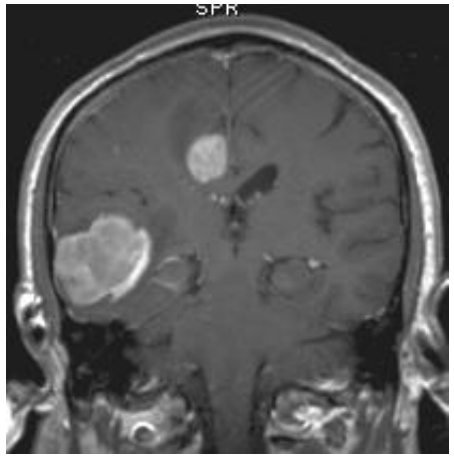
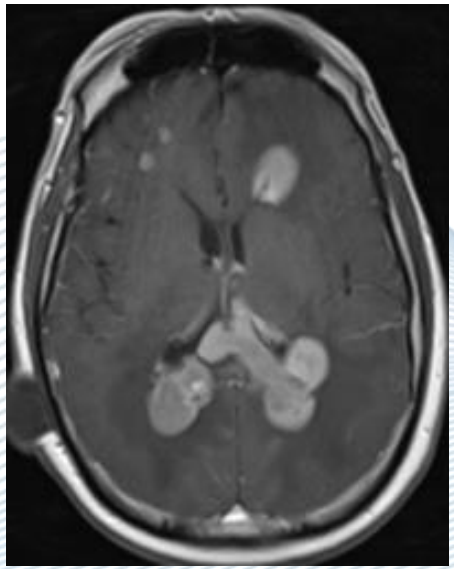
Primary CNS Lymphoma

Standard of Care and New Strategies

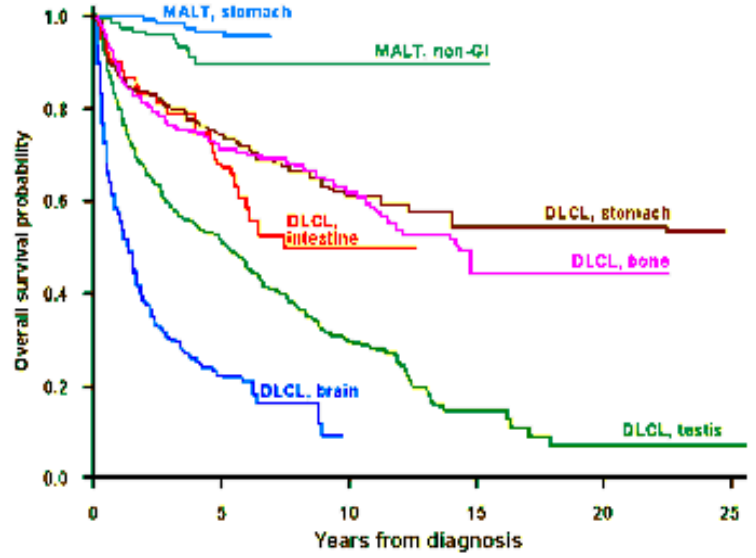
Andrés J. M. Ferreri
IRCCS San Raffaele Scientific Institute, Milano, Italy
Università Vita-Salute San Raffaele, Milano, Italy

PCNSL: DIFFICULTIES AND SOLUTIONS

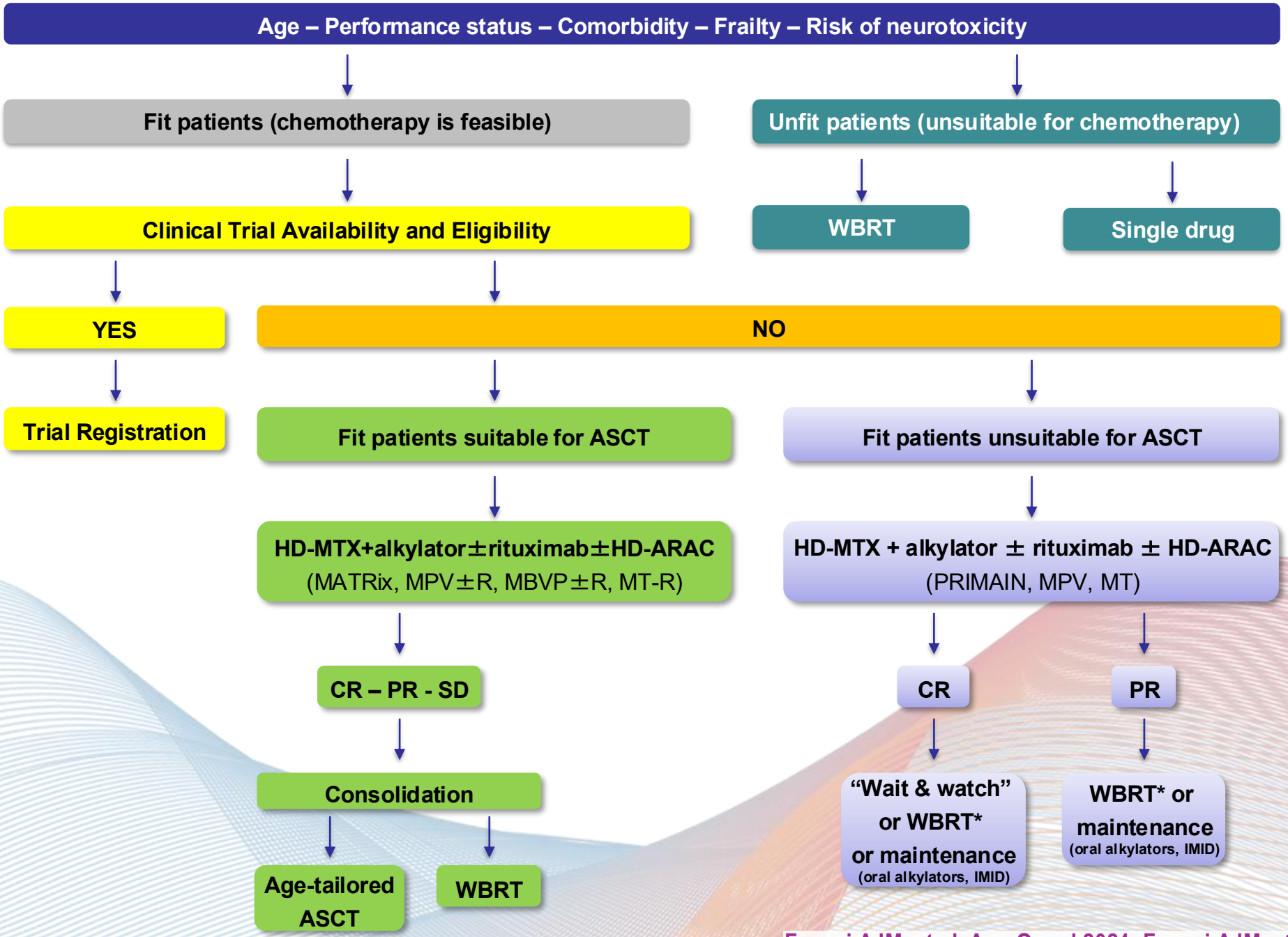




- High proportion of elderly pts (median age 68 ys, range 18-85)
- Poor PS at presentation (ECOG score ≥2 in 65% of pts)
- Biopsy not performed/or delayed
- Delayed diagnosis/Initiation of therapy
- Palliative treatment considered
- Consensus regarding treatment options lacking
- Few referral centers
- Pts can not be/are not referred to other centers
- **Broad consensus among multidisciplinary experts**
- **Improvement of time to diagnosis**
- **Recommendations for different patient subgroups**

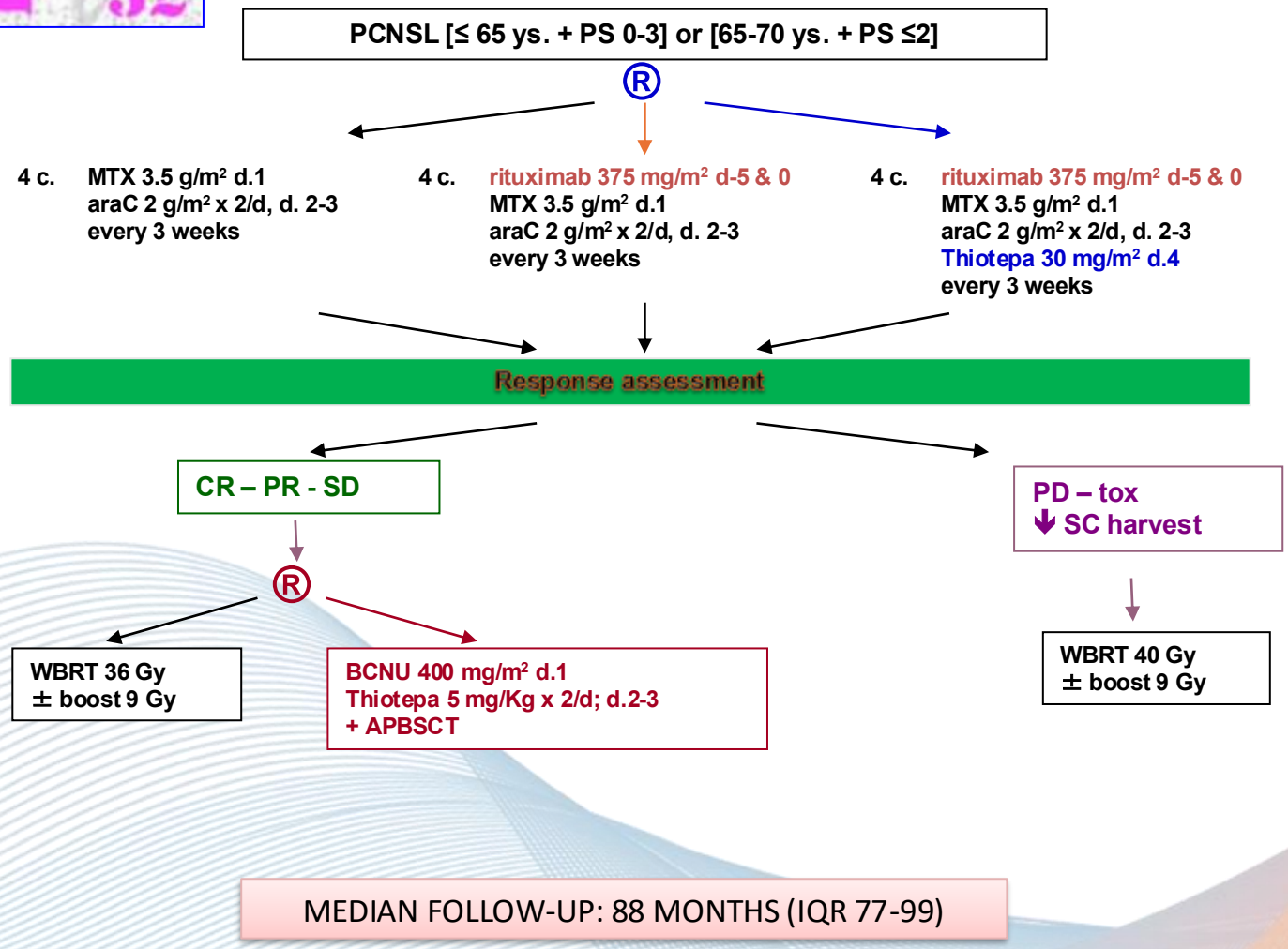


Ferreri AJM, et al. Nature Rev Dis Primer 2023

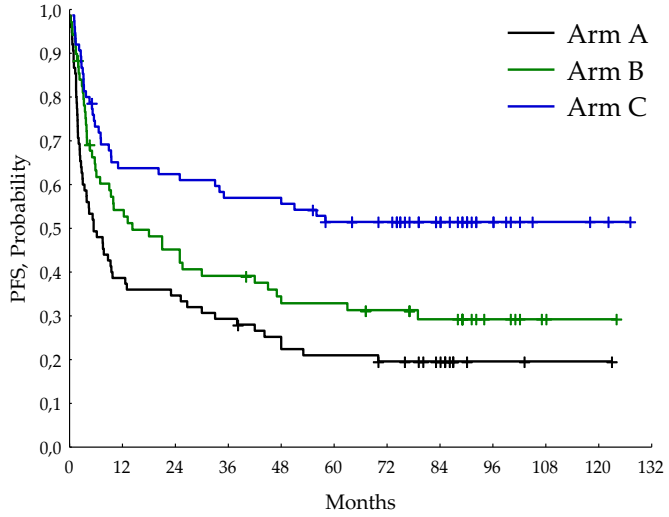


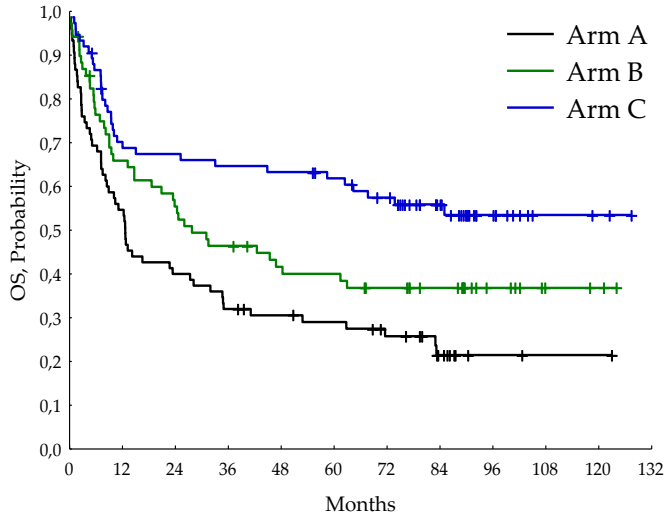
Ferreri AJM, et al. Ann Oncol 2024; Ferreri AJM, et al. Hemasphere 2024

The IELSG #32 trial: MATRix efficacy



MEDIAN FOLLOW-UP: 88 MONTHS (IQR 77-99)





