CAR-T E LBCL: DOVE SIAMO E DOVE ANDIAMO

LBCL: ALGORITMO DI TRATTAMENTO

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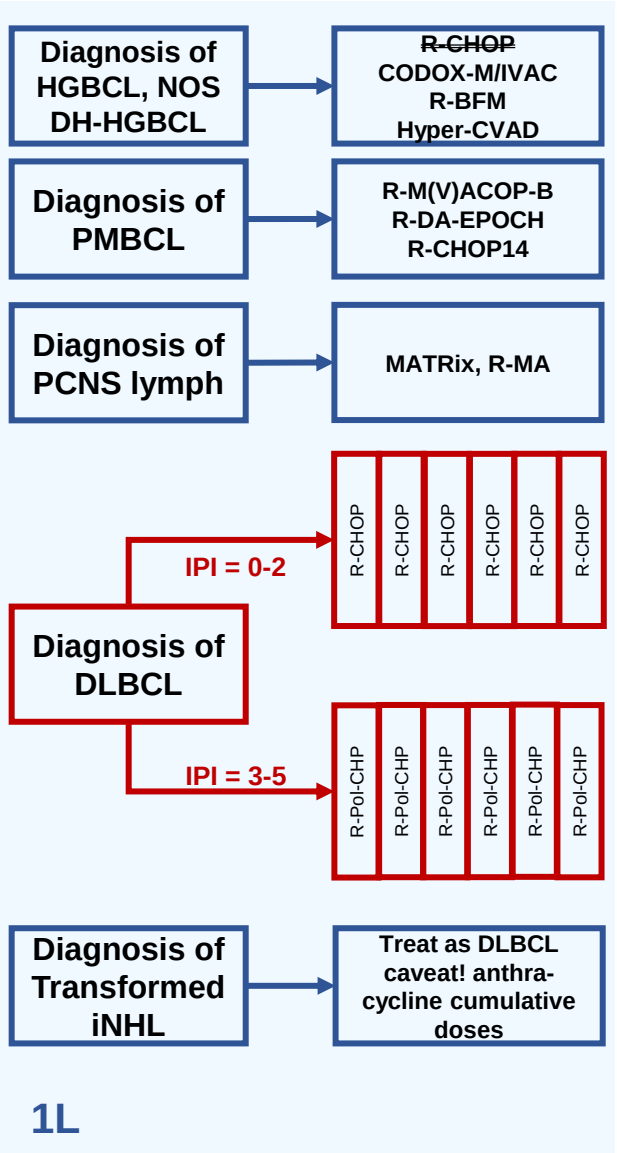
CAR-T:
e la storia continua...
migliorando

Bologna, 10 Marzo 2025
Royal Hotel Carlton

Disclosures of: ALESSANDRO BROCCOLI

Company name	Research support	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Sandoz	X				X	X
Gilead					X	X
Merck	X					X
Janssen	X			X		X
Takeda		X		X	X	X
Kyowa Kirin					X	
Incyte						X
Recordati						X
Astra Zeneca				X		
Roche				X		
Eli Lilly						X
GlaxoSmithKline				X	X	
Beigene					X	

Large B-cell lymphoma treatment algorhythm



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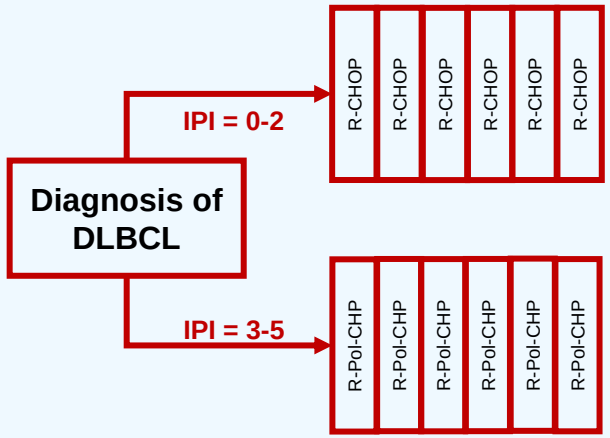
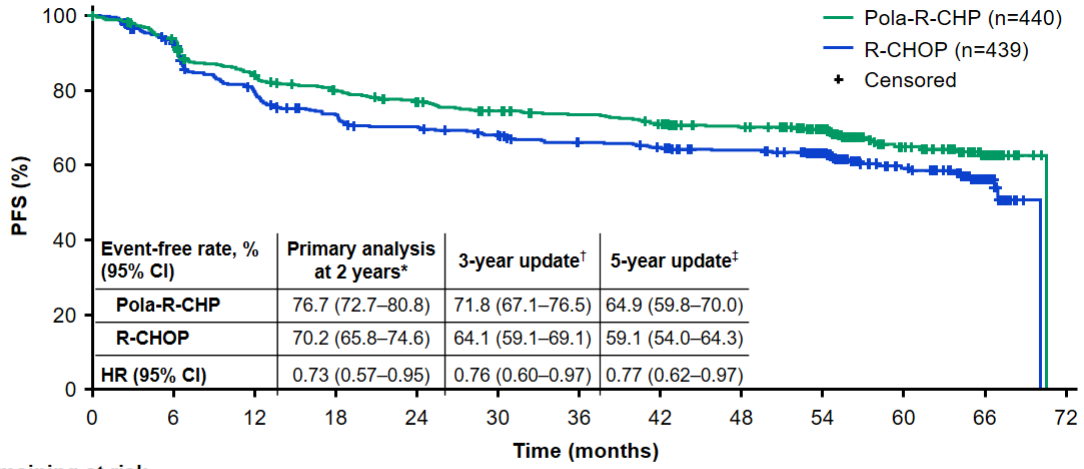
Large B-cell lymphoma treatment algorhythm



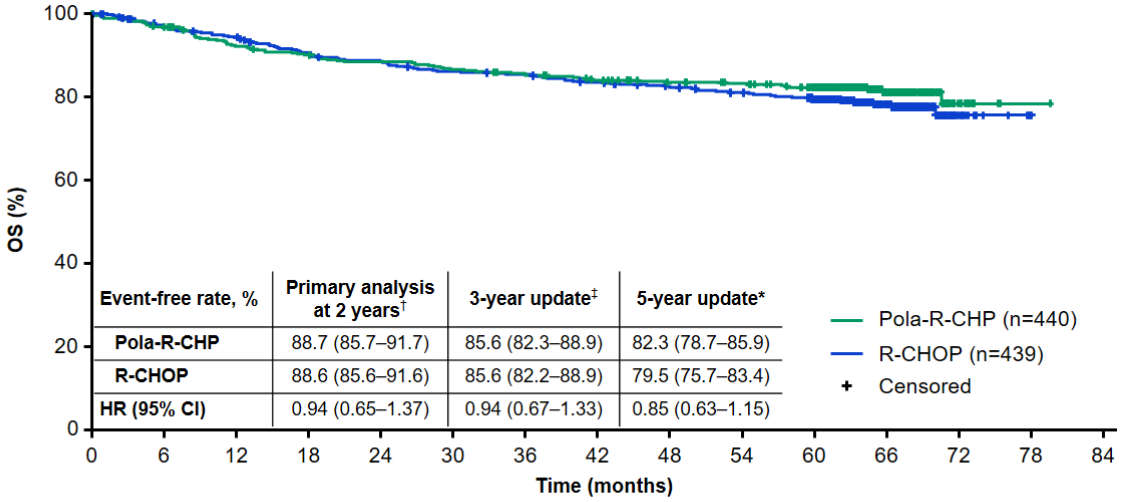
1L

Five-year analysis of the POLARIX study: Prolonged follow-up confirms positive impact of polatuzumab vedotin plus rituximab, cyclophosphamide, doxorubicin, and prednisone (Pola-R-CHP) on outcomes



Patients remaining at risk

Pola-R-CHP	440	407	357	335	318	303	292	280	258	213	100	56	NE
R-CHOP	439	391	332	302	287	274	258	251	240	192	95	54	NE

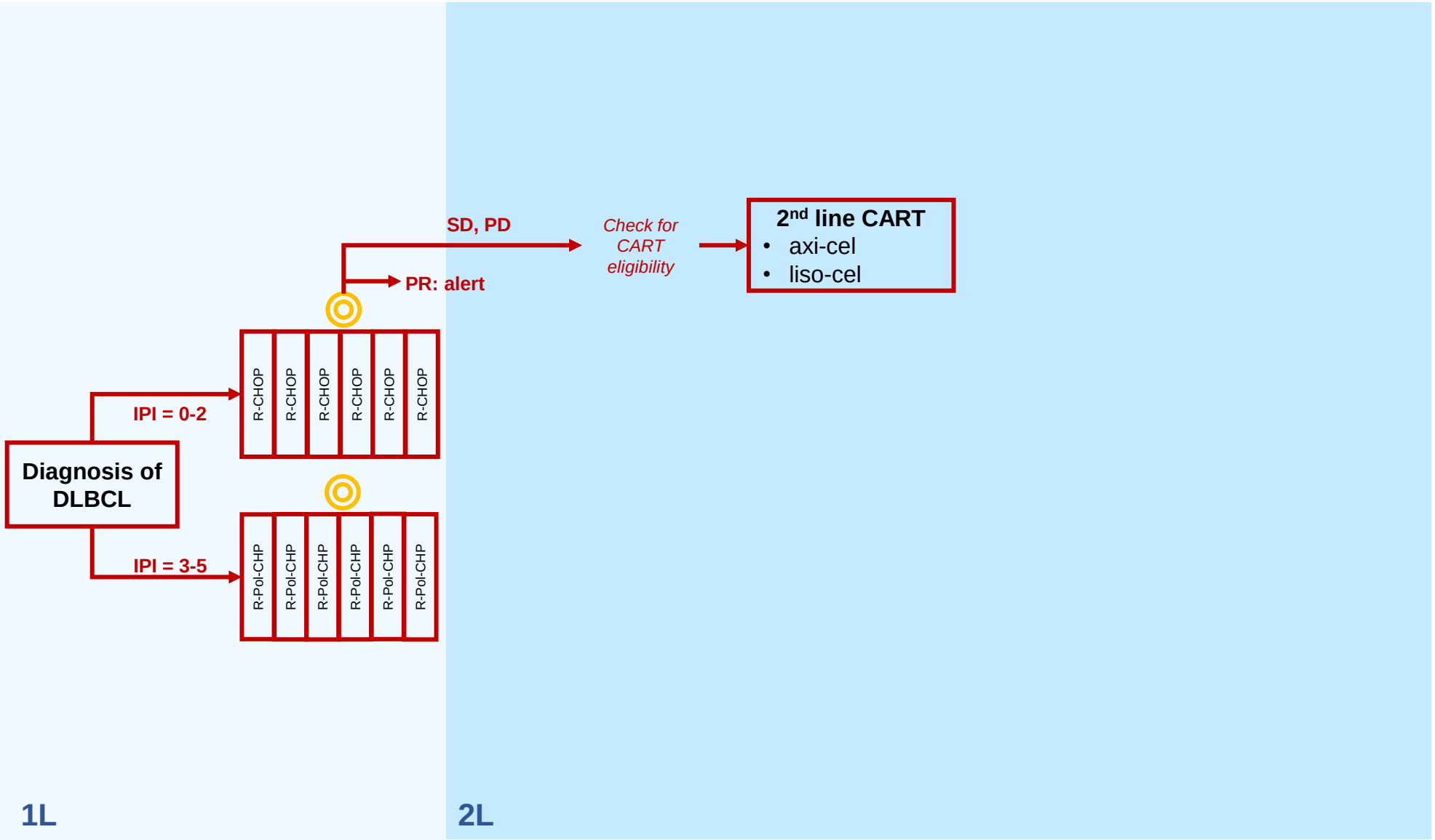


Patients remaining at risk

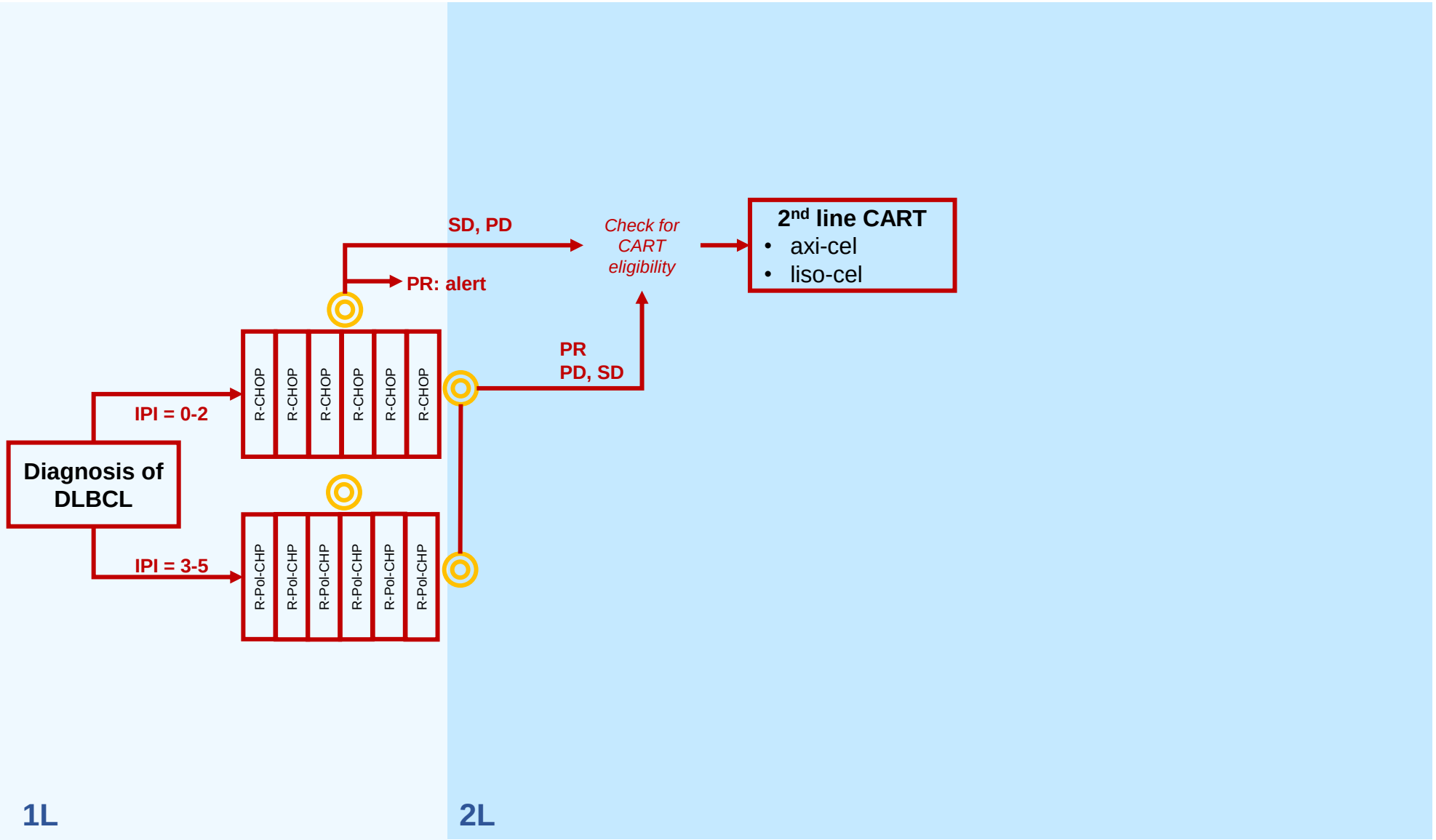
Pola-R-CHP	440	424	399	389	381	373	366	355	343	338	319	124	12	1	NE
R-CHOP	439	415	403	382	372	361	357	347	338	329	311	128	13	1	NE

