La terapia cellulare CAR-T è più efficace del trapianto autologo nella terapia di seconda linea dei linfomi B a grandi cellule ricaduti precocemente?

GITMO

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CONVEGNO EDUCAZIONALE GITMO

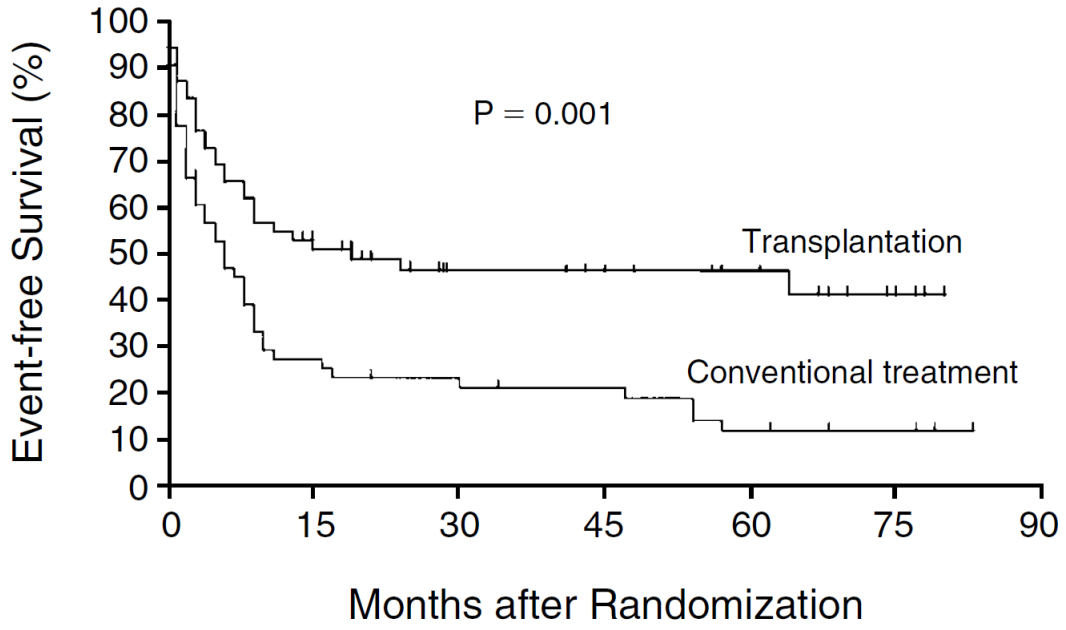
HOT QUESTIONS IN TRASPLANTATION AND CELLULAR THERAPIES

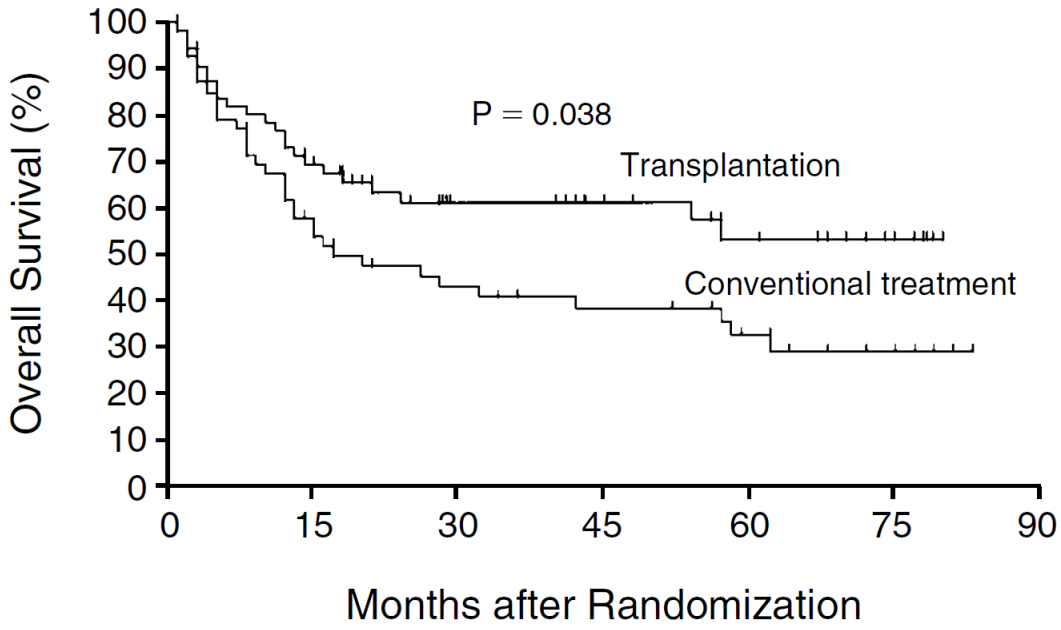
Udine
13-14 novembre 2023
Aula Polifunzionale - Ospedale di Udine