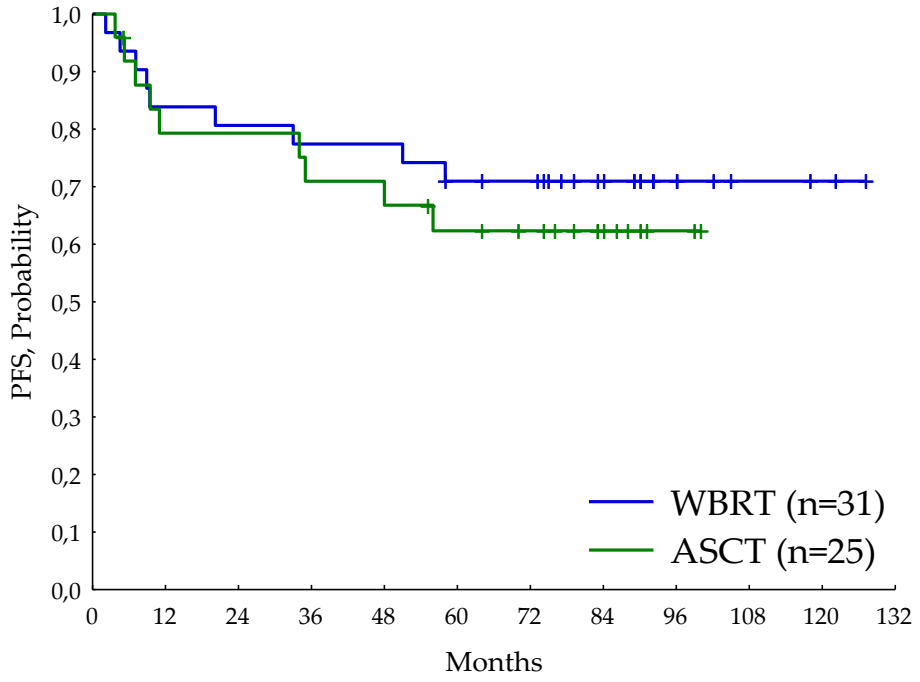
Ferreri AJM, et al. Leukemia 2022

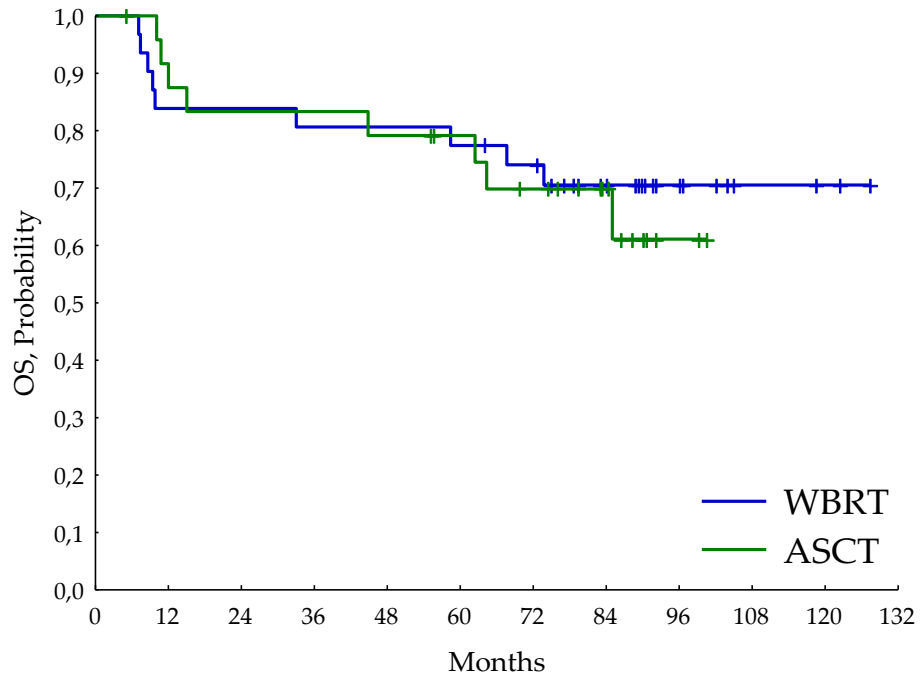
Recommendations: Induction Therapy

- Induction including methotrexate (MTX) at a minimum dose of 3 g/m^2 delivered in a 3-h infusion [I, A].
- Combinations of HD-MTX with other drugs that cross the BBB and have been tested in prospective (preferably randomised) trials are recommended [I, A].
- The benefit of adding rituximab to HD-MTX-based polychemo remains unclear. The balance between tolerability and efficacy should be discussed with patients and their carers [II, B].
- Intrathecal Chemo is not recommended, except for pts with CSF disease who are unable to receive MTX at 3 g/m^2 or for pts with persistence of CSF/meningeal disease at the EoT [III, D].
- Intravitreal Chemo is not recommended, except for pts with persistent intraocular lymphoma at the EoT [III, D].
- SOC for patients unfit for HD-MTX-based chemo? Valid (but incompletely investigated) palliative options: upfront WBRT [III, B], corticosteroids, oral alkylating agents, BTK inhibitors, and immunomodulators [V, C]

CONSOLIDATION AFTER MATRIX

MEDIAN FOLLOW-UP: 88 MONTHS (IQR 77-99)





Patients treated with MATRIX + consolidation had a 7-year OS of 70%, without a difference between WBRT and ASCT.

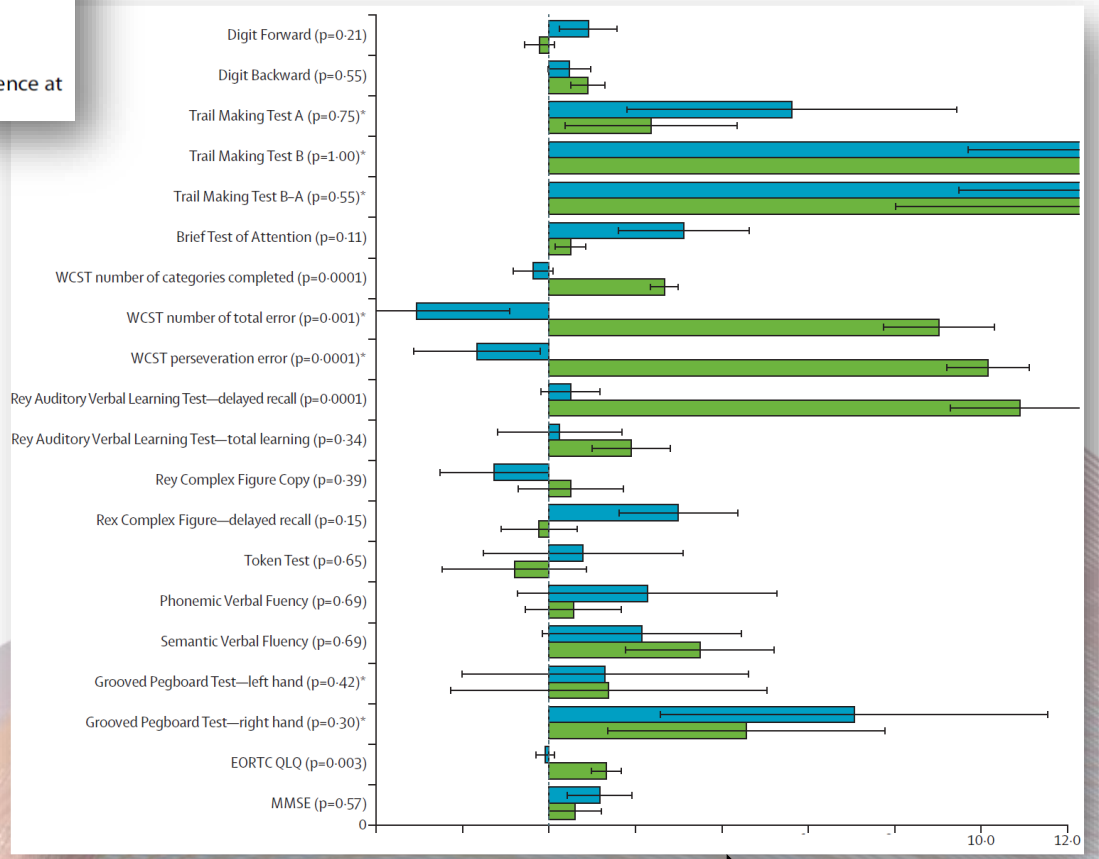
IELSG32 Trial: Long-term Toxicity

Table 1. Disease- and treatment-related events according to induction and consolidation arm (per-protocol bases)

	Total	Arm A ($n=75$)	Arm B ($n=69$)	Arm C ($n=75$)	WBRT[a] ($n=70$)	ASCT[a] ($n=60$)	Others[b] ($n=74$)
Toxic deaths (1st line)	15	7 (9%)	3 (4%)	3 (4%)	0 (0%)	2 (2%)	-
Progressive disease	66	26 (35%)	18 (26%)	13 (17%)	4 (4%)	2 (2%)	3 (4%)
Relapse after response	51	19 (25%)	17 (25%)	15 (20%)	22 (31%)	19 (32%)	10 (14%)
Salvage therapy	75	30 (40%)	22 (32%)	23 (31%)	15 (21%)	18 (30%)	42 (57%)
Second tumors[c]	8	1/38 (3%)	2/47 (4%)	5/59 (8%)	5/67 (7%)	3 (5%)	0 (0%)
Deaths during/after salvage[d]	7	4 (13%)	0 (0%)	3 (13%)	2 (13%)	2 (11%)	3 (4%)
Deaths of lymphoma	96	43 (57%)	32 (46%)	21 (28%)	19 (27%)	16 (27%)	61 (82%)
Deaths in relapse-free patients[e]	14	2/17 (12%)	6/28 (21%)	6/42 (14%)	9/44 (20%)	3/37 (8%)	2/6 (33%)

[a]Actually delivered consolidation regardless of random allocation.
[b]Denominator: all patients who did not receive WBRT or ASCT; patients died of toxicity during first line were excluded.
[c]Denominator: patients who completed the first-line treatment.
[d]Cause of deaths: bacterial septicemia (2), pneumonia, varicella-zoster virus encephalitis, stroke, brain aspergillosis, unknown.
[e]Cause of deaths: infections (4), cognitive decline (3), second tumor (2), car accident (1), unknown (4). Denominator: patients without lymphoma recurrence at the last visit.

