohort and 1 (9.1%) in auto-

HCT cohort had disease recurrence. Two-year PFS was 83% overall, 81% for the WBRT pts and 87% for the auto-HCT pts, with a p value of 0.65 for log-rank comparison of PFS for the WBRT vs auto-HCT pts. Two-year OS was 96% for the entire cohort, 94% for the WBRT pts and 100% for the auto-HCT pts, with a p value of 0.27 for log-rank comparison of OS for the WBRT vs auto-HCT pts.

Conclusion

In this real-world cohort of PCNSL pts not treated as part of a clinical trial, we observed excellent outcomes using the modified RTOG 0227 induction regimen. PFS and OS at 2 yrs in our cohort exceeds those reported with any prospective clinical trial to date, and with zero TRM to date. This data indicates that the modified RTOG 0227 induction with either WBRT or auto-HCT consolidation represents a very tolerable and highly effective option for first line therapy of PCNSL, for both younger and older pts.

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Table 1. Patient characteristics and treatment outcomes

CLINICAL CHARACTERISTICS AND OUTCOME	ENTIRE COHORT (N=29)	WBRT COHORT (N=18)	AUTO-HCT COHORT (N=11)
Median age at diagnosis, yrs	62 (40-78)	64 (45-78)	56 (40-67)
Male gender (%)	18 (62)	10 (55.5)	8 (72.7)
ECOG PS at diagnosis (%)			
0-1	25 (86.2)	15 (83.3)	10 (90.9)
2-4	4 (13.8)	3 (16.6)	1 (9.1)
Deep brain structures involved (%)	18 (62)	11 (61.1)	7 (63.6)
Positive CSF cytology (%)			
Yes	4 (13.8)	3 (16.6)	1 (9.1)
No	22 (75.8)	13 (72.2)	9 (81.8)
Unknown	3 (10.3)	2 (11.1)	1 (9.1)
Ocular involvement at diagnosis (%)	4 (13.8)	3 (16.6)	1 (9.1)
Elevated CSF protein at diagnosis (%)			
Yes	19 (65.5)	13 (72.2)	6 (54.5)
No	4 (13.8)	2 (11.1)	2 (18.2)
Unknown	6 (20.7)	3(16.7)	3 (27.3)
Elevated serum LDH at diagnosis	16 (55.2)	11 (61.1)	5 (45.4)
IELSG risk group (%)			
Low (0-1)	4 (13.8)	2 (11.1)	2 (18.2)
Intermediate (2-3)	12 (41.4)	8 (44.4)	4 (36.4)
High (4-5)	7 (24.1)	5 (27.8)	2 (18.2)
Unknown	6 (20.7)	3 (16.7)	3 (27.2)
Avg no. of MTX cycles	4	4	5
Avg no. of total cycles of TMZ	7	11	2
Avg Cumulative TMZ dose (mg/m^2)	5913	8971	909
ORR (%)	93.1	94.4	90.9
CRR (%)	27.5	27.7	27.2
Consolidation treatment (%)			
WBRT	18 (62)	18 (100)	0 (0)
Auto-HCT	11 (38)	0 (0)	11 (100)
Median dose of WBRT (Gy)	36 (23.4-36)	36 (23.4-36)	0
Conditioning regimen for Auto-HCT (%)			
BCNU/TT (carmustine/thiotepa)	7 (24.1)	0 (0)	7 (63.6)
Bu/TT/Cy (busulfan/thiotepa/cyclophosphamide)	4 (13.8)	0 (0)	4 (36.4)
Disease Recurrence (%)	5 (17.2)	4 (22.2)	1 (9.1)
2 yr PFS (%) (p=0.65)	83	81	87
2 yr OS (%) (p=0.27)	96	94	100

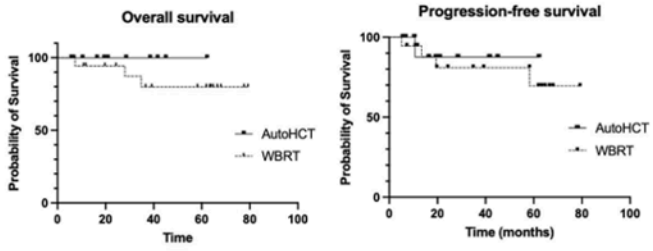

Figure 1. 2-year OS and PFS curves comparing auto-HCT vs WBRT consolidation after RTOG 0227 induction

Figure 1

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