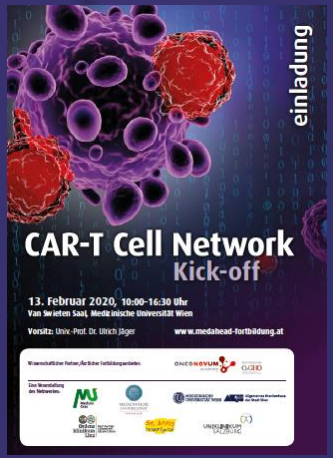
Sequencing therapies for patients with high-risk DLBCL



COMPREHENSIVE CANCER CENTER VIENNA

MEDICAL UNIVERSITY OF VIENNA

Vienna General Hospital

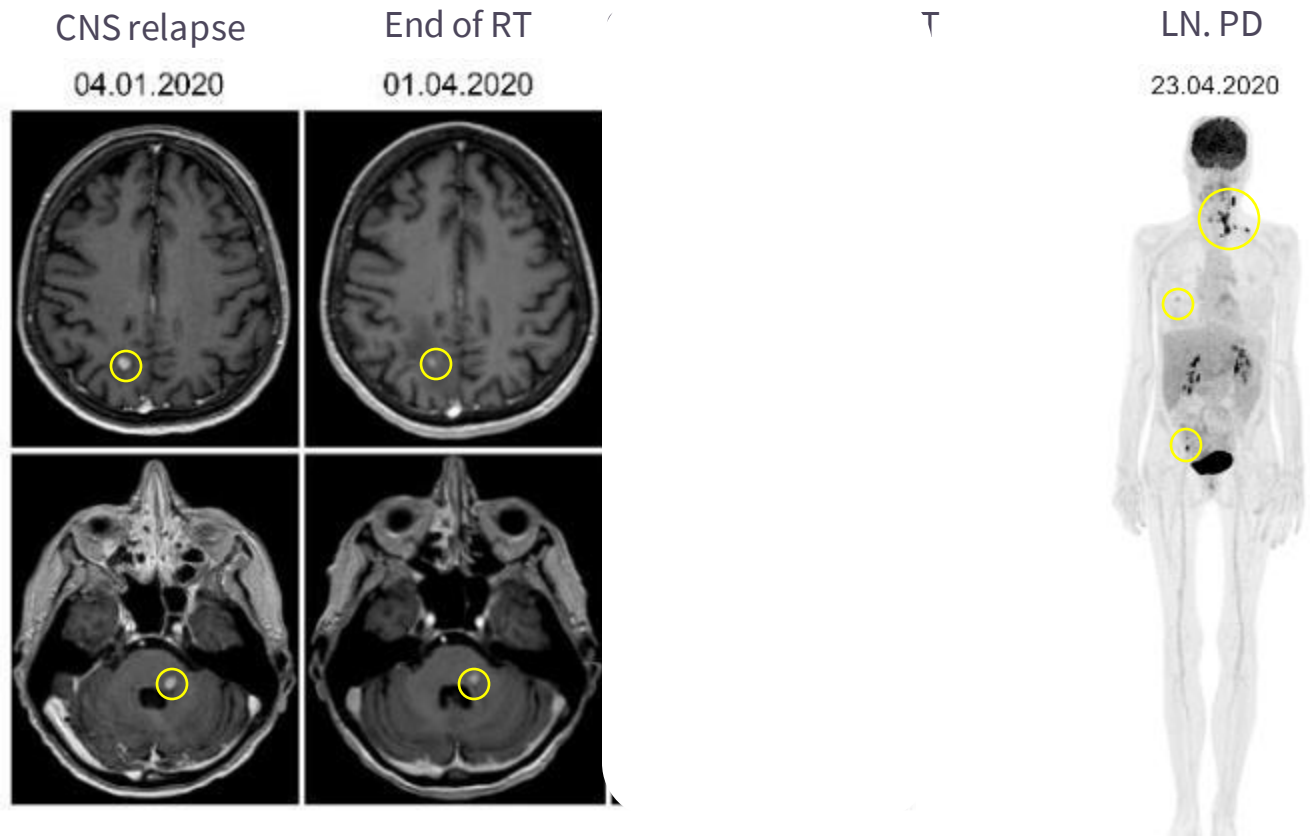
Case report: Female patient, 59 years old

