

QUINTO EVENTO NAZIONALE

SIE incontra i pazienti

**I nuovi farmaci nei
Linfomi**

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Bologna, Royal Hotel Carlton



SIE incontra i pazienti

Disclosures of **Beatrice Casadei**

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Celgene-BMS						X	
Kite-Gilead					X	X	X
Novartis					X	X	
Takeda						X	
Roche			X		X	X	
Janssen						X	
Lilly					x		
Abbvie					x		
BeOne					x		
MSD					x		

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I nuovi farmaci nei Linfomi

Linfoma di Hodgkin

1. Anticorpi farmaco coniugati (ADC)
2. Anticorpi bispecifici
3. Inibitori di proteine (inibitore di PRMT5)
4. Terapia cellulare

Linfomi non-Hodgkin B

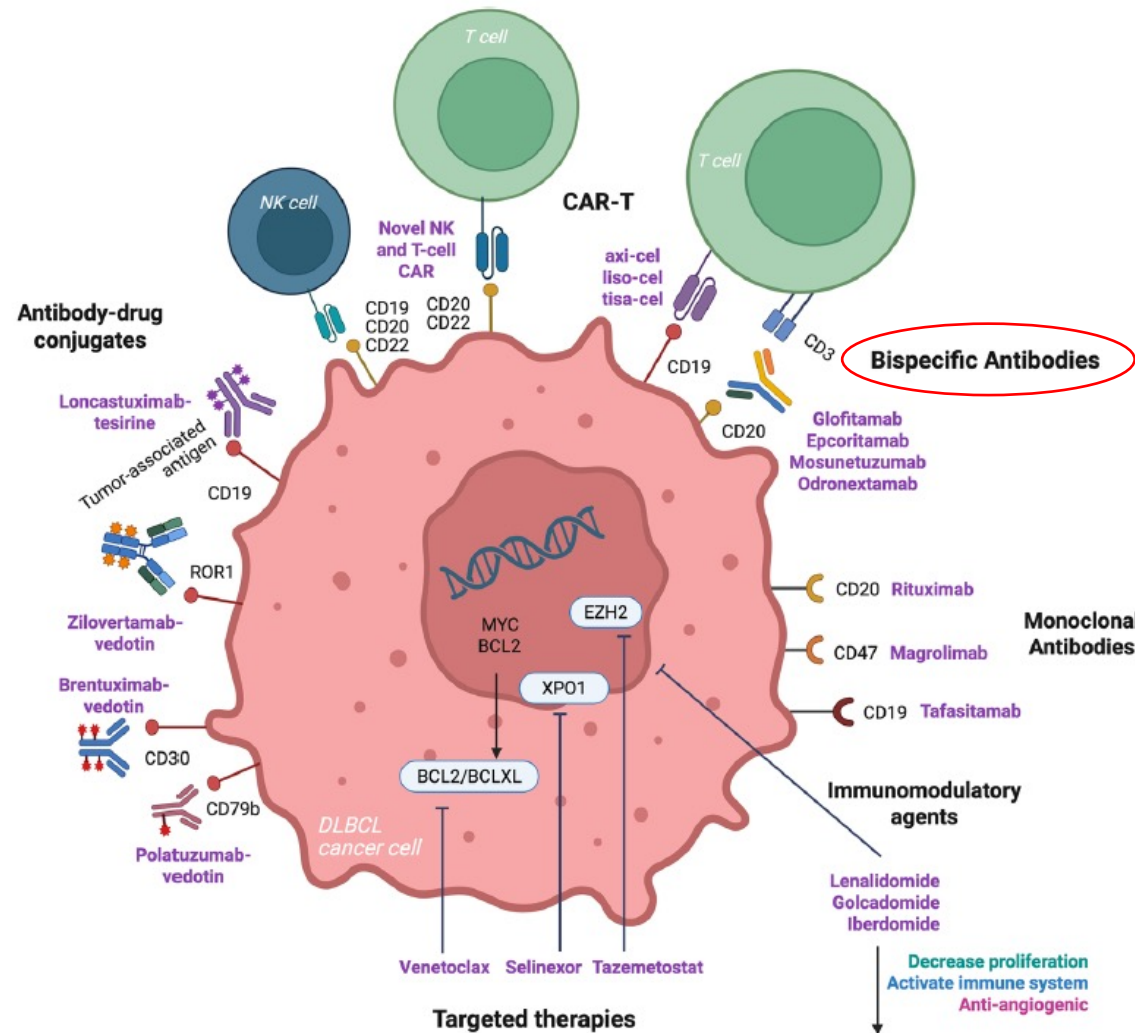
1. Anticorpi bispecifici
2. ADC
3. Anticorpi monoclonali
4. Immunomodulanti
5. Inibitori di chinasi/proteine
6. Protein degrader

Linfomi non-Hodgkin T

1. Inibitori di chinasi/proteine
2. Anticorpi monoclonali
3. Terapia cellulare

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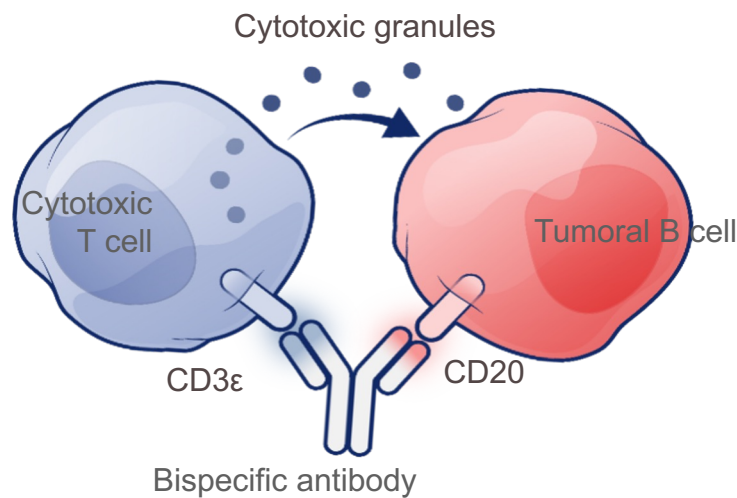
I nuovi farmaci nei Linfomi non-Hodgkin B



DLBCL
 FL
 MZL (clinical trial)
 MCL (clinical trial)

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Gli Anticorpi Bispecifici e le Loro Attuali Indicazioni



	Glofitamab	Epcoritamab	Mosunetuzumab
Construct	CD20xCD3	CD20xCD3	CD20xCD3
CD20:CD3 ratio	2:1	1:1	1:1
Administration	EV, 12 cycles (21 days)	SC, until PD or severe toxicity (28days cycle)	EV, 17 cycles (21 days)
AIFA approval status	<ol style="list-style-type: none"> 1. Adult patients with DLBCL NOS after ≥ 2 lines of systemic therapy 2. Plus Gemox in Adult patients with DLBCL RR to a previous systemic therapy and not eligible to ASCT (COOMING SOON in 2L) 	<ol style="list-style-type: none"> 1. Adult patients with DLBCL NOS after ≥ 2 lines of systemic therapy 2. Adult patients with r/r FL after ≥ 2 lines of systemic therapy 	<ol style="list-style-type: none"> 1. Adult patients with r/r FL after ≥ 2 lines of systemic therapy

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Gli Anticorpi Bispecifici: Efficacia e Tossicità

