High-Grade B-cell Lymphomas

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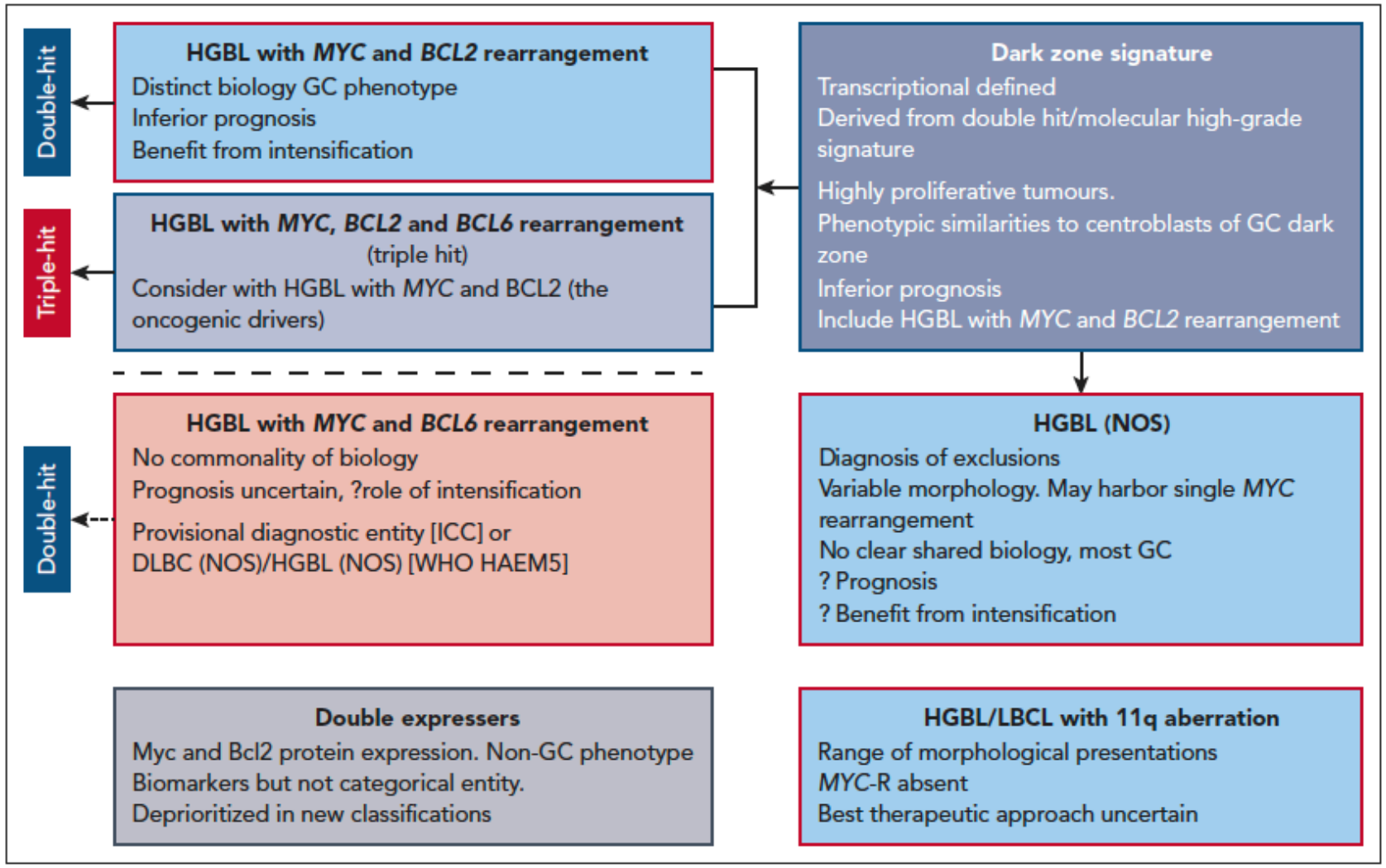
Disclosures of Carmelo Carlo-Stella

Company name	Research support	Consultant	Stockholder	Speakers bureau	Advisory board	Other
ADC Therapeutics	X	X		X	Honorarium	Honorarium
Karyopharm Tx				X		
Celgene/BMS				X	Honorarium	Honorarium
Incyte					Honorarium	Honorarium
Hoffmann-La Roche Ltd	X			X	Honorarium	Honorarium
Janssen Oncology					Honorarium	Honorarium
Takeda					Honorarium	Honorarium
Merck Sharp & Dohme				X	Honorarium	Honorarium
AstraZeneca					Honorarium	Honorarium
Gilead					Honorarium	Honorarium
SOBI				X	Honorarium	Honorarium
AbbVie				X		
Genmab				X		

Classification of the HGBCL



Mature aggressive B-cell lymphomas harboring rearrangements of MYC, BCL2, and BCL6.