MEDIZINISCHE UNIVERSITÄT WIEN

2019	Jan	• Diagnosis: DLBCL GCB; DHS (Green) 2; CS IVB (bone marrow infiltration, osteolytic lesions, multiple LN manifestations); aaIPI = high-intermediate; CNS-IPI = 3/intermediate • Mutations: *CREBBP* Received six cycles of R-CEOP in community hospital: refractory after six cycles
	Jul	• LN biopsy showed persisting DLBCL • New: multiple CNS lesions—referred to University Hospital • ASCT or CAR T-cell therapy planned 26/07/2019: T-cell apheresis successful 28/07/2019: Started therapy for relapsed disease with GMALL-Burkitt protocol Block A1 + i.th. therapy
	Sep	PET-CT: CMR—therefore underwent stem cell harvest for planned ASCT in second CR
	Nov	After Block C1: paresthesias in tongue, lips, and left side of face: CNS PD - i.th. triple therapy
2020	Jan	CSF still positive (132/3 cells)
	Mar	CNS radiation, **CAR T-cell therapy planned**

aaIPI, age-adjusted International Prognostic Index; ASCT, autologous stem-cell transplantation; CAR, chimeric antigen receptor; CMR, complete metabolic response; CNS, central nervous system; CS, clincal stage; CSF, cerebrospinal fluid; DHS, double-hit score; DLBCL, diffuse large B-cell lymphoma; GCB, germinal center B-cell like; GMALL, German multicenter study group for adult acute lymphoblastic leukemia; i.th., intrathecal; IPI, International Prognostic Index; LN, lymph node; PD, progressive disease; PET-CT, positron emission tomography-computed tomography; R-CEOP, rituximab, cyclophosphamide, etoposide, vincristine, prednisone.

Case report: Female patient, 59 years old[1]



CAR, chimeric antigen receptor; CMR, complete metabolic response; CNS, central nervous system; CR, complete response; LN, lymph node; PD, progressive disease; RT, radiotherapy.