Francesco Onida - Università di Milano

AUTOLOGOUS BONE MARROW TRANSPLANTATION AS COMPARED WITH SALVAGE CHEMOTHERAPY IN RELAPSES OF CHEMOTHERAPY-SENSITIVE NON-HODGKIN'S LYMPHOMA

THIERRY PHILIP, M.D., CESARE GUGLIELMI, M.D., ANTON HAGENBEEK, M.D., RENIER SOMERS, M.D., HANS VAN DER LELIE, M.D., DOMINIQUE BRON, M.D., PIETER SONNEVELD, M.D., CHRISTIAN GISSELBRECHT, M.D., JEAN-YVES CAHN, M.D., JEAN-LUC HAROUSSEAU, M.D., BERTRAND COIFFIER, M.D., PIERRE BIRON, M.D., FRANCO MANDELLI, M.D., AND FRANCK CHAUVIN, M.D.





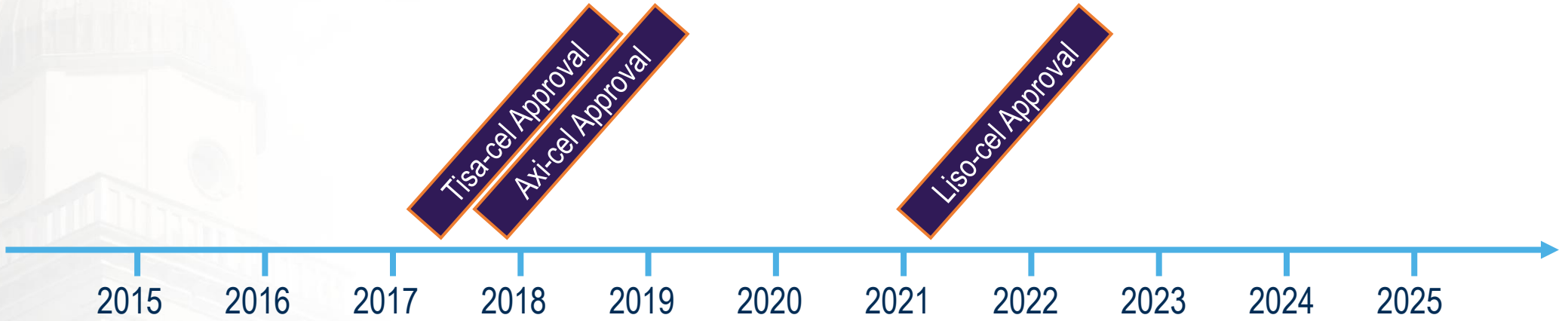
Annals of Oncology 26 (Supplement 5): v116–v125, 2015
doi:10.1093/annonc/mdv304

Diffuse large B-cell lymphoma (DLBCL): ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

First relapse/progress	
Eligible for transplant	Not eligible for transplant
Platinum-based chemotherapy regimens (i.e. R-DHAP, R-ICE, R-GDP) as salvage treatment For chemosensitive patients: R-HDCT with ASCT as remission consolidation Consider allogeneic transplantation in patients relapsed after R-HDCT with ASCT or in patients with poor-risk factors at relapse	Platinum- and/or gemcitabine-based regimens Clinical trials with novel drugs
>2 relapse/progress	
Eligible for transplant	Not eligible for transplant
Allogeneic transplantation Clinical trials with novel drugs	Clinical trials with novel drugs Palliative care