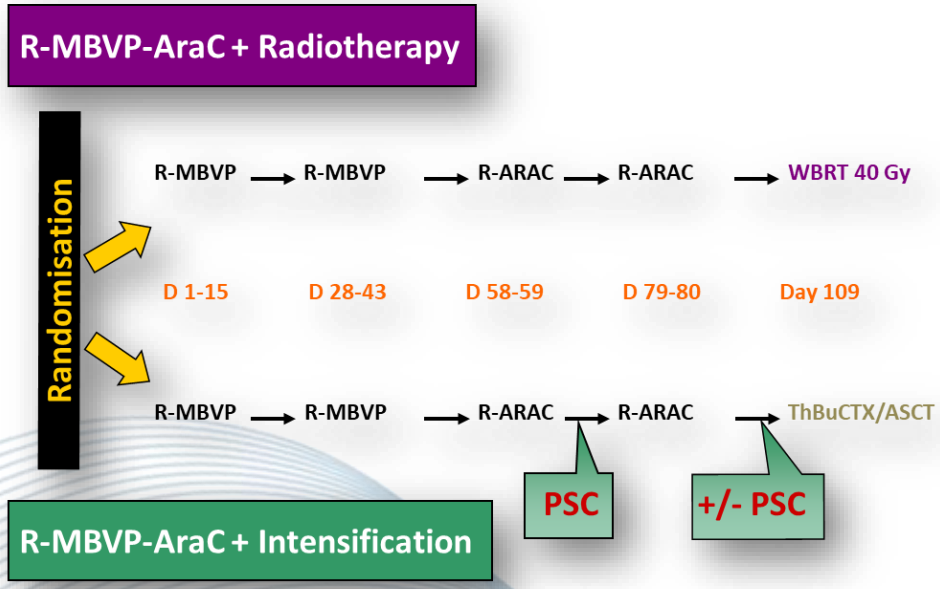
WBRT
ASCT

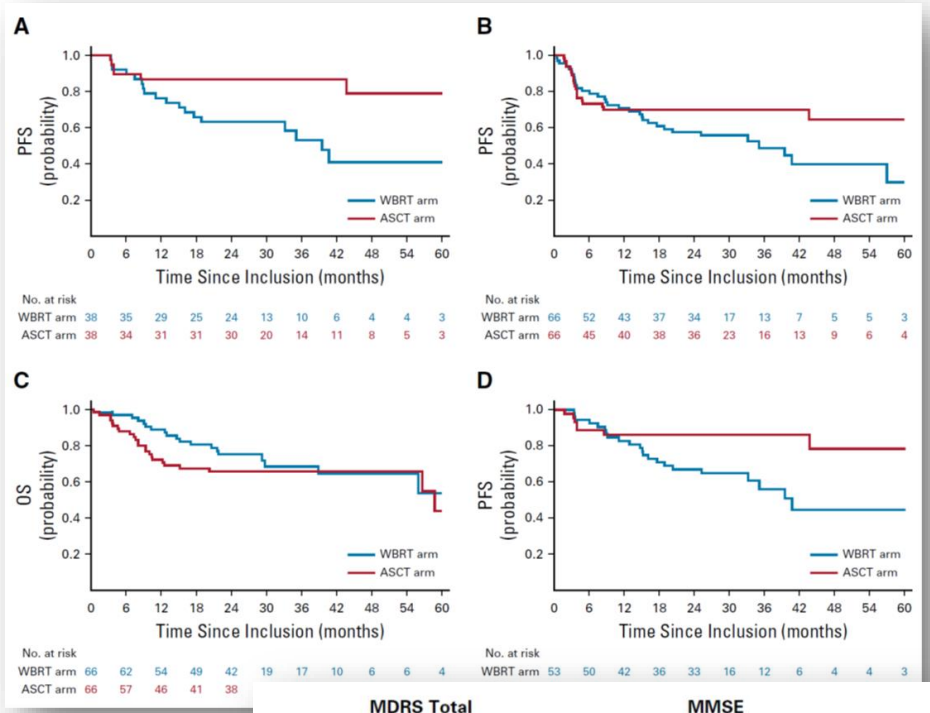


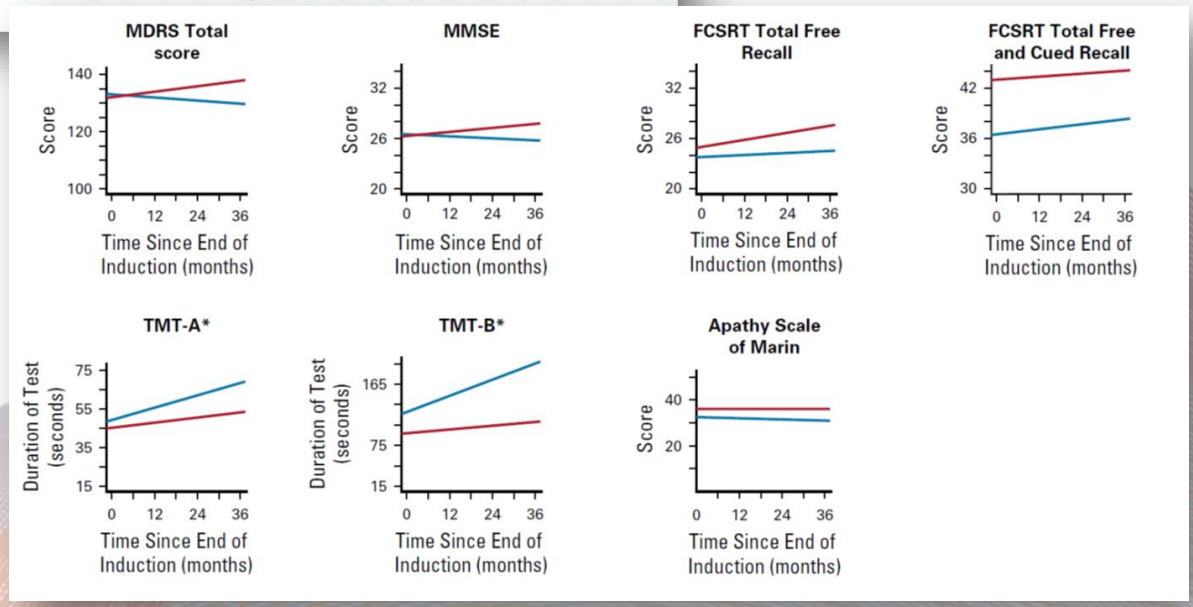
Improvement

Ferreri AJM, et al. Leukemia 2022

PRECIS Trial

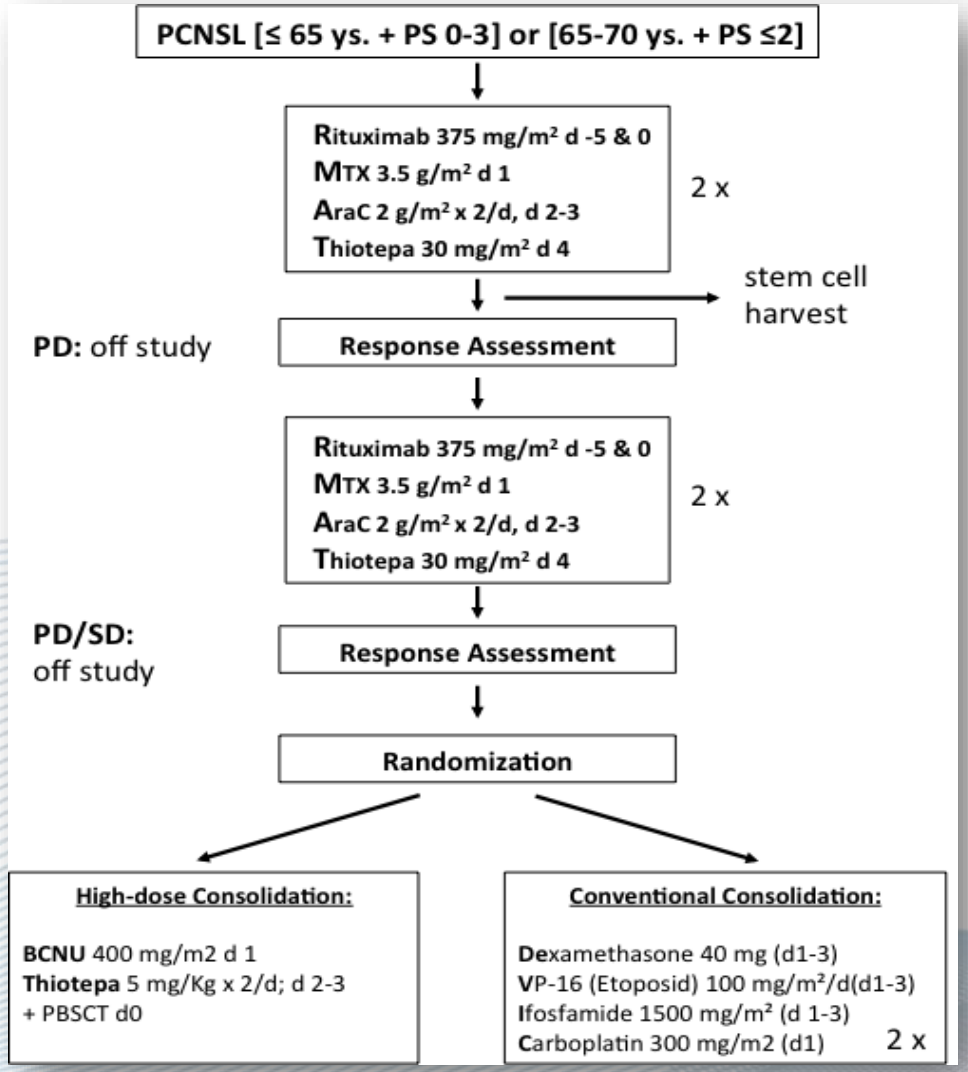


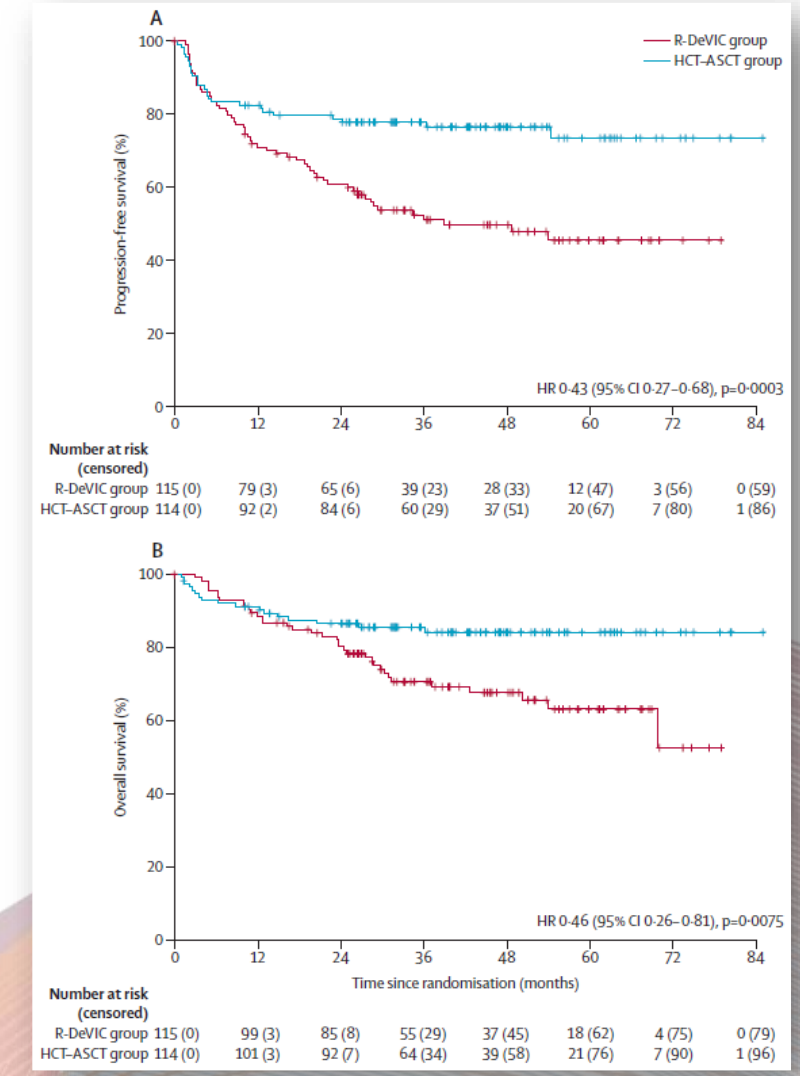




Houillier C, et al. JCO 2019

THIOTEPA-CONDITIONED ASCT IS SOC





Illerhaus G, Ferreri AJM, et al. The Lancet 2026

ASCT in the elderly: the MARTA trial

Induction

Rituximab 375 mg/m² (d 0, 4)
Methotrexate 3.5 g/m² (d 1)
Cytarabine 2x2 g/m²/d (d 2-3) (q3w)

SC harvest

Rituximab 375 mg/m² (d 0, 4)
Methotrexate 3.5 g/m² (d 1)
Cytarabine 2x2 g/m²/d (d 2-3)

Response Assessment (MRI)

PD: off study

Consolidation

Rituximab 375 mg/m2 (d -8)
Busulfan 3.2 mg/kg/d (d -7-(-6))
Thiotepa 5 mg/kg/d (d -5-(-4))
ASCT (d 0)

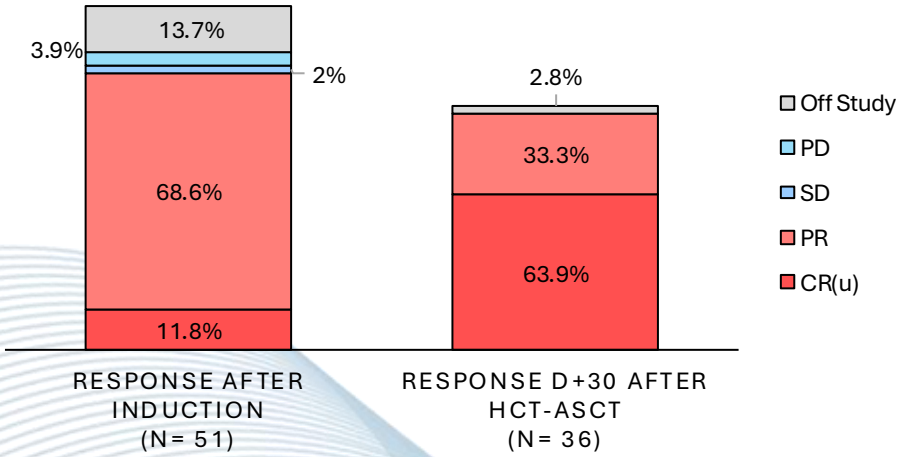
Total duration of treatment: ~ 10 weeks

Schorb et al. Lancet Haematol 2024

MARTA trial: outcome

median follow-up: 23 months

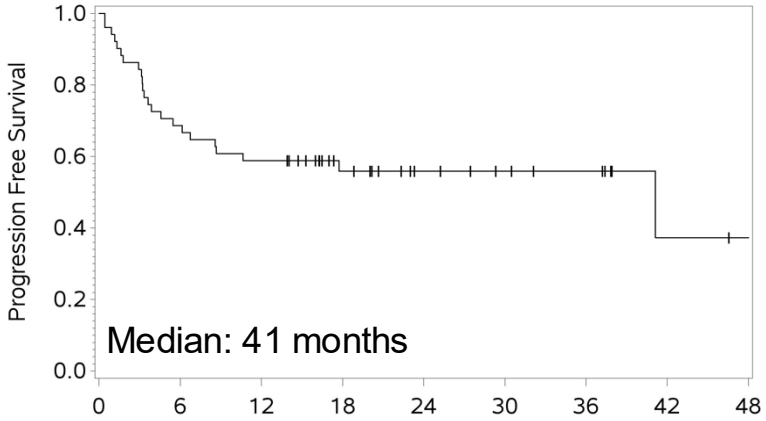
Median age 72 yo (65-80)
70-74: 35%
75-80: 35%

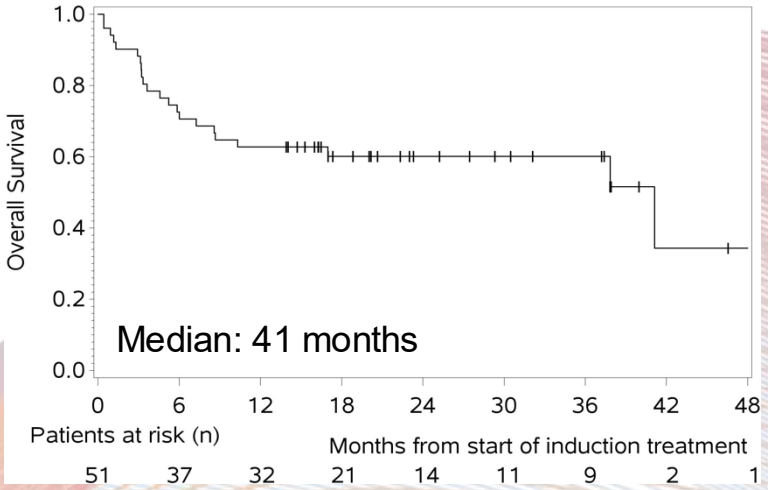


Treatment related deaths	
Induction	Consolidation
3.7%	2.7%

71% received ASCT

Intention-to-Treat





Recommendations: Consolidation WBRT

- Consolidation WBRT at a dose of 36-40 Gy/20 fractions for young patients who are not suitable candidates for ASCT [I, A].

- Consolidation WBRT at a dose of 36-40 Gy should be avoided or deferred in elderly pts [I, D].

- Reduced-dose WBRT (23.4 Gy) is an option for patients with responsive disease after induction chemo, but the longer-term effects on cognitive function remain to be defined, especially in elderly patients [III, B].