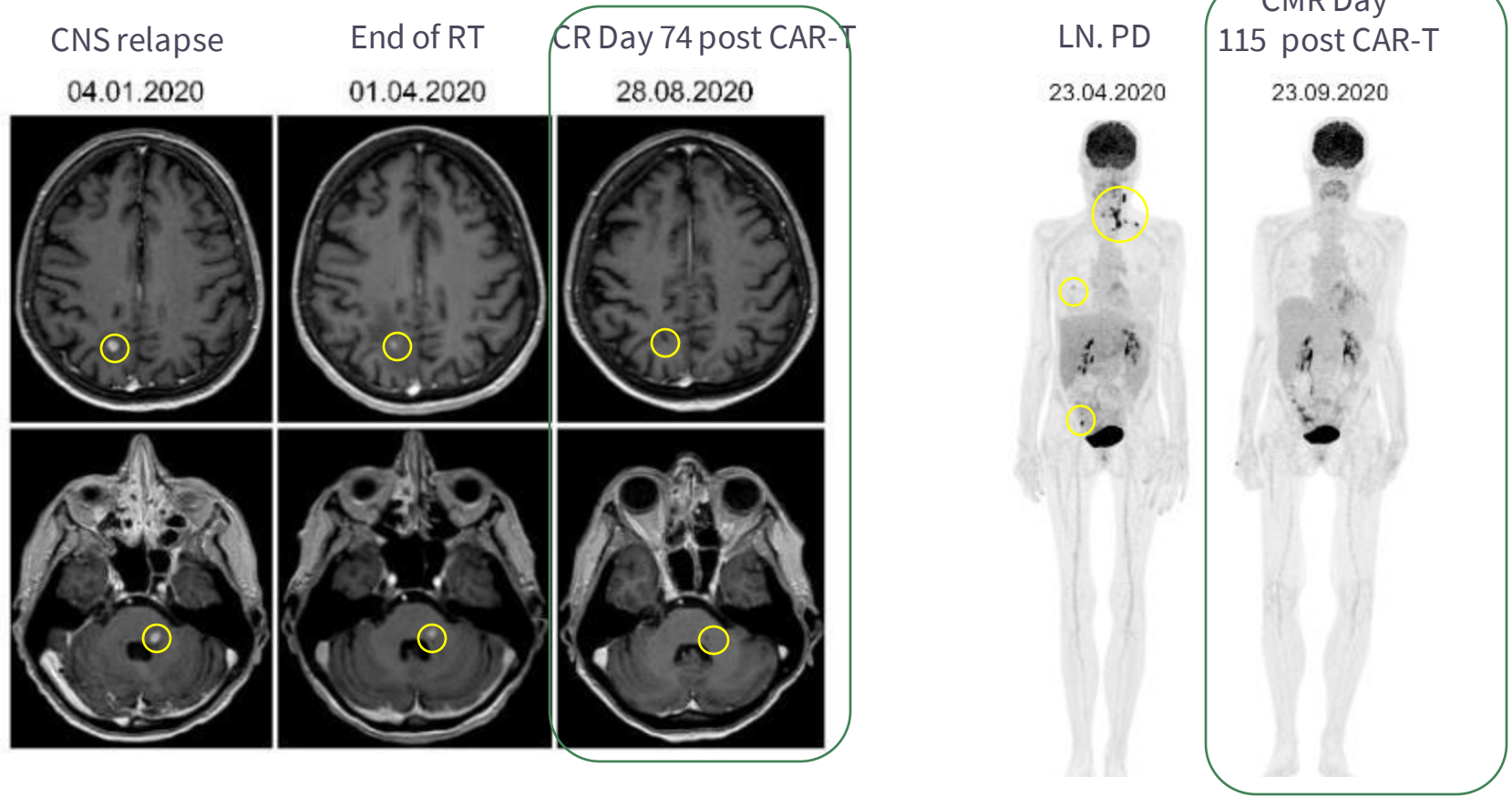
1. Courtesy: Marius Mayerhöfer, MUW/MSKCC.

Case report: Female patient, 59 years old

2020	Apr	CAR T-cell therapy planned • PD (multiple LN manifestations) • Bridging with rituximab-polatuzumab-dexamethasone
	Jun	16/06/2020: Infusion with CAR T cells • No CRS, but ICANS 1 under Keppra prophylaxis
	Sep	Outcome at Month 3: PET-CT + MRI negative = CMR Ig deficiency (received Ig substitution ×4 until 2022)
2021	May	Responded to SARS-CoV2 vaccination (6% $CD19^+$ B lymphocytes)
2022		
2023	Apr	Update: Patient is now in CCR for 3 years (13% $CD19^+$ B lymphocytes)

CAR, chimeric antigen receptor; CCR, clinical complete response ; CMR, complete metabolic response; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; Ig, immunoglobulin; LN, lymph node; MRI, magnetic resonance imaging; PD, progressive disease; PET-CT, positron emission tomography-computed tomography; SARS-CoV2, severe acute respiratory syndrome coronavirus 2.

Case report: Female patient, 59 years old[1]



CAR, chimeric antigen receptor; CMR, complete metabolic response; CNS, central nervous system; CR, complete response; LN, lymph node; PD, progressive disease; RT, radiotherapy.

