Abstract: P1237

Title: GENE EXPRESSION PROFILING OF RELAPSED AND REFRACTORY PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA REVEALS ENRICHMENT OF IMMUNE SIGNALING PATHWAYS

Abstract Type: Poster Presentation

Topic: Lymphoma biology & translational research

Background:

Primary Central Nervous System Lymphoma (PCNSL) presents a challenging diagnosis with poor prognosis, particularly in the relapsed/refractory setting. This necessitates a deeper understanding of disease biology to refine treatment strategies.

Aims:

Here, we investigated the clinicopathologic characteristics influencing survival patterns of Asian patients with PCNSL and explored tumor immuno-oncologic signals in relapsed/refractory disease (R/R PCNSL).

Methods:

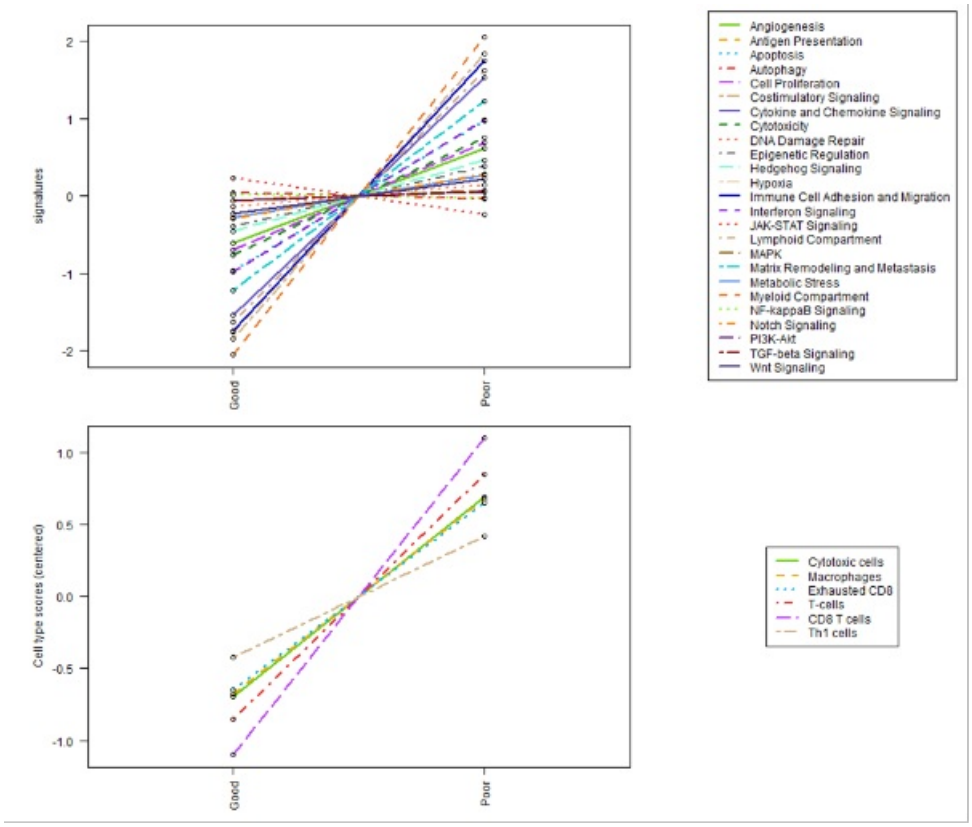
We conducted a retrospective study on a cohort of PCNSL patients (n=127) treated at the National Cancer Centre Singapore and the National Cancer Institute of Singapore from 2000 to 2019. All patients received contemporary high-dose methotrexate-based chemotherapy. Overall survival (OS) and progression-free survival (PFS) were calculated using the Kaplan-Meier method. Formalin-fixed paraffin-embedded (FFPE) tissue from initial tumor biopsies were used for gene expression profiling using the NanoString PanCancer IO360 panel. One group comprised patients with primary refractory disease or early relapse within 2 years from diagnosis ("high-risk", n=3), while the second group comprised patients without relapse more than 5 years from diagnosis ("good-risk", n=3).

Results:

Median age at diagnosis was 59 years (range: 20-78) and most were male (59%). Induction therapy consisted of methotrexate, vincristine, procarbazine (MVP) with (40.9%) or without (59.1%) rituximab (R-MVP). Consolidation radiotherapy was administered to 100 patients (78.7%), while consolidation chemotherapy using cytarabine was administered to 69 patients (54.3%). None of the patients underwent upfront stem cell transplant. Median follow-up duration was 5.9 years (range: 2 months to 13 years). In the overall cohort, median PFS and OS were 3.3 and 4.5 years, respectively. In the "high-risk" group (n=35, 27.5%), median OS was 1.7 years (95%CI 0.88-2.18). Cell of origin with non-germinal centre is associated with poorer prognosis. Analysis of immuno-oncologic pathway signatures showed that the "high-risk" group was enriched in myeloid and lymphoid compartments, immune cell adhesion and migration, costimulatory signaling, as well as cytokine and chemokine signaling pathways. Cell type profiling revealed a higher infiltration of CD8 T-cells, macrophages and Th-1 cells in the high-risk group. Interestingly, differential gene expression analysis demonstrated that *TIGIT* (log2foldchange 3.01, p=0.042) and *HAVCR2* (log2foldchange 2.00, p=0.0339) were amongst the top upregulated genes in the high-risk group, whilst *WNT11* (log2foldchange -6.00, p=0.0174) and *CD44* (log2foldchange -3.58, p=0.00359) were significantly downregulated.

Summary/Conclusion:

We observed a significant proportion of "high-risk" PCNSL characterized by dismal prognosis and tumor upregulation of immune checkpoints *TIGIT* and *HAVCR2*, supporting immune evasion as a disease mechanism. This represents a potential avenue for integrating immunotherapy into existing treatment regimens.



Keywords: Genomics, CNS lymphoma, Diffuse large B cell lymphoma