Nel Linfoma B a Grandi Cellule

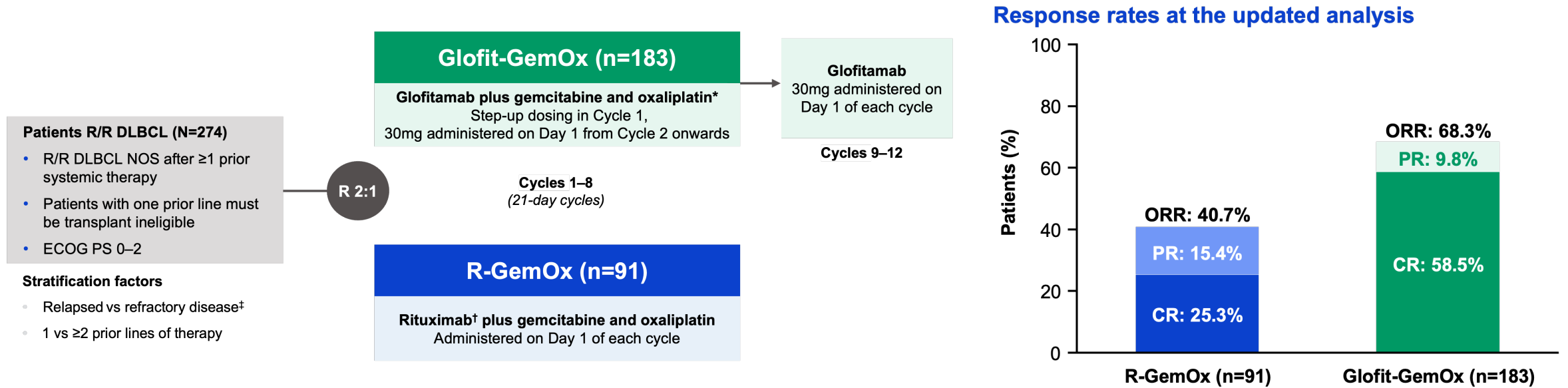
Agent and trial	Ph	Route	Pts n	Prior tx median (range)	Primary ref. %	Prior CART, %	ORR/CR%	Median Follow-up, mo	Median DoR/CR mo	Median PFS, mo	Median OS, mo	CRS (any/gr ≥3), %	ICANS (any/gr ≥3) %
Glofitamab	I/II	EV, fixed duration	155	3 (2-7)	58	33	52/40	32.1	18.4/29.8	4.9	11.5	63/4	8/3
Epcoritamab	I/II	SC, Until PD	148	3 (2-11)	61	38	59/41	31	20.8/36.1	4.4	NR	52/3	6/0.6

Nel Linfoma Follicolare

Agent and trial	Ph	Administration	Pts n	POD24 %	Prior tx median	ORR (CR), %	Follow-up median, mo	PFS median, mo	OS median, mo	CRS (any/gr ≥3), %	ICANS (any/gr ≥3), %	Infections gr ≥3, %
Mosunetuzumab (GO29781) ^{1,2}	II	EV, fixed duration	90	52	3 (2-4)	78 (60)	49.4	24	NR	44/2	5/0	16
Epcoritamab ⁵ (EPCORE-NHL)	I/I	SC, Until PD	214	42	3 (2-4)	82 (62.5)	36	15.4	NR	59/2	6/2	19

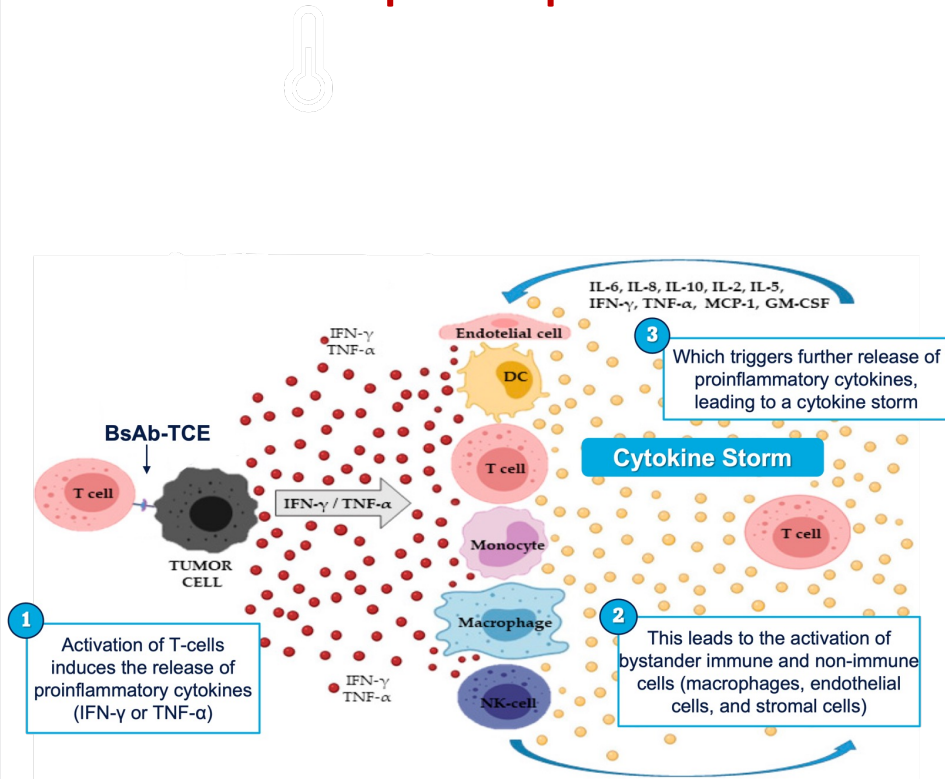
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Gli Anticorpi Bispecifici in associazione alla chemioterapia



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Gli Anticorpi Bispecifici: La Sindrome da Rilascio delle Citochine



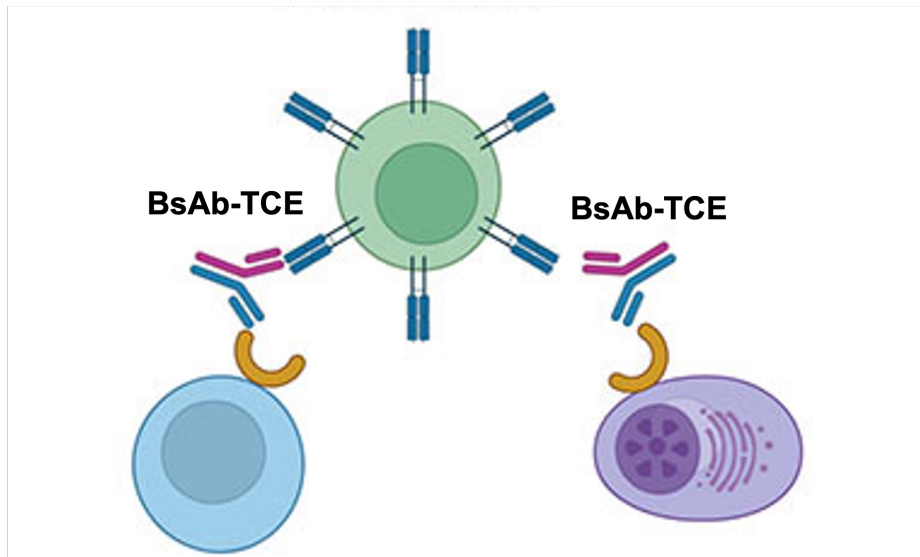
	Glofitamab				Epcoritamab				
Time Course for CRS Occurrence	42,8%	25,2%	26,0%	0,9%	5,8%	11,8%	42,8%	4,9%	3,0%
	C1D8	C1D15	C2	C3+	C1D1	C1D8	C1D15	C1D22	C3+D1
Dose (mg)	2.5	10	30	30	0.16	0.80	48	48	48
Time to CRS onset hours, median	13.5				20[†]				
Duration of CRS hours, median (range)	30.5 (0.5 – 317)				48 (24 – 648)				

Nel Linfoma diffuso a grandi cellule RR

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Gli Anticorpi Bispecifici: Le infezioni