Salles G. *Blood (ASH annual meeting abstracts)*. 2024; 144: 469a

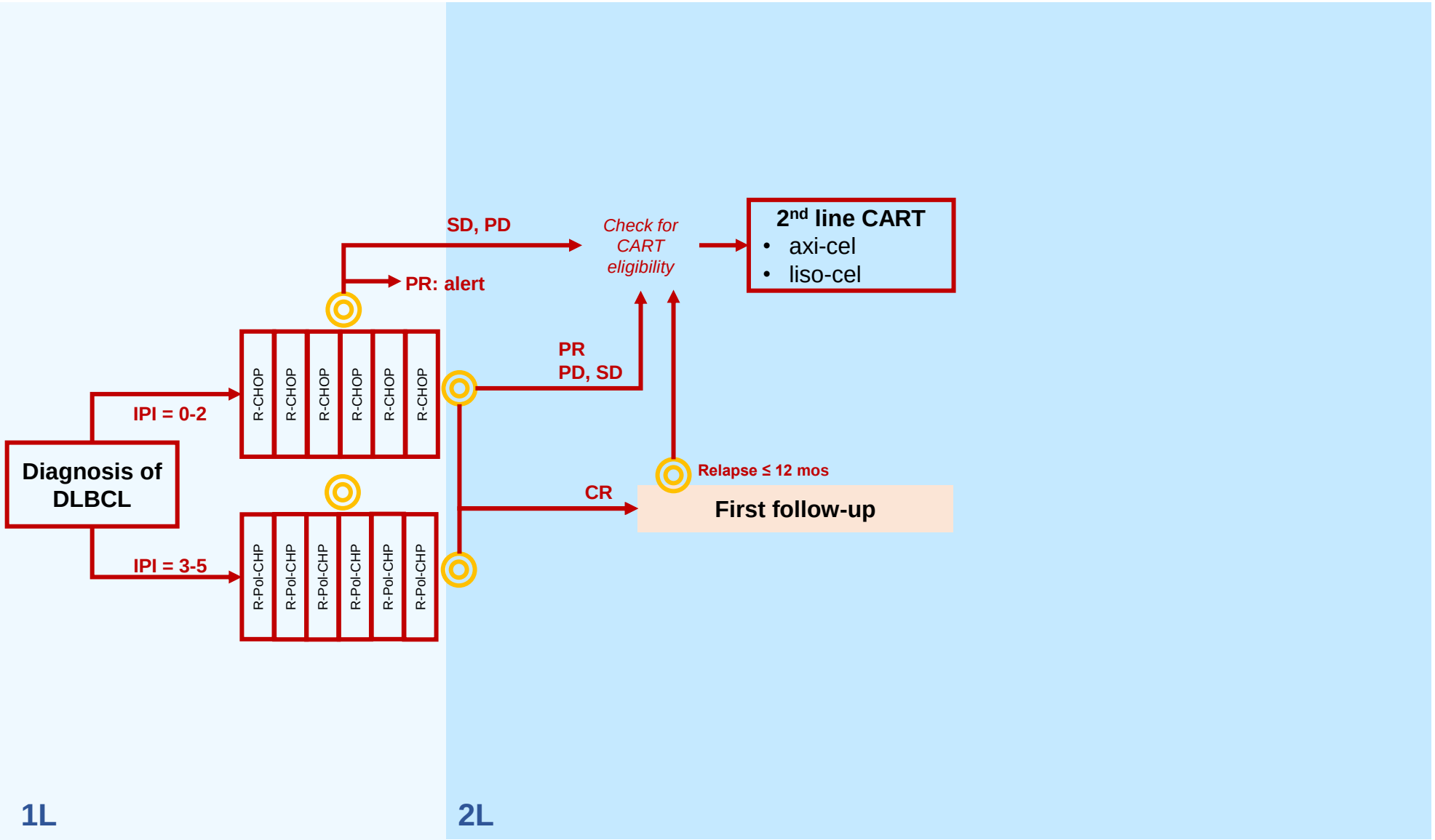
Large B-cell lymphoma treatment algorhythm



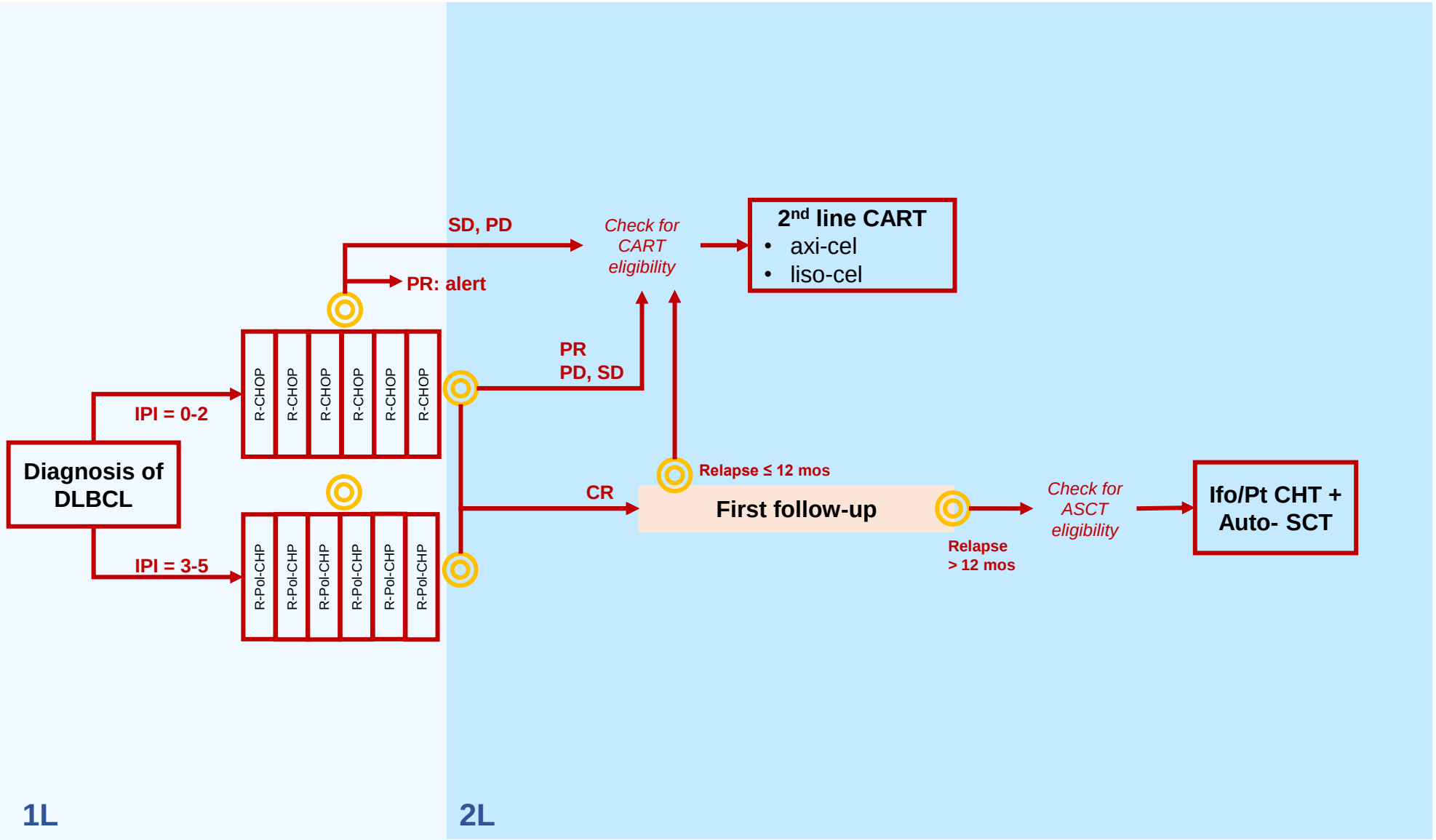
Large B-cell lymphoma treatment algorhythm



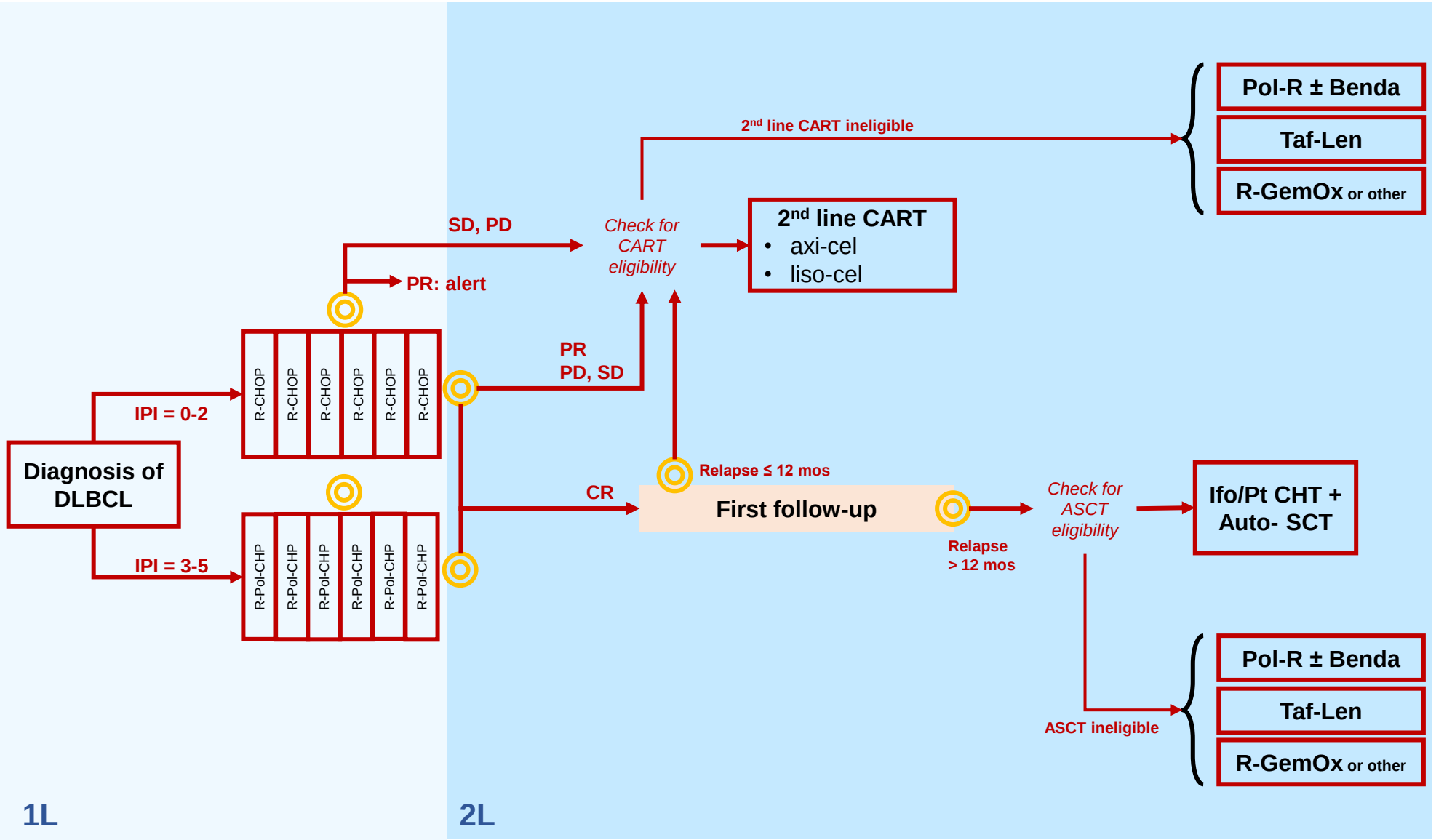
Large B-cell lymphoma treatment algorhythm



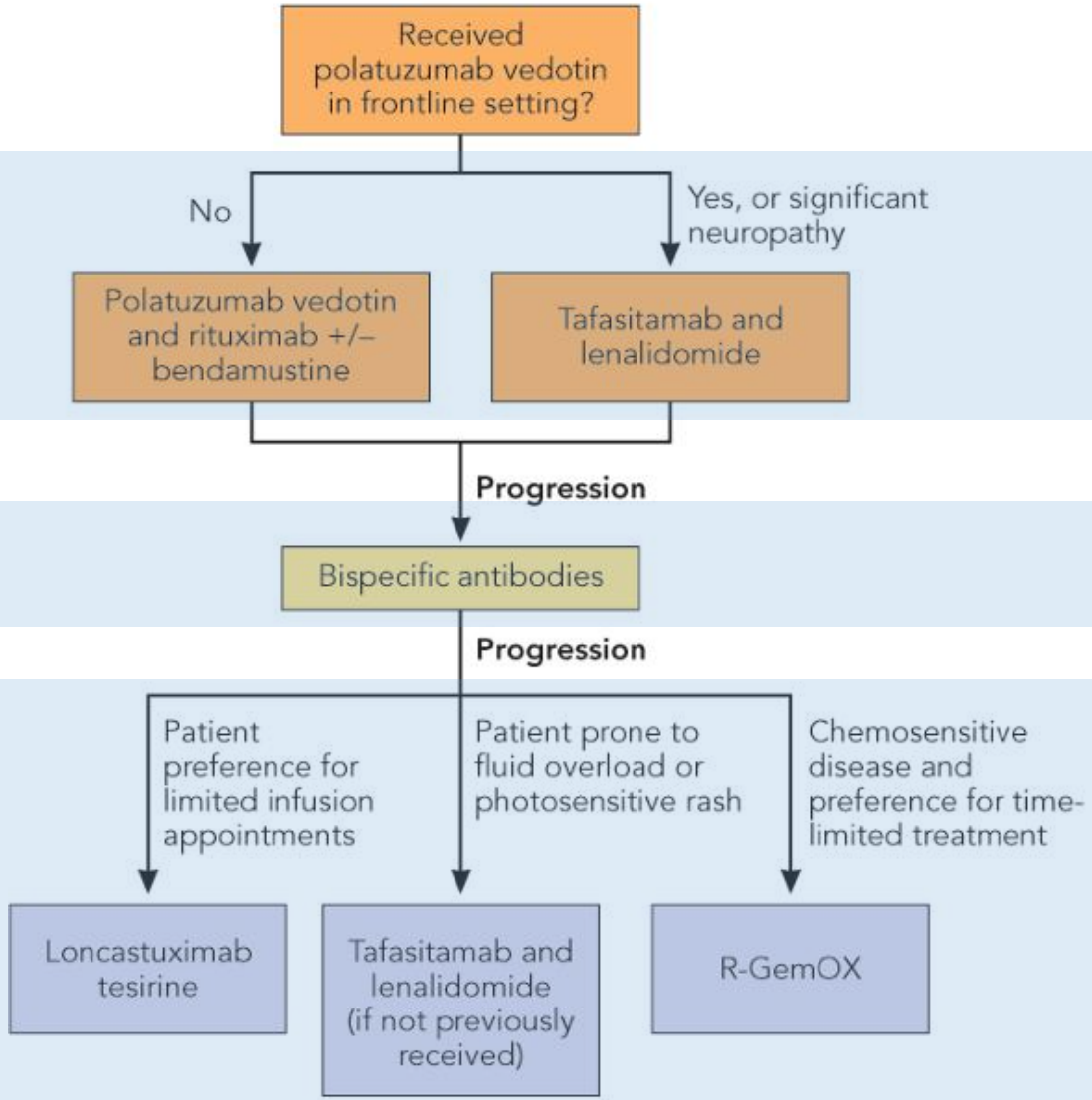
Large B-cell lymphoma treatment algorhythm



