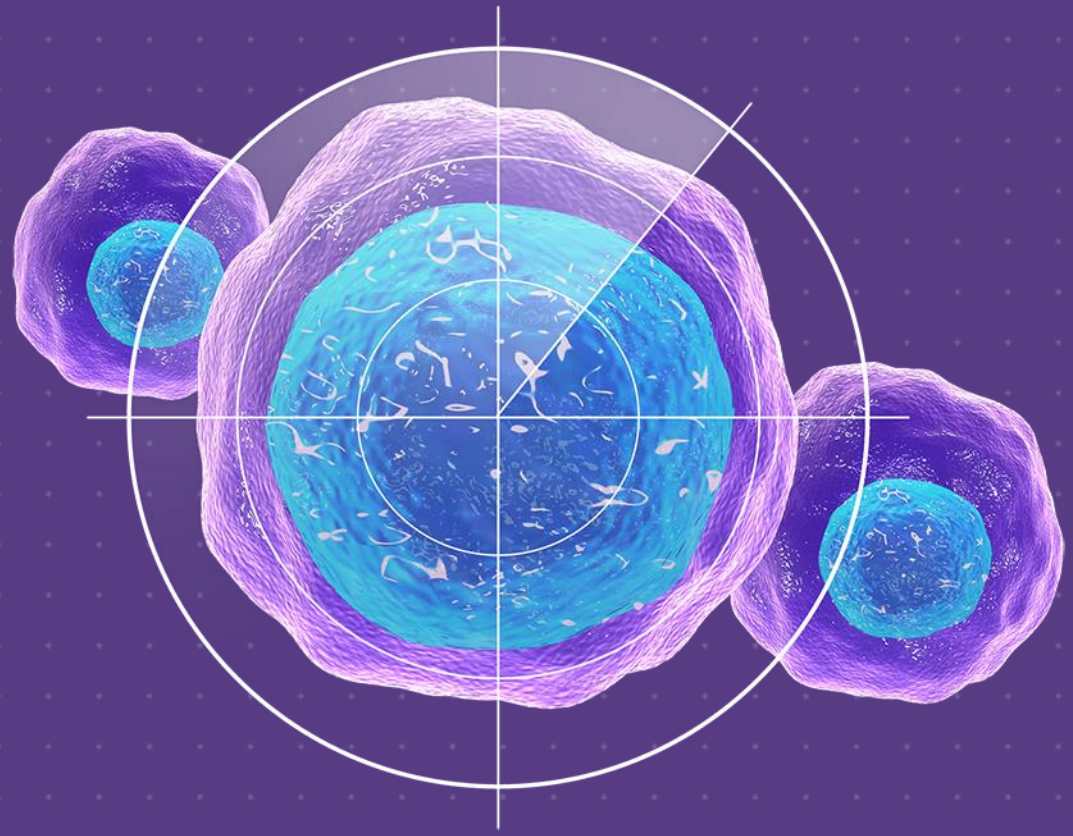
LymphomaHub

VIRTUAL SATELLITE SYMPOSIUM

How I treat relapsed/refractory disease – DLBCL and CLL

November 8, 2020



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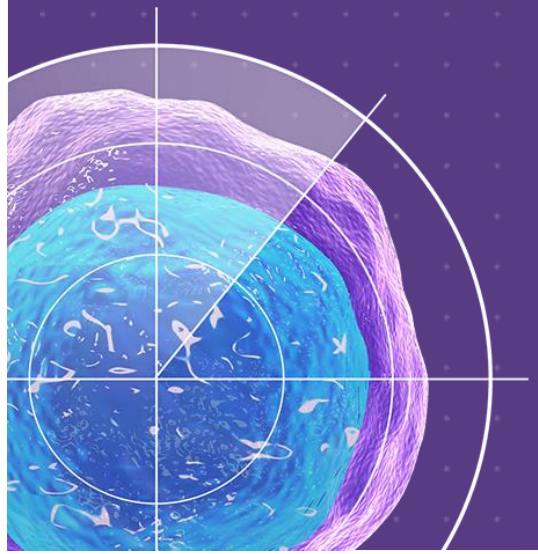
Scientific Education Support

Case 1:
Patient with R/R DLBCL – US perspective

Professor Kieron Dunleavy

George Washington University Cancer Center

Washington DC, US



Disclosures

	Research funding	Advisory Board
Celgene/BMS		√
Bayer		√
AstraZeneca		√
AbbVie		√
Atara		√
Janssen		√
Karyopharm		√
Morphosys		√
Genmab		√
Kymera		√
Pharmacyclics		√
Daiichi Sankyo		√

