Clinical characterisation of High grade B-cell lymphoma in a population-based cohort. Comparative study for the years 2016-2021 with data from the Cancer Registry of Baden-Württemberg.

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AEK 21st International AEK Cancer Congress

Purpose

High-grade B-cell lymphoma (HGBL) not otherwise specified (NOS), and HGBL with MYC and BCL2 rearrangements are recently introduced diagnostic categories for aggressive B-cell lymphomas. Data from the literature reveal that about 15% of DLBCL show HGBL-like GEP signature in gene expression analysis. For most of patients, advanced stage disease is observed at diagnosis. Optimal treatment of HGBL NOS, and HGBL double hit and triple hit lymphomas has not been established yet. The purpose of the present study is to explore the reporting frequency, therapy choice and clinical outcome of patients with HGBL double hit, triple hit and HGBL NOS diagnosed over the last five years and reported to the cancer registry of Baden-Württemberg.

Methods

Diffuse large B cell lymphoma of adult patients diagnosed between 2016 and 2021 and reported to the clinical cancer registry are included. Data required for identification of HGBL with MYC rearrangement in combination with BCL2 and/or BCL6 rearrangement, HGBL NOS, or B-cell lymphoma unclassifiable with features intermediate between diffuse large B cell lymphoma and Burkitt lymphoma, replaced in 2016 by the WHO with the former two categories, are obtained from the pathology reports (1-3). By the same way, DLBCL NOS along with the cell of origin [germinal center B cell (GCB) versus non germinal center B-cell (non-GCB) according to Hans´s-algorithm (4)] are extracted by the same way. Survival analysis of HGBL vs DLBCL NOS GCB and non-GCB is performed using Kaplan Meier methodology.

Results

Cohort: We considered a cohort of 3.617 patients with diffuse large B-cell lymphoma (ICD-O 9680/3) and available pathology report. **Tumour characteristics**: Among them, 99 tumours are identified as HGBL (2.7%), mostly being double hit lymphomas with MYC and BCL2 or BCL6 rearrangement, followed by HGBL NOS and triple hit lymphomas with MYC, BCL2 and BCL6 rearrangement (Figure 1). **Clinical presentation**: HGBL is observed more frequently in males (>55%) and elderly patients. Compared to DLBCL NOS, advanced stage disease and high IPI score are reported more frequently (Figure 2).