Large B-cell lymphoma treatment algorhythm



Treatment of elderly patients (poor eligibility to CAR T-cells)



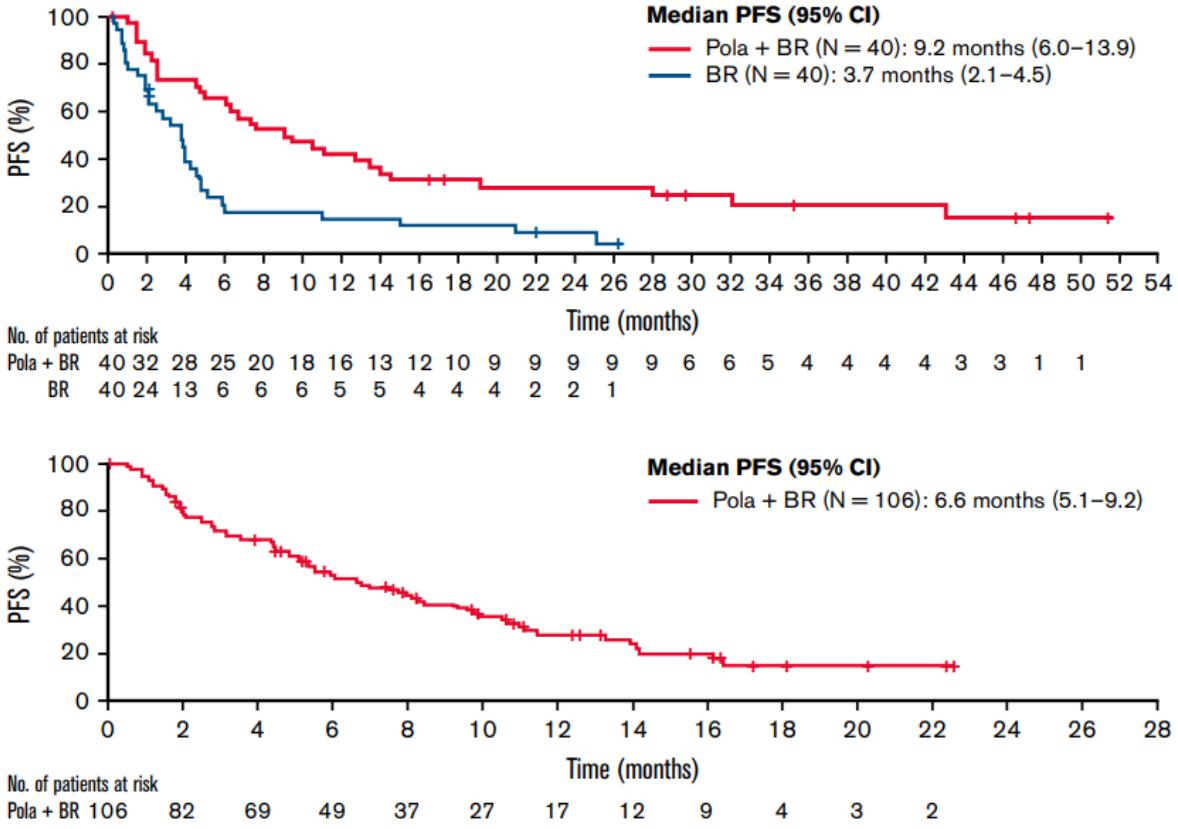
2nd line
Choose between available agents
Do not repeat polatuzumab vedotin if used frontline

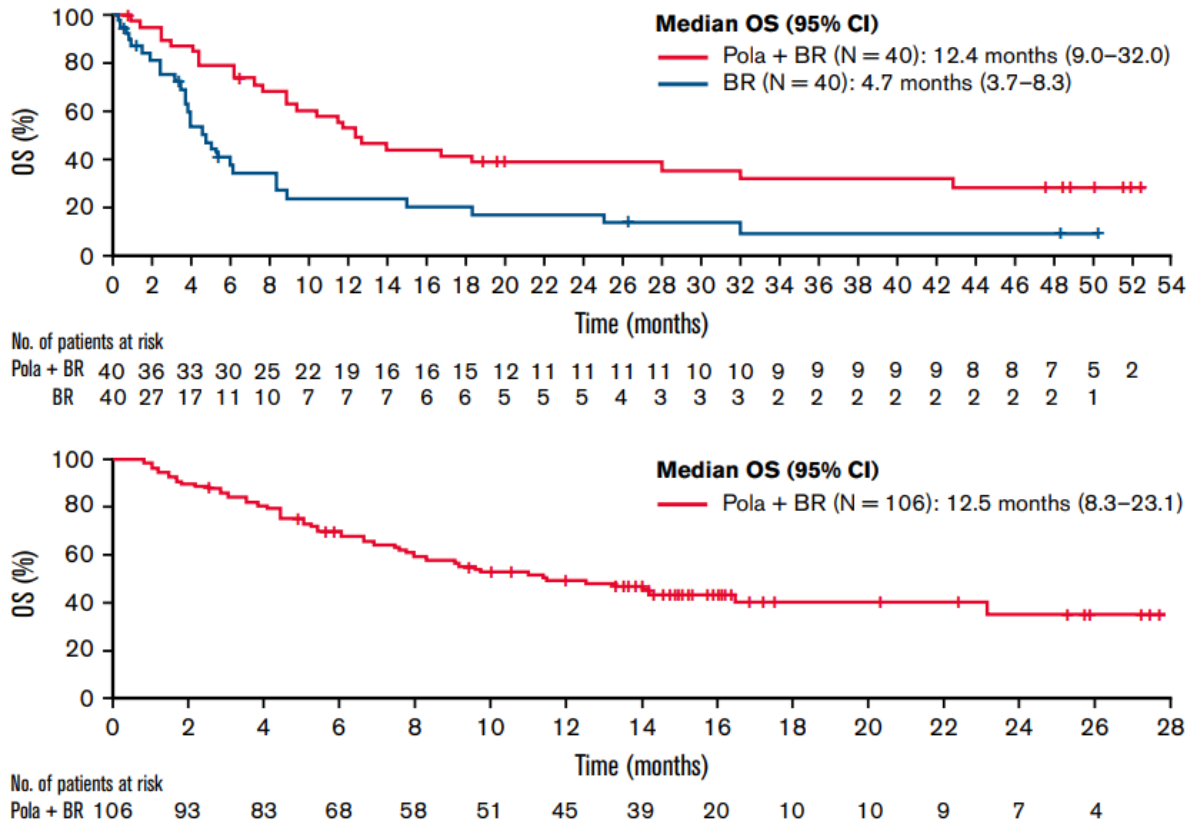
3rd line

4th line
Do not repeat previously applied regimens
Take into account the drug-specific side effects
Evaluate patient's fitness and compliance

Wallace DS. *Blood*. 2025; 145: 277-289

Polatuzumab vedotin plus bendamustine and rituximab in relapsed/refractory DLBCL: survival update and new extension cohort data





Sehn L. *Blood Adv*. 2022; 6: 533-543

Tafasitamab + lenalidomide

Registration phase 2 study

- 80 patients with relapsed (or refractory) diffuse large B-cell lymphoma evaluable for efficacy.
- Patients not eligible for high-dose chemotherapy and autologous stem cell transplant.
- Primary refractory patients initially not eligible (overall representing 19% of enrolled patients).
- Median age at enrolment was 72 years, ranging from 62 to 76 years.
- 50% of patients received 1 prior systemic treatment, overall 93% of patients received ≤ 2 lines of systemic therapy.
- Bulky disease present in 19% of the cases.
- Median time from diagnosis to tafasitamab + lenalidomide therapy: 27 months.

5-year update

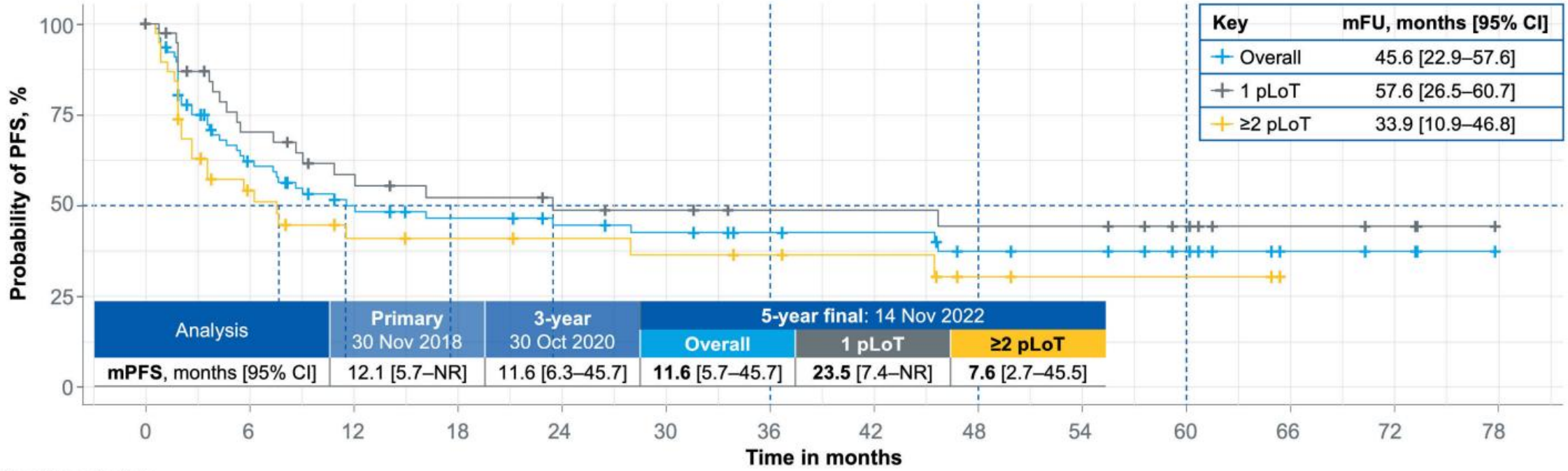
- Best OR rate of 57.5% with CR rate of 40%.
- Median PFS 11.6 months, better for patients receiving tafasitamab + lenalidomide as 2nd line, 23.5 months.
- Patients achieving a CR maintain the response for > 36 months in > 75% of the cases.
- Patients with more favorable disease presentation (relapse or progression > 12 months, no bulky disease, lower IPI score) have better response rates.

Real life experience

- Much more disappointing results due to a higher number of patients with comorbidities and high-risk disease features.

Salles G. *Lancet Oncol*. 2020; 21: 978-988 – Duell J. *Haematologica*. 2024; 109: 553-566 – Qualls DA. *Blood*. 2023; 142: 2327-2331

Tafasitamab for patients with relapsed or refractory diffuse large B-cell lymphoma: final 5-year efficacy and safety findings in the phase II L-MIND study

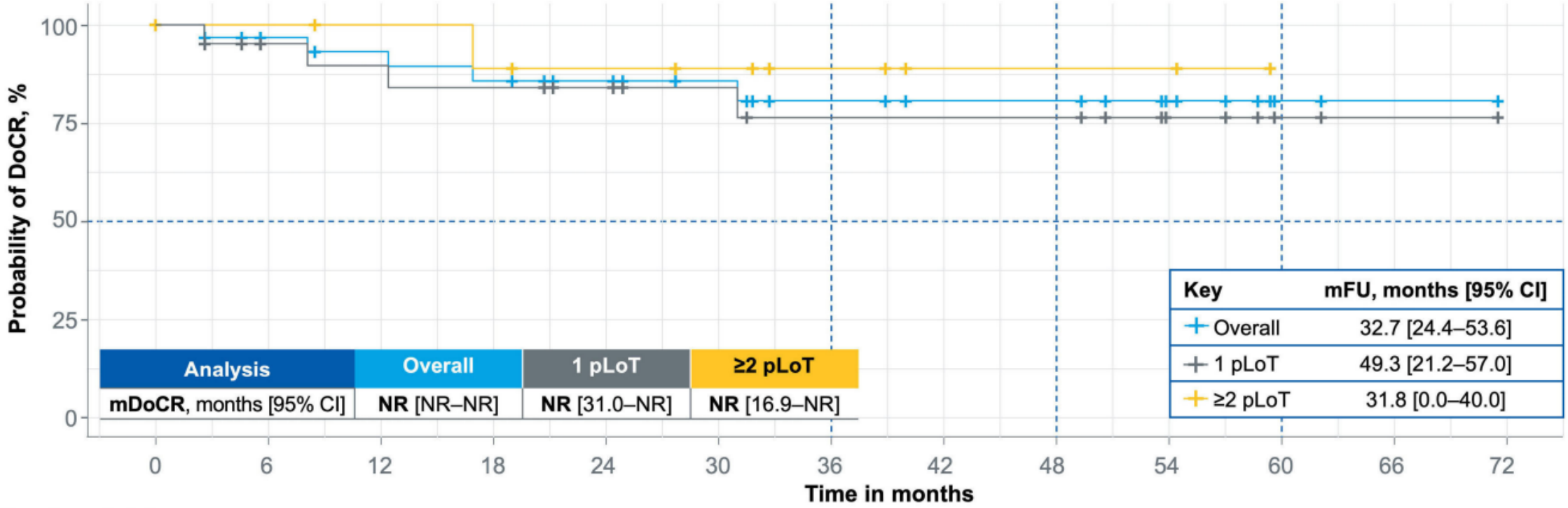


Number at risk:

Overall	80	42	30	26	23	21	18	17	13	12	9	4	3	0
1 pLoT	40	25	19	16	14	13	11	11	10	10	7	4	3	0
≥2 pLoT	40	17	11	10	9	8	7	6	3	2	2	0	0	0

Duell J. *Haematologica*. 2024; 109: 553-566

Tafasitamab for patients with relapsed or refractory diffuse large B-cell lymphoma: final 5-year efficacy and safety findings in the phase II L-MIND study



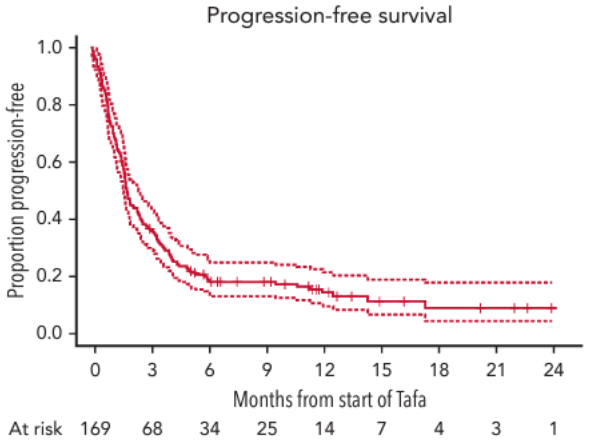
Number at risk:

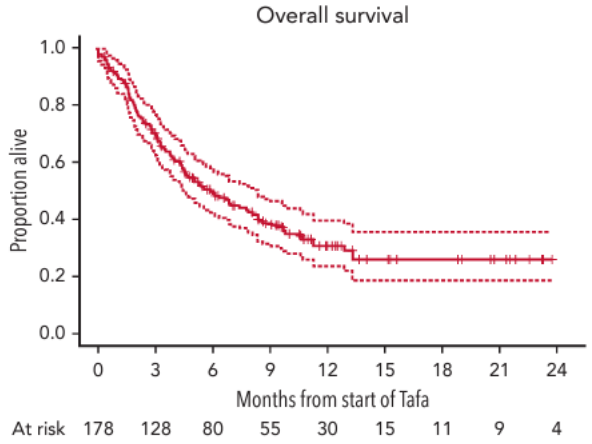
Overall	33	27	25	23	20	17	13	11	11	7	2	1	0
1 pLoT	21	17	16	15	13	11	9	9	9	5	2	1	0
≥2 pLoT	12	10	9	8	7	6	4	2	2	2	0	0	0