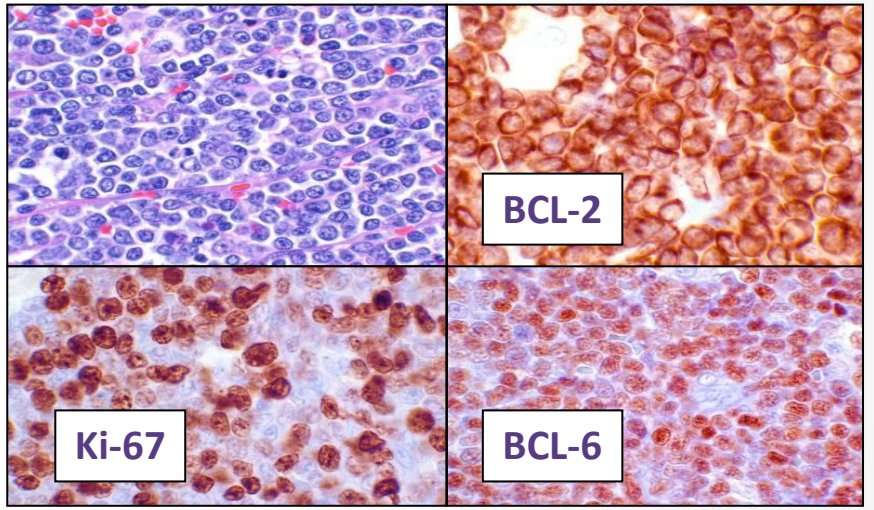
Case 1

- 68-year-old male
  - Previously well
  - No significant medical history
- 4-week history: fevers, night sweats, weight loss, and bilateral neck lymphadenopathy
- All labs normal except LDH > 2ULN
- Imaging: diffuse lymphadenopathy both sides of diaphragm
- Biopsy of large neck lymph node performed

LDH, lactate dehydrogenase; ULN, upper limit of normal.

Case 1

- DLBCL (no follicular component)
- CD20+, CD10–, BCL6+
- IHC: MYC+++ (80%), BCL2+ (60%)
- FISH: No *MYC* or *BCL2* rearrangement



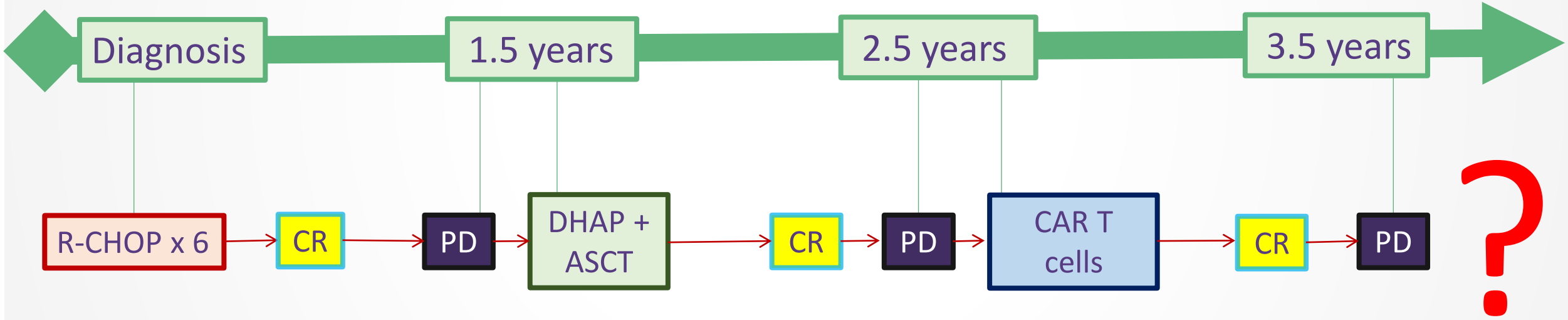
- Bone marrow biopsy and CSF negative

DLBCL. Stage III. Non-GCB subtype

'Double-expresser' lymphoma

CSF, cerebrospinal fluid; DLBCL, diffuse large B-cell lymphoma; FISH, fluorescence *in situ* hybridization; GCB, germinal center B-cell like; IHC, immunohistochemistry.