Annals of Oncology 26 (Supplement 5) 2015

Expansion of the Field of Cellular Immunotherapy for DLBCL



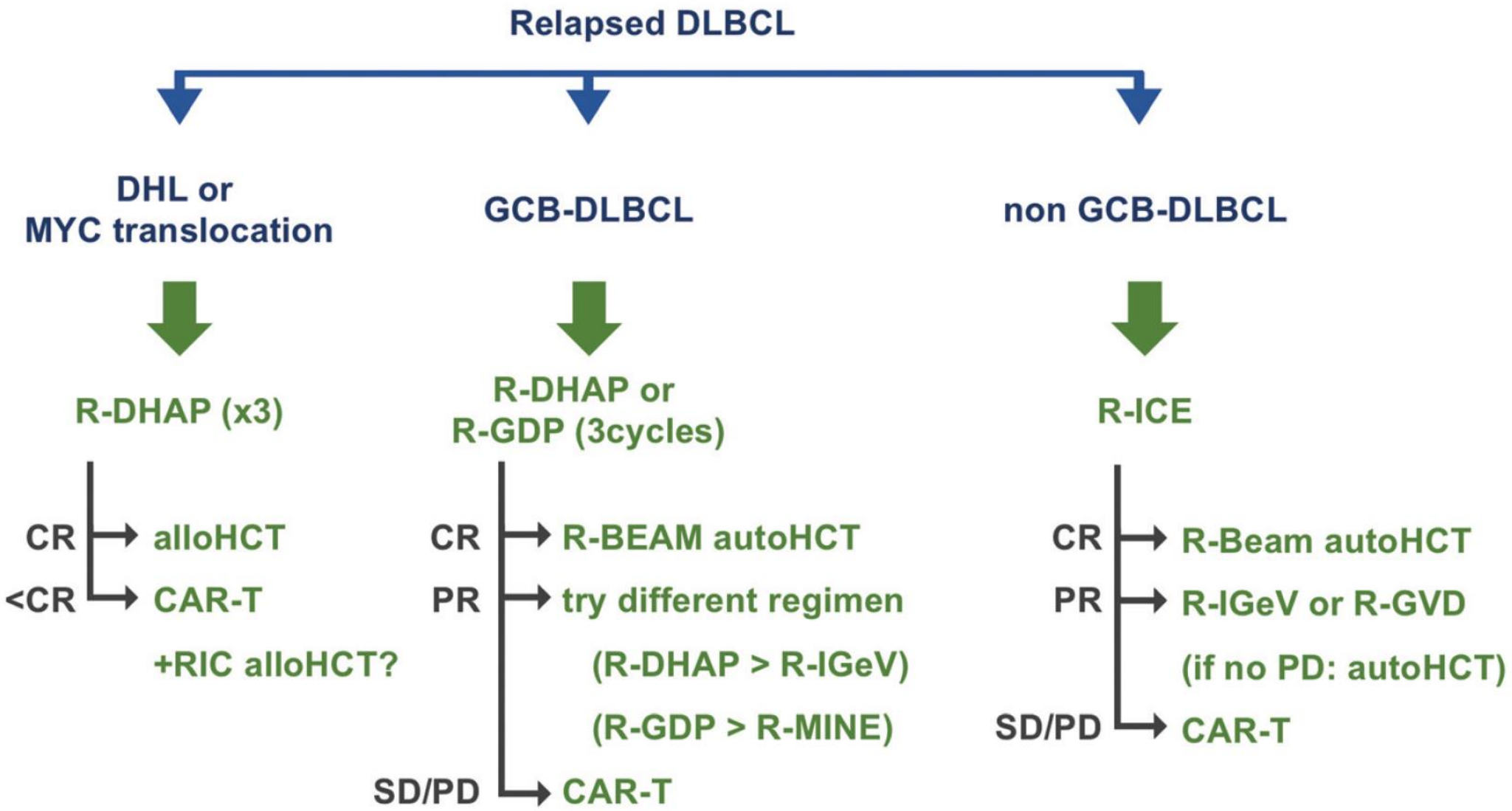


Figure 1. **Authors' algorithm for the treatment of relapsed DLBCL.**

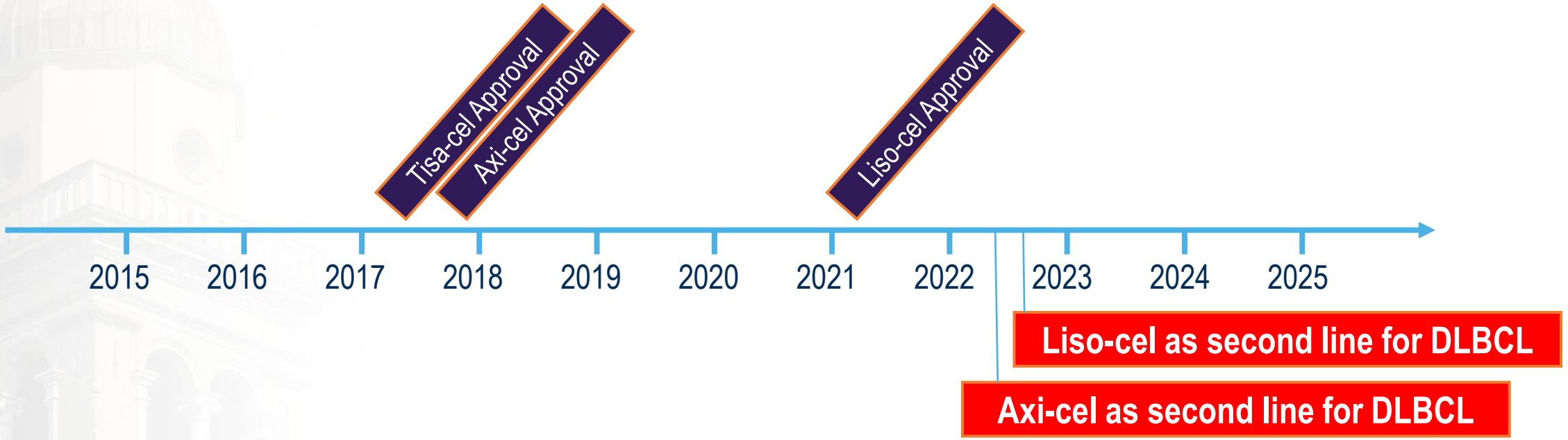
Lekakis LJ & Moskowitz CH. HemaSphere 2019

Anti-CD19 CAR T Cells for Aggressive 2L LBCL

	APPROVED PRODUCTS		NOT APPROVED
	Axicabtagene Ciloleucel[1] (KTE-C19)	Lisocabtagene Maraleucel[2] (JCAR017)	Tisagenlecleucel[3] (CTL019)
Pivotal Trial	ZUMA-7 NCT03391466	TRANSFORM NCT03575351	BELINDA NCT03570892
Phase	Phase 3	Phase 3	Phase 3
Dose Level	2×10^6 cells	1×10^8 cells	2.9×10^8 cells
Conditioning Chemotherapy	FLU 30 mg/m^2 and CY 500 mg/m^2 × 3 days	FLU 30 mg/m^2 and CY 300 mg/m^2 × 3 days	FLU 25 mg/m^2 + CY 250 mg/m^2 × 3 days *or* Bendamustine 90 mg/m^2 × 2 days
Evaluable Patients (N)	DLBCL (N = 180)	DLBCL (N = 92)	DLBCL (N = 162)
Response Rates	ORR = 83% CR = 65%	ORR = 86% CR = 66%	Tisagenlecleucel was not superior to standard salvage therapy

1. YESCARTA. Package insert. Kite Pharma, Inc.; 2022.
2. Kamdar M, et al. Lancet. 2022;399:2294-308.
3. Bishop MR, et al. NEJM. 2022;386(7):629-39.

Expansion of the Field of Cellular Immunotherapy for DLBCL



ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ESMO OPEN SCIENCE FOR OPTIMAL CANCER CARE

REVIEW

How I treat diffuse large B-cell lymphoma

T. Melchardt[1,2,3,4], A. Egle[1,2,3,4] & R. Greil[1,2,3,4*]

[1]IIIrd Medical Department at the Paracelsus Medical University Salzburg, Cancer Center, Salzburg; [2]Salzburg Cancer Research Institute, Salzburg; [3]Austrian Group for Medical Tumor Therapy (AGMT), Salzburg; [4]Cancer Cluster, Salzburg, Austria