Oncogenic hits that promote cellular proliferation and inhibit apoptosis, conferring clinically high-risk disease and potential resistance to chemotherapy

A. J. Davies, Blood 2024

First-line Therapy for HGBCL DH/TH

- Retrospective analyses have demonstrated the poor outcome of DHL/THL with conventional R-CHOP chemotherapy
- Retrospective analyses showed that chemotherapy intensification was associated with an improvement in CR rates and PFS, but there was little to indicate an improved OS
- In a meta-analysis from 11 studies of 394 patients, with 91 received **DAEPOCH-R** that was superior for PFS, but did not show any survival advantage (1)
- In 53 patients with MYC rearranged HGBCL, DAEPOCH-R showed 48-month PFS 73% for patients with DHL (2)
- CALGB/Alliance 50303 randomized study showing no advantage of DA-EPOCH-R over R-CHOP (3)

1. Howlett C , Br J Haematol, 2015; 2. Dunleavy K, Lancet Haematol, 2018; 3. Bartlett NL, J Clin Oncol, 2019

First-line Therapy for HGBCL DH/TH

- **R-CODOX-M/R-IVAC** regimen evaluated prospectively in a single-arm phase 2 study of high-risk DLBCL, of which **12% of patients had DHL**. Treatment was well tolerated in younger patients with good performance status; however, treatment-related mortality was 4.3% with a 2-year PFS of 67.9% for the whole cohort.(1)
- A retrospective review of patients with DHL receiving R-CODOX/R-IVAC reported 2-year
- OS and PFS of 61% and 47%, respectively.(2)

1. McMillan AK, Ann Oncol, 2020; 2. Sun H, Clin Lymphoma Myeloma Leuk. 2015.

First-line Therapy for HGBCL DH/TH

- Primary analysis of **POLARIX trial**: on 45 of 879 were DH patients. The subgroup analysis did not favor polatuzumab.
- An extended data set of 93 DH/TH patients was analyzed (FDA): the CR rate favored Pola-R-CHP(88.4%) compared with R-CHOP (64%) in patients with DHL/THL with a PFS HR of 0.45 (95% CI, 0.21-1.08) and OS of 0.42 (95% CI, 0.15-1.19).
- Further analysis by the sponsor revealed that 108 patients, of 665 tested, had a DZsig+ (26% with BCL2 and/or BCL6 translocations).(1) Patients who were DZsig+ and treated with Pola-RCHP had a better outcome compared with those receiving R-CHOP

1. Morschhauser F, Blood. 2023; 142(suppl 1):3000-3003

First-line Therapy for HGBCL DH/TH

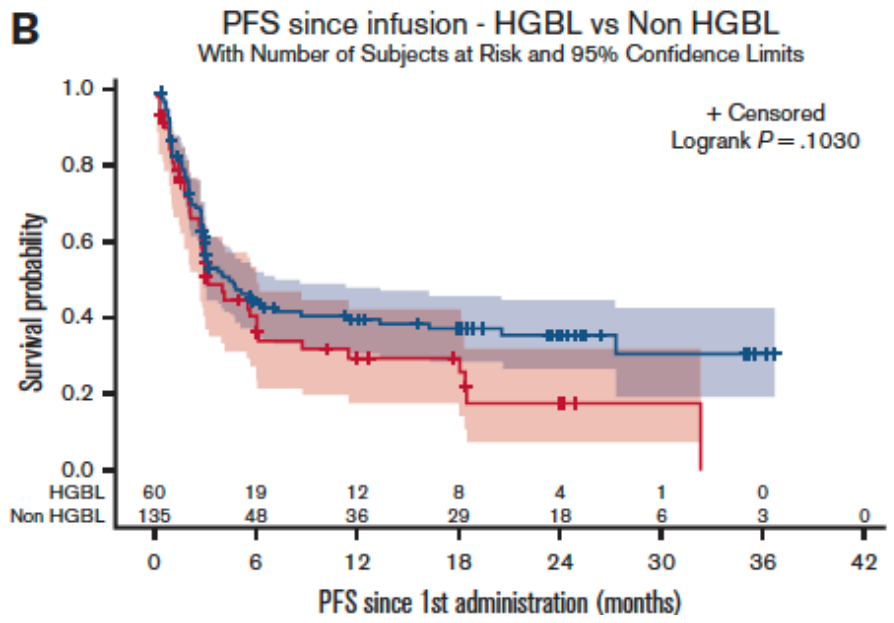
- DA-EPOCHR, R-CODOX-M/R-IVAC [III, B]
- Pola-R-CHP seems superior to R-CHOP in DH/TH
- Offer R-CHOP21 only in unfit patients
- ASCT consolidation after first-line treatment is not recommended [IV, B].80

Therapy for Rel/Ref HGBCL

- In the **ZUMA-7** study of axi-cel, 16% of patients had HGBL (including MYC/BCL2 ± BCL6). In the whole population, HR for EFS was 0.40 (95% CI, 0.31-0.51) in favor of CAR-T and 0.28 (95% CI, 0.14-0.59) in the population with DHL
- In the T**RANSFORM** study of lisa-cel, the EFS HR in the whole population (n = 184) was 0.35 (95% CI,0.23-0.53), and it was 0.4 (95% CI, 0.19-0.90) in the 43 patients in the HGBL group.