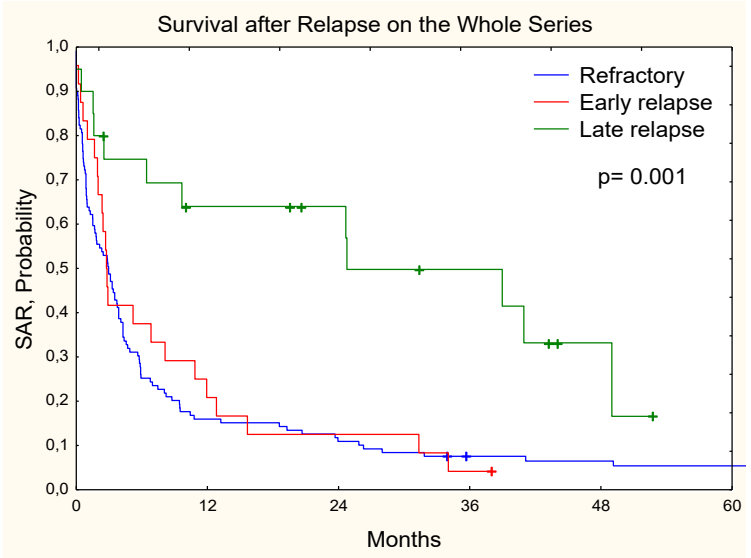
Prognosis of R/R-PCNSL: IELSG Randomized Trials

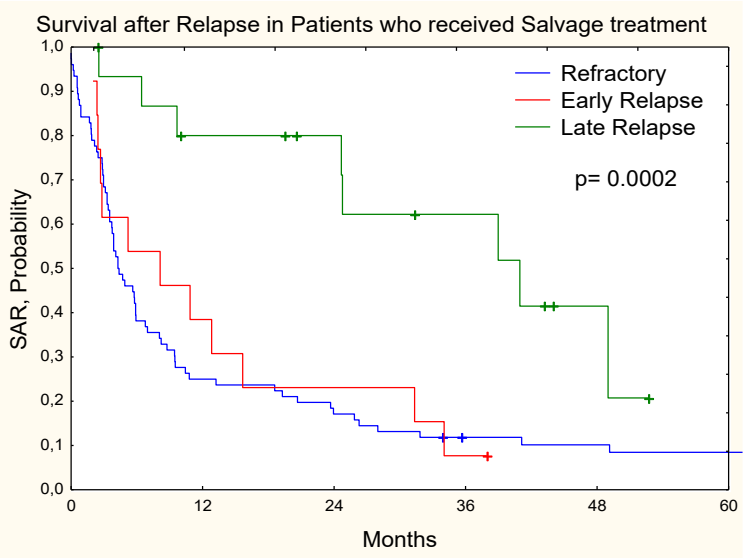
Mortality of rrPCNSL is ≈90%

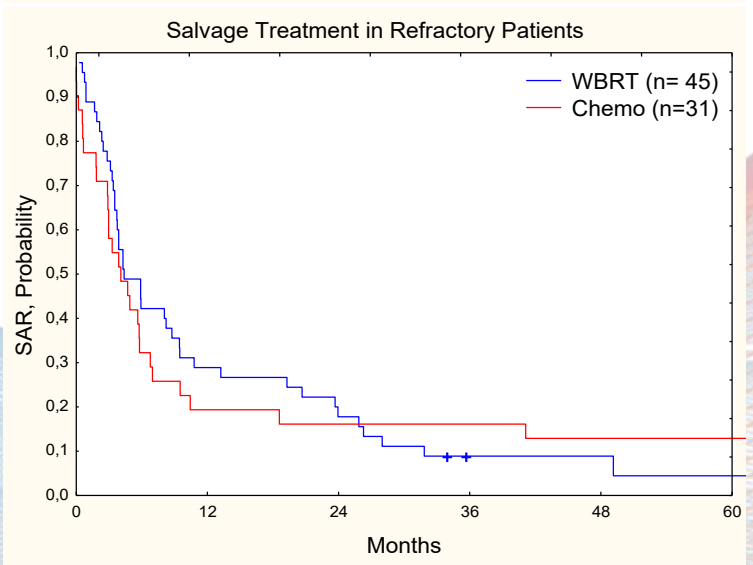
1/3 are not candidates for salvage.

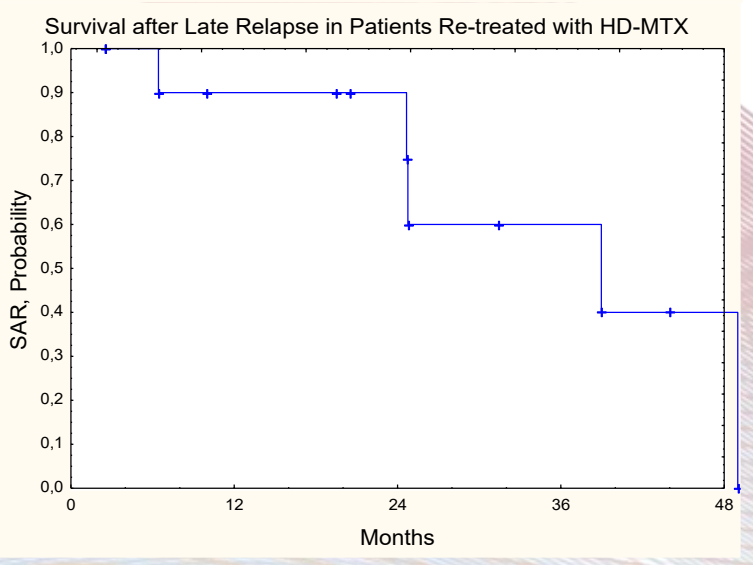
Efficacy of salvage therapy appears to be independent of the 1L.