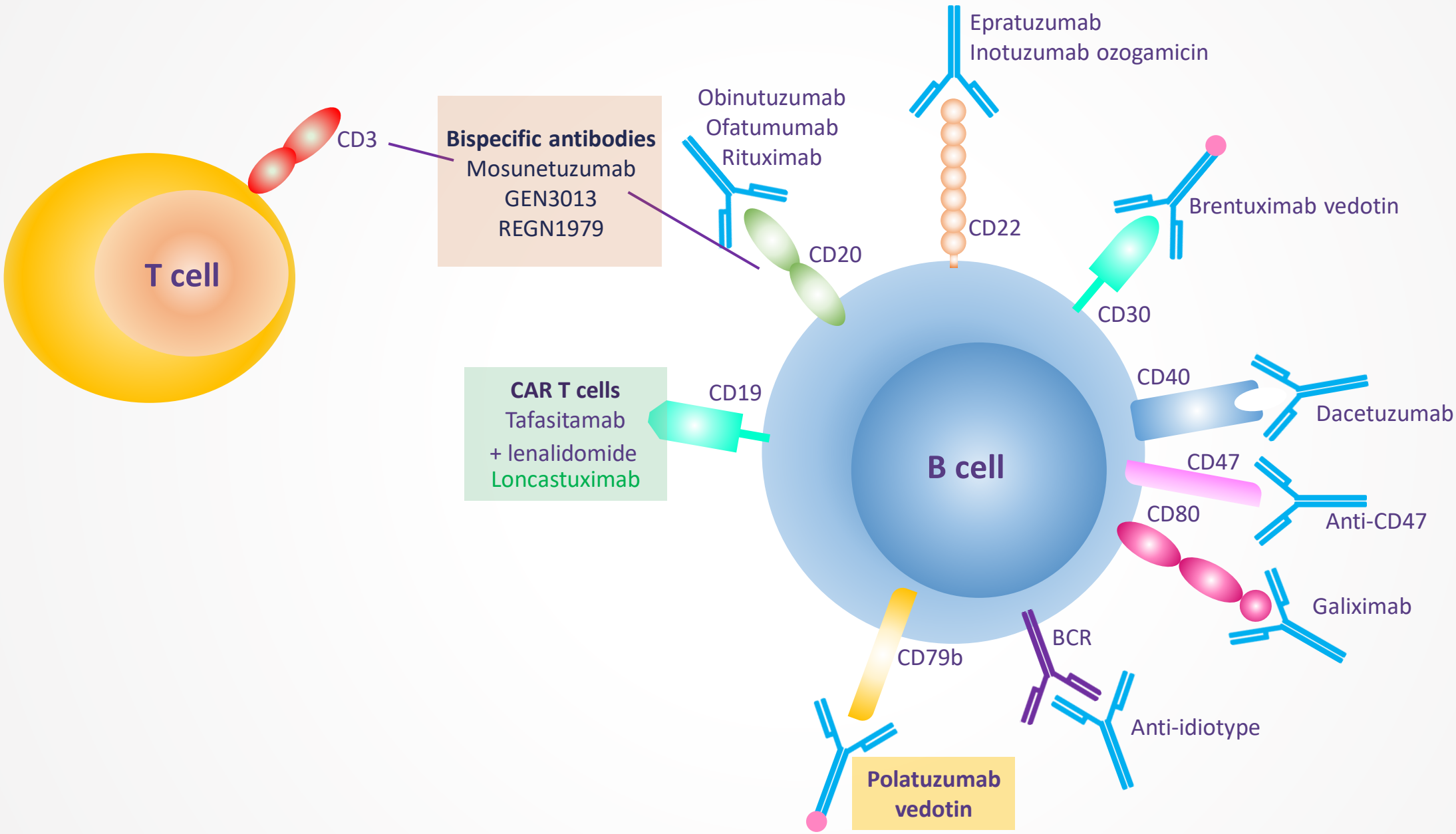
Case 1: Treatment course



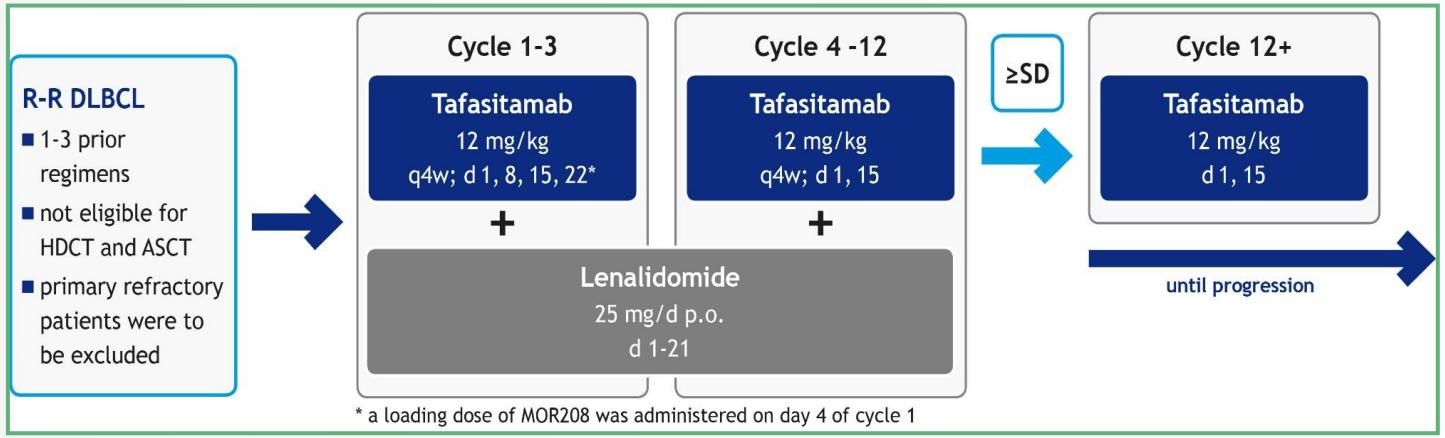
ASCT, autologous stem cell transplantation; CAR, chimeric antigen receptor; CR, complete response; DHAP, dexamethasone + high-dose cytarabine + cisplatin; PD, progressive disease; R-CHOP, rituximab + cyclophosphamide + doxorubicin + vincristine + prednisone.

Next steps: Options

- FDA-approved options
  - Tafasitamab + lenalidomide
  - Polatuzumab + bendamustine with rituximab (pola-BR)
  - Selinexor
- Clinical trial options
  - Bispecific antibodies
  - Novel antibody–drug conjugates
- Other options
  - Further immunochemotherapy platforms
  - Allogeneic stem cell transplant options


T cell
CD3
Bispecific antibodies
Mosunetuzumab
GEN3013
REGN1979
Obinutuzumab
Ofatumumab
Rituximab
CD20
Epratuzumab
Inotuzumab ozogamicin
CD22
Brentuximab vedotin
CD30
CAR T cells
Tafasitamab
+ lenalidomide
Loncastuximab
CD19
B cell
CD40
Dacetuzumab
CD47
Anti-CD47
CD80
Galiximab
BCR
Anti-idiotype
CD79b
Polatuzumab vedotin