T-cell Exhaustion



PATIENT-RELATED FACTORS

- Age
- Performance Status (PS)
- Comorbidities
- Immunoparesis (low IgG levels)
- Cytopenia (neutropenia & lymphopenia)

DISEASE-RELATED FACTORS

- Tumor burden
- Refractory disease
- Disease type
- Genetic status
- Renal dysfunction

TREATMENT FACTORS

- Previous intensive treatment
- Recent CAR T therapy
- Most recent line of therapy
- Glucocorticoid cumulative dose/prior glucocorticoid use & duration

PATIENT HISTORY

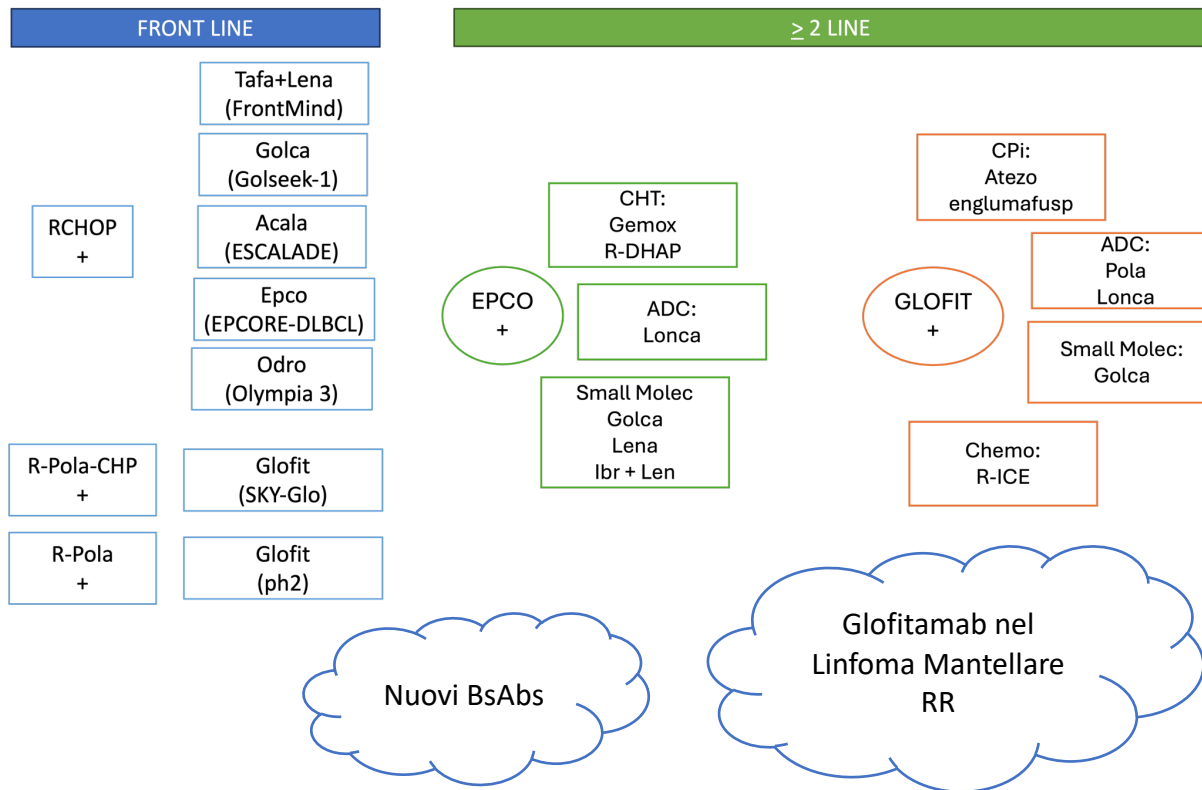
- Number of previous infections
- Type(s) of previous infections
- History of hospitalization due to infection
- Baseline DNA-virus exposure, including VZV, CMV, & HBV

- T-cell activation, proliferation, & exhaustion
- Cytopenias (Neutropenia)
- Hypogammaglobulinemia

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Prossimi Passi nel Mondo degli Anticorpi Bispecifici

Linfomi Aggressivi (DLBCL e MCL)



Linfomi Indolenti (FL, MZL)

anti-CD20xCD3 bsAbs				anti-CD19xCD3 bsAb
EPCORE FL-2 ¹	OLYMPIA-1 ^{2*}	OLYMPIA-2 ^{3*}	MorningLyte ⁴	SOUNDTRACK-F1 ⁵
Induction: Epcor + R ²	Induction: Odron monotherapy	Induction: Odron + CHOP/CVP	Induction: Mosun + Len	Induction: AZD0486 + R
Maintenance: ± epcor maintenance	Maintenance: + odron maintenance	Maintenance: ± odron maintenance	Maintenance: + mosun maintenance	Maintenance: + R maintenance
vs	vs	vs	vs	vs
Induction: • R/G-CHOP • R/G-Benda • R ²	Induction: • R-CHOP/CVP • R-Benda	Induction: • R-CHOP	Induction: • R/G-CHOP • R/G-Benda	Induction: • R-CHOP/CVP • R/Benda
Maintenance: + R maintenance	Maintenance: + R maintenance	Maintenance: + R maintenance	Maintenance: + R maintenance	Maintenance: + R maintenance (with R-CHOP/CVP only)

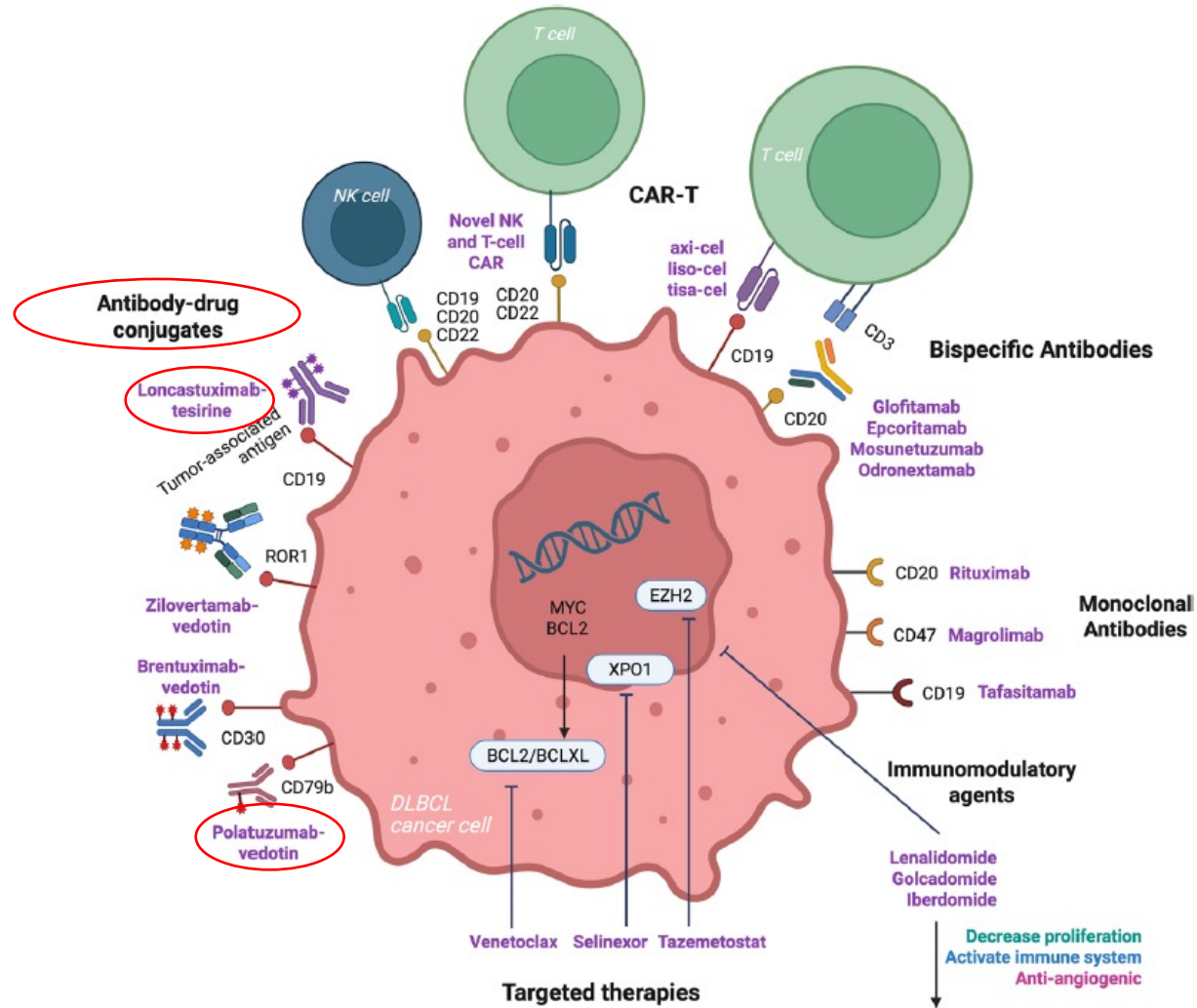
EPCORE [®] FL-1 ³	Celestimo ⁴	OLYMPIA-5 ⁵
epcoritamab + R²	mosunetuzumab + len	odronextamab + len
vs	vs	vs
R²		