Annals of Oncology 2023

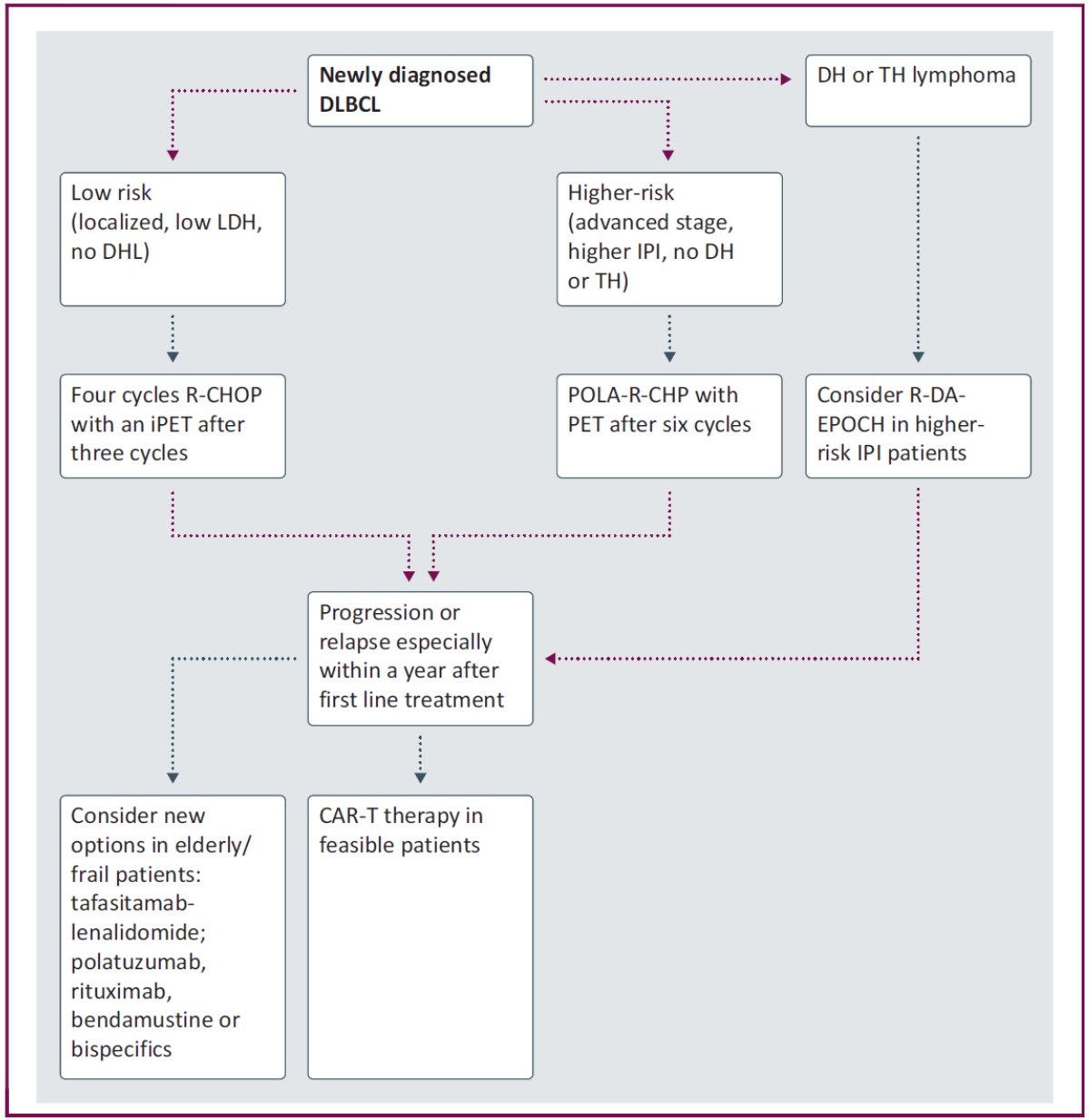
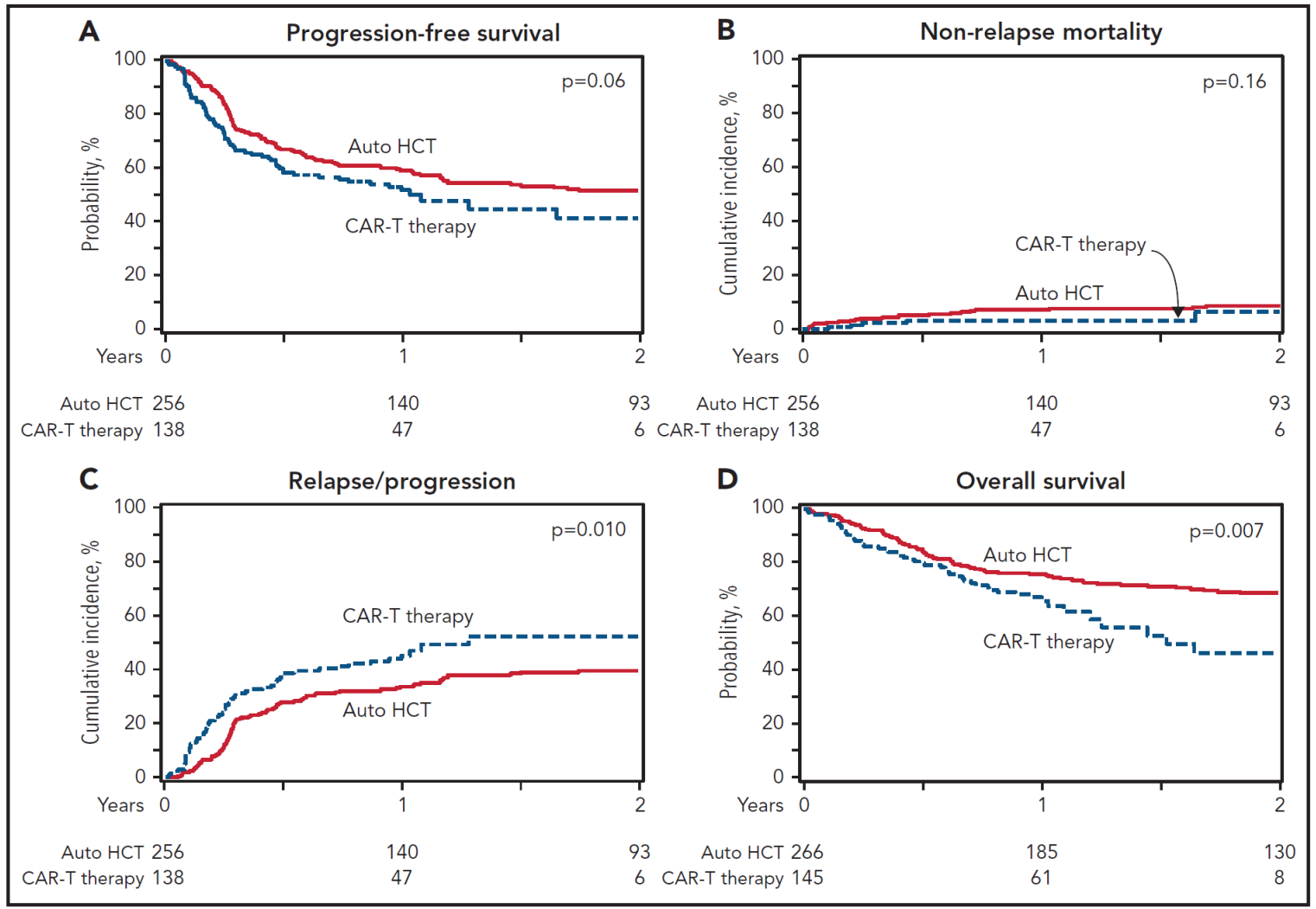