Ferreri AJM, et al. ASH 2021

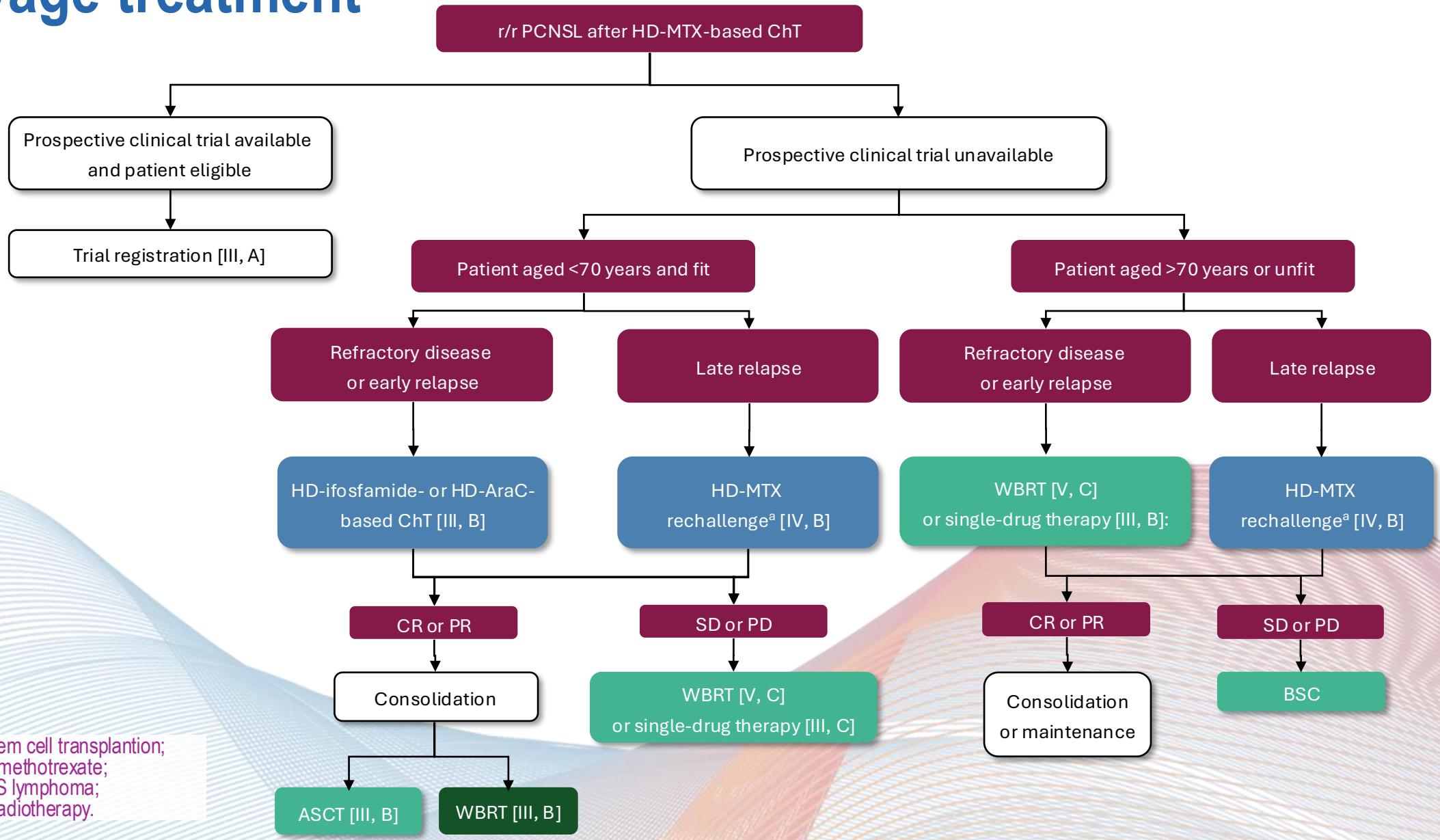






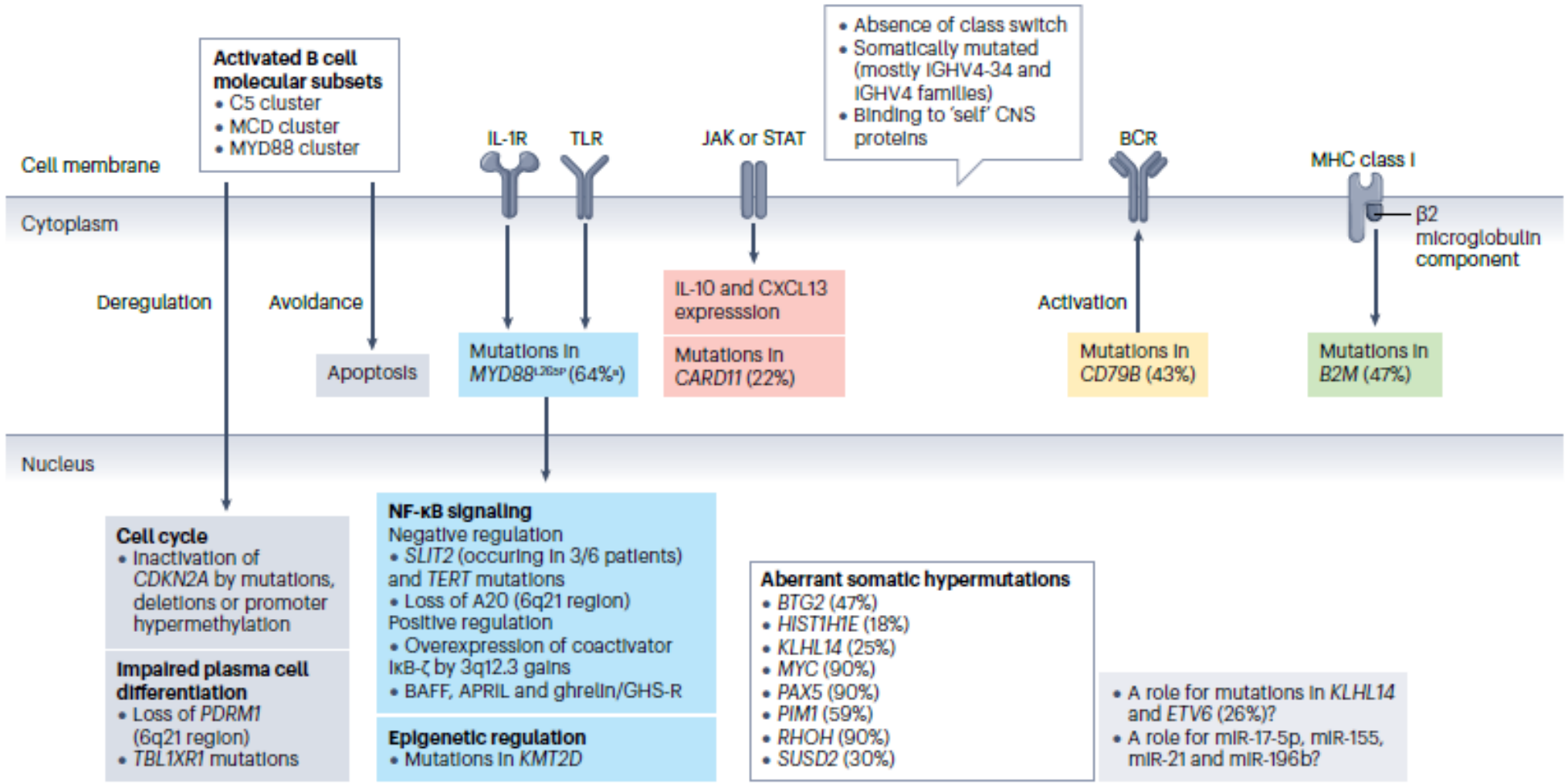


Salvage treatment



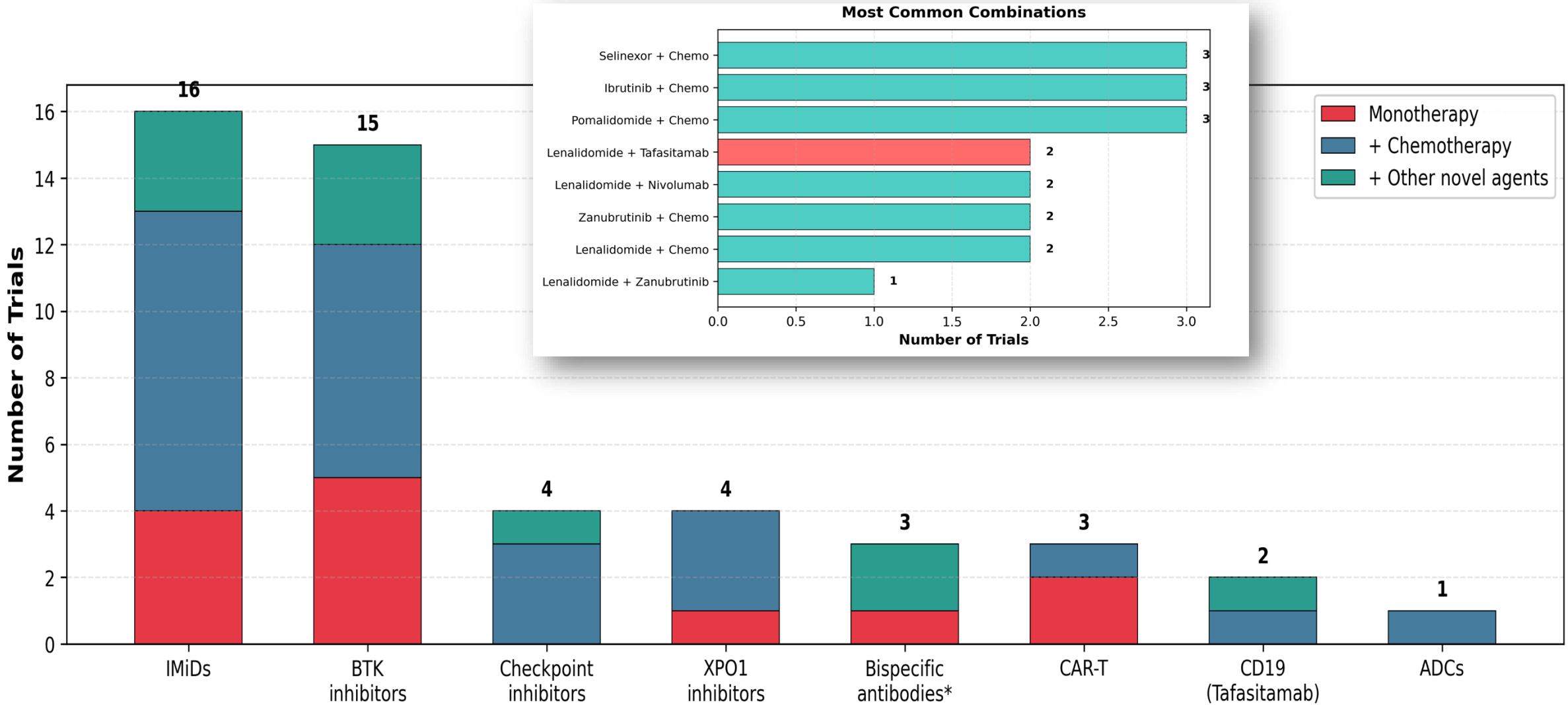
ASCT, autologous stem cell transplantion;
HD-MTX, high-dose methotrexate;
PCNSL, primary CNS lymphoma;
WBRT, whole brain radiotherapy.

Signaling Pathways



Ferreri A.J.M., *et al. Nat Rev Dis Pirmers* 2023

Novel Agents in CNS Lymphoma Clinical Trials (n=38 CNS-specific trials)



Clinicaltrials.gov: searched on 14/10/25

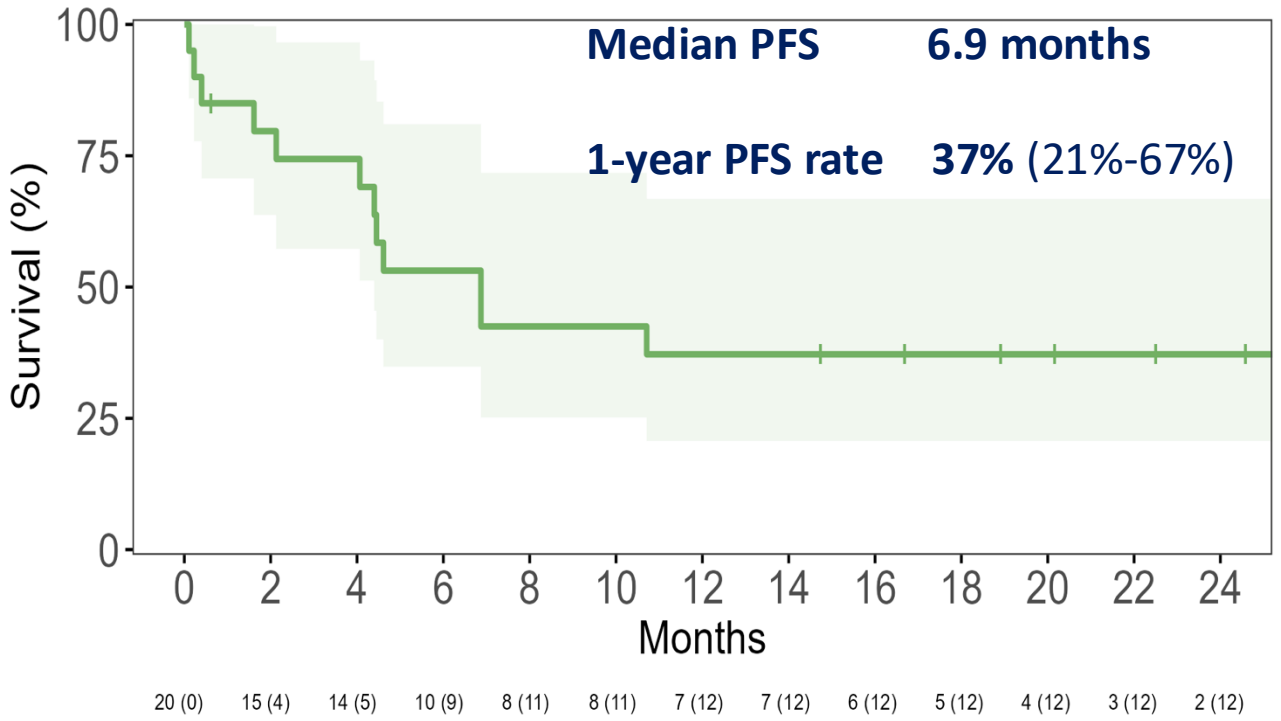
With thanks to Dr Benjamin Kasenda

Summary of BTKi and iMiD data in rrPCNSL

	Drug	Study	N	Results	Ref
iMiDs	Lenalidomide 25 mg + Rituximab	Phase II	50	Best ORR = 67 % ORR end of induction = 36 % median PFS = 7 months	Ghesquières *2019*
	Pomalidomide 3, 5, 7, 10 mg + Dex	Phase Ib/II	25	ORR = 48 % median PFS = 5 months	Tun *2018*
IBTK	Ibrutinib 560 mg/840 mg	Phase I Phase II	13 PCNSL 31 SCNSL	ORR = 70 % median PFS = 4.6 months	Grommes *2017*
	Ibrutinib 560 mg	Phase II	52	ORR = 52 % @ 2 months median PFS = 4.8 months	Soussain *2019*
	Tirabrutinib	Phase I/II	44	ORR: 64% median PFS = 2.9 months	Narita 2021

Zanubrutinib monotherapy in rrPCNSL – CR/CRu at 8 weeks

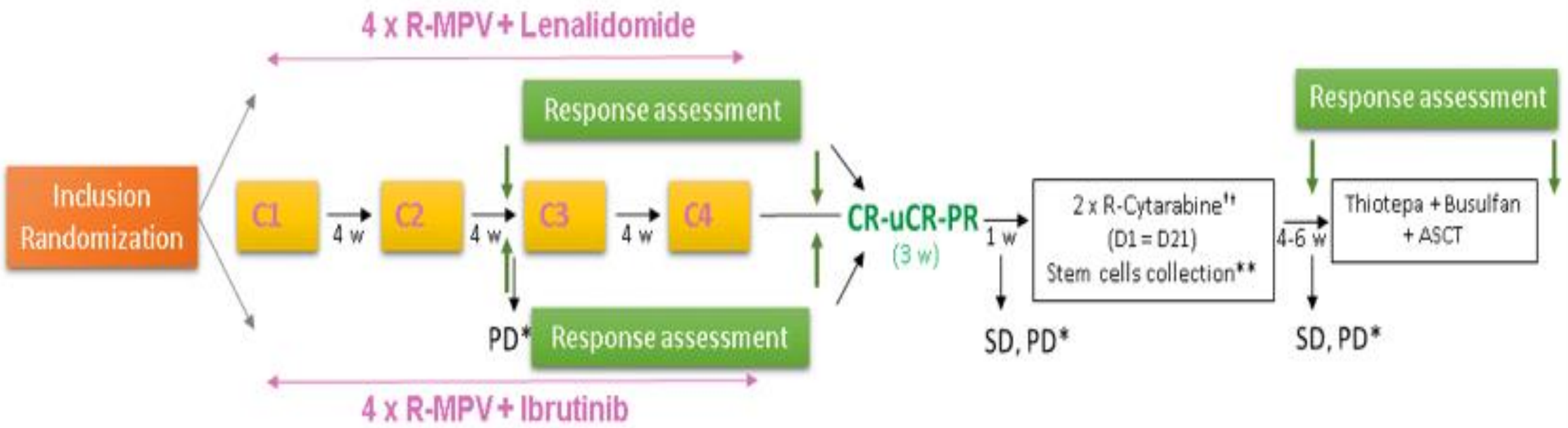
- ORR by IRC = 55% (95% CI 52%, 80%)
- CRR by IRC = 35% (95% CI 29%, 59%)



Event type	Patients (n=20)	SAE (n=10)
Number of SAEs	7 (35%)	10
Infections & infestations	3 (15%)	5 (50%)
Lung infection	1 (5%)	1 (10%)
COVID	2 (10%)	2 (20%)
Sepsis	1 (5%)	1 (10%)
Other (NOS)	1 (5%)	1 (10%)
Nervous System Disorders	3 (15%)	3 (30%)
Seizure	2 (10%)	2 (20%)
Hydrocephalus	1 (5%)	1 (10%)
Gastrointestinal disorders	2 (10%)	2 (20%)
Diarrhoea	1 (5%)	1 (10%)
Vomiting	1 (5%)	1 (10%)

Fox CP *et al* Abstract 087 ICML 2025

Lenalidomide or Ibrutinib in combination **with** Rituximab-Methotrexate Procarbazine Vincristine (**R-MPV**) as a targeted induction treatment for patients aged 18 to 65 with a newly diagnosed Primary Central Nervous System Lymphoma (PCNSL): Phase IB/II non comparative multicentric study

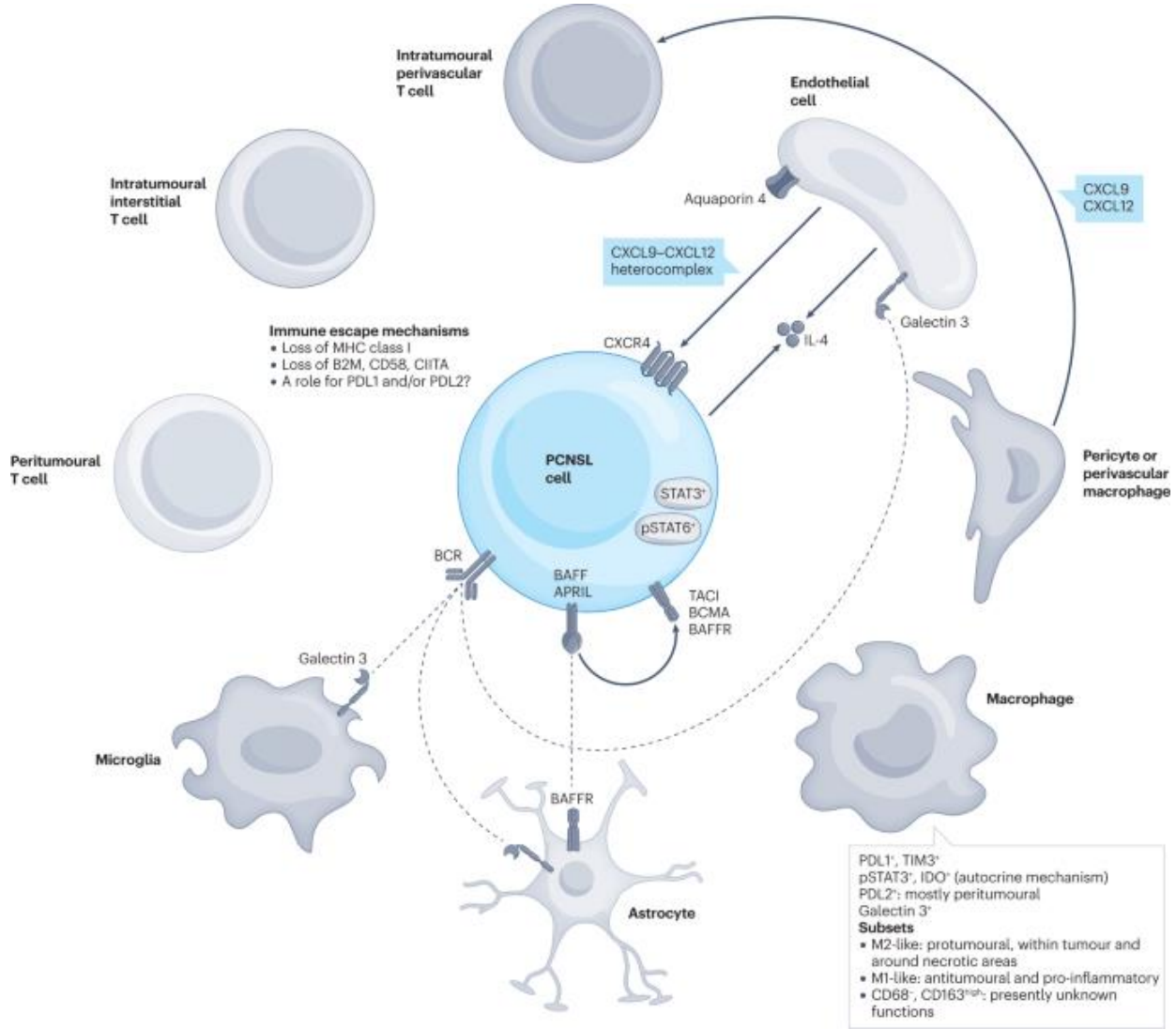


- Phase II primary endpoint: CR/CRu rate (by central review) after induction phase