1. Courtesy: Marius Mayerhöfer, MUW/MSKCC.

Selection algorithm for patients with DLBCL in clinical routine: Austrian CAR-T Cell Network[1]

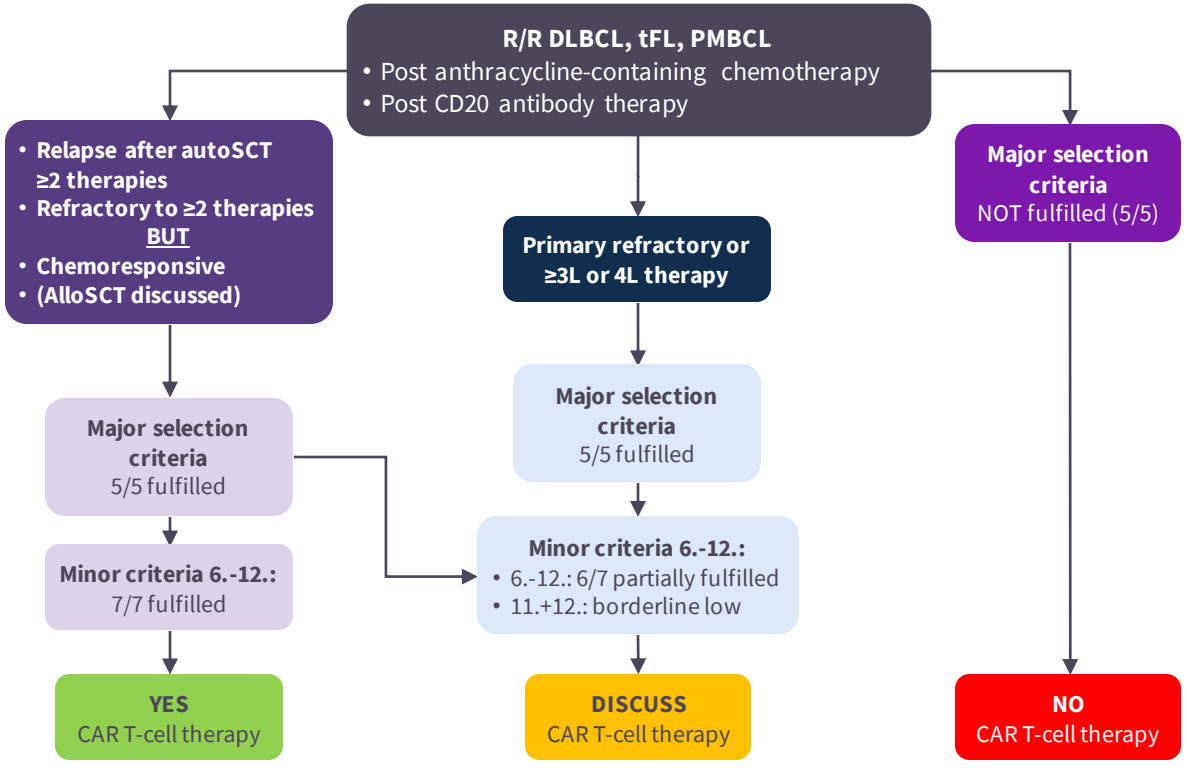
Major criteria*		
1	Cardiac function	EF >50%
2	Lung function	SpO_2 >91–92% at room air
3	ECOG performance status	0–1
4	CNS	• No involvement • No major neurologic disease as contraindication
5	Infection	No active or uncontrolled infection
Minor criteria*		
6	ANC	≥1.0 G/L
7	ALC	>0.1–0.3 G/L
8	Renal function	eGFR ≥60 mL/min/1.73 m^2
9	Liver function	Serum ALT/AST <2.5 × ULN
10	Liver function	Total bilirubin <2.0 mg/dL
11	Platelets	≥50–75 G/L
12	Hb	>8.0 g/dL

No active/symptomatic CNS involvement at time of infusion (first amendment proposed)

ALC, absolute lymphocyte count; ALT/AST, alanine aminotransferase/aspartate aminotransferase; ANC, absolute neutrophil count; CAR, chimeric antigen receptor; CNS, central nervous system; DLBCL, diffuse large B-cell lymphoma; ECOG, Eastern Cooperative Oncology Group; EF, ejection fraction; eGFR, glomerular filtration rate; G/L, giga/liter; Hb, hemoglobin; SpO2, oxygen saturation; ULN, upper limit of normal.
*Based on available protocols/recommendations for routine use/clinical studies/RWE data.