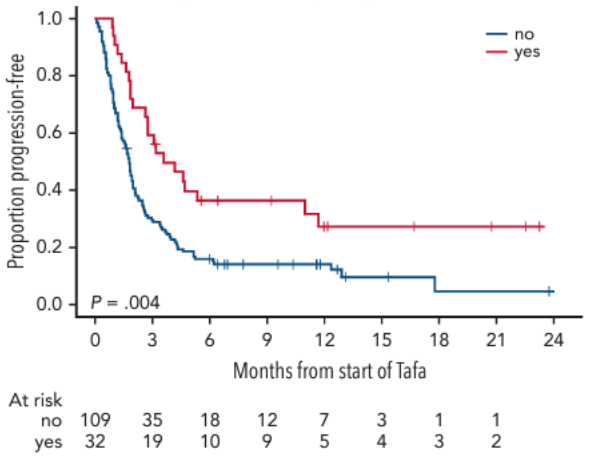
Duell J. *Haematologica*. 2024; 109: 553-566

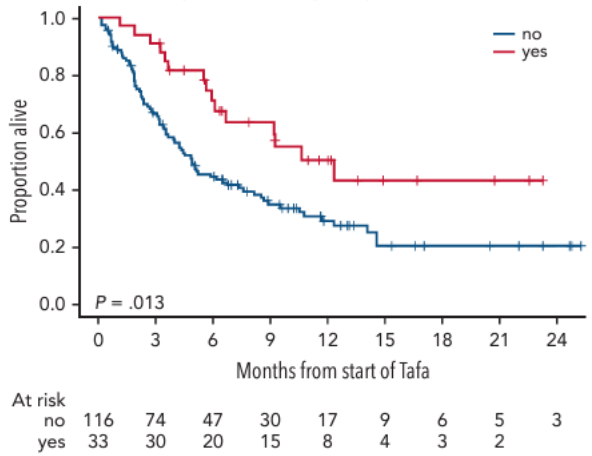
Tafasitamab and lenalidomide in large B-cell lymphoma: real-world outcomes in a multicenter retrospective study

Characteristic	Real world	L-MIND
Number of patients	178	81
Female sex	87 (49)	37 (46)
Age (y), median (range)	75 (26-94)	72 (41-86)
Race		
White, all ethnicity	161 (90)	72 (89)
Asian	9 (5)	2 (2)
Other or unknown	8 (4)	1 (1)
Diagnosis		
DLBCL-NOS	96 (54)	72 (89)
Transformed indolent lymphoma	59 (33)	7 (9)
HGBCL (nontransformed)	19 (11)	2 (2)
Other	4 (2)	0 (0)
Cell of origin by immunohistochemistry		
GCB	100 (56)	38 (47)
Non-GCB	62 (35)	21 (26)
Unknown	16 (9)	22 (27)
Risk (IPI)		
0-2	43 (27)	40 (49)
3-5	114 (73)	41 (51)
Ann Arbor stage		
I-II	20 (12)	20 (25)
III-IV	149 (88)	61 (75)
Prior lines of therapy for DLBCL		
Median (range)	2 (0-11)	2 (1-4)
0	12 (7)	0 (0)
1	49 (28)	40 (49)
2	49 (28)	35 (43)
3	27 (15)	5 (6)
4	13 (7)	1 (1)
≥5	28 (16)	0 (0)
Primary refractory (progression within 6 months of first-line therapy)	87 (49)	15 (18)
Refractory to last therapy	118 (67)	36 (44)



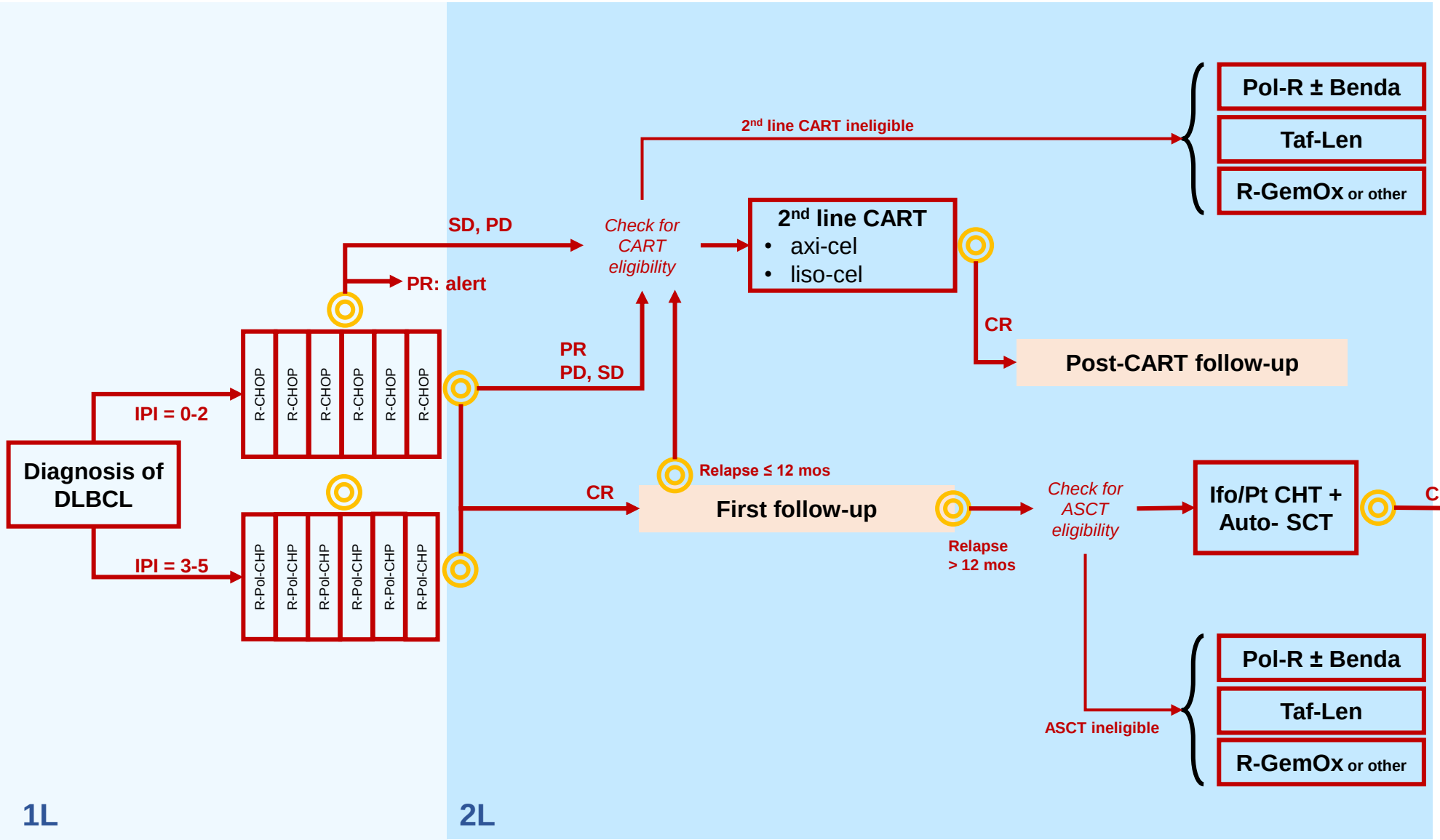




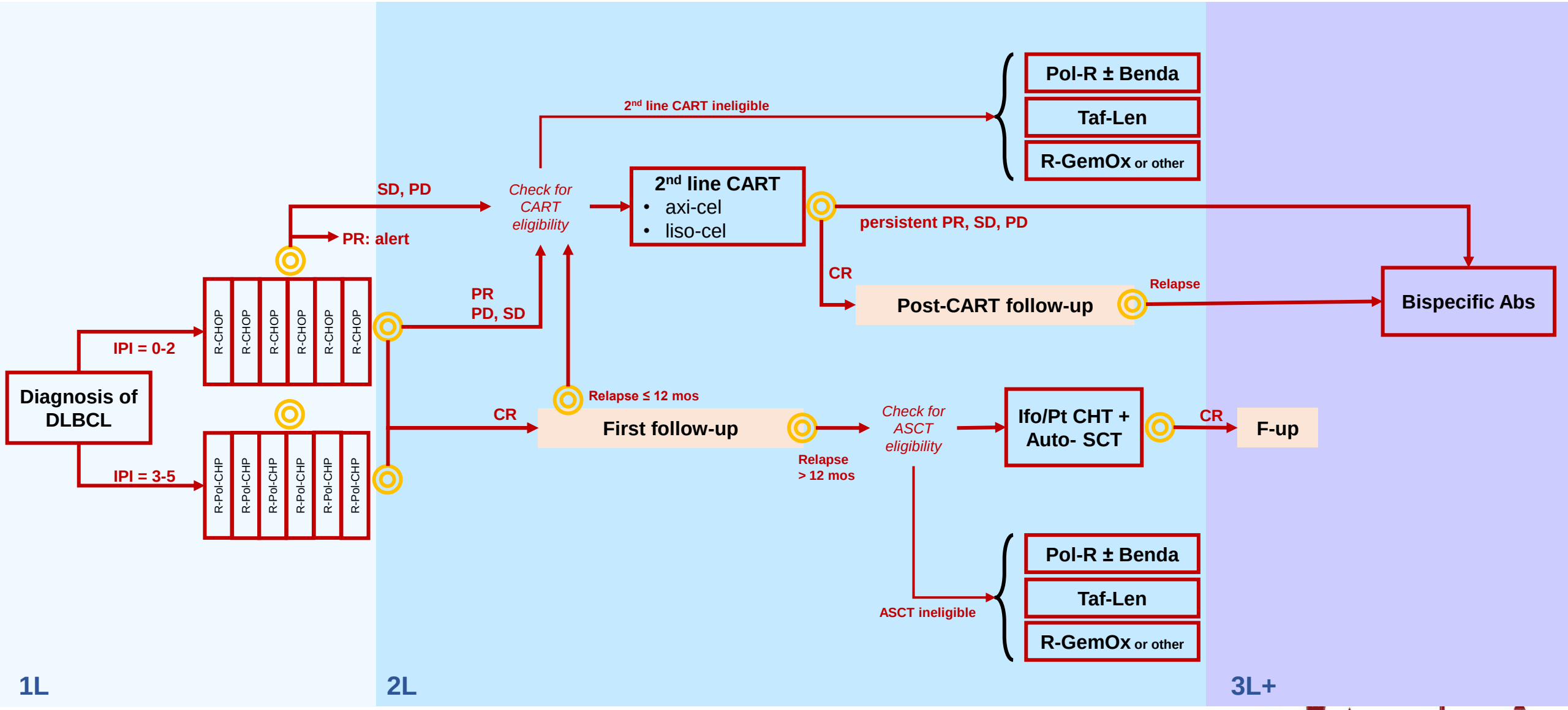


Qualls DA. *Blood*. 2023; 142: 2327-2331

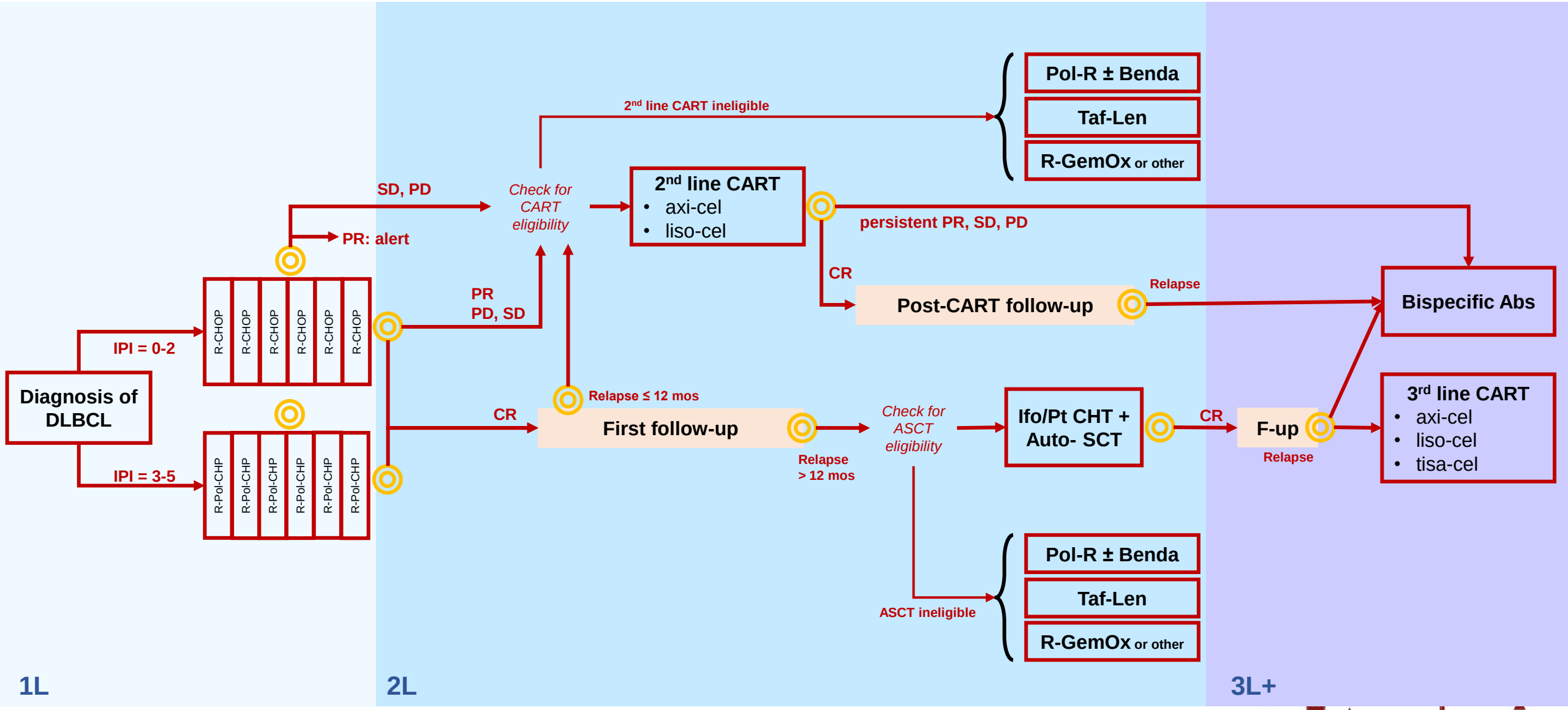
Large B-cell lymphoma treatment algorhythm