L-MIND study



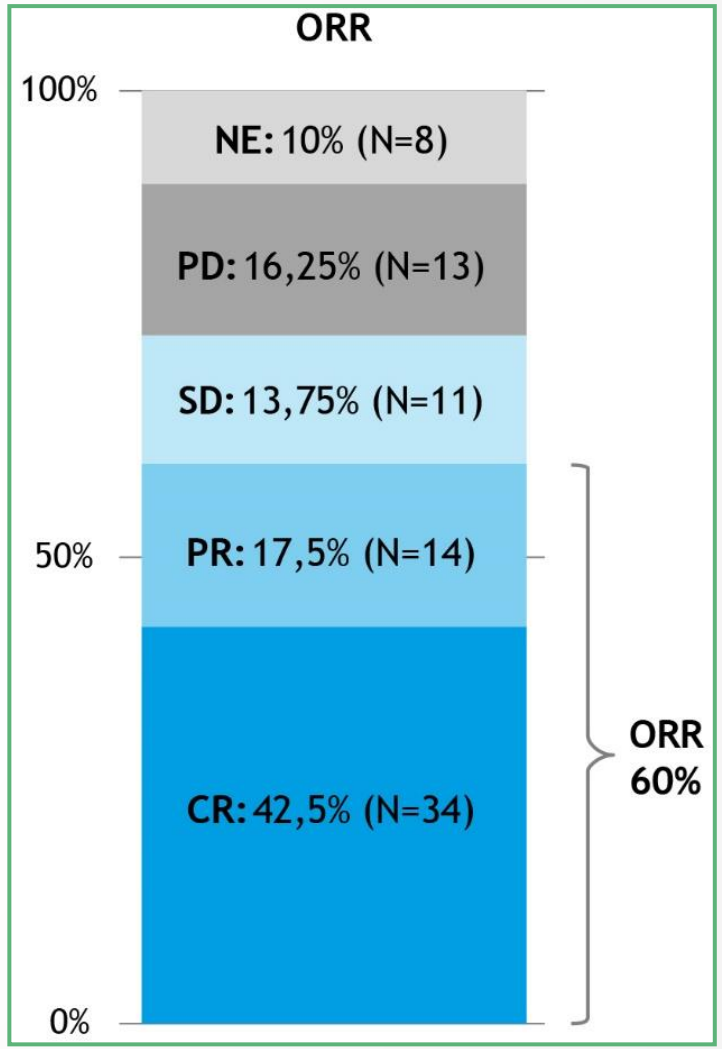
N=80

Primary endpoint

- ORR (IRC)

Secondary endpoints

- PFS
- DoR
- OS
- Safety of the tafasitamab + lenalidomide combination
- Exploratory and biomarker-based analyses

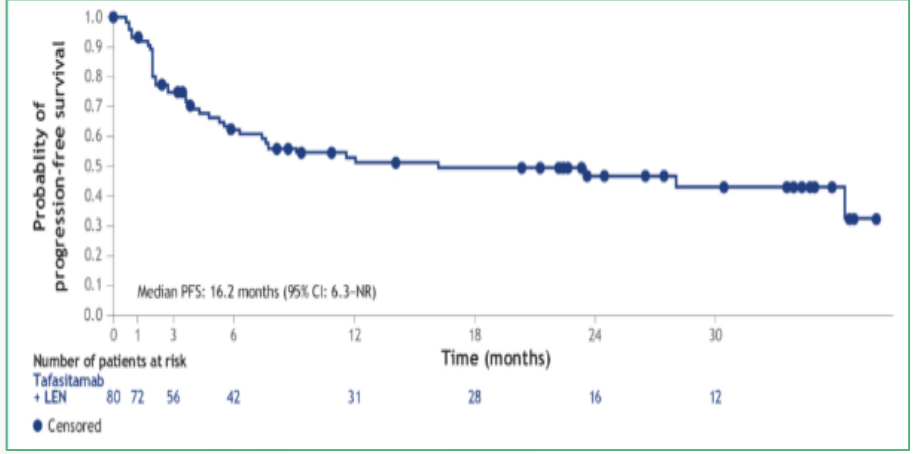


Salles G, et al. *Lancet Oncol.* 2020;21:978–88.

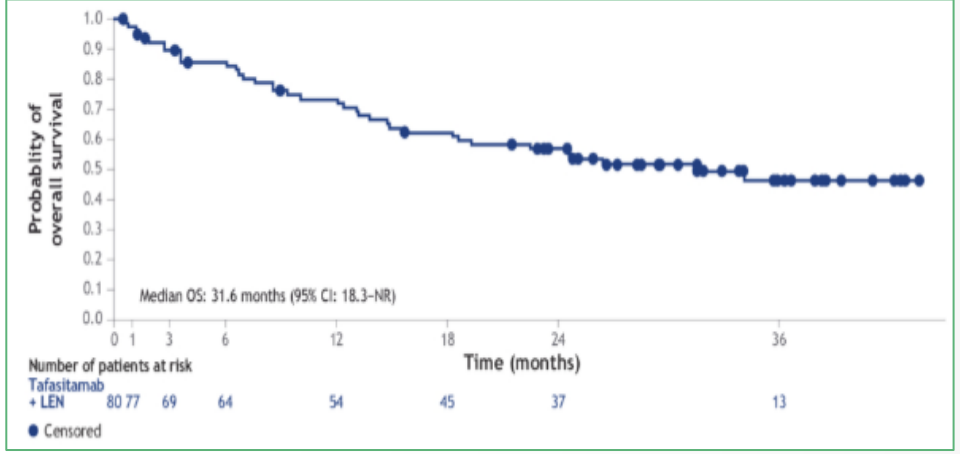
ASCT, autologous stem cell transplantation; CR, complete response; DLBCL, diffuse large B-cell lymphoma; DoR, duration of response; HDCT, high-dose chemotherapy; IRC, independent review committee; NE, not evaluable; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; p.o., orally; R/R, relapsed/refractory; SD, stable disease.