- MZL:**
- Mosu+Lena
 - ELM2 (Odronextamab)
 - Olympia5_ Odron+Lena

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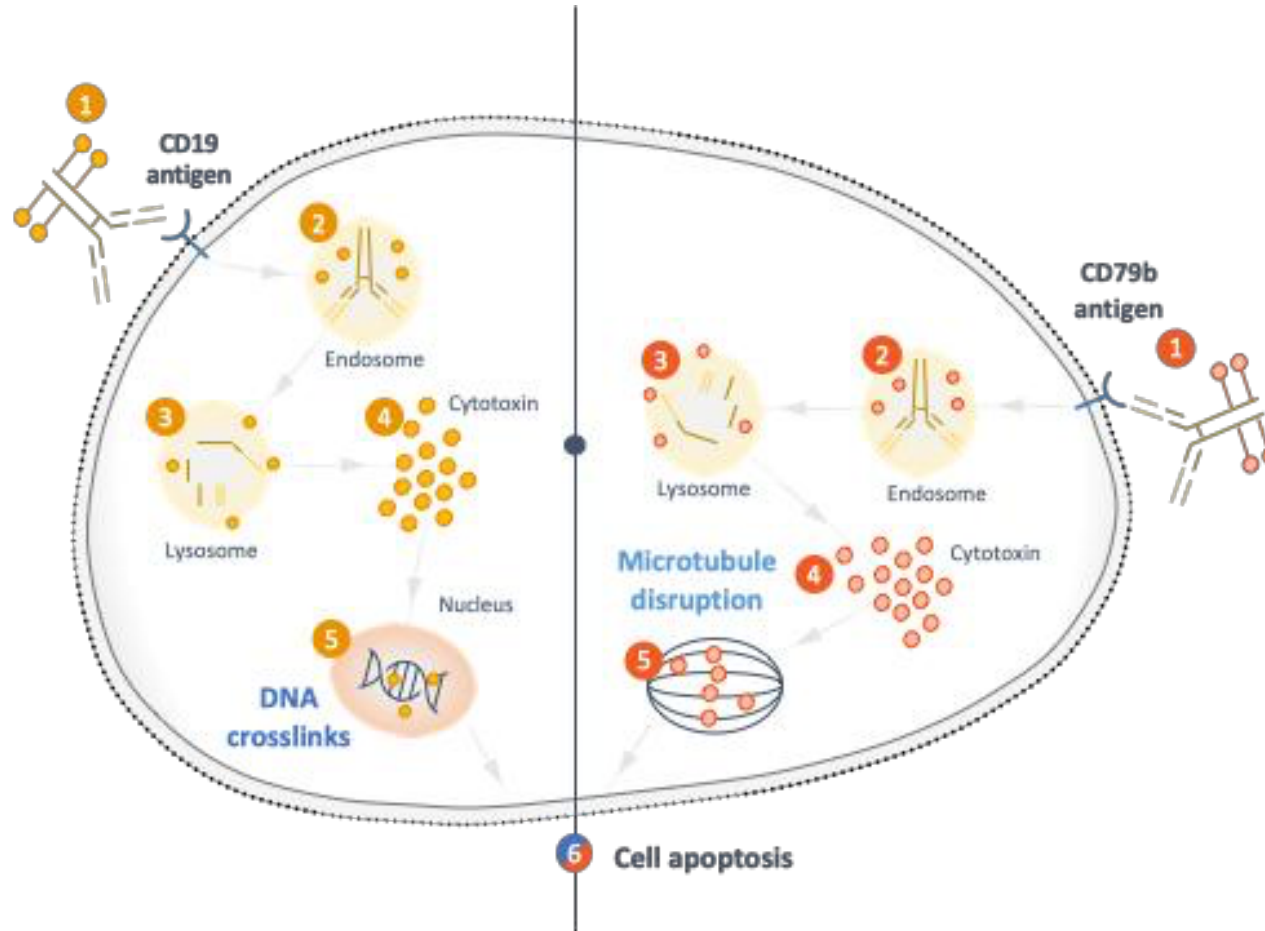
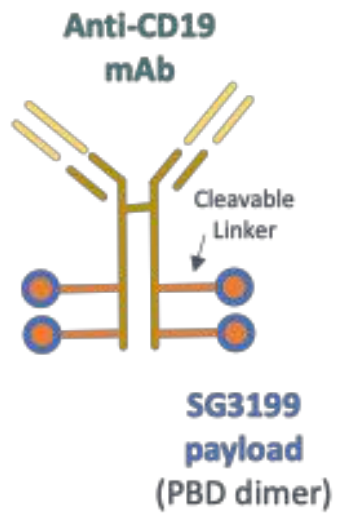
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DLBCL
 FL (clinical trial)
 MZL (clinical trial)