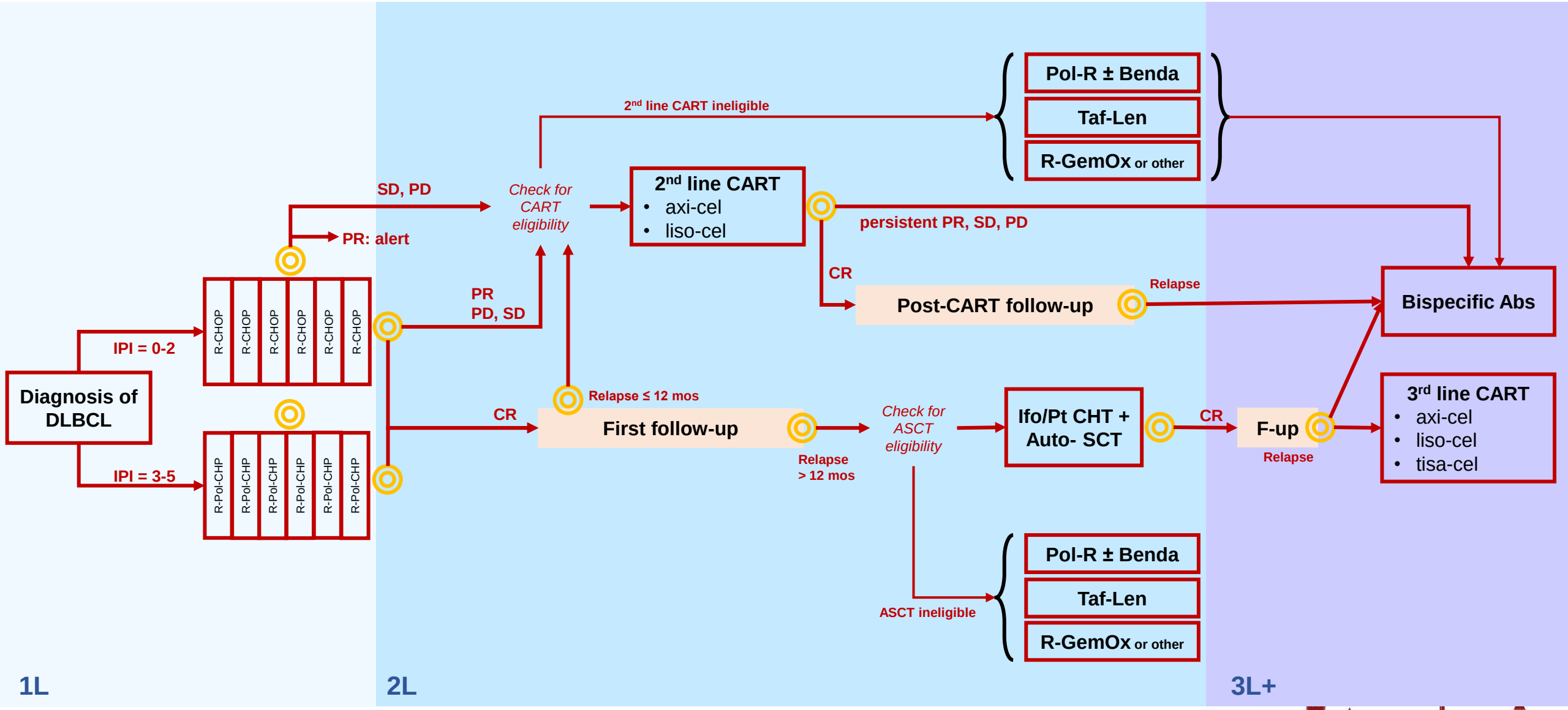
Large B-cell lymphoma treatment algorhythm



Large B-cell lymphoma treatment algorhythm



Large B-cell lymphoma treatment algorhythm



Glofitamab and epcoritamab at a glance

	Glofitamab	Epcoritamab
Construct	2:1 anti-CD20 x anti-CD3	1:1 anti-CD20 x anti-CD3
Route of administration	Intravenous	Subcutaneous
Treatment duration	Up to 12 cycles (8.5 months)	Until progression or unacceptable toxicity
CRS-mitigating strategy	Obinutuzumab 7 days before	Corticosteroids days 1 → 4
Schedule and ramp-up	• Every week for the first 3 weeks • Ramp-up: 2.5 mg/10 mg/30 mg • Then every 3 weeks	• Every week for the first 12 weeks • Ramp-up: 0.16 mg/0.8 mg/48 mg • Then every 2 weeks for 2 months • Then monthly (cycle 10+) until PD or toxicity
CRS incidence (any grade)	64.3%	51.0%
CRS grade 3-4	3.9%	3.0%
Highest CRS incidence timepoint	Cycle 1, day 8+, first dose (2.5 mg)	Cycle 1, day 15+, full dose (48 mg)

Glofitamab

Registration phase 2 study

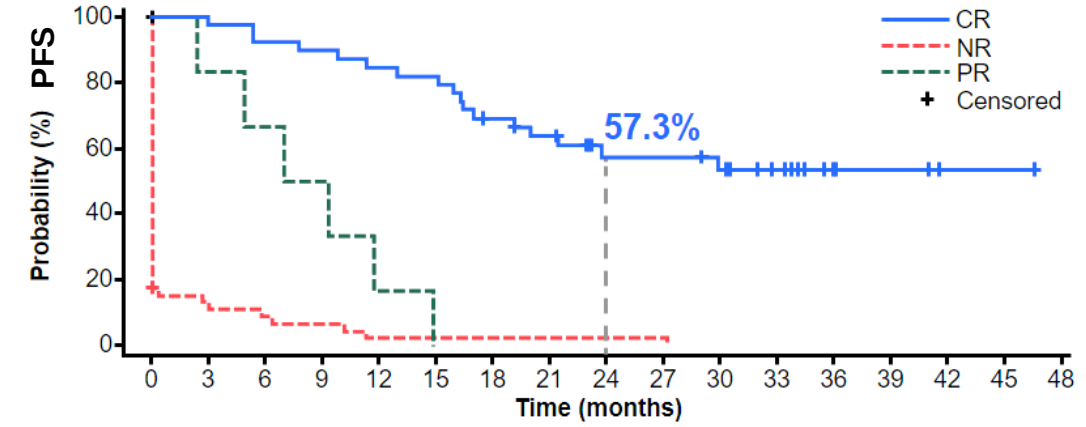
- Fixed duration treatment: every 3 weeks up to 12 cycles (8.5 months).
- 155 patients with pretreated large B-cell lymphoma (including tFL, HGBCL and PMBCL) evaluable for efficacy.
- Two previous lines in 40% of patients; three or more lines in 60%.
- Median age at enrolment was 66 years, ranging from 21 to 90 years.
- All patients received previous anti-CD20 treatment. Refractory to anti-CD20 therapy: 83%.
- Previous CAR T-cell therapy in 33% of pretreated patients. Refractory to previous CAR T-cell: 30%.
- Refractoriness to last previous therapy: 86%.

3-year update

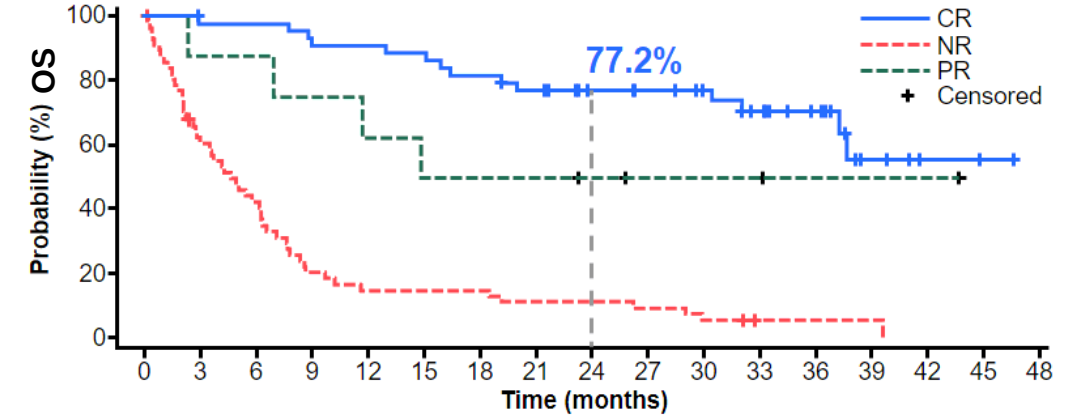
- Complete responses remaining durable after fixed-duration glofitamab, OR rate of 52% with CR rate of 40%.
- More than half of patients in CR at the end of treatment are still in CR at 24 months.
- There is evidence of immune recovery 12-18 months after the end of treatment.

Dickinson M. *N Engl J Med*. 2022; 387: 2220-2231 – Dickinson M. *Blood (ASH annual meeting abstracts)*. 2024; 144: 865a

Fixed-duration glofitamab monotherapy continues to demonstrate durable responses in patients with relapsed or refractory large B-cell lymphoma: 3-year follow-up from a pivotal Phase II study

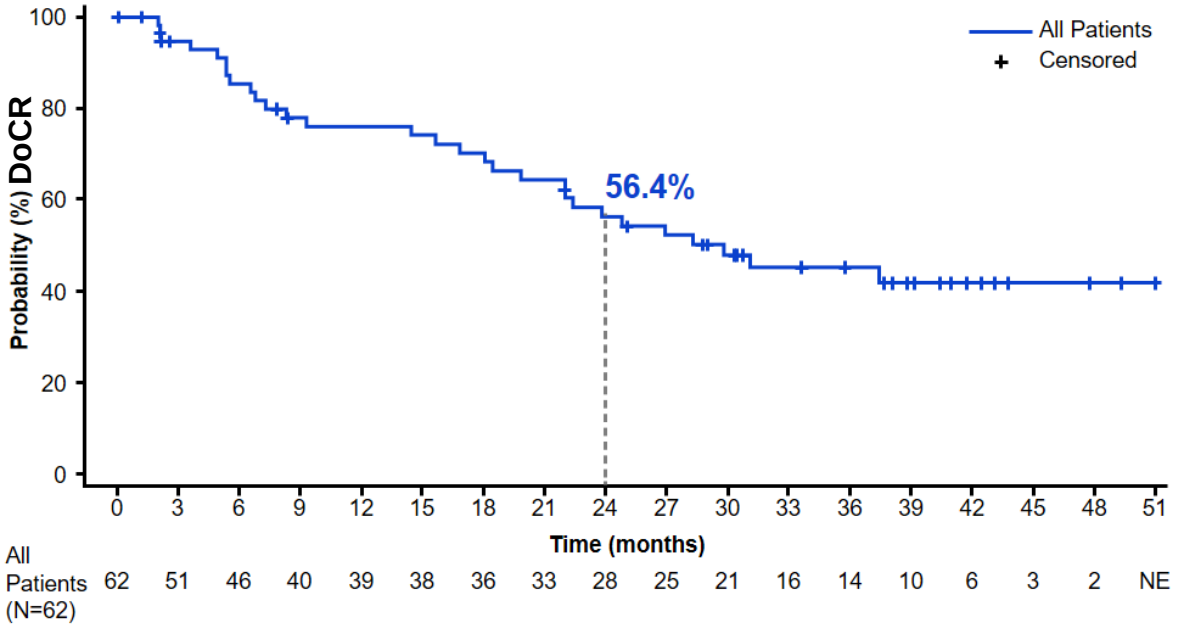


CR (N=45)	45	38	36	35	33	32	26	23	16	16	14	10	4	3	1	1	NE
NR (N=57)	57	5	4	3	1	1	1	1	1	1	NE	NE	NE	NE	NE	NE	NE
PR (N=8)	8	5	4	3	1	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE	NE



CR (N=45)	45	43	43	40	40	39	36	33	28	26	23	19	13	5	2	1	NE
NR (N=57)	57	33	23	11	8	8	8	6	6	5	3	1	1	1	NE	NE	NE
PR (N=8)	8	7	7	6	5	4	4	4	3	2	2	2	1	1	1	NE	NE

Responses assessed at the end of treatment



All Patients (N=62)	62	51	46	40	39	38	36	33	28	25	21	16	14	10	6	3	2	NE

Duration of complete response
Complete responses achieved at any time during treatment

Dickinson M. *Blood (ASH annual meeting abstracts)*. 2024; 144: 865a

Epcoritamab

Registration phase 2 study

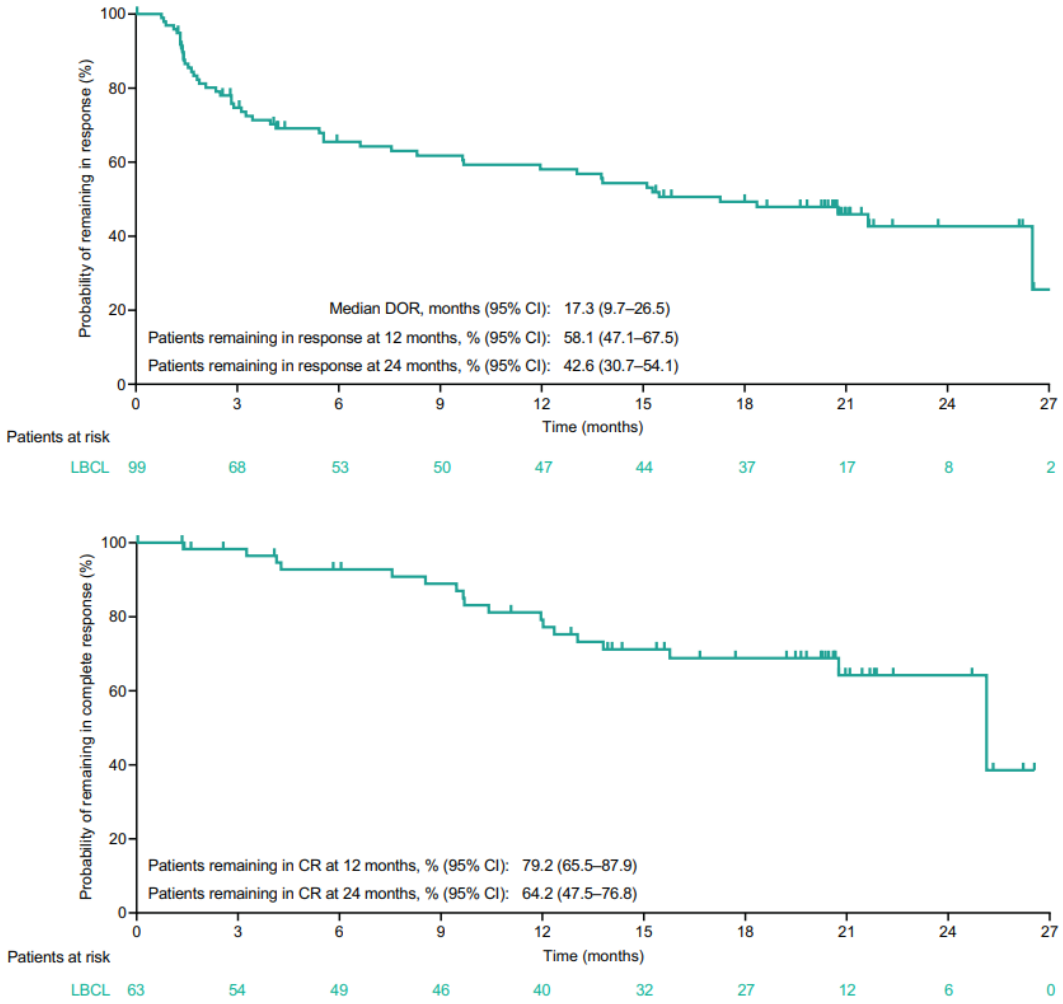
- Continuous treatment until progression or unacceptable toxicity.
- 157 patients with pretreated large B-cell lymphoma (including t-iNHL, HGBCL, PMBCL and FL3B) evaluable for efficacy.
- Median of 3 prior lines of therapy; three or more lines in 71% of patients.
- Median age at enrolment was 64 years, ranging from 20 to 83 years.
- Previous CAR T-cell therapy in 39% of pretreated patients. Progression within 6 months of previous CAR T-cell: 75%.
- Refractoriness to last previous therapy: 83%.