L-MIND study: Long-term outcomes

IRC-Assessed PFS after > 24 months follow-up



OS after > 24 months follow-up



Salles G, et al. Abstract #EP1201. EHA 2020.

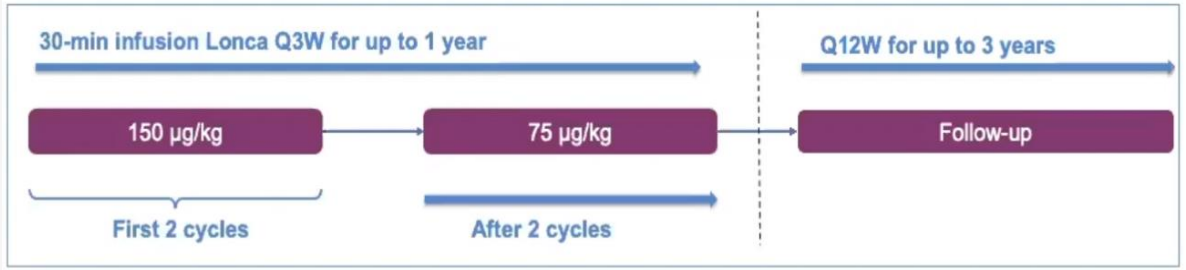
CI, confidence interval; IRC, independent review committee; LEN, lenalidomide; NR, not reached; OS, overall survival; PFS, progression-free survival.

Loncastuximab tesirine (ADCT-402)

Study Design: Single-arm, Open-label Phase 2 Study

Patient population:
Patients with R/R DLBCL following ≥2 lines of prior systemic therapy

Primary objective:
Evaluate efficacy, using ORR (central review), and safety of the full Phase 2 study population



Futility requirements met:
ORR for first 52 patients[1]

Total enrolment:
145 patients

1. Carlo-Stella C, *et al. Blood.* 2019;134(Supp1):757. DLBCL, diffuse large B-cell lymphoma; Lonca, loncastuximab tesirine; ORR, overall response rate; Q3W, every 3 weeks; Q12W, every 12 weeks; R/R, relapsed/refractory.

Baseline Characteristics

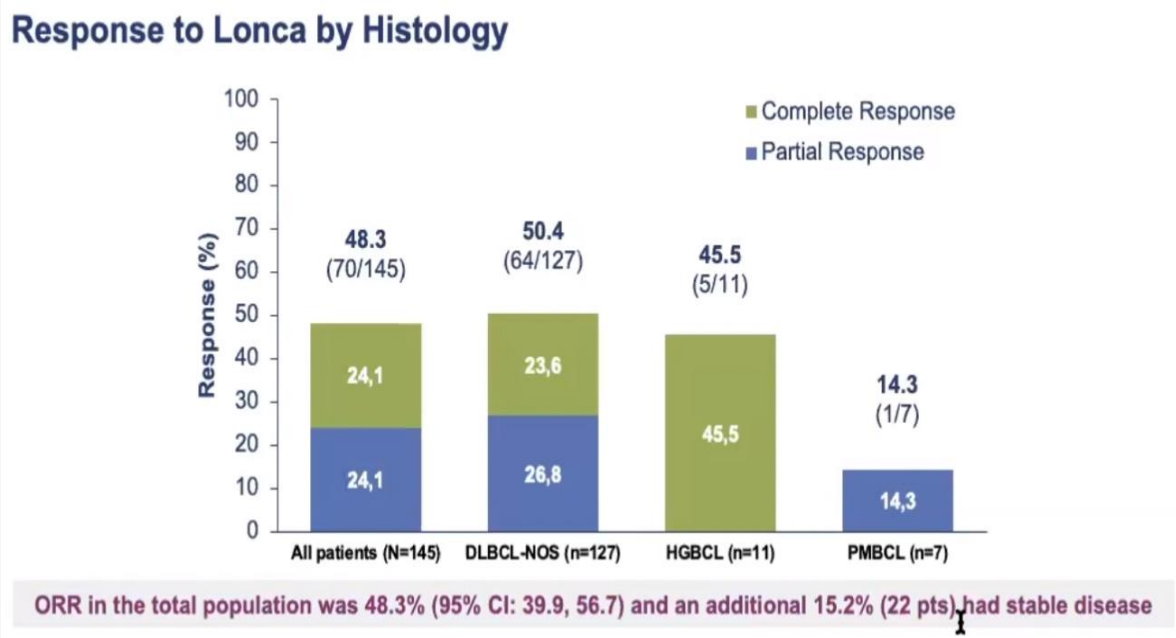
Patient characteristics		Total (N=145)
Sex, n (%)	Female	60 (41.4)
	Male	85 (58.6)
Age, years, median (min, max)		66.0 (23–94)
Histology, n (%)	DLBCL	127 (87.6)
	HGBCL	11 (7.6)
	PMBCL	7 (4.8)
Double/triple hit, n (%)		15 (10.3)
Double/triple expressor, n (%)		20 (13.8)
Transformed disease, n (%)		29 (20.0)
Stage, n (%)	I–II	33 (22.8)
	III–IV	112 (77.2)