Outcome of high-grade B-cell lymphoma compared with other large B-cell lymphoma after CAR-T rescue: a DESCAR-T LYSA study

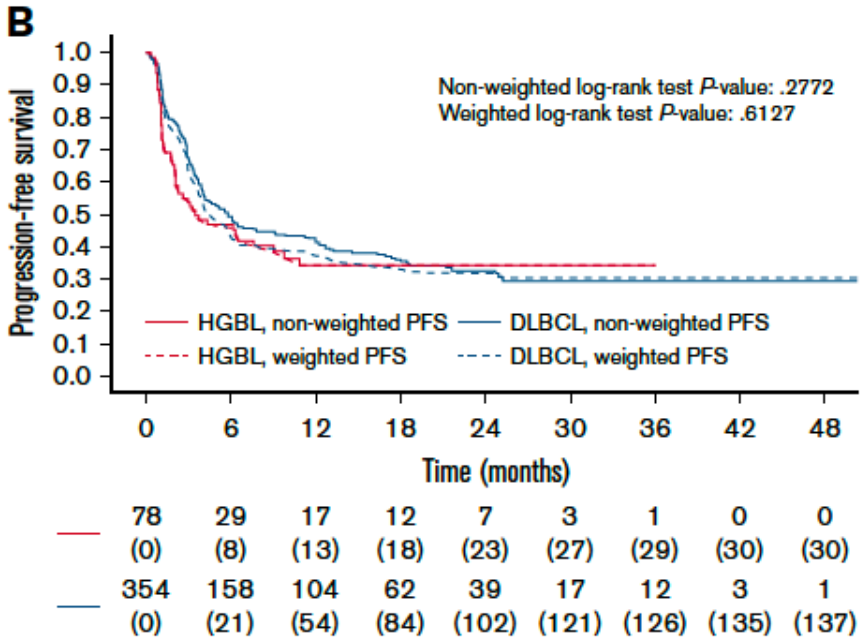
Xavier Phina-Ziebin,[1] Emmanuel Bachy,[2] François-Xavier Gros,[3] Roberta Di Blasi,[4] Charles Herbaux,[5] Jacques Olivier Bay,[6] Sylvain Carras,[7] Pierre Bories,[8] Olivier Casasnovas,[9] Fabrice Jardin,[10] Franck Morschhauser,[11] Blandine Guffroy,[12] Mohamad Mohty,[13] Elodie Gat,[14] Julien Calvani,[15] Marie-Cécile Parrens,[16] Elsa Poullot,[17] Alexandra Traverse-Glehen,[18] and Louise Roulin[1]



PFS and OS were not significantly different between HGBL and non-HGBL

Outcomes of CAR T-cell therapy in high-grade B-cell lymphomas compared to DLBCL: a weighted comparison analysis

Anna Dodero,[1,*] Giusy Ceparano,[1,2,*] Beatrice Casadei,[3] Piera Angelillo,[4] Stefania Bramanti,[5] Maria Chiara Tisi,[6] Silva Ljevar,[7] Federico Stella,[2] Annalisa Chiappella,[1] Barbara Botto,[8] Ilaria Cutini,[9] Giada Zanirato,[1] Patrizia Chiusolo,[10] Anna Maria Barbui,[11] Mirko Farina,[12] Alice Di Rocco,[13] Giovanni Grillo,[14] Jacopo Olivieri,[15] Mauro Krampera,[16] Marco Ladetto,[17] Anna Guidetti,[1,2] Pier Luigi Zinzani,[3,18] Cristiana Carniti,[1] and Paolo Corradini[1,2]



There was no statistically significant difference in PFS between patients with HGBL-DH/TH lymphomas vs other high-grade histotypes.

Efficacy and Safety of Glofitamab Plus Polatuzumab Vedotin in Relapsed/Refractory Large B-Cell Lymphoma Including High-Grade B-Cell Lymphoma: Results From a Phase Ib/II Trial

Martin Hutchings, MD, PhD[1]; Anna Sureda, MD, PhD[2]; Francesc Bosch, MD, PhD[3]; Thomas Stauffer Larsen, MD, PhD[4]; Paolo Corradini, MD[5]; Abraham Avigdor, MD[6]; María José Terol, MD, PhD[7]; Antonio Rueda Dominguez, MD, PhD[8]; Antonio Pinto, MD[9]; Alan Skarbnik, MD[10]; Raul Cordoba, MD, PhD[11]; Judit Meszaros Jørgensen, MD, PhD[12]; Pier Luigi Zinzani, MD, PhD[13,14]; Wilfred Leung, PhD[15]; Alessia Bottos, PhD[16]; Donghang Li, PhD[17]; James Relf, MD[18]; Maneesh Tandon, MBChB[18]; Gila Sellam, PhD[16]; and Giuseppe Gritti, MD, PhD[19]