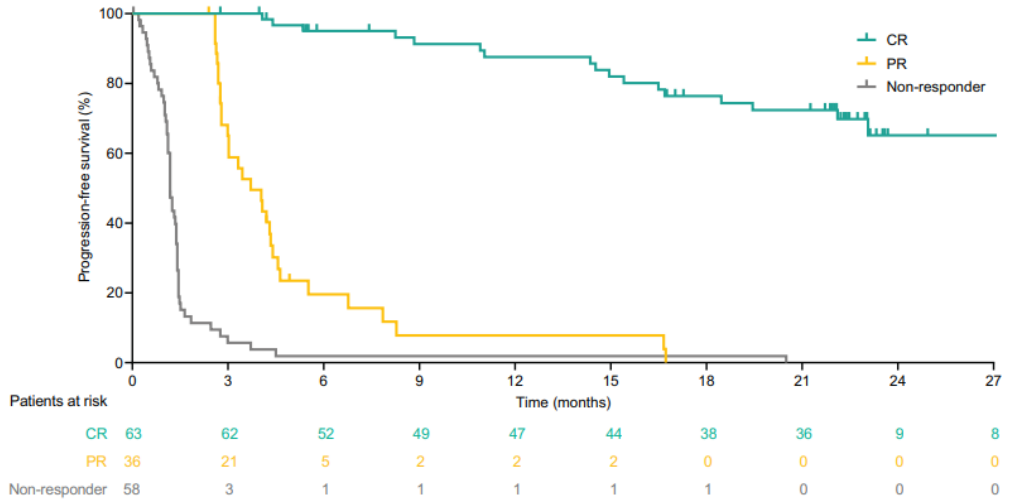
Long-term update

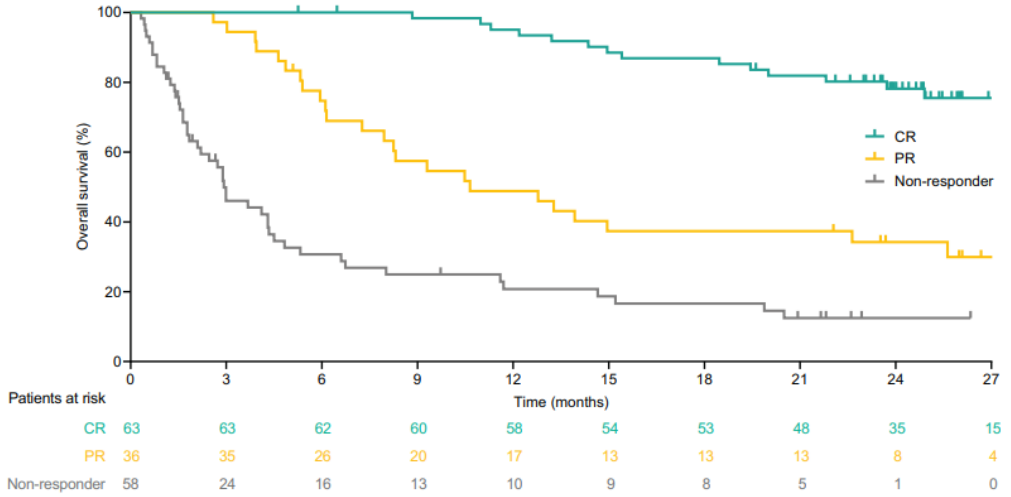
- Median follow-up: 27.4 months.
- Median time to CR was 2.6 months.
- Best OR rate of 63% with CR rate of 38.9%.
- 64.2% of patients achieving a CR at any time during treatment are still in CR at 24 months.

Thieblemont C. *J Clin Oncol*. 2023; 41: 2238-2247 – Thieblemont C. *Leukemia*. 2024; 38: 2653-2662

Epcoritamab in relapsed/refractory large B-cell lymphoma: 2-year follow-up from the pivotal EPCORE NHL-1 trial







Thieblemont C. *Leukemia*. 2024; 38: 2653-2662

Predicting bispecific antibody failure in diffuse large B-cell lymphoma

Poor prognostic marker	Cohort	Bispecific antibody analyzed	Number	Timepoint assessed	Outcome measure affected
ECOG >0	Retrospective	CD20/CD3	*N*=143	≥1 prior line of therapy	Inferior OS
Male sex	Prospective	• Glofitamab • Epcoritamab	• *N*=154 • *N*=157	>1 prior line of therapy	Lower CR rate
Chemotherapy refractoriness	Prospective + Retrospective	• Glofitamab • CD20/CD3	• *N*=154 • *N*=104	≥1 prior line of therapy	• Lower CR rate • Inferior PFS/OS
High inflammatory markers: IL-6, IL-8, CRP	Prospective	Glofitamab	*N*=119	≥1 prior line of therapy	Lower CR rate
Increased LDH	Retrospective	CD20/CD3	*N*=104	≥1 prior line of therapy	Inferior PFS/OS
TMTV ≥ median	Retrospective	Glofitamab	*N*=144	>1 prior line of therapy	Inferior PFS
Tumor: <10% CD20 expression	Retrospective	Mosunetuzumab	*N*=161	≥2 prior therapies	Reduced ORR
Tumor: molecular aberrations *MYC*, *TP53*, *RHOA*, *CD274*, *GNAI2*	Retrospective	• Glofitamab • CD20/CD3	*N*=33 *N*=36	>1 prior line of therapy	• Reduced ORR • Inferior PFS/OS
TME: increased "exhausted" CD8 T cells	Retrospective	CD20/CD3	*N*=7	>1 prior line of therapy	Higher relapse rate

CR, complete response; CRP, C-reactive protein; ECOG, Eastern Cooperative Oncology Group; IL, interleukin; LDH, lactate dehydrogenase; N, number; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; TME, tumor microenvironment; TMTV, total metabolic tumor volume.

Barraclough A. *Hematology*. 2024; 2024: 318-320

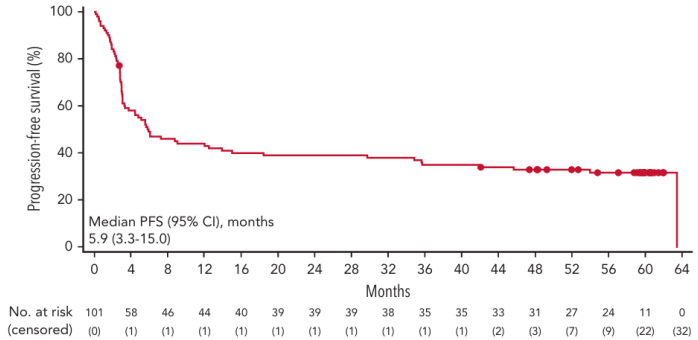
Pivotal phase 2 trials with 3rd line CAR T-cells (1)

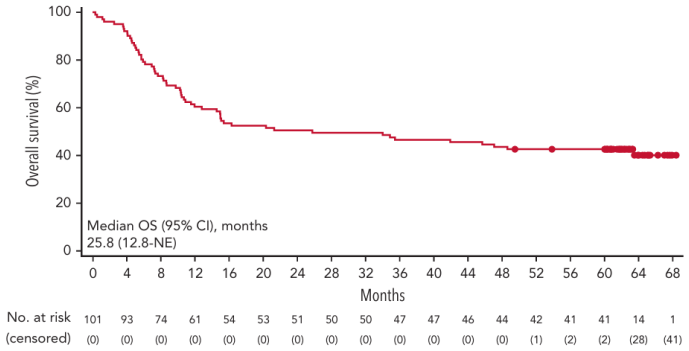
	ZUMA-1 Axicabtagene ciloleucel	JULIET Tisagenlecleucel	TRANSCEND-001 Lisocabtagene maraleucel
Age (years)	58	56	63
DLBCL, NOS	76%	80%	51%
Bridging therapy	0	92%	59%
ORR	83%	53%	73%
CR	58%	39%	53%
Median follow-up (mos)	63.1	40.3	19.9
Median DoCR (mos)	62.2	N.R.	26.1
Median PFS (mos)	5.9	2.9	6.8
Median OS (mos)	25.8	11.1	27.3
CRS grade ≥ 3	11%	22%	2%
ICANS grade ≥ 3	32%	12%	10%

Neelapu SS. *Blood*. 2023; 141: 2307-2315 – Schuster SJ. *Lancet Oncol*. 2021; 22: 1403-1415 – Abramson JS. *Blood*. 2024; 143: 404-416

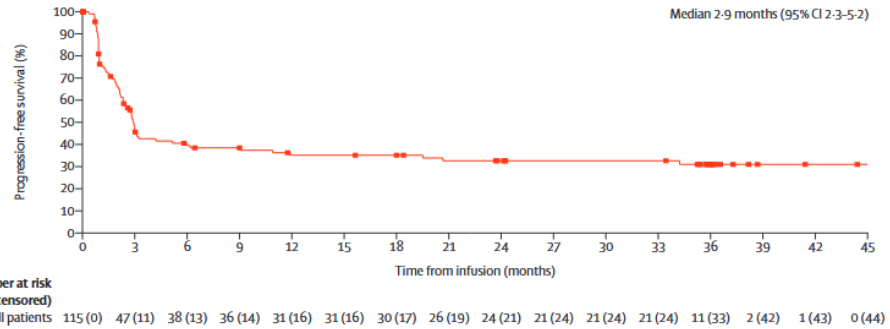
Pivotal phase 2 trials with 3rd line CAR T-cells (2)

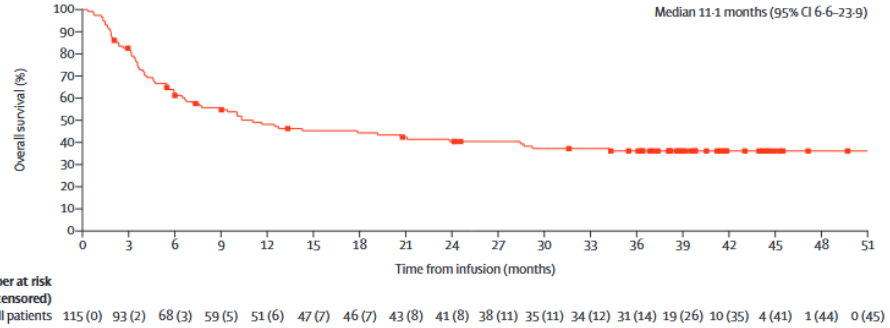
ZUMA-1





JULIET





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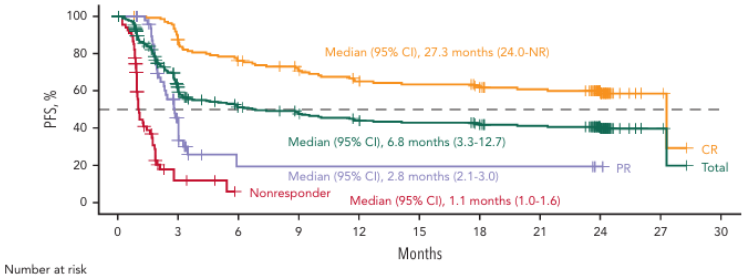
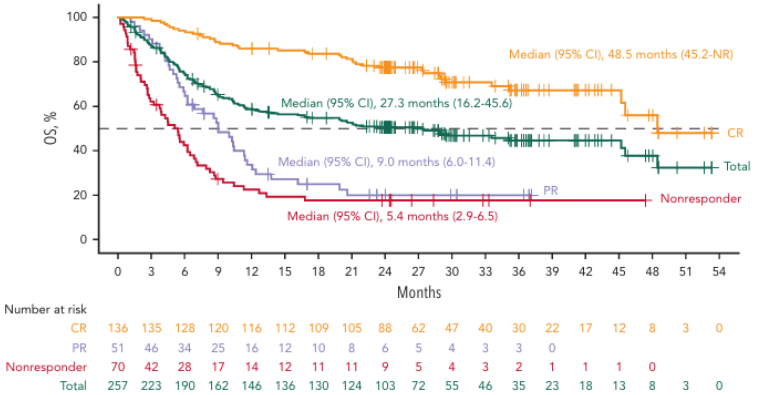




Neelapu SS. *Blood*. 2023; 141: 2307-2315 – Schuster SJ. *Lancet Oncol*. 2021; 22: 1403-1415 – Abramson JS. *Blood*. 2024; 143: 404-416

The difficult choice between bispecific antibodies and CAR T-cells as 3rd line

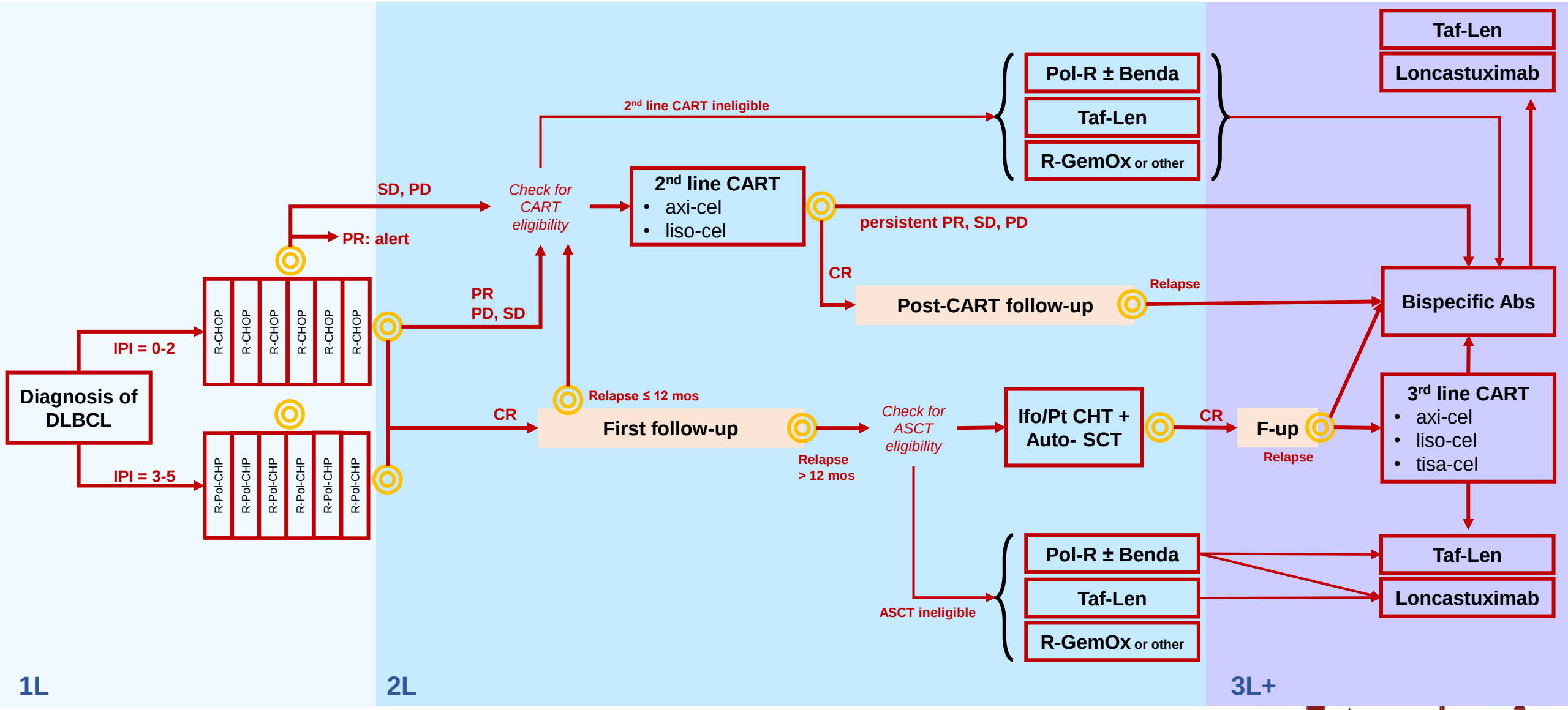
CAR T-cells	Bispecific Antibodies
Excellent efficacy	Excellent efficacy
Manufacturing process (3-4 weeks)	Available off-the-shelf
Usually inpatient, followed by period of time proximal to administering center for monitoring	Usually outpatient, initially with weekly visits that ultimately space out depending on product
"One and done"	Months (fixed duration) or continuous treatment
Requires lymphodepleting chemotherapy +/– bridging	No lymphodepleting chemotherapy or bridging
Higher risk of, and less predictable, CRS and NT	Less risk of, and more predictable, CRS and NT
Infections and cytopenias are common; likely higher rates and more prolonged	Infections and cytopenias are common; potentially lower rates but more follow up needed
Durable responses with years of follow up	Longer follow up needed for response durability