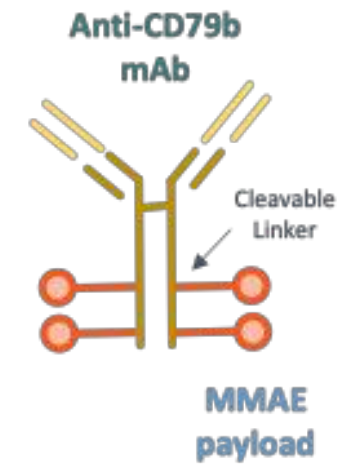


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Loncastuximab tesirine



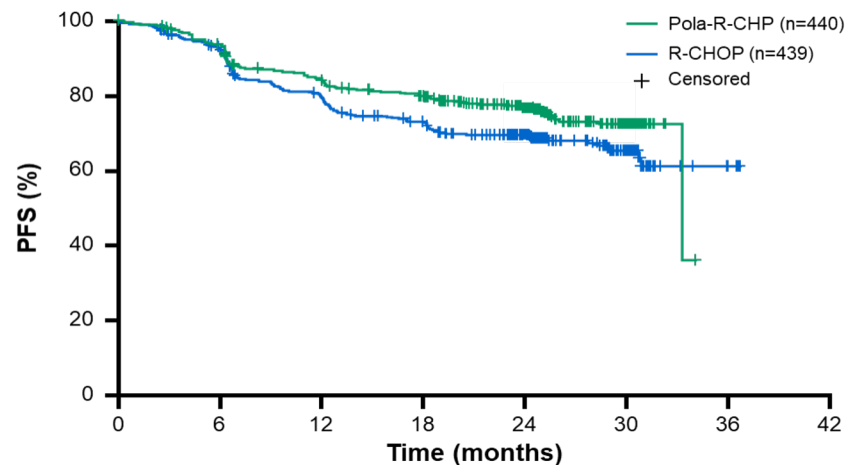
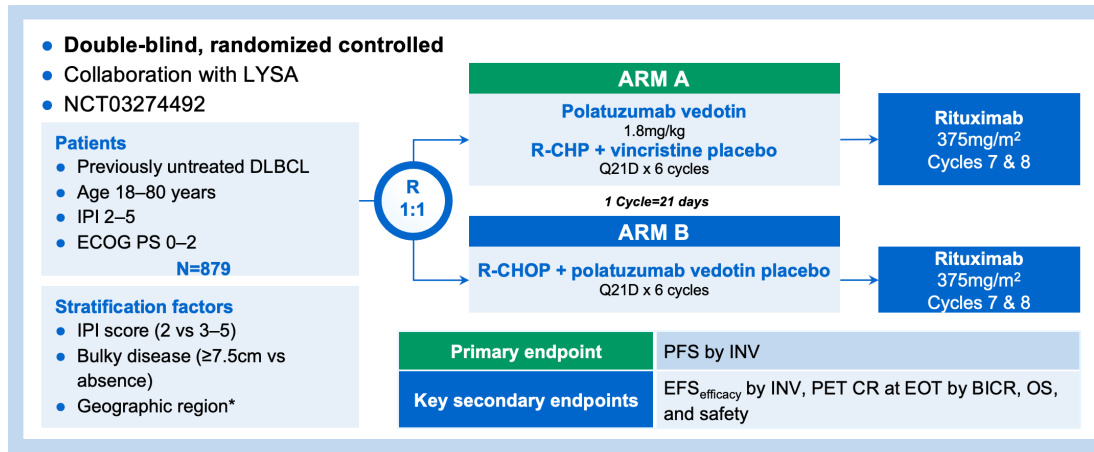
Polatuzumab vedotin



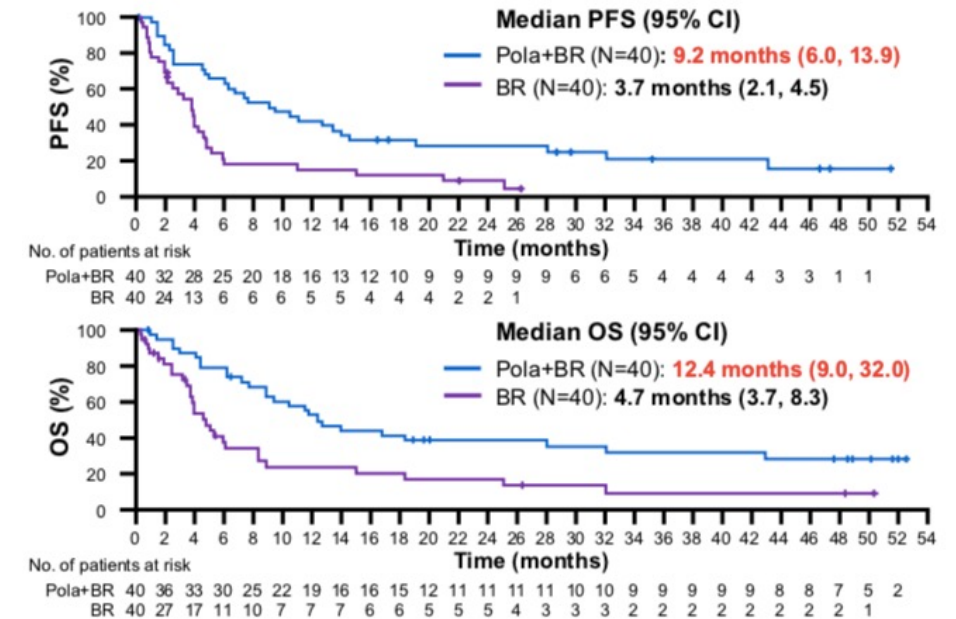
1. Alderuccio et al. Blood Rev 2022
2. Joubert et al. Pharmaceuticals (Basel) 2020.

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Polatuzumab Vedotin nel Linfoma Diffuso a Grandi Cellule



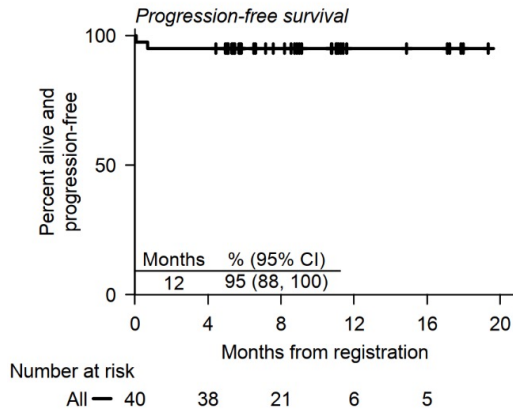
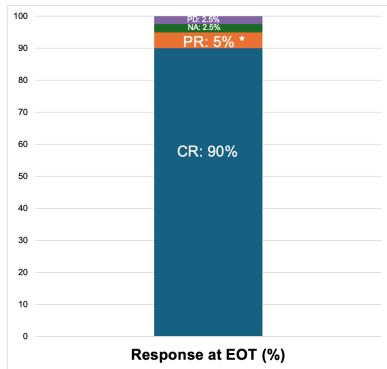
2L:
 Polatuzumab Vedotin + Bendamustina-Rituxumab in pazienti non eleggibili a trapianto autologo



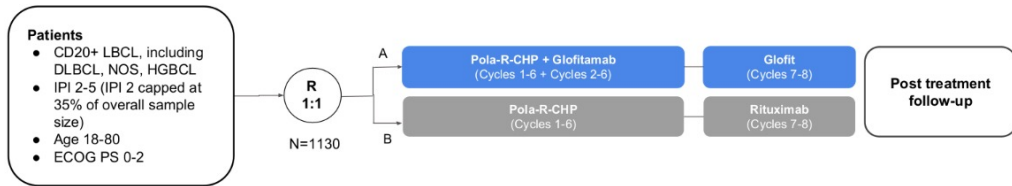
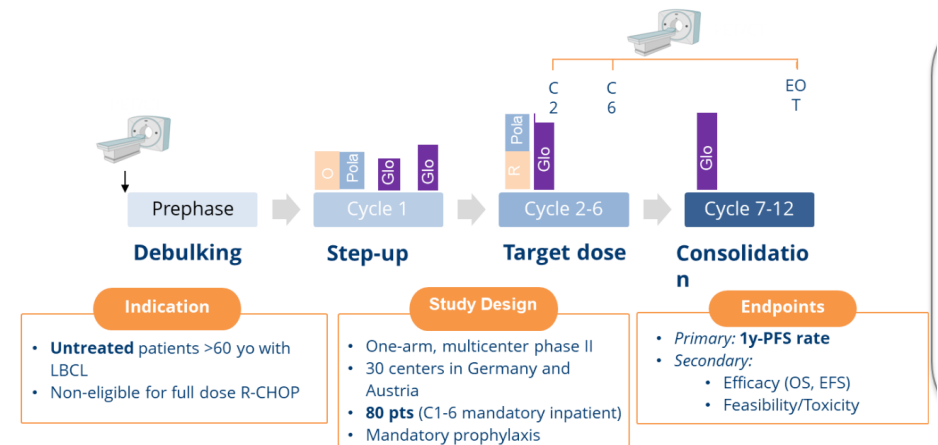
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Polatuzumab Vedotin: Prossimi Passi