  (A'Hern: P0 = 45%; P1 = 65%, alpha = 8%; beta = 9%)
- n=92 patients from 20 centers randomized: March 2022-August 2024

With thanks to Dr Carole Soussain

Biological and molecular properties of the microenvironment



Ferreri, A.J.M., *et al. Nat Rev Dis Pirmers* 2023

ICI: much promise but little evidence of activity

	CheckMate 647	Acsé trial
clinicaltrials.gov	NCT02857426	NCT02779101
Phase Trial	BMS global registration study	Phase II, single Institution
Sites	International	Medical University of Vienna
Sample size	47	50
Results	Final	Preliminary
Drug	Nivolumab	Pembrolizumab
ORR (%)	6	26
Median PFS (months)	1,4	2,6
SAE	6 deaths due to infections or bleeding	Not reported

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GLA study NCT05583071- a pilot single-arm trial

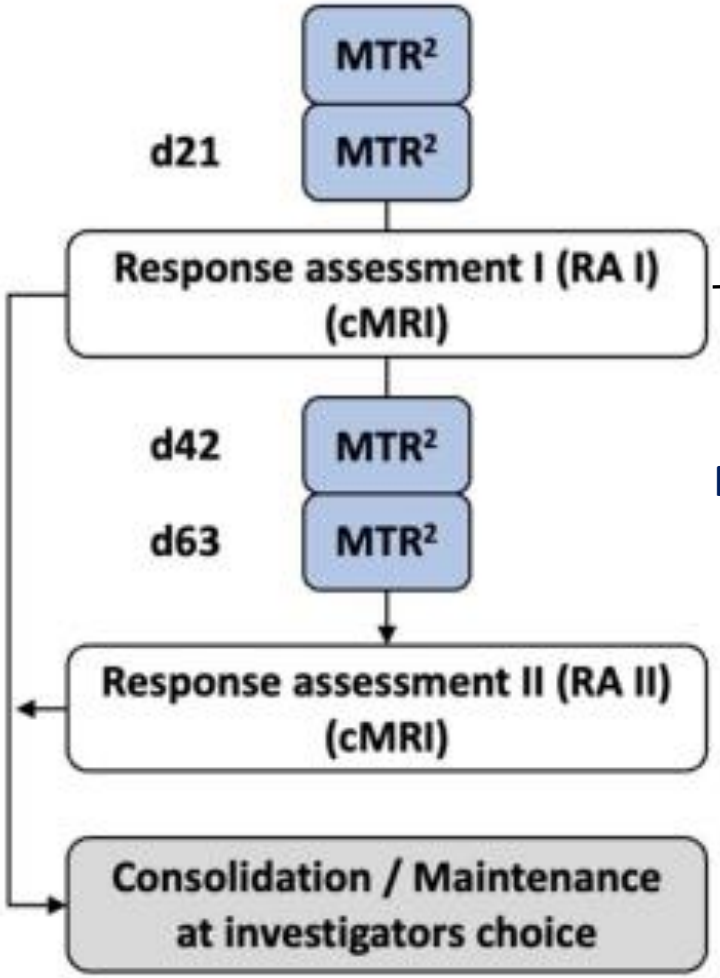
MTR²

Rituximab:
375 mg/m² d-1, d5

Tafasitamab-cxic (Monjuvi®):
12 mg/kg body weight d-1, d5

Methotrexate:
3500 mg/m² d1

Lenalidomide (Revlimid®):
20 mg/day d4-17 cycle 1
25 mg/day d4-17 subsequent cycles



Primary endpoint CRR ≥2 cycles

With thanks to Dr. Gerald Illerhaus

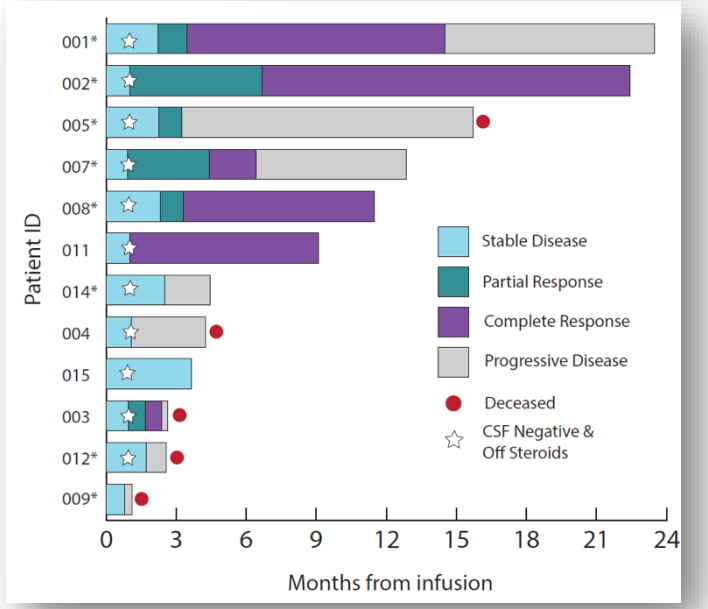
CAR T-cells: A selective therapy in PCNSL

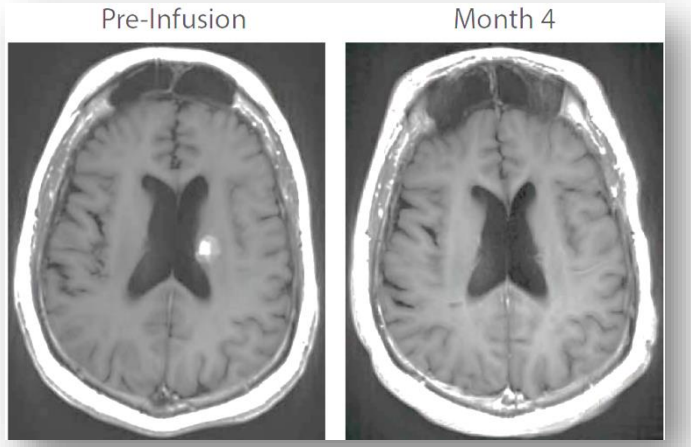
Study	Time	Median follow-up	Patients (n)	ORR (%)	CR (%)	OS	PFS	CRS (%)	CRS≥3 (%)	Median CRS onset	ICANS (%)	ICANS≥3 (%)	Median ICANS onset
Yu et al. (73)	2024	316d	22	90.9	68.2	NR***	NR	72.7	4.5	4d	36.4	4.5	8d
Mercadal et al. (74)	2024	26m	24	61	48	–	–	66.7	0	3.5d	33	8	6d
Frigault et al. (75)	2022	12.2m*	12	58.3	50	–	–	58.3	0	4d**	50	8	5d
Choquet et al. (41)	2024	20.8m	25	56	8	21.2m (median)	8.4m (median)	92	–	1d	68	20	1d
Karschnia et al. (76)	2023	12m	18	39	33	–	3.5m (median)	–	–	–	44.4	16.7	2.5d
Lacan et al. (77)	2023	12m	13	38	31	20m (median)	3m (median)	–	–	–	–	–	–

Anti-CD19 CAR-T for PCNSL: First prospective trial

Median age (range) – yr	63, (34-81)
Male:Female	7:5
Infused/Enrolled	12/13
ECOG performance status – no %	
• 0-1	7/12
• 2+	5/12
Disease location	
• Parenchymal	11/12
• Leptomeningeal enhancement/CSF+	2/12
Cell of origin	
• Germinal center B-cell type	1/12
• Non-germinal center B-cell type	11/12
Median no. of previous lines of anti-neoplastic therapy, (range)	4, (2-9)
Prior methotrexate-based regimen	
• Yes	12/12
• No	0/12
Prior thiotepa based ASCT	
• Yes	3/12
• No	9/12
BTKi refractory	
• Yes	12/12
• No	0/12
IMiD refractory$	
• Yes	4/12
• No	8/12
TEDDI-R refractory	
• **Yes**	6/12
• **No**	6/12
Prior radiotherapy	
• Yes	4/12
• No	8/12
Bridging therapy (including high dose steroids)	
• Yes	12/12
• No	0/12
Median Vein-to-Vein Time (days)	33, (27-37)

Cytokine release syndrome (CRS)$	
• Any CRS	7/12
• Grade 1	7/12
• Grade 2	-
• Grade 3	-
• Grade 4	-
Required tocilizumab	-
Median onset of CRS (day post infusion)	4
Median duration of CRS (day post infusion)	2
Immune Cell Associated Neurotoxicity Syndrome (ICANS)$	
• Any ICANS	6/12
• Grade 1	3/12
• Grade 2	2/12
• Grade 3	1/12
• Grade 4	-
Required corticosteroids	
• At time of infusion for disease control*	4/12
• Additional provided for ICANS following infusion	6/12
Median onset (day post infusion)	5
Median duration (day post infusion)	3





Frigault M, et al. Blood 2022

Received: 27 November 2023 | Revised: 24 February 2024 | Accepted: 26 March 2024
DOI: 10.1002/ajh.27316

RESEARCH ARTICLE

CAR T-cell therapy induces a high rate of prolonged remission in relapsed primary CNS lymphoma: Real-life results of the LOC network

Retrospective 27 PCNSL who had leukapheresis for CAR-T cells from the 3L:

- Median age: 68, median of 3 previous lines (ASCT in 14/27)

- 25 received CAR T-cells (tisa-cel 16, axi-cel 9)

Controls: *PCNSL treated with any treatment, at least in the third line and not eligible for ASCT*

Choquet et al. et al. Am J Hematol. (2024)

Bridging therapy	26 (96%)
Type of bridging therapy (CAR T-cell group) or treatment at studied relapse (control group)	
HD-MTX-based CT	7 (26%)
HD-AraC-based CT	3 (11%)
(R)-lenalidomide	2 (8%)
(R)-ibrutinib	5 (20%)
(R)-lenalidomide-ibrutinib	2 (8%)
(R)-ICE	3 (12%
(R)-temozolomide	2 (8%)
Anti PD1 as monotherapy	0
WBRT alone	0
Other CT regimens	2 (8%)
WBRT as consolidation	0

	CAR T-cell group	Control group
Response to bridging therapy (CAR T-cell group) or early response[a] to treatment at studied relapse (control group)		
Complete or partial response	14 (54%)	89 (41%)
Stable or progressive disease	12 (46%)	130 (59%)
Disease status at CAR T-cell infusion ($N = 25$)		
Complete response	2 (8%)	NA
Partial response	12 (48%)	
Stable disease	2 (8%)	
Progressive disease	9 (36%)	
Delay between leukapheresis and CAR T-cells infusion: median (range) (days)	41 (27–91)	NA

TABLE 2 Response to CAR T-cells.

Response	CR	PR	PD
At 1 month	8 (32%)	11 (44%)	6 (24%)[a]
At 3 months	14 (56%)	3 (12%)	8 (32%)
Best response	16 (64%)	4 (16%)	5 (20%)[a]
Best response in each CNS compartment			
Brain	12 (60%)	4 (20%)	4 (20%)
CSF	7 (87%)	0	1 (13%)
Eye	2 (67%)	0	1 (33%)
Best response according to the type of CAR T-cells			
Axi-cel	8 (89%)	1 (11%)	0 (0%)
Tisa-cel	8 (50%)	3 (19%)	5 (31%)
Best response according to the disease status at CAR T-cell injection			
CR or PR	12 (86%)	1 (7%)	1 (7%)
SD or PD	4 (36%)	3 (27%)	4 (36%)

[a]One patient was in progression at 1 month, but then achieved PR without any further treatment and maintained this PR during several months. The progression at 1 month probably corresponded to a flare effect (already described in Alcantara et al, Blood 2022).

Received: 27 November 2023 | Revised: 24 February 2024 | Accepted: 26 March 2024
DOI: 10.1002/ajh.27316

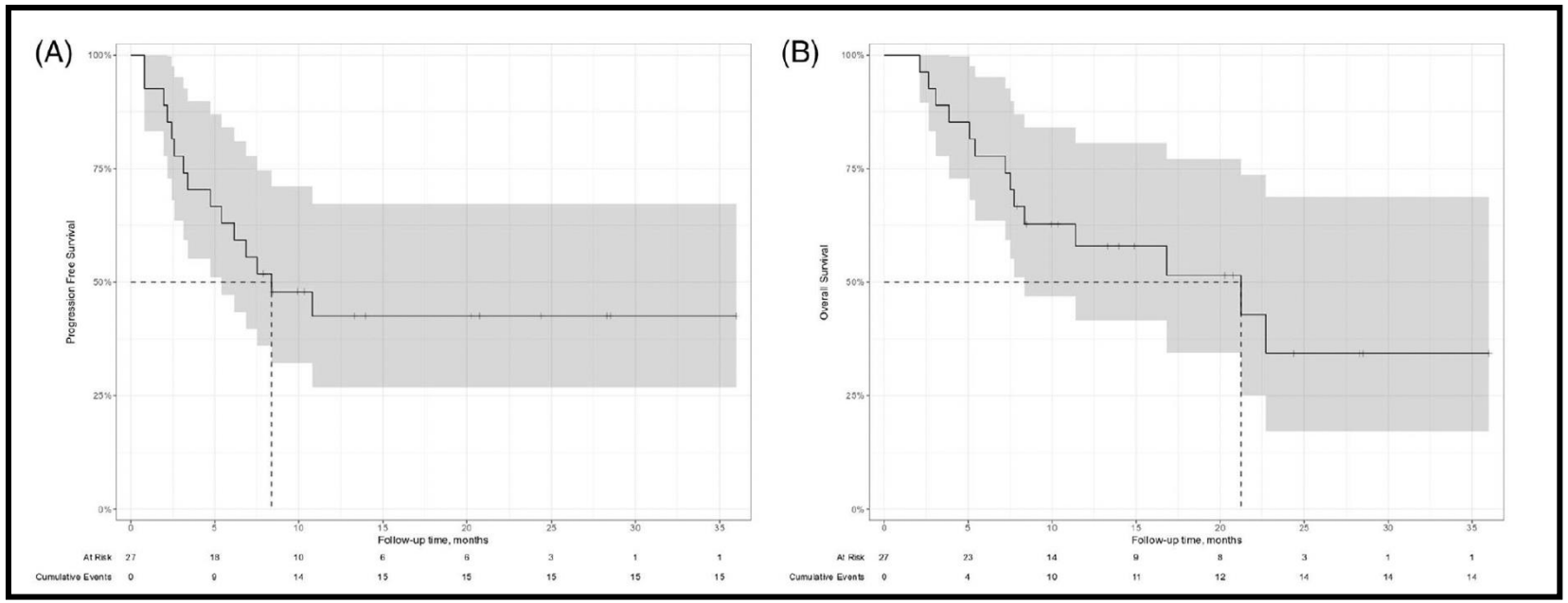
RESEARCH ARTICLE

AJH WILEY

CAR T-cell therapy induces a high rate of prolonged remission in relapsed primary CNS lymphoma: Real-life results of the LOC network