Haydu JE. *Blood Adv*. 2024; 8: 4700-4710

Assessing eligibility to either bispecific antibodies or CAR T-cells in 3rd line

	CAR T-cells	Bispecific antibodies
Age limitations	≥ 18 and ≤ 75 years	≥ 18 years
Performance status (ECOG)	0-1	0-1
Antigen expression	$CD19^+$ if anti-CD19 pretreated	$CD20^+$ required
Infections	Absent or all inactive	Absent or all inactive
Immune-mediated diseases	None	*Not specified*
Creatinine clearance	≥ 60 mL/min	≥ 30 mL/min
Left ventricle ejection fraction	≥ 50%	*Not specified*
Cardiovascular diseases	None	None
Pulmonary function	$SatO_2$ > 92%	*Not specified*
Thromboembolism	None within 6 months	*Not specified*
Liver function	AST/ALT ≤ 2.5 x ULN Bilirubin ≤ 1.5 mg/dL	Child Pugh A
Bone marrow function	ANC ≥ 1,000/mmc Hb ≥ 8 g/dL Plt ≥ 75,000/mmc	*Not specified*

Large B-cell lymphoma treatment algorhythm



Loncastuximab tesirine

Registration phase 2 study

- 149 patients with relapsed (or refractory) diffuse large B-cell lymphoma, high-grade B-cell lymphoma with double/triple hit features, primary mediastinal B-cell lymphoma and transformed diffuse large B-cell lymphoma.
- Median age at enrolment was 66 years, ranging from 56 to 71 years.
- Median number of previous systemic therapies was 3.
- Bulky disease was an exclusion criterion (6% of patients overall).
- Patients were refractory to the most recent therapy in 58% of the cases.
- Previous CART therapy was given in 9% of enrolled patients.

2-year update

- Best OR rate of 48.3% with a CR rate of 24.1%.
- Median time to first response (complete or partial): 41 days.
- Deep responses observed in patients with adverse disease features.
- Median PFS 4.93 months, but not reached for patients achieving a CR.
- Patients achieving a CR maintain the response for > 36 months in > 70% of the cases.

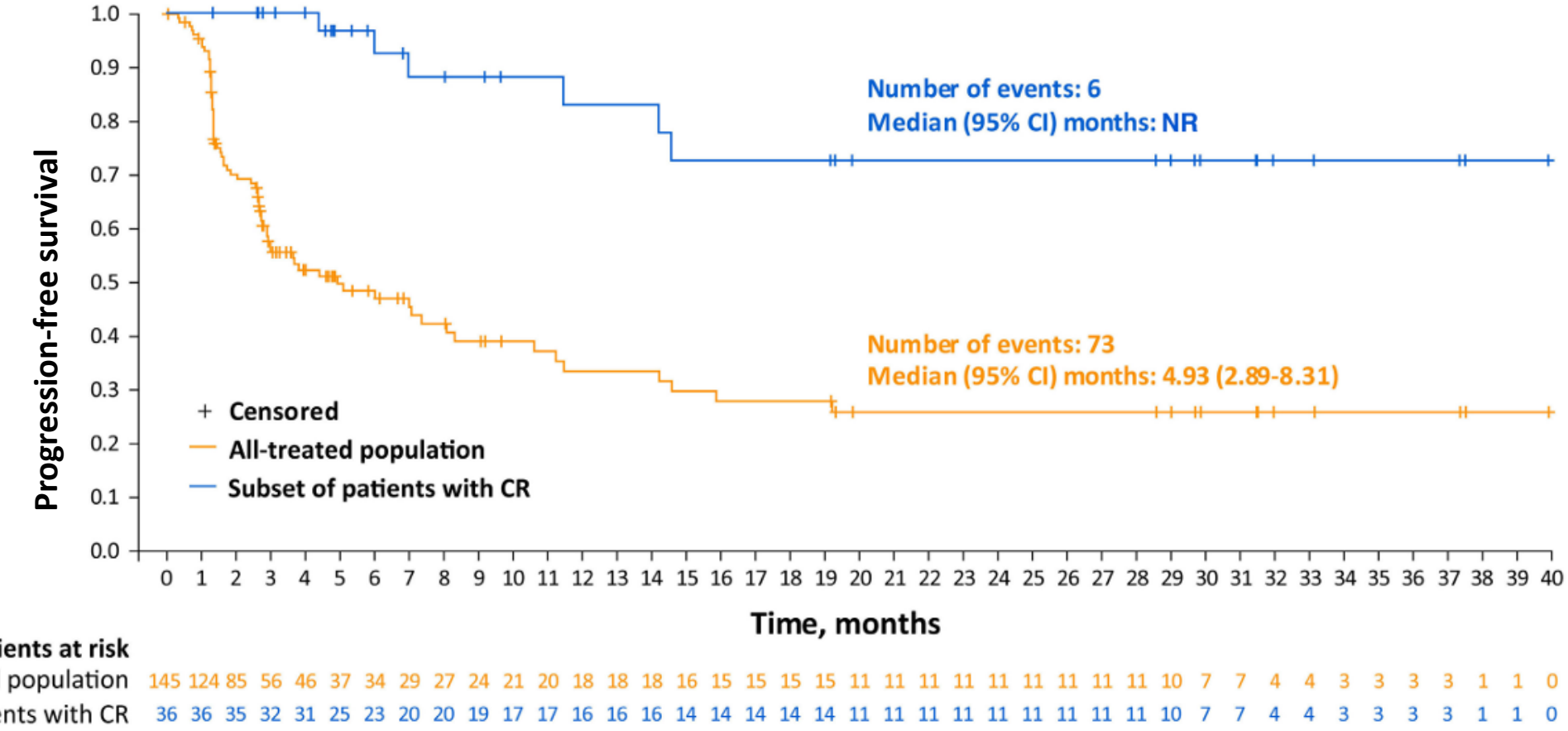
Caimi PF, *Lancet Oncol* 2021; 22: 790-800 – Caimi PF. *Haematologica*. 2024; 109: 1184-1193

Loncastuximab tesirine in relapsed/refractory diffuse large B-cell lymphoma: long-term efficacy and safety from the phase II LOTIS-2 study

	All-treated N=145	Best response of CR N=36	Patients with CR who were event-free ≥1 year N=16	Patients with CR who were event-free ≥2 years N=11
Sex, N (%)				
Female	60 (41.4)	22 (61.1)	13 (81.3)	9 (81.8)
Age in years, N (%)				
Median (range)	66.0 (23-94)	67.5 (45-94)	71.0 (53-84)	70.0 (53-82)
<65	65 (44.8)	13 (36.1)	3 (18.8)	3 (27.3)
≥65 to <75	59 (40.7)	15 (41.7)	7 (43.8)	5 (45.5)
≥75	21 (14.5)	8 (22.2)	6 (37.5)	3 (27.3)
Race, N (%)				
White	130 (89.7)	34 (94.4)	15 (93.8)	11 (100)
Black or African American	5 (3.4)	1 (2.8)	0	0
Asian	3 (2.1)	0	0	0
Other	7 (4.8)	1 (2.8)	1 (6.3)	0
ECOG score, N (%)				
0	58 (40.0)	19 (52.8)	9 (56.3)	7 (63.6)
1	78 (53.8)	14 (38.9)	6 (37.5)	3 (27.3)
2	9 (6.2)	3 (8.3)	1 (6.3)	1 (9.1)
Histology, N (%)				
DLBCL, NOS	128 (88.3)	31 (86.1)	11 (68.8)	8 (72.7)
HGBCL	10 (6.9)	5 (13.9)	5 (31.3)	3 (27.3)
Primary mediastinal DLBCL	7 (4.8)	0	0	0
Transformed DLBCL, N (%)	30 (20.7)	7 (19.4)	4 (25.0)	2 (18.2)
Double/triple hit, N (%)				
Double hit	12 (8.3)	5 (13.9)	5 (31.3)	3 (27.3)
Triple hit	3 (2.1)	0	0	0
Stage, N (%)				
I-II	33 (22.8)	9 (25.0)	3 (18.8)	2 (18.2)
III-IV	112 (77.2)	27 (75.0)	13 (81.3)	9 (81.8)
Prior systemic therapies, N (%)				
Median (range)	3.0 (2-7)	3.0 (2-7)	2.0 (2-7)	2.0 (2-7)
2 prior lines	63 (43.4)	15 (41.7)	10 (62.5)	8 (72.7)
3 prior lines	34 (23.4)	5 (13.9)	2 (12.5)	1 (9.1)
>3 prior lines	48 (33.1)	16 (44.4)	4 (25.0)	2 (18.2)
Refractory, N (%)				
Primary refractory	29 (20.0)	5 (13.9)	2 (12.5)	0
Refractory to last therapy	89 (61.4)	11 (30.6)	5 (31.3)	4 (36.4)
Prior SCT, N (%)	24 (16.6)	8 (22.2)	1 (6.3)	1 (9.1)
Prior CAR T therapy, N (%)	14 (9.7)	3 (8.3)	2 (12.5)	0

Caimi PF. *Haematologica*. 2024; 109: 1184-1193

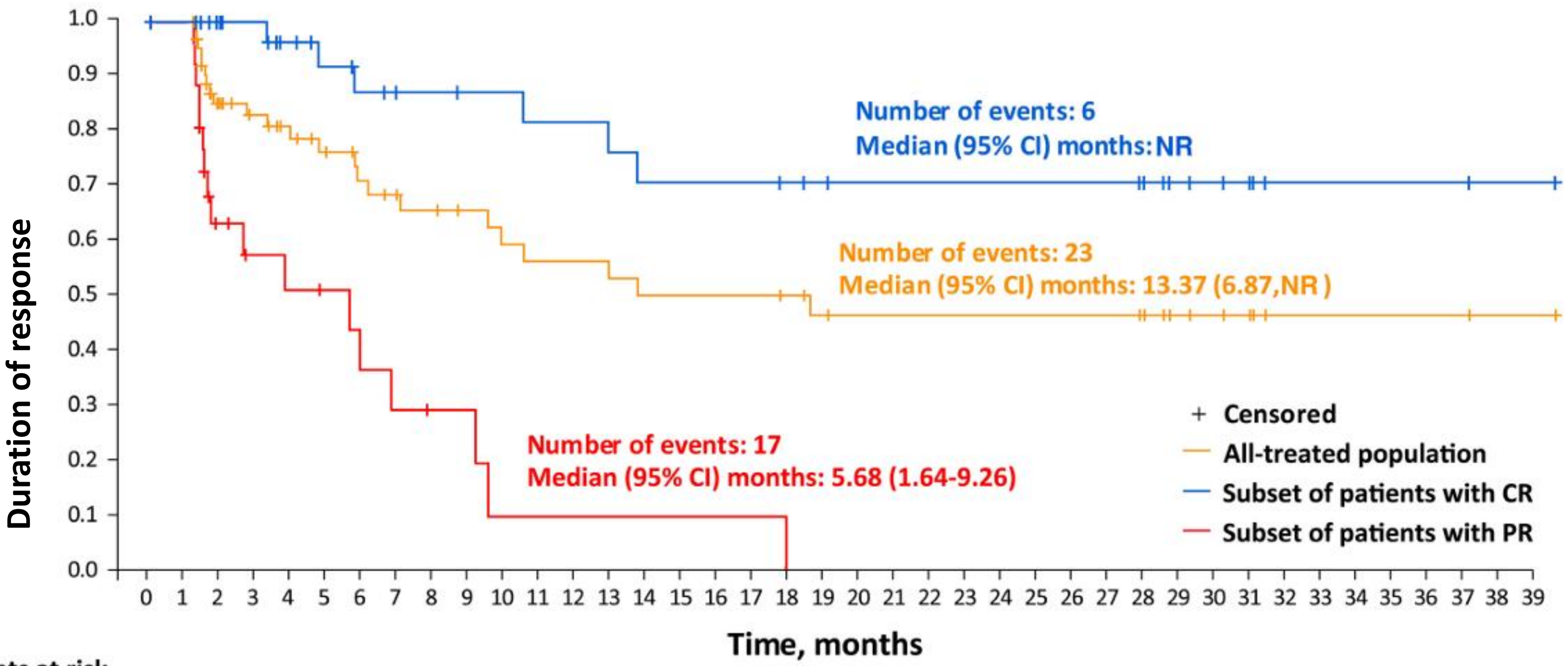
Loncastuximab tesirine in relapsed/refractory diffuse large B-cell lymphoma: long-term efficacy and safety from the phase II LOTIS-2 study



Patients at risk																																						
All-treated population	145	124	85	56	46	37	34	29	27	24	21	20	18	18	18	16	15	15	15	15	11	11	11	11	11	11	11	11	11	10	7	7	4	4	3	3	3	3	1	1	0
Subset of patients with CR	36	36	35	32	31	25	23	20	20	19	17	17	16	16	16	14	14	14	14	14	11	11	11	11	11	11	11	11	11	10	7	7	4	4	3	3	3	3	1	1	0

Caimi PF. *Haematologica*. 2024; 109: 1184-1193

Loncastuximab tesirine in relapsed/refractory diffuse large B-cell lymphoma: long-term efficacy and safety from the phase II LOTIS-2 study