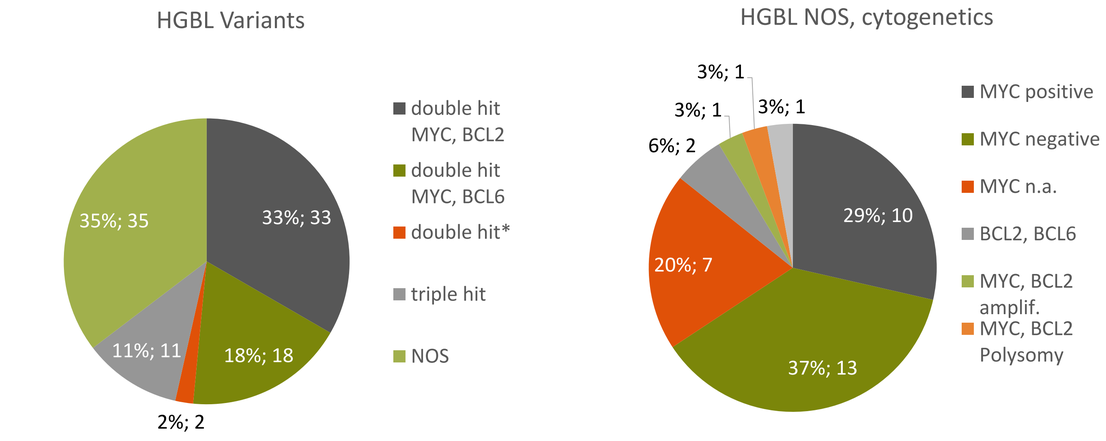

Figure 1. HGBL Variants (left). Cytogenetics of HGBL NOS (right). Double hit*: double hit reported without specification of cytogenetics; MYC positive: MYC rearranged; MYC negative: not rearranged; MYC n.a.: information on MYC rearrangement not available. BCL2, BCL6: BCL2 and BCL6 rearrangement without MYC rearrangement. MYC, BCL2 amplif.: MYC rearrangement plus BCL2 amplification. MYC, BCL2 Polysomy: MYC rearrangement plus BCL2 Polysomy. BCL6: BCL6 rearrangement without MYC rearrangement.

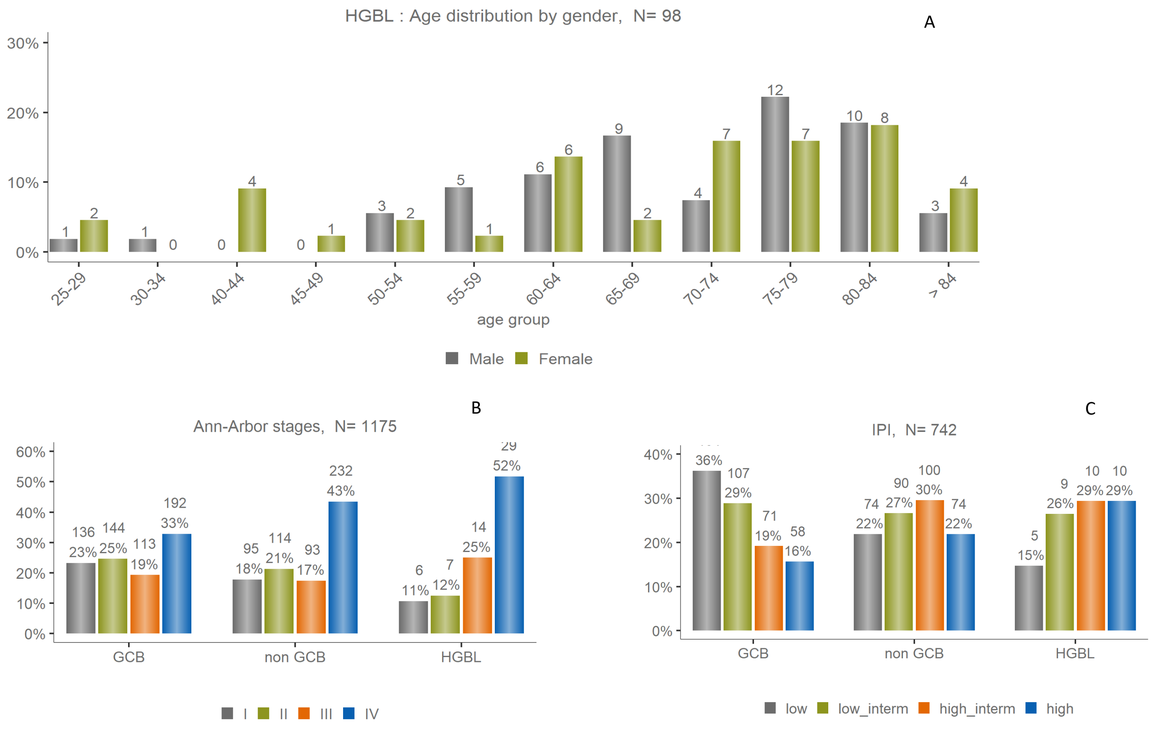

Figure 2A-2C HGBL patients |Age distribution by gender (A) | Ann Arbor stages (B) and international prognostic groups (IPI) (C) of HGBL patients compared to DLBCL NOS GCB and non-GCB patients. For one patient with HGBL, age was not reported.