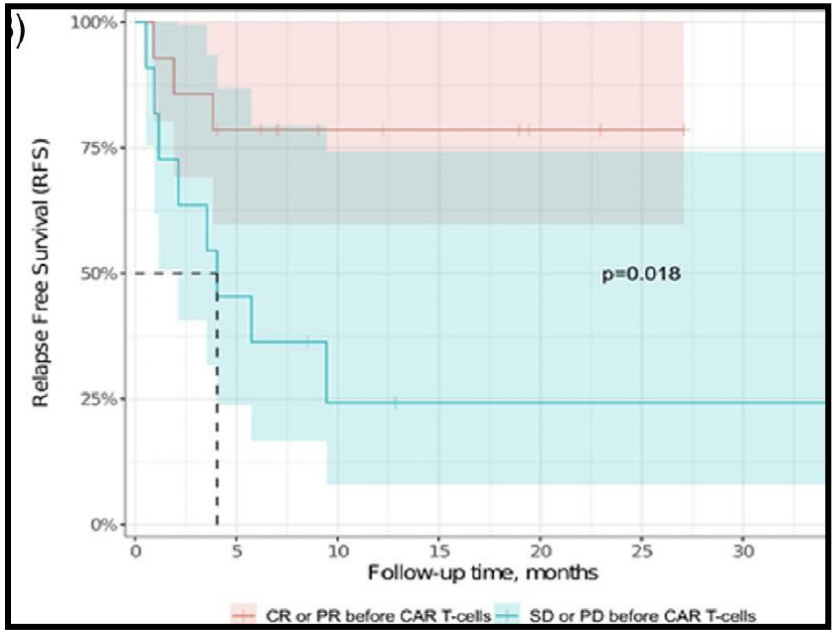
Responses and Outcomes

Choquet et al. et al. Am J Hematol. (2024)



From leukapheresis	
Median PFS	8.4 mo [5.4-NR]
6 mo PFS	63% [47–84]
12 mo PFS	43% [27–67]

From leukapheresis	
Median OS	21.2 mo [8.4-NR]
6 mo OS	77% [64–79]
12 mo OS	58% [242–81]
18 mo OS	51% [34–77]



Received: 27 November 2023 | Revised: 24 February 2024 | Accepted: 26 March 2024
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RESEARCH ARTICLE

AJH WILEY

CAR T-cell therapy induces a high rate of prolonged remission in relapsed primary CNS lymphoma: Real-life results of the LOC network

Safety

Choquet et al. et al. Am J Hematol. (2024)

Three patients experienced grade 4 neurotoxicity with a neurological deterioration lasting more than 3 months.

1 of them died from neurotoxicity
1 patient fully recovered 6 months after CAR T-cell infusion
1 patient was still experiencing neurological recovery 9 months after CAR T-cell infusion.

	CRS	ICANS
Any Grade	23/25 (93%)	17/25 (68%) Axi-cel 8/9 (89%) Tisa-cel 9/16 (56%)
Grade 3-4	2 (8%)	5/25 (20%) Axi-cel 2/9 (22%) Tisa-cel 3/16 (19%)
Median Time to Onset	1 day (0–5)	5 days (1–9)
Median Time to Resolution	4 days (2–9)	6 days (1–270+)

A Pilot Study of Axicabtagene Ciloleucel in Relapsed/Refractory Primary and Secondary Central Nervous System Lymphomas (PCNSL & SCNSL)

L Nayak, UN Chukwueke, S Hogan, C Meehan, R Redd, E Lee, AI Kim, LN Gonzalez Castro, JR McFaline Figueroa, IC Arrillaga-Romany, M Murakami, R Huang, U Gerdemann, J Kaminski, D Mao, S Filosto, M Mattie, S Poddar, P Armand, LS Kean, CA Jacobson

Dana-Farber Cancer Institute; Boston Children's Hospital; Mass General Brigham; Kite, A Gilead Company

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Date of preparation: June 2024

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Axi-Cel in CNSL – Patients and Methods

Nayak et al. ACO (2024) – Abstract #2006

Patient Characteristics		N=18 (%)
Gender	Men Women	10 (56) 8 (44)
Age (years)	Median (range)	62 (33-81)
PCNSL *v* SCNSL	PCNSL SCNSL Systemic & Ocular	13 (72) 4 (22) 1 (6)
Tumor Location	Parenchymal CSF cytology +ve CSF atypical/suspicious Eye Systemic	17 (94) 0 (0) 3 (17) 2 (11) 1 (6)
Number of prior treatments • Prior ASCT	Median (range)	3 (1-7) 6 (33%)
Time from diagnosis to enrollment	Days (range)	489 (150-8665)
Time from last tx to enrollment	Days (range)	72 (4-1273)

24 patients screened

- 6 screen fails-
  - organ function (n=2),
  - infection (n=2),
  - progression (n=1),
  - pt preference (n=1)

Axi-cel was successfully manufactured in **18/18** patients underwent leukapheresis

5/18 patients received palliative **targeted RT** immediately prior to screening for the trial

No bridging therapy after consenting

Stable/lower doses of dexamethasone allowed & tapered to 2mg qd by axi-cel infusion (except in 1 patient)

- 5 patients continued steroids from screening to treatment

Axi-Cel in CNSL – Safety

Nayak et al. ACO (2024) – Abstract #2006

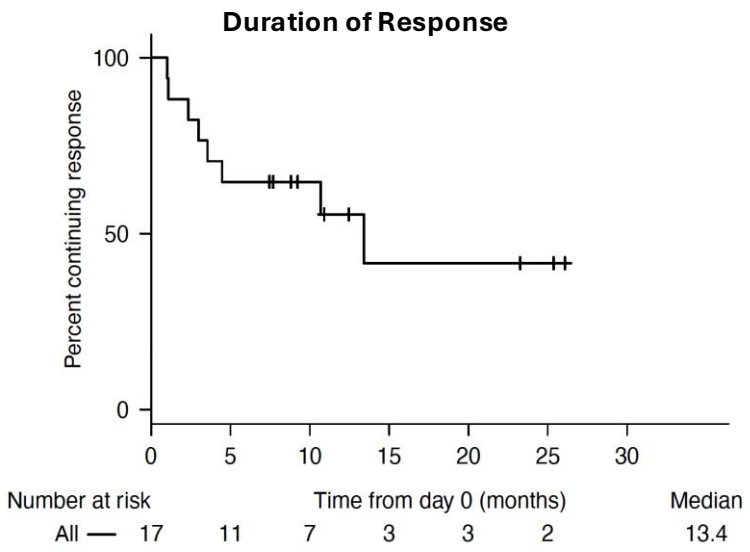
	CRS	ICANS
Any grade, n (%)	16 (89%)	8 (44%)
Grade 3+, n (%)	0 (0)	5 (28%)
Median time to onset (range)	2 days (1-6)	6 days (3-9)
Median duration (range)	5.5 days (1-9)	4 days (1-56)
Toci administered, n (%)	14 (78%)	N/A
Median number of doses (range)	1 (1-2)	N/A
Dex administered, n (%)	13 (72%)	5 (29%)
Median number of doses (range)	1 (1-7)	2 (1-9)

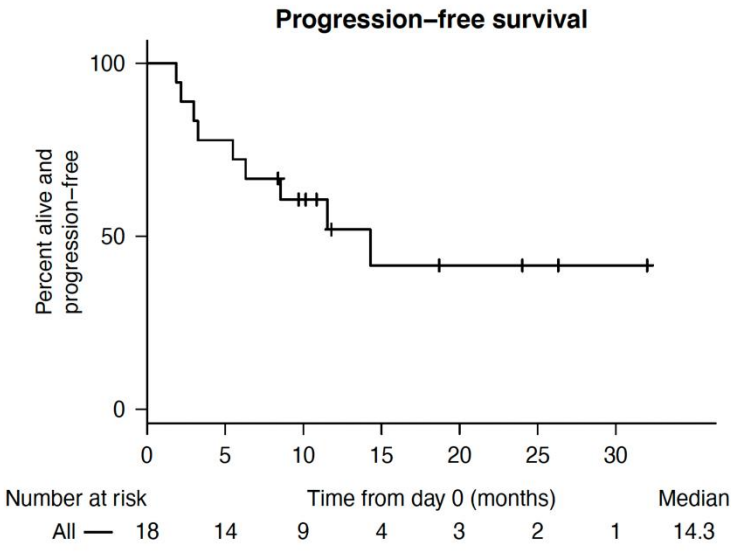
	1m	3m
Prolonged grade 3+ cytopenias	10/18 (56%)	0/18 (0%)
Neutropenia	7/18 (39%)	0/18 (0%)
Thrombocytopenia	1/18 (6%)	0/18 (0%)
Anemia	5/18 (28%)	0/18 (0%)

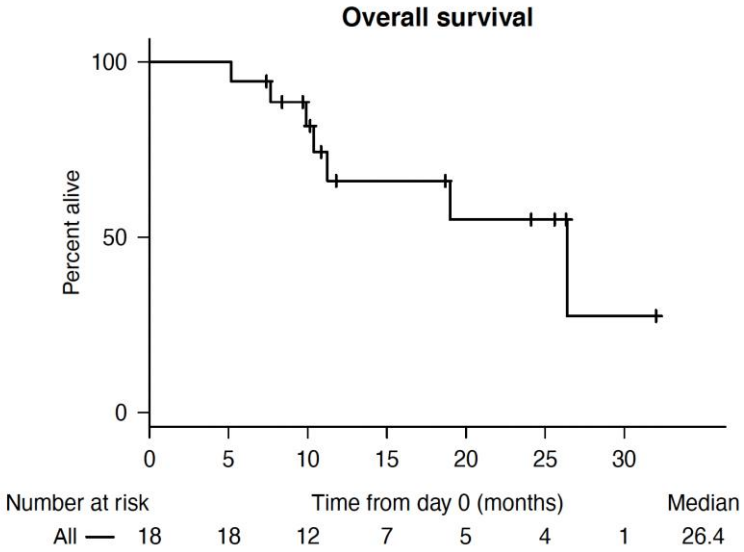
- No TLTs
- No Grade 4/5 ICANS
- Grade 3 Ommaya infection req removal : 2 patients
- Grade 3 electrographic focal status epilepticus : 1 patient
- Grade 2 low grade renal cell carcinoma : 1 patient
- Grade 4 myelodysplastic syndrome (at 12 mo): 1 patient
- Death due to PD : 7 patients

Axi-Cel in CNSL – Efficacy

- Median f/u: 24 mo
- ORR: 17/18 (94%)
  - uCR/CR: 12/18 (67%)
  - PR: 5/18 (28%)
- Median time to best response : 3 mo





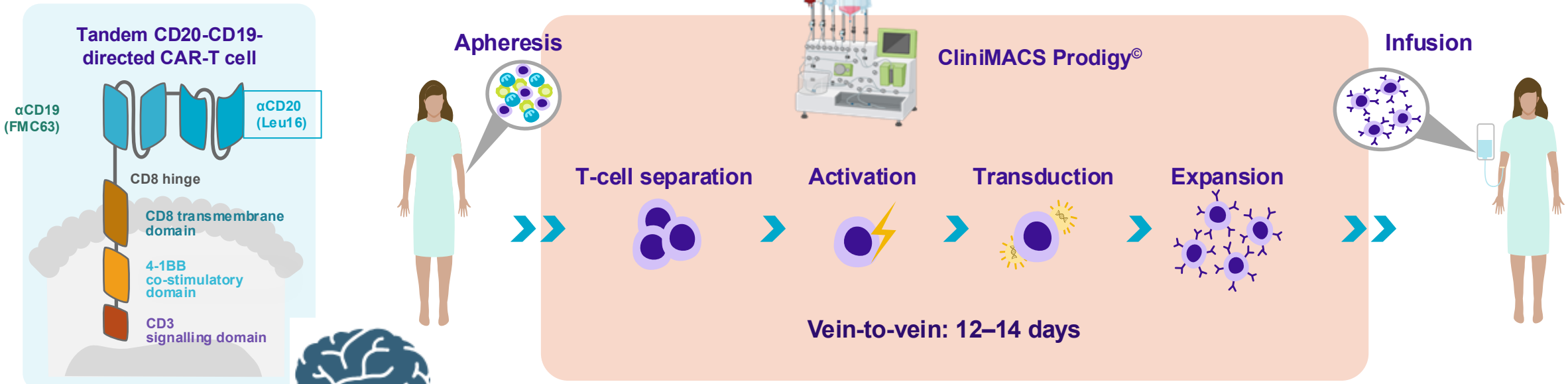


New Autologous CAR-T

Tandem CD20-19-Directed Non-Cryopreserved CAR-T Cells– Zamtocabtagene Autoleucel (Zamto-cel) - in Patients with Relapsed/Refractory CNS Lymphoma (CNSL). First Analysis of CNSL cohort in DALY-II US