1. Greinix HT, et al. *memo*. 2020;13:27-31.

Selection algorithm for patients with DLBCL in clinical routine: Austrian CAR-T Cell Network[1]



2019–2022

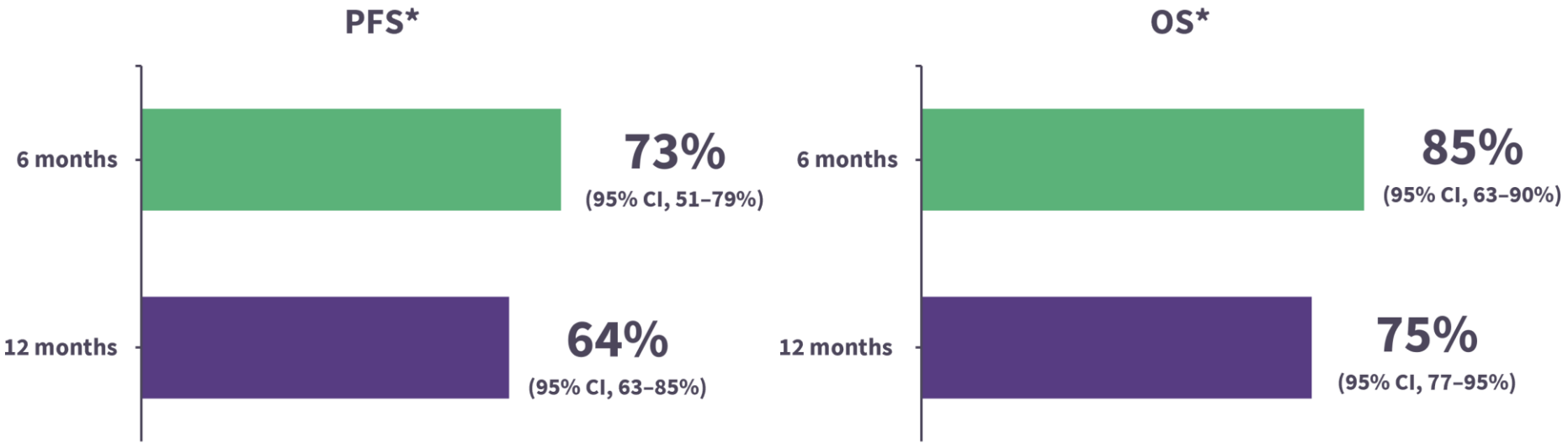
Major changes to the algorithm from 2022 onwards

- CAR T given in second line
- Less stringent for CNS manifestations
- Less stringent in general

alloSCT, allogeneic stem cell transplant; autoSCT, autologous stem cell transplant; CAR, chimeric antigen receptor; DLBCL, diffuse large B-cell lymphoma; PMBCL, primary mediastinal B-cell lymphoma; R/R, relapsed/refractory; SCT, stem cell transplant; tFL, transformed follicular lymphoma.

1. Greinix HT, et al. *memo*. 2020;13:27-31.

Probability of OS and PFS of patients with R/R LBCL infused with commercial CAR-T compounds[1]



CAR, chimeric antigen receptor; CI, confidence interval; LBCL, large B-cell lymphoma; OS, overall survival; PFS, progression-free survival; R/R, relapsed/refractory.
*Data from 65 patients treated with axicabtagene ciloleucel or tisagenlecleucel.

1. Rudzki CJ. Poster #2964. EBMT-EHA 5th European CART-cell Meeting; Feb 9, 2023; Rotterdam, NL.

Conclusions

- Special populations can be included
- Sequencing has changed to earlier CAR T-cell therapy use (first-line in high-risk DLBCL not in CCR, second-line)
- Secondary CNS lymphoma can be successfully treated, preferably in CR, but this is not mandatory (Keppra prohylaxis)
- CAR T-cell therapy preferred to ASCT—CR not required

ASCT, autologous stem cell transplant; CAR, chimeric antigen receptor; CCR, clinical complete response; CNS, central nervous system; CR, complete response; DLBCL, diffuse large B-cell lymphoma.

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