Abstract:

Background: Nodal peripheral T-cell lymphomas (nPTCLs) encompass a heterogeneous group of mature and aggressive lymphoid malignancies, including peripheral T-cell lymphoma, not otherwise specified (PTCL/NOS), angioimmunoblastic T-cell lymphoma (AITL) and anaplastic large cell lymphoma (ALCL) ALK-positive and ALK-negative. Their differential diagnosis and prognosis are an issue in the clinical practice. Accurate biomarkers to refine the different subtypes of nPTCLs and to stratify their prognosis are essential to improve their treatment approach. The aim of this study was to test the prognostic impact of *GATA3* gene expression, and its capability to discriminate the different subtypes of nPTCLs.

Patients and Methods: From 2000 to 2017, 80 patients with nPTCLs were eligible for *GATA3* gene expression analysis that was assessed retrospectively by quantitative real time PCR (qRT-PCR) of neoplastic biopsies in Formalin-Fixed Paraffin-Embedded samples (FFPE).

Results: Median age was 49 years old (IqR 34-59), 43/80 (53.7%) were male. Median follow-up was 1.72 years. Of them, 36.3% were classified as PTCL/NOS, 31.2% ALK-negative ALCL, 21.2% ALK-positive ALCL and 11.3% AITL. The majority of cases had advanced stage (III/IV). Two-year estimated overall survival (OS) and progression-free survival (PFS) were 52.2% and 39.5%, respectively. The median *GATA3* gene expression level was 0.49% (range 0 – 7.07) in all cohort, it was 0.11% for ALK-positive ALCL, 0.46% for ALK-negative ALCL, 0.86% for PTCL/NOS and 0.67% for AITL. The difference of *GATA3* gene expression among distinct variants of nPTCLs was statistically significant ($p < 0.001$). *GATA3* gene expression levels ≥ 0.71% discriminate PTCL/NOS from ALK-negative ALCL and AITL with sensitivity of 62% and specificity of 80.3%. *GATA3* gene expression levels ≥ median was associated with poor 2-year OS for PTCL/NOS (46.7% x 21.4%, $p=0.04$) and for ALK-negative ALCL (85.7% x 54.5%, $p=0.04$).

Conclusion: Despite the relative small and heterogeneous group of patients with nPTCLs, *GATA3* gene overexpression may be an important biomarker associated with poor prognosis in PTCL/NOS and ALK-negative ALCL. Moreover it may also discriminate different subtypes of nPTCLs. Further studies with larger series of patients should confirm our findings.