Primary therapy: Information on primary therapy of HGBL is available for 75 patients and includes mainly CHOP-based regimens. Intensified therapy with DA-EPOCH-R was reported for seven patients. Following induction, eleven patients underwent autologous stem cell transplantation with high-dose chemotherapy (conditioning protocol was BEAM N=7, TEAM N=2, BCNU/Thiotepa N=1, not specified N=1).

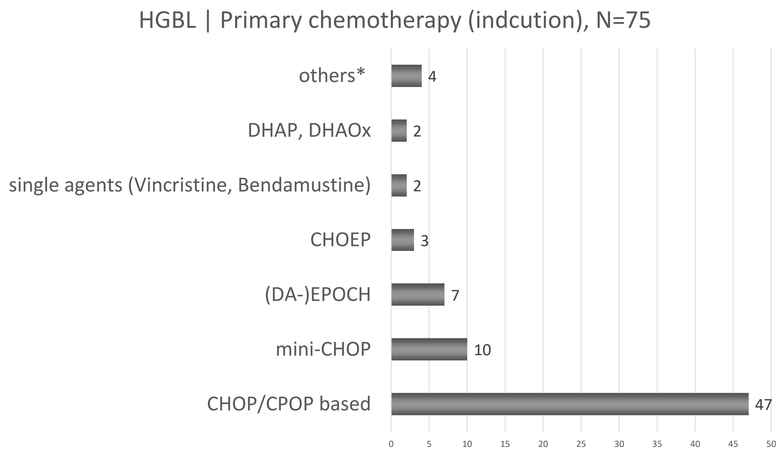

Figure 3. Primary chemotherapy of patients with HGBL. Others: R-MTX only, analogous to IELSG, C/H/O, „Block A1“. CHOP/CPOP based protocols include some mixed protocols (one case with CHOP/ mini-CHOP, one with CHOP/CHOEP, two with CHOP/DHAOx. 22 patients received in addition MTX, one MTX plus Cytarabine and one MTX, Cytarabine and Dexamethasone. All patients were given also Rituximab.

Overall survival: HGBL patients show inferior two-year survival rates compared to DLBCL NOS. Higher Ann Arbor stages, IPI score and age of patients with HGBL must be taken into account for the interpretation of survival data (Figure 4).

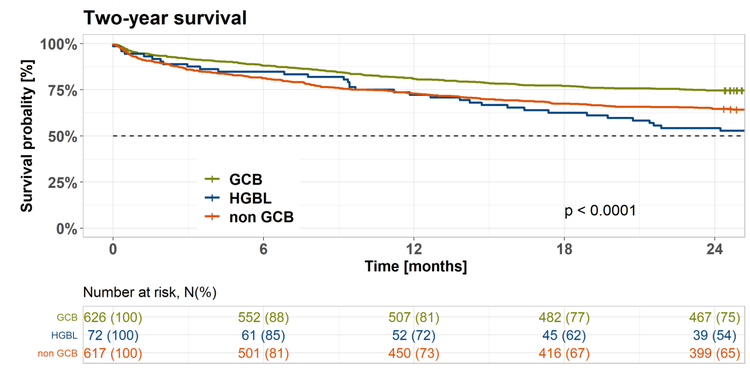

Figure 4. Overall two-year survival of patients with HGBL, DLBCL NOS GCB and non-GCB diagnosed in 2016-2020 (Kaplan-Meier Analysis).

Discussion and Conclusion

In comparison to the frequency of HGBL reported in the literature from gene expression analysis, the number of HGBL in our cohort is likely to be underestimated. Partially, missing data on cytogenetics may be responsible, as evaluation of MYC-rearrangement was not always reported. In agreement with data from the literature, HGBL harbour an inferior prognosis compared to DLBCL NOS, GCB and non-GCB. However, higher Ann Arbor stages and IPI score of patients with HGBL must be taken into account for the interpretation of survival.

Yet no standard therapy has been defined for HGBL so far (3). This patient group should be considered for clinical trials (5) for testing new therapy approaches. Directly targeting MYC is one option but still considered impossible but alternative methods are under investigation (6).

References

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