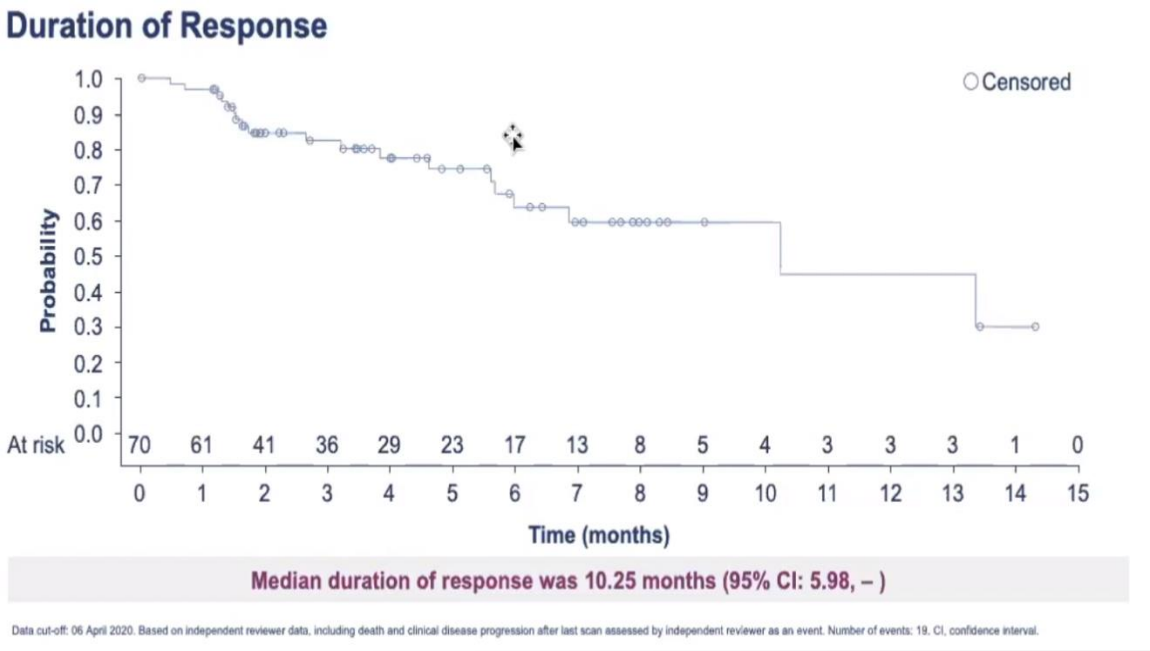
Patient treatment history		Total (N=145)
No. of previous systemic therapies,* median (range)		3 (2–7)
First-line systemic therapy response, n (%)	Relapse	99 (68.3)
	Refractory†	29 (20.0)
	Other‡	17 (11.7)
Last-line systemic therapy response,¶ n (%)	Relapse	43 (29.7)
	Refractory†	84 (57.9)
	Other‡	18 (12.4)
Refractory to all prior therapies, n (%)	Yes	25 (17.2)
	No	115 (79.3)
	Other‡	5 (3.4)
Prior stem cell transplant, n (%)	Allogeneic	2 (1.4)
	Autologous	21 (14.5)
	Both	1 (0.7)

145 patients were enrolled and received a mean of 4.3 cycles of Lonca (range: 1–15)

Carlo-Stella C, et al. Abstract #S233. EHA 2020.

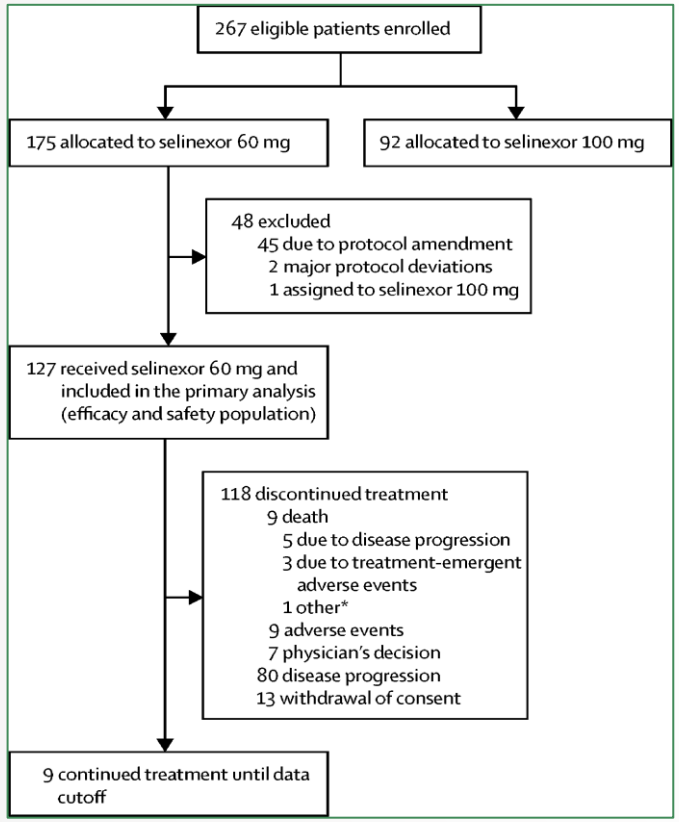
Loncastuximab tesirine (ADCT-402)