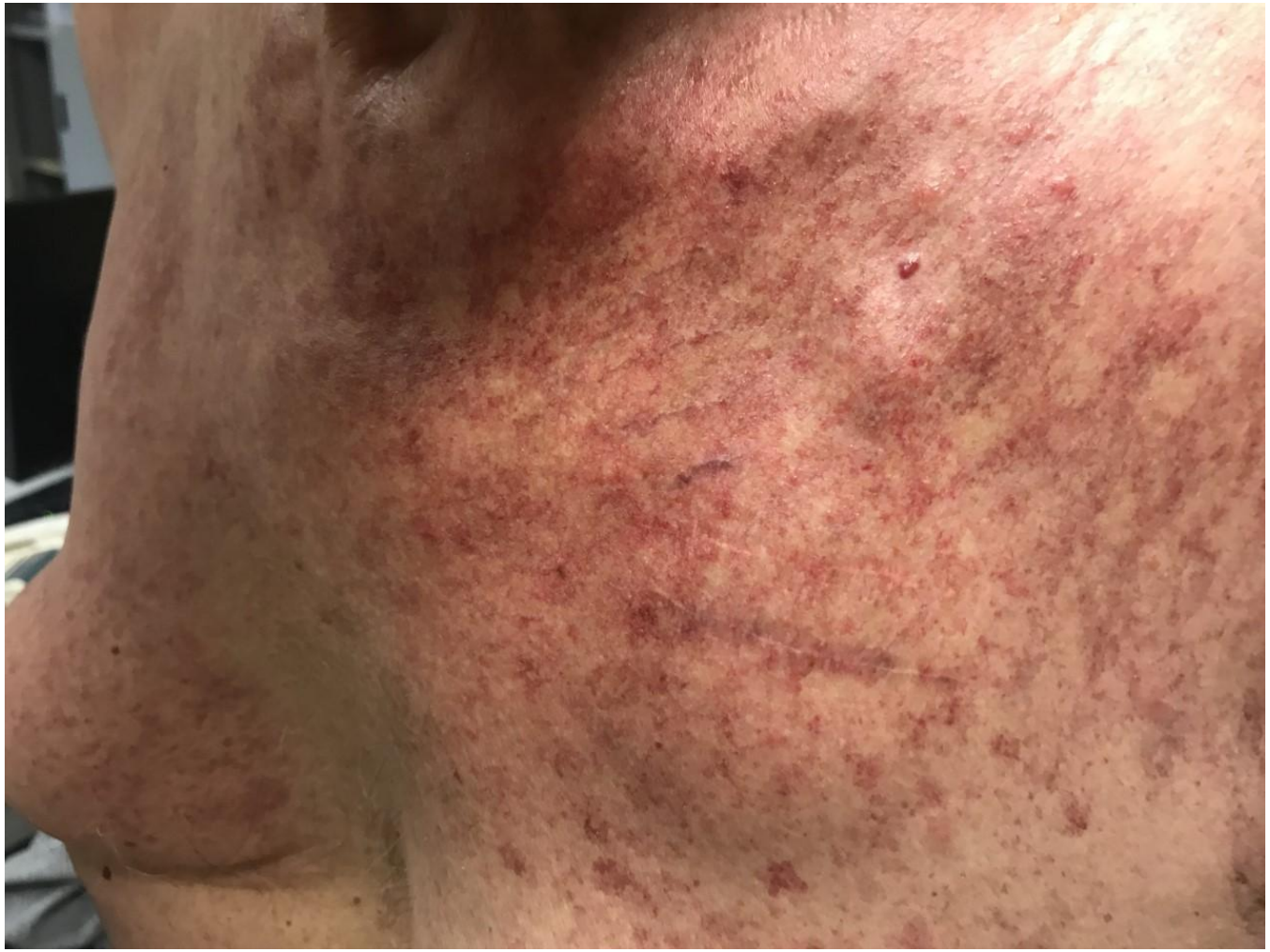


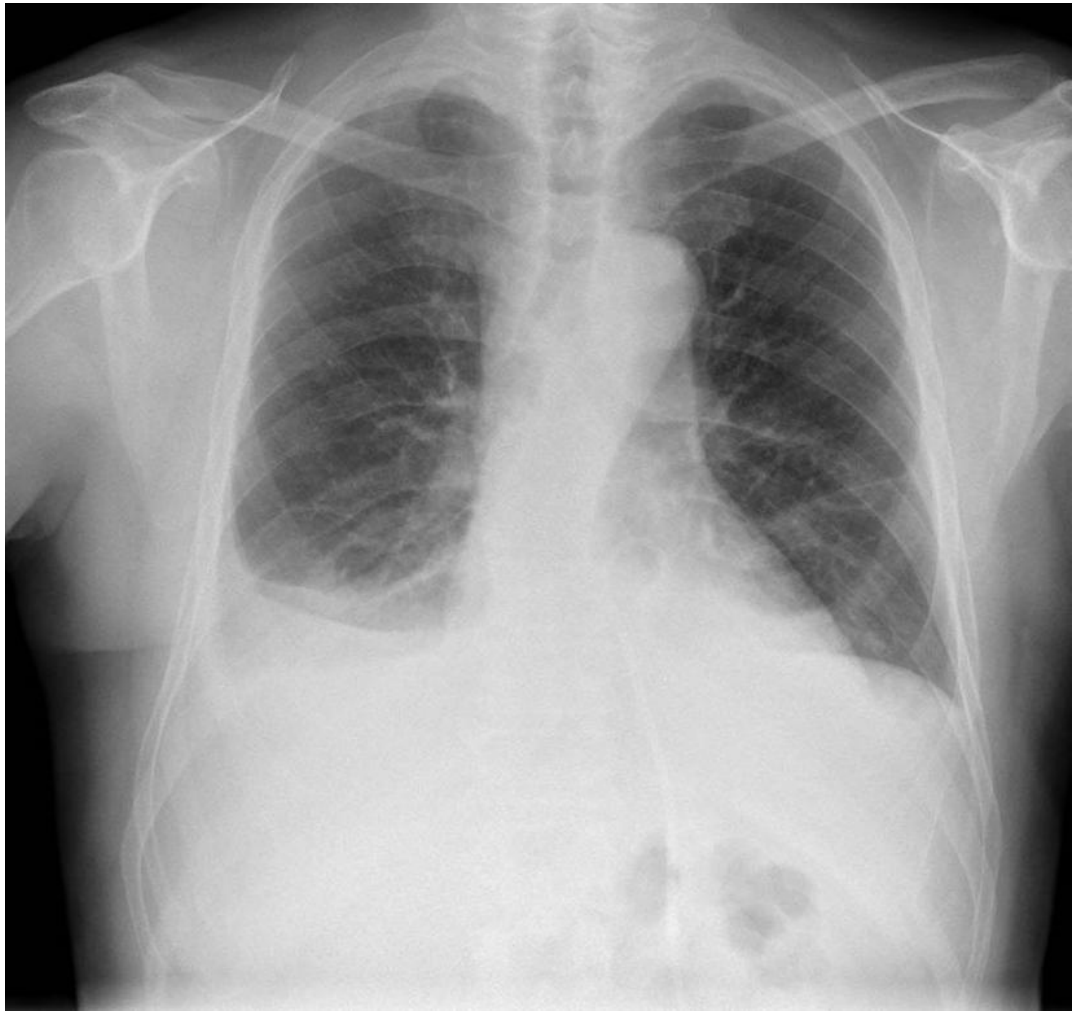
Patients at risk

All-treated population	70	63	42	38	33	29	25	22	21	20	18	17	17	16	15	15	15	15	13	11	11	11	11	11	11	11	11	11	7	6	5	2	2	2	2	2	2	1	1	0
Subset of patients with CR	36	35	30	29	25	22	20	18	18	17	17	16	16	15	14	14	14	14	12	11	11	11	11	11	11	11	11	11	7	6	5	2	2	2	2	2	2	1	1	0
Subset of patients with PR	34	28	12	9	8	7	5	4	3	3	1	1	1	1	1	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Caimi PF. *Haematologica*. 2024; 109: 1184-1193

Loncastuximab tesirine: toxicity aspects

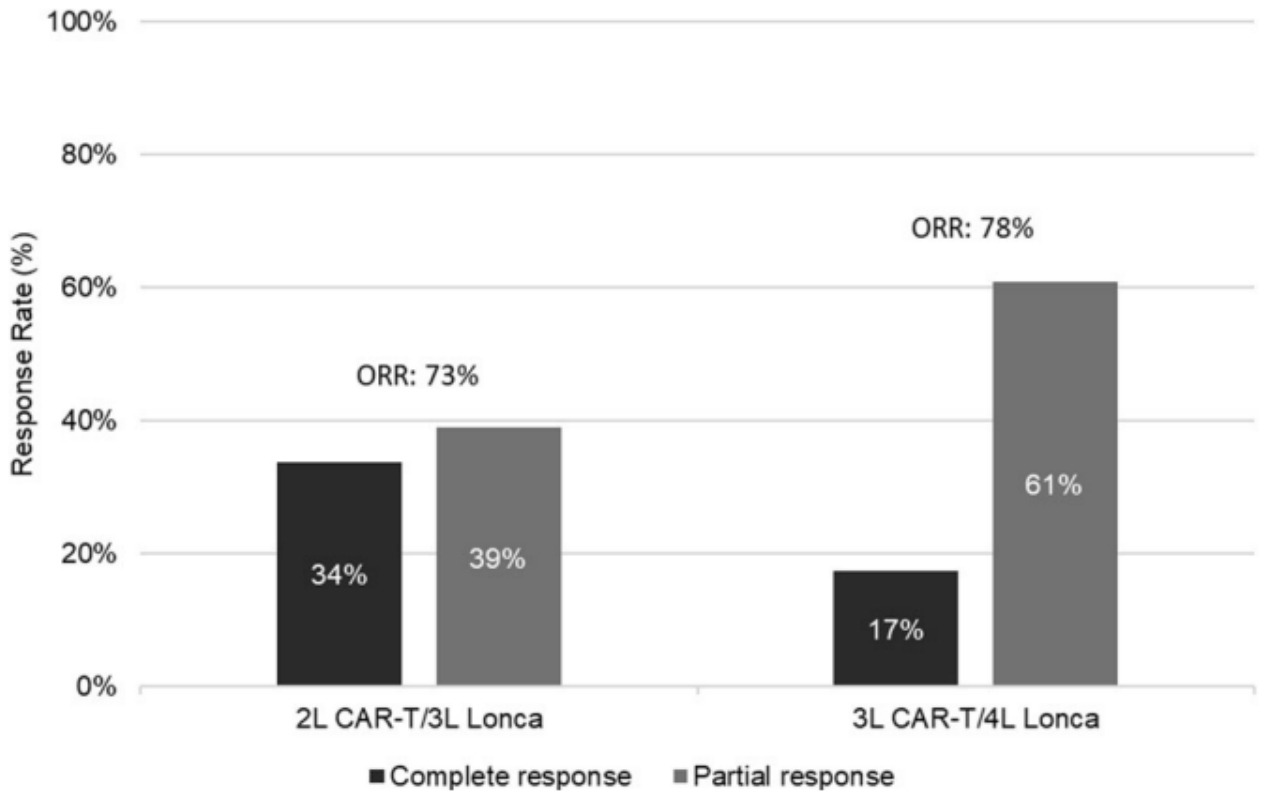




Author's personal archive

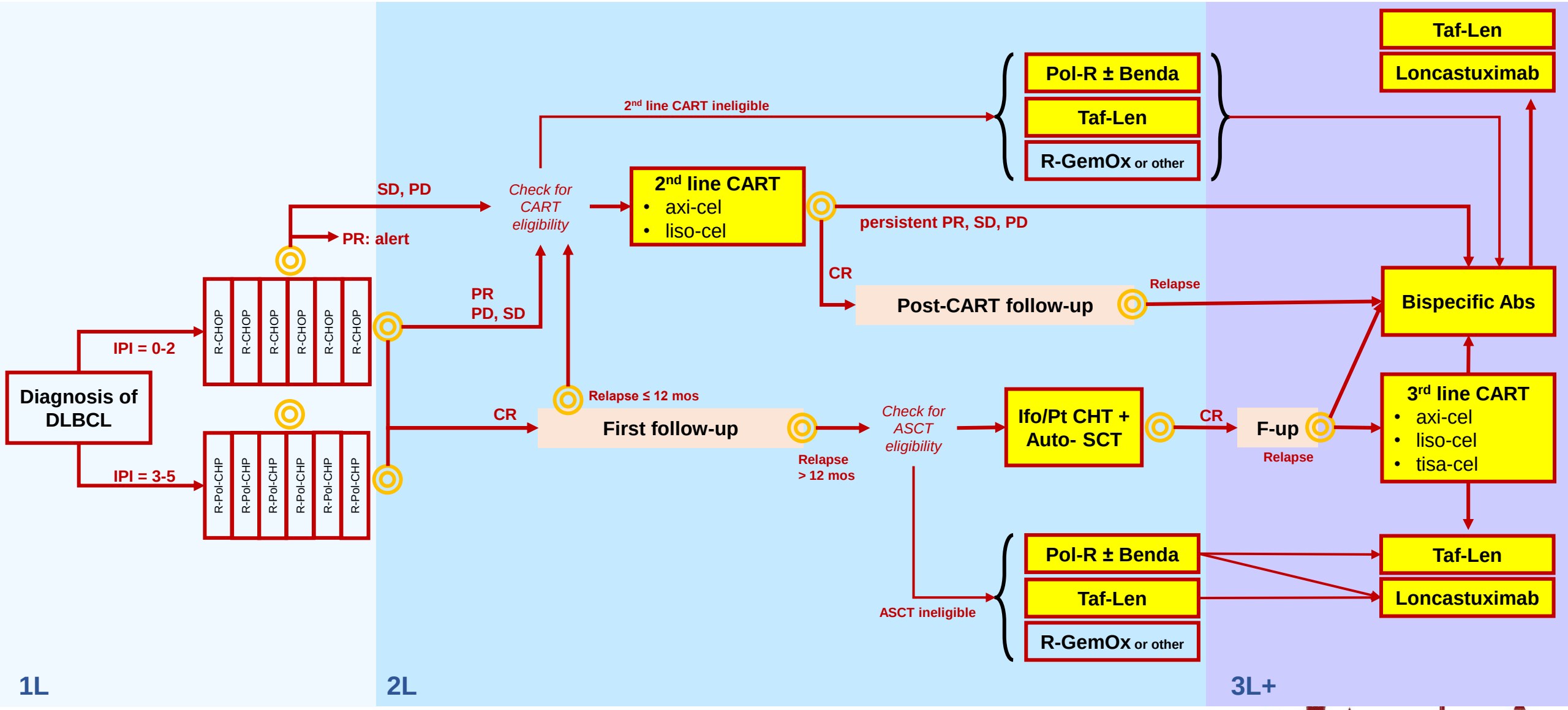
	Loncastuximab line of therapy	
	3rd Line *N* = 95 (%)	4th Line *N* = 23 (%)
Overall response rate	69 (73%)	18 (78%)
Best overall response		
Complete response	32 (34%)	4 (17%)
Partial response	37 (39%)	14 (61%)
Stable disease	18 (19%)	3 (13%)
Progressive disease	4 (4%)	2 (9%)
Death	4 (4%)	0 (0%)
Duration of response		
Median (95% CI)	NR (8, NR)	7.6 (6.0, 8.9)
12-month DOR, (%)	68%	22%
Progression-free survival		
Median (95% CI)	NR	12.0 (8.1, 12.0)
12-month PFS, (%)	77%	27%
24-month PFS, (%)	NR	22%
Overall survival		
Median (95% CI)	NR	NR (19.3, NR)
12-month OS, (%)	84%	95%
24-month OS, (%)	79%	64%

Outcomes with loncastuximab tesirine following CAR T-cell therapy in patients with relapsed or refractory diffuse large B-cell lymphoma



Epperla N. *Blood Cancer J*. 2024; 14: 210

Large B-cell lymphoma treatment algorhythm



Based on Author's experience

Concluding remarks

- Patients require careful evaluation and staging before (prognosis) and during initial (and subsequent) treatment(s) and need to be closely followed (clinically + PET) after each line of therapy.

- The detection of early signs and symptoms of relapse is of paramount importance at any time when you deal with an aggressive disease with potentially effective treatment options following first line.

- The timing of the relapse (e.g. early *versus* late ⇨ 2nd line CART *versus* salvage ASCT, if feasible) and the quality of the response (e.g. CR *versus* PR ⇨ salvage ASCT *versus* 3rd line CART) are informative for treatment decisions.

- Treatment-emergent adverse events, patient's comorbidities, rapidity of response are the main factors on which further treatment choices should rely on.

- Adherence to the same enrolment criteria used in registration trials may be of importance when applying more advanced lines of therapy (e.g. tafasitamab + lenalidomide).

- Logistic concerns may exist and should be taken into consideration to enhance compliance: ease of initiation, outpatient administration options, fixed duration *versus* continuous therapy, need of a caregiver etc.