In 1 Linea in associazione a R-CHP e GLofitamab



In 1 Linea in associazione a R+Glofitamab



Patients

- CD20+ LBCL, including DLBCL, NOS, HGBCL
- IPI 2-5 (IPI 2 capped at 35% of overall sample size)
- Age 18-80
- ECOG PS 0-2

Stratification Factors

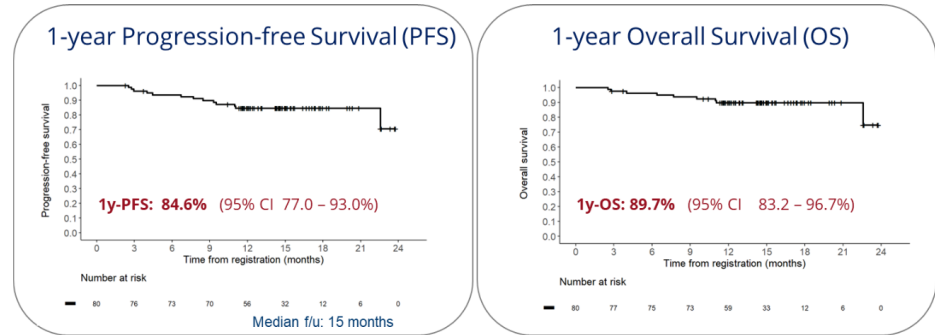
- IPI 2 vs IPI 3-5
- bulky disease defined as one lesion ≥7.5 cm (present vs absent)

Primary EP: PFS with 2-year follow-up (IRC)

Key Secondary EPs*: PFS in IPI 3-5 (IRC), OS, EFS_{efficacy} (IRC)

Selected Secondary EPs (no adjustment for multiplicity): PFC (INV), ORR, DOR, DOCR, DFS, safety, PK, PROs, ctDNA

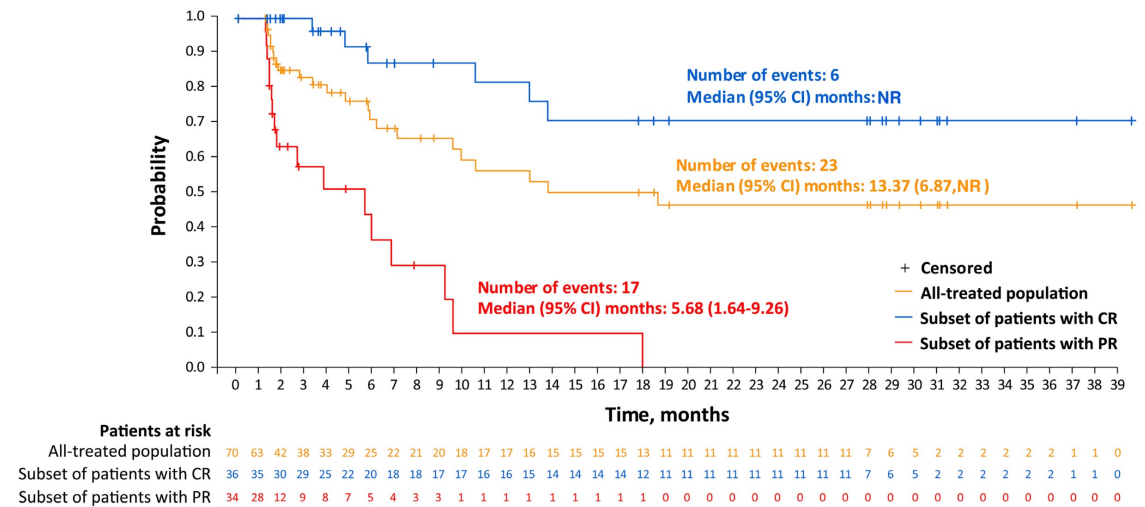
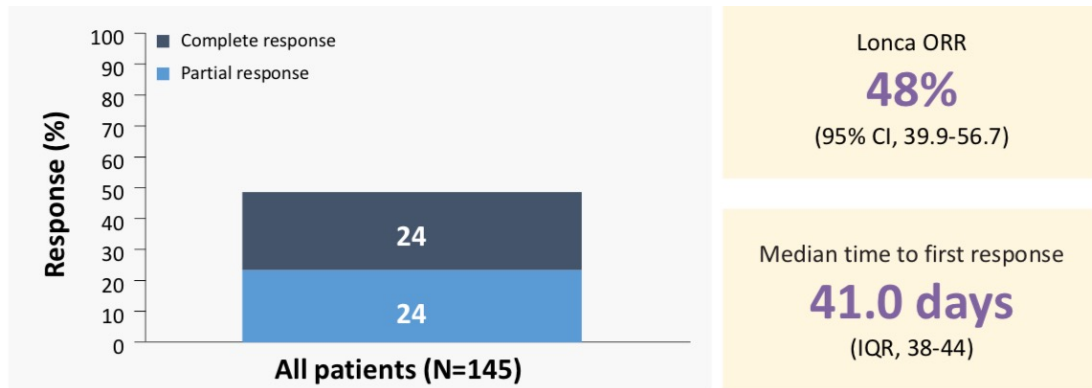
Exploratory: Biomarkers



Chapuy B. et al, oral presentation ASH 2025 Blood (2025) 146 (Supplement 1): 61.

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Loncastuximab Teserine: dati attuali nel DLBCL

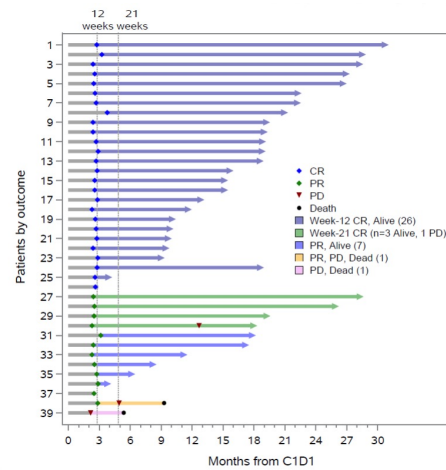
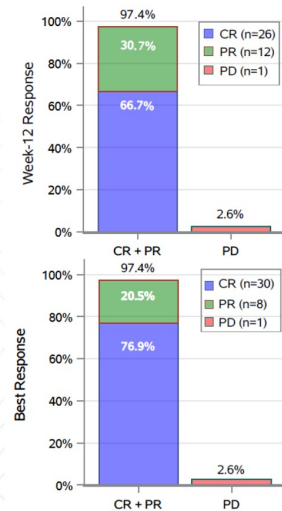


3L+ (also after CART), DLBCL (also HGBCL)
CD19 expression is not a predictor of response
Until PD (??)