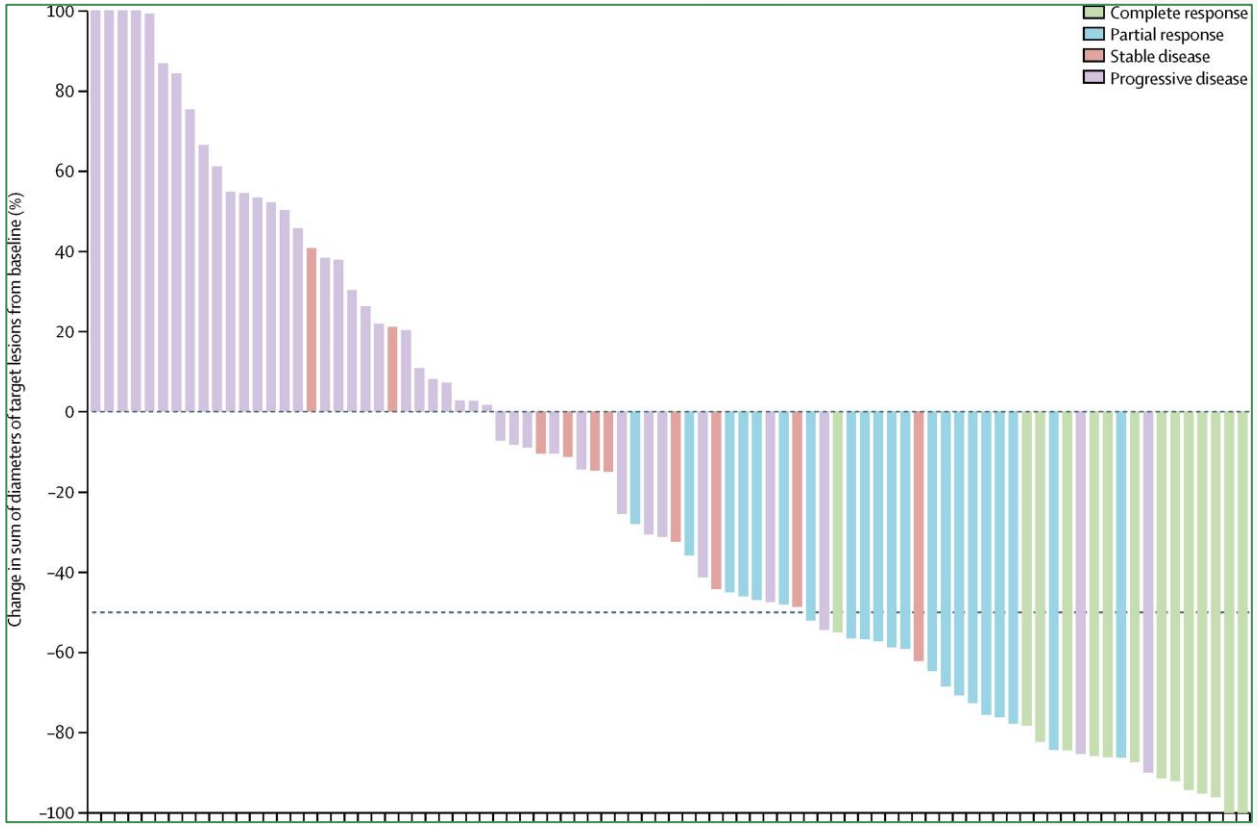




Carlo-Stella C, et al. Abstract #S233. EHA 2020.

