Molecular Characterization of Gastrointestinal Diffuse Large B-Cell Lymphoma

Romée Jansen (1), Tim Dekker (1), Ruben de Groen (1), Fleur de Groot (1), Esther Kret (1), Lorraine de Haan (2), Susan Blommers (1), Lizan Hardi (3), Wietske den Hartog (4), Valeska Terpstra (5), Liane te Boome (6), Els Ahsmann (7), Henriette Levenga (8), Isabelle Focke-Snieders (9), Ward Posthuma (10), Lianne Koens (11), Marie José Kersten (12), Patty Jansen (2), Joost Vermaat (1)

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1) LUMC, Hematologie, Leiden
2) LUMC, Pathologie, Leiden
3) Alrijne Ziekenhuis, Interne Geneeskunde, Leiderdorp
4) Alrijne Ziekenhuis, Pathologie, Leiderdorp
5) Haaglanden MC, Pathologie, Den Haag
6) Haaglanden MC, Interne Geneeskunde, Den Haag
7) Groene Hart Ziekenhuis, Pathologie, Gouda
8) Groene Hart Ziekenhuis, Interne Geneeskunde, Gouda
9) Reinier de Graaf Ziekenhuis, Pathologie, Delft
10) Reinier de Graaf Ziekenhuis, Interne Geneeskunde, Delft
11) Amsterdam UMC, Pathologie, Amsterdam
12) Amsterdam UMC, Hematologie, Amsterdam

Introduction:

Approximately 30% of diffuse large B-cell lymphoma (DLBCL) cases arise from extranodal sites. The gastrointestinal tract is the most common, resulting in gastrointestinal DLBCL (GI-DLBCL). GI-DLBCL is linked to a relatively poor prognosis compared to DLBCL with nodal localizations. Despite its prevalence, the molecular characteristics of GI-DLBCL remain poorly understood.

Methods:

A homogeneous cohort of GI-DLBCL with Ann Arbor stage I and II, treated with R-(mini)-CHOP was assembled. The GI-DLBCL cases were limited to localizations in the stomach, small intestine, and large intestine. For comparison, a cohort of patients with strictly nodal DLBCL, also limited to Ann Arbor stage I and II, was included. Targeted next-generation sequencing (tNGS) was performed using a custom developed AmpliSeq panel (including 129 B-cell lymphoma-related genes) on the IonTorrent platform. Targeted gene expression profiling

(tGEP) using the nCounter system (NanoString) with the BLYMF777 probe set was used to assess key pathways and tumor microenvironment interactions.

Results:

In this preliminary analysis, 37 GI-DLBCL cases were compared to 42 cases of nodal DLBCL. The GI-DLBCL cohort showed enrichment for mutations in *TP53* (*P*=0.04), *TET2* (*P*=0.04), *KRAS* (*P*=0.02), and *PTPN6* (*P*=0.02) compared to the comparator cases of nodal DLBCL. *TP53* mutations were associated with poor 2-year overall survival (*P*=0.032) in univariable analysis. Additional analyses, including gene expression profiling, are underway to further delineate the molecular differences between GI-DLBCL and nodal DLBCL, with a focus on transcription pathways and contents of the tumor microenvironment.

Conclusion:

Preliminary results highlight distinct molecular features in GI-DLBCL compared to nodal-DLBCL, including significant enrichment of *TP53* mutations, which are associated with poor 2-year survival. These findings underscore the prognostic importance of *TP53* mutations in GI-DLBCL, with further gene expression analyses to be presented at the DHC meeting.