Figure 1. **My approach to DLBCL outside a clinical trial.**

ASCT vs CAR-T for relapsed DLCBL in PR



Shadman M et al. Blood 2022

CAR T Therapy: Acute Toxicities

- Cytokine release syndrome
- Immune effector cell-associated neurotoxicity syndrome (ICANS)
- Cytopenias and their consequences (ICAHT)
- Acute infusion toxicity
- Tumor lysis
- MAS or HLH (may be life threatening if not managed by expert multidisciplinary team)
- Anaphylaxis
- Coagulopathy
- **Economic issues**

Lee DW, Santomasso BD, Locke FL, et al. *Biol Blood Marrow Transplant*. 2019;25(4):625-638.

Key Points

- Patients with relapsed DLBCL after 2 or more lines of therapy, including ASCT, represent a group with poor prognosis. CAR-T cell therapy offers long-term survival for a proportion of these patients.

- In the setting of primary refractory disease or disease that relapsed within a year following first-line chemotherapy, 2 out of 3 clinical trials that compared CAR-T cell therapy to ASCT favored the first modality in terms of progression-free survival. However, a retrospective registry study favored ASCT in patients who achieved objective response to salvage chemotherapy (chemosensitive).

Which is the preferred second-line treatment option for patients with relapsed or refractory DLBCL?