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Loncastuximab Teserine: Prossimi Passi

R+Lonca
RR FL

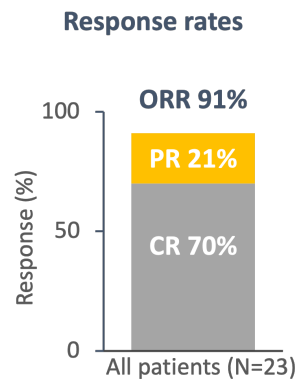


The null hypothesis was rejected (one-sided $p < 0.0001$)

Lonca
RR MZL



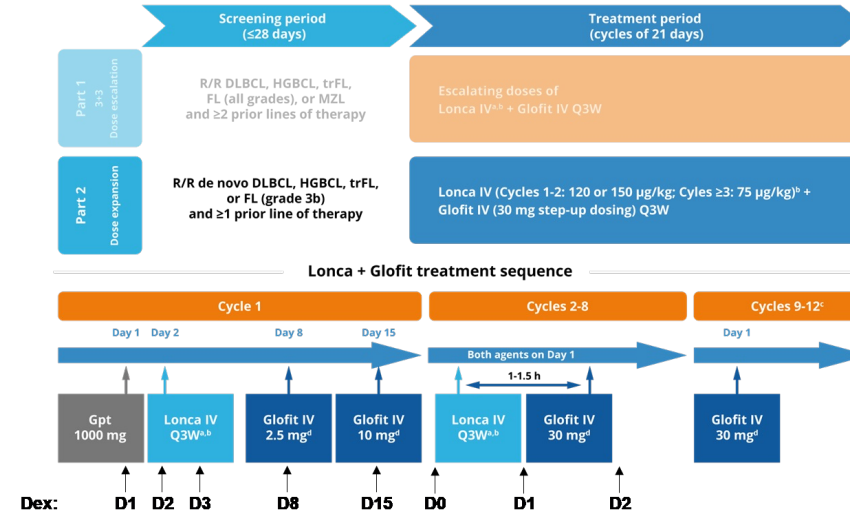
- 23 patients enrolled
- Median age was 65 years (range 45–82)
 - 100% had ECOG PS 0–1
 - 83% had stage III/IV disease
 - 48% had POD24
 - 61% had relapsed disease
 - 39% were refractory
 - Median no. of prior LoT was 2 (range 1–4)



Additional efficacy findings

- 93% of CRs currently maintained
 - 64% of POD24 patients achieved CR
 - 1 patient received prior CAR-T and achieved CR
- 67%** 18-mo DoCR **92%** 12-mo PFS

LOTIS-7: Glofit+Lonca in RR DLBCL

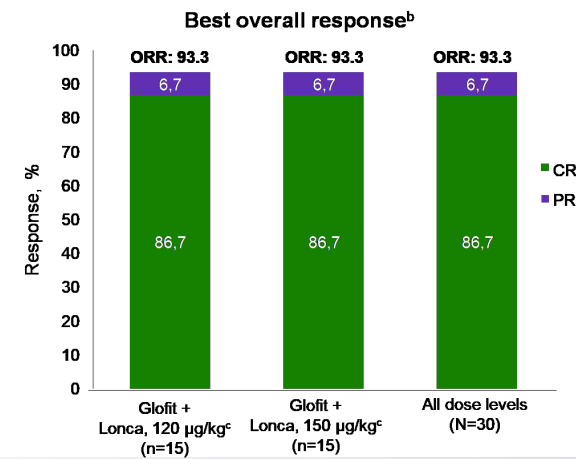


Study population

- Patients with 3L+ R/R B-NHL (part 1) and 2L+ R/R LBCL (part 2)
- ECOG PS score of 0-2
- Prior autologous SCT (>100 days) or CAR-T therapy (>100 days) is allowed
- Measurable disease (per 2014 Lugano Classification)
- Excludes patients with clinically significant third-space fluid accumulation

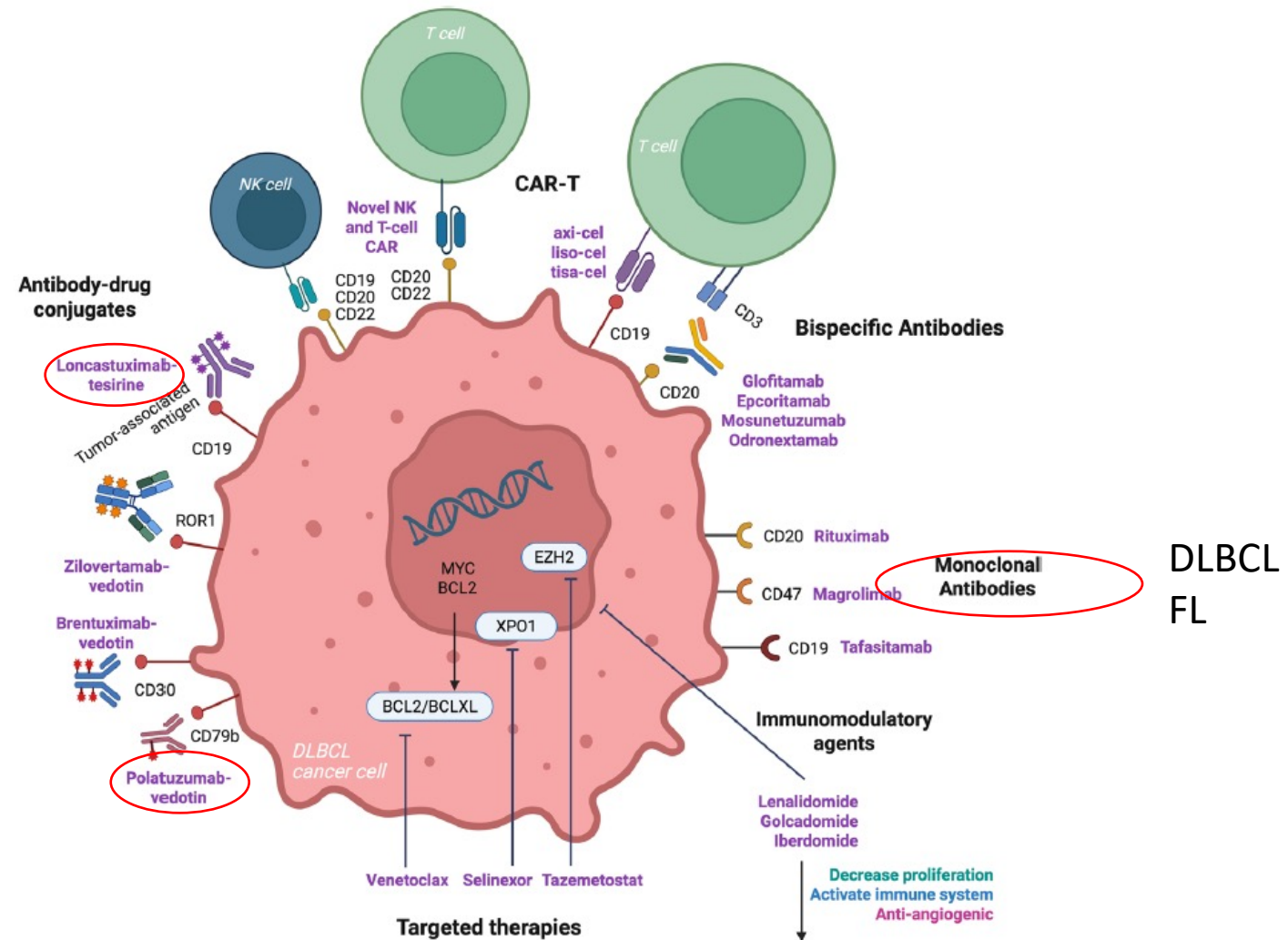
Endpoints

- **Primary:** safety and tolerability; MTD and/or RDE
- **Secondary:** ORR, DOR, CR rate, PFS, RFS, and OS; PK and immunogenicity
- **Exploratory:** Glofit concentration in circulation; biomarker and PK correlations with clinical outcomes



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Tafasitamab: Indicazione nel DLBCL

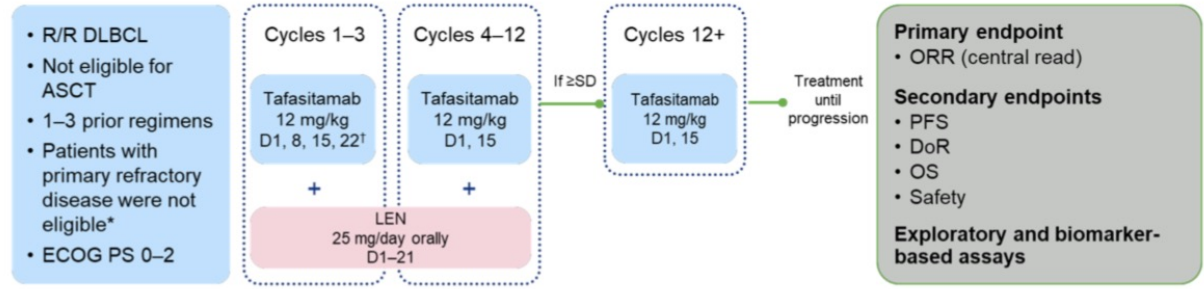
Tafasitamab
Anti-CD19 monoclonal antibody immunotherapy

Affinity-matured CD19 binding site

Enhanced Fc portion

- ADCC ↑
- ADCP ↑
- Direct cell death

Open-label, single-arm, multicenter, global, Phase II study; **N=81**



NCT02399085¹

*Primary refractory is defined as no response to, or progression/relapse during/within 6 months of, front-line therapy; 15 patients with refractory disease were included under an early version of the protocol.

