00293 Prognostic Factors and Molecular Mechanisms in Early-relapse Diffuse Large B-Cell Lymphoma in the Rituximab Era

Jasmin Koh[1], Lim Soon Thye[2], Nagavilli Somasundaram[2]

[1]Duke-NUS Medical School, [2]Singapore General Hospital

Aims: Despite first-line chemotherapy, 40% of patients with Diffuse Large B-cell Lymphoma (DLBCL) relapse and do poorly even with salvage therapy. We aimed to investigate the differences in genomic profiles and clinical characteristics between 2 groups of patients—the early relapsers (ER) and those who achieve continuous complete remission (cCR) after curative intent rituximab-based chemotherapy (RBC).

Methodology: Clinical variables of ER and cCR DLBCL patients who received RBC from 1992 to 2017 were compared in a retrospective analysis. Data was obtained from the Singapore Lymphoma Study database. NanoString gene expression profiling (GEP) was carried out on formalin-fixed paraffin embedded tissue (FFPET) to characterize the genomic profiles of 96 patients—48 with ER and 48 in cCR.

Result: Of 484 patients, 145 had ER, 40 had LR and 299 had cCR. Median survival (95% CI) in years was 1.4(1.2, 1.9), 10.1 and not reached for the 3 groups respectively. ER patients more likely presented with age>60 [1.68(1.17-2.41), elevated lactate dehydrogenase (LDH) [2.63(1.57-4.42)], >1 extra-nodal site of disease [3.30(2.20-4.97)], Stage III/IV disease [3.87(2.65-5.63)] and central nervous system (CNS) involvement [5.72(2.19-14.91). Subtyping by Hans criteria was not associated with outcome. Multivariate analysis showed age>60, elevated LDH, late stage disease as well as CNS involvement to be associated with ER. GEP showed cell-of-origin (COO) subtypes to be independent of outcomes, and unclassified phenotype associated with ER. Interferon-gamma (IFN-γ) and chemokine-receptor-3 (CXCR3) pathways were enriched in ER. MAPK3 had a significant role in these pathways.

Conclusion: In the rituximab era, patients with ER have worse outcomes. Clinical factors predicted for poor outcomes and GEP subtyping shows that the unclassified group of DLBCLs is associated with worse prognosis. IFN-γ and CXCR3 molecular pathways could be driving pathogenesis behind ER independent of the established classified COO subtypes.