Patrick B. Johnston, David B. Miklos, Neel K. Gupta, Nathan Denlinger, Jason Romancik, Amelia A. Langston, Matthew S. McKinney, Mitchell E. Horowitz, Sunil H. Abhyankar, Farrukh T. Awan, Praveen Ramakrishnan Geethakumari, Nirav N. Shah, Ugonma Chukwueke, Johanna Theruvath, Kimberly C. Coleman, Madhavi Nallewar, Marek Ancukiewicz, Dorota Klysz, Esther Eromosele, Sabrina Holley, Remigiusz Kaleta, Anna Wijatyk, Lakshmi Nayak and Caron A. Jacobson

Zamto-cel – an investigational autologous tandem CD20-CD19-directed non-cryopreserved CAR-T cell product for patients with CNSL



Inclusion criteria

- Adult patients with:
  r/r PCNSL or SCNSL
- At least one prior line
- Measurable CNS disease
  (at least 1cm in one direction)

Treatment

Lymphodepletion is initiated during manufacturing

Lymphodepletion chemotherapy

Zamto-cel | 2.5 x 10^6 | CAR-T cells/kg

Enrollment and Response

- Enrollment goal: 30 pts
  (15 PCNSL, 15 SCNSL)
- Response assessment:

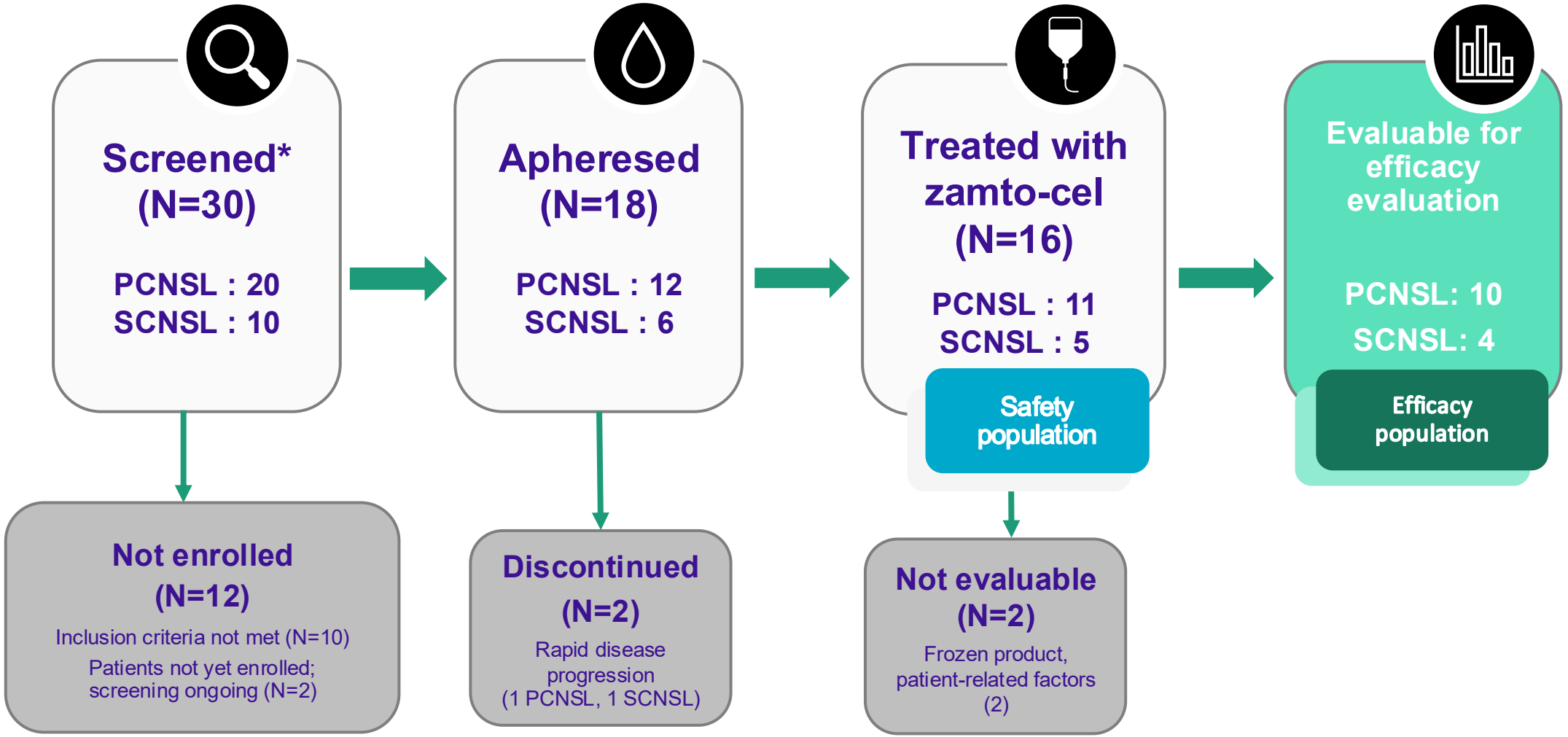
- CNS disease: IPCG (MRI/CSF)
- Systemic disease: Lugano (PET-CT)

Endpoints

Primary: ORR, defined as BOR of either CR or PR
Secondary: CRR at 1 and 6 months; DOR; PFS; OS; safety; PK;

BOR, best overall response; CAR-T cell, chimeric antigen receptor T cell; CR, complete response; CRR, complete response rate; Cy/Flu, Cyclophosphamide/Fludarabine; DOR, duration of response; FU, follow-up; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PR, partial response; r/r DLBCL, relapsed/refractory diffuse large B-cell lymphoma.

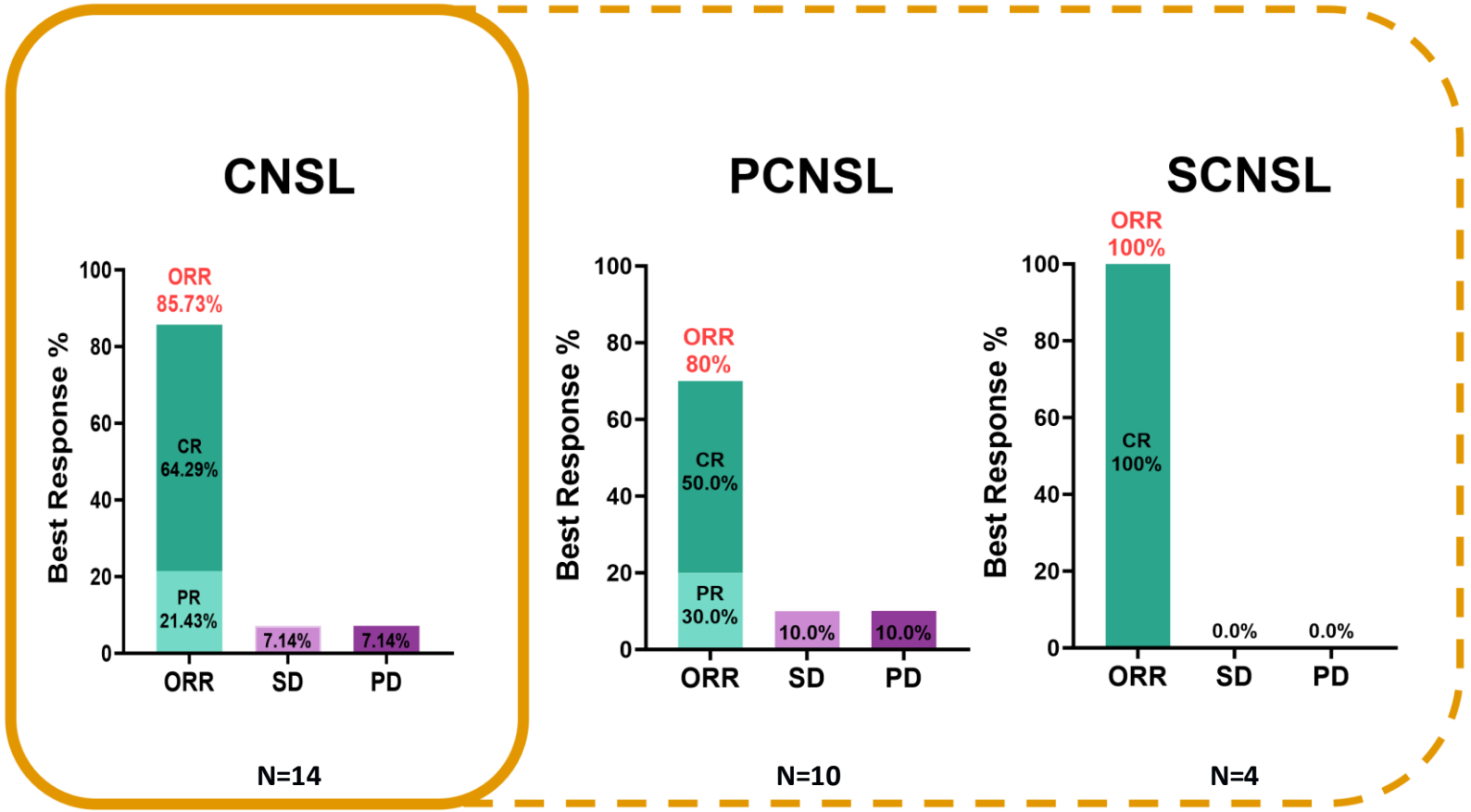
Patient disposition:
Only half of screened patients were infused



*Patient inclusion cut-off: 6 Nov 2024.

Patient disposition:
In total 14 CNSL patients were evaluated for efficacy

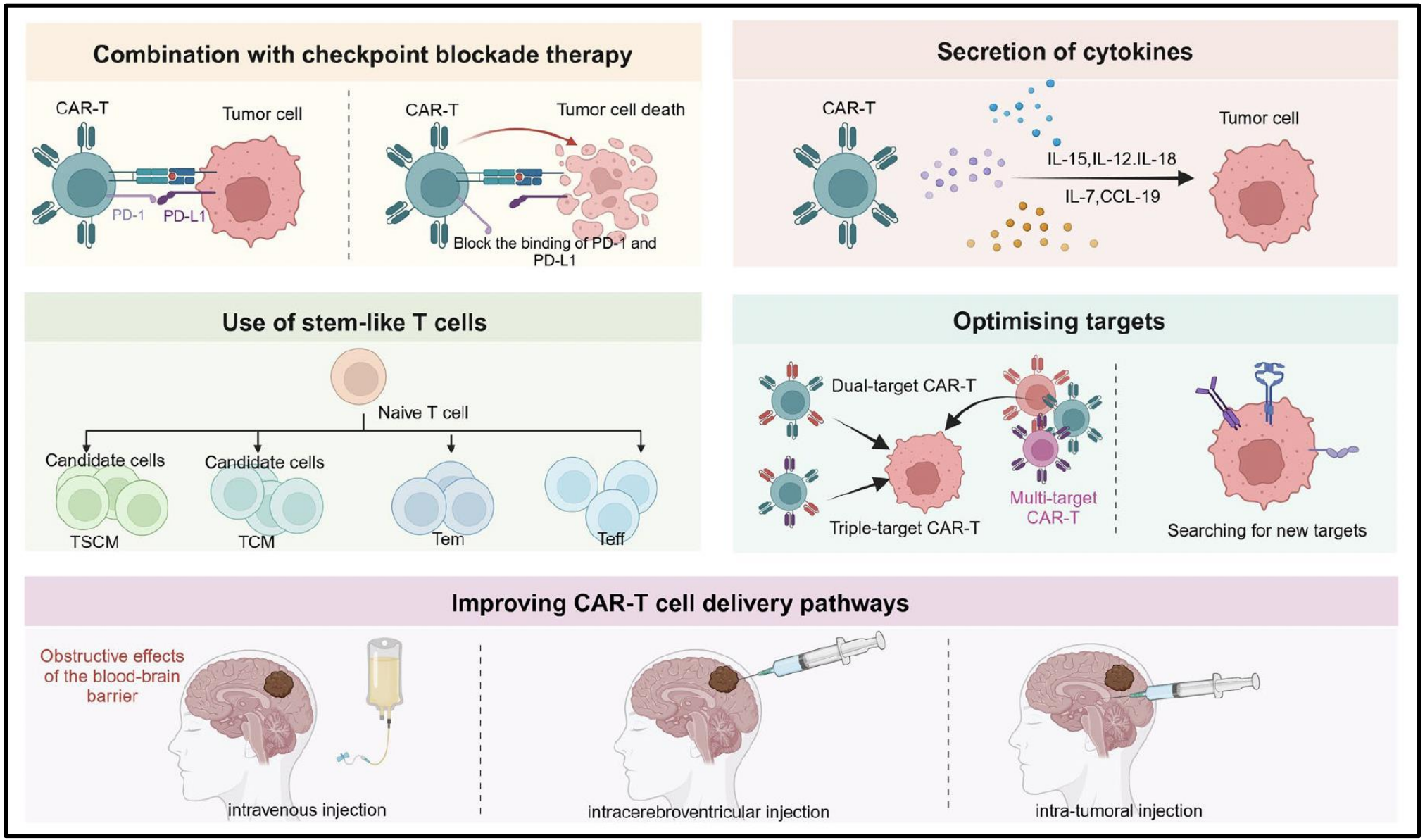
EFFICACY



Assessed by investigator

- mITT, modified intention-to-treat
- **Data cut-off: 20 Apr 2025.

Strategies to enhance CAR-T cell therapy for CNS tumors



Zhou et al. Biomarker Research (2024)

PCNSL: Outlook 2026

Improved diagnosis	Tumor cell free-DNA Biomarkers in CSF and/or plasma (biomarkers-informed therapy) Progress in neuroimaging (IPCG consensus) and new tracers for PET Radiomics
Generalizability of trial results	Results of prospective trials in real-life studies Use of international guidelines in rioutine clinical practice
New therapies	Modern molecular and genetic technologies Targetable molecules and pathways New immunotherapies effective against systemic LBCL Non-surgical BBB permeabilization
Ad hoc trials in elderly patients	To reduce treatment-related complications and neurotoxicity Specific geriatric scales in treatment selection and customization
In vitro models	Syngeneic and orthotopic xenograft Insights into pathogenesis (tumor cells-microenvironment interactions) Biological characteristics of tumor cells from PCNSL pts (no cell lines) To investigate new therapeutic agents or strategies

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