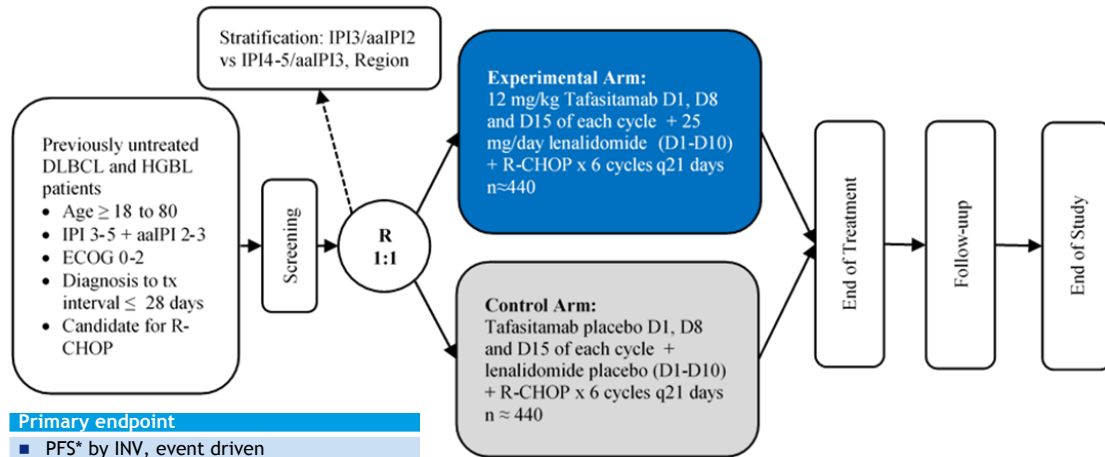
Characteristics	Primary analysis	3-year follow-up	Final 5-year data	5-year data for patients with 1 prior line of therapy, N=40	5-year data for patients with ≥2 prior lines of therapy, N=40
Data cut-off date	Nov 30, 2018	Oct 30, 2020	Nov 14, 2022	Nov 14, 2022	Nov 14, 2022
Best ORR, N (%) [95% CI]	48 (60.0) [48.4-70.9]	46 (57.5) [45.9-68.5]	46 (57.5) [45.9-68.5]	27 (67.5) [50.9-81.4]	19 (47.5) [31.5-63.9]
CR rate, N (%) [95% CI]	34 (42.5) [32.0-54.0]	32 (40.0) [29.2-51.6]	33 (41.3) [30.4-52.8]	21 (52.5) [36.1-68.5]	12 (30.0) [16.6-46.5]
PR rate, N (%)	14 (17.5)	14 (17.5)	13 (16.3)	6 (15.0) [5.7-29.8]	7 (17.5) [7.3-32.8]
				NR [9.1-NR]	NR [26.1-NR]
				23.5 [7.4-NR]	7.6 [2.7-45.5]
				NR [24.6-NR]	15.5 [8.6-45.5]

2L DLBCL, non transplant and non CAR-T eligible, IPI 0-2, relapsed Until PD

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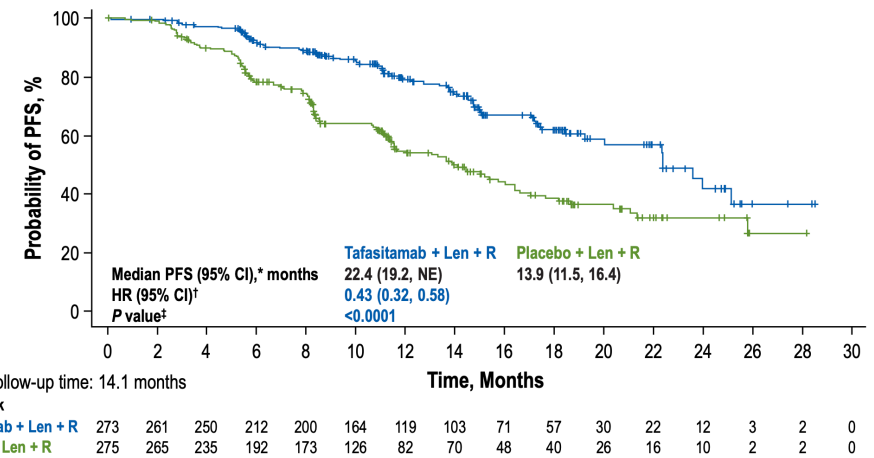
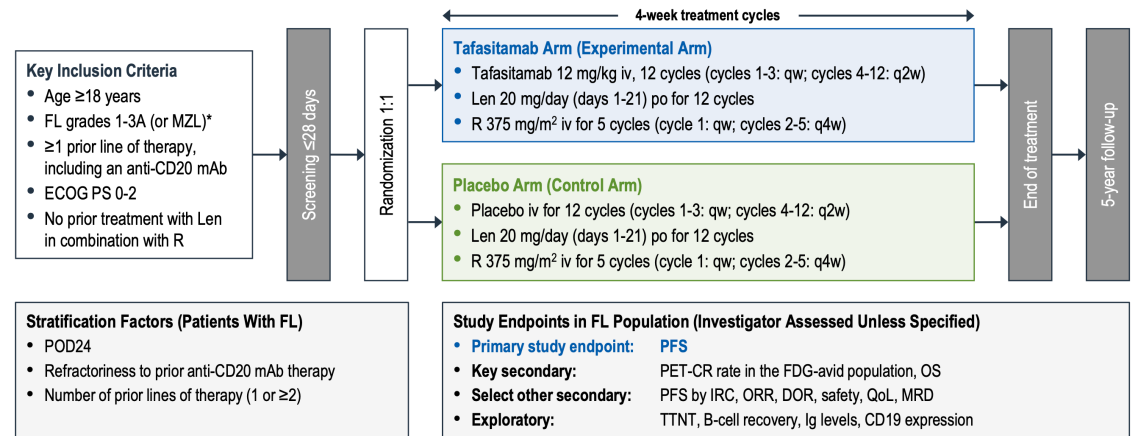
Tafasitamab: Prospettive Future

In 1 Linea nel DLBCL



- Primary endpoint**
- PFS* by INV, event driven
 - Primary analysis: 274 events
 - Interim analysis (futility): 100 events
- Sample size**
- N= 880 incl. drop outs
 - Assumptions
 - Projected PFS increase @36 months from -57% (control) to -68%
 - HR = 0.70, Power: 83%
 - Accrual: 21 months (350 sites)
 - Annual Drop-out: 15%

In 2 Linea nel FL



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Linfomi non-Hodgkin B

1. Anticorpi bispecifici
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3. Anticorpi monoclonali
4. Immunomodulanti
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6. Protein degrader

Linfomi non-Hodgkin T

1. Inibitori di chinasi/proteine
2. Anticorpi monoclonali
3. Terapia cellulare

SIE incontra i pazienti

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