Selinexor – XPO1-mediated nuclear transport





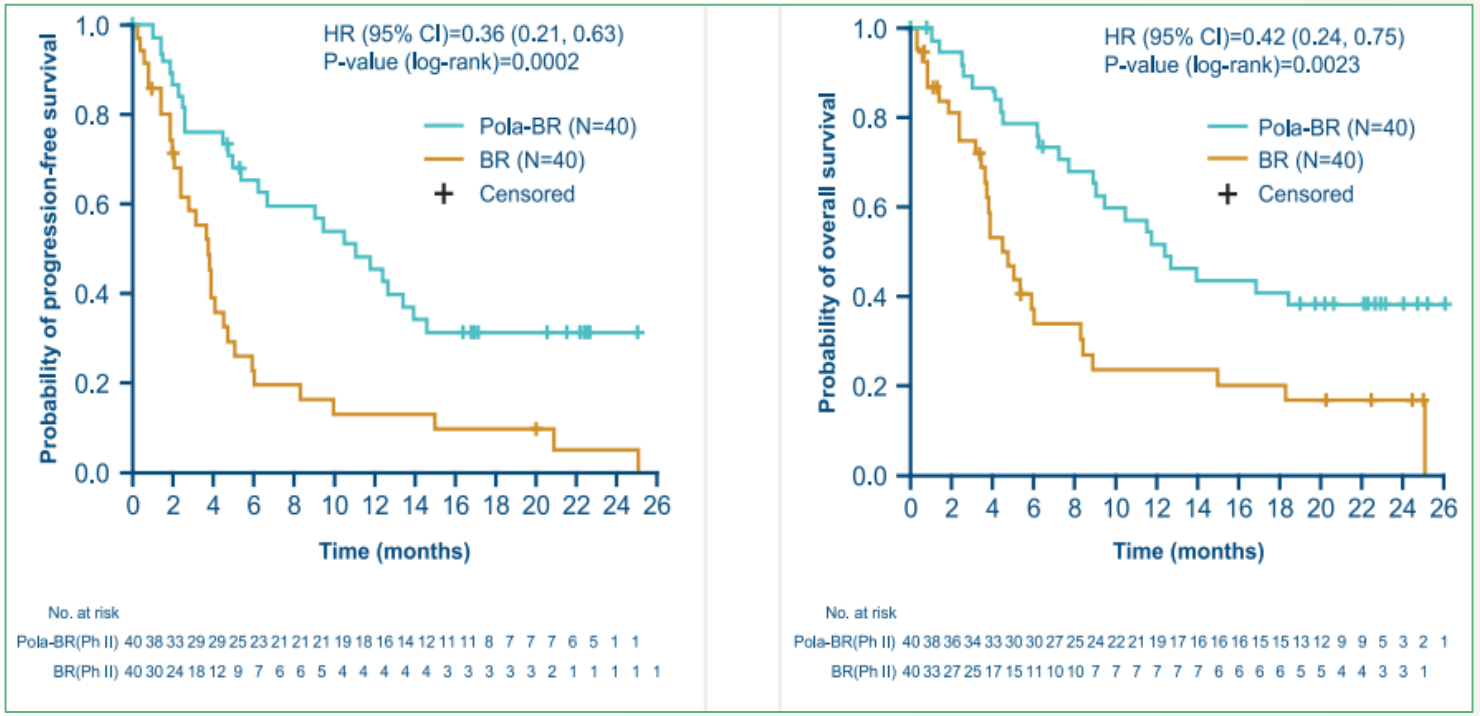
Kalakonda N, *et al. Lancet Haematol.* 2020;7:e511-22.
*One patient died due to pneumonia 38 days after the last dose of the study drug.

Polatuzumab vedotin: DLBCL

- Randomized phase 2 study
- Pola-BR vs BR in R/R DLBCL

R/R DLBCL
1+ prior Rxs
NE for ASCT

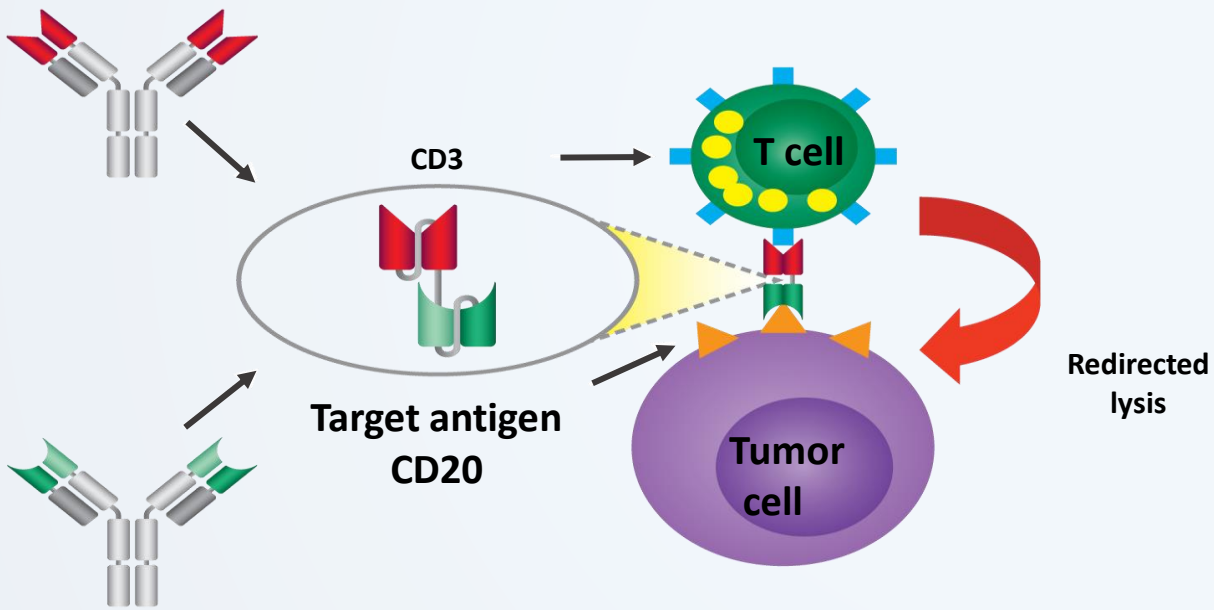
- Higher CR: 40% vs 18% (p = 0.03)
- Median PFS: 9.5 v 3.7m (HR = 0.36, p < 0.001)
- Median OS: 12.4 v 4.7 m (HR = 0.42, p < 0.002)



- Ongoing phase 3 (POLARIX)
- Frontline DLBCL: R-CHOP vs R-CHP+Pola

Sehn LH, et al. *J Clin Oncol*. 2020;38(2):155-165.
BR, bendamustine + rituximab; CR, complete response; DLBCL, diffuse large B-cell lymphoma; m, months; OS, overall survival; PFS, progression-free survival; Pola, polatuzumab vedotin; R-CHOP, rituximab + cyclophosphamide + doxorubicin + vincristine + prednisone; R-CHP, rituximab + cyclophosphamide + doxorubicin + prednisone; R/R, relapsed/refractory.

Bispecific antibodies (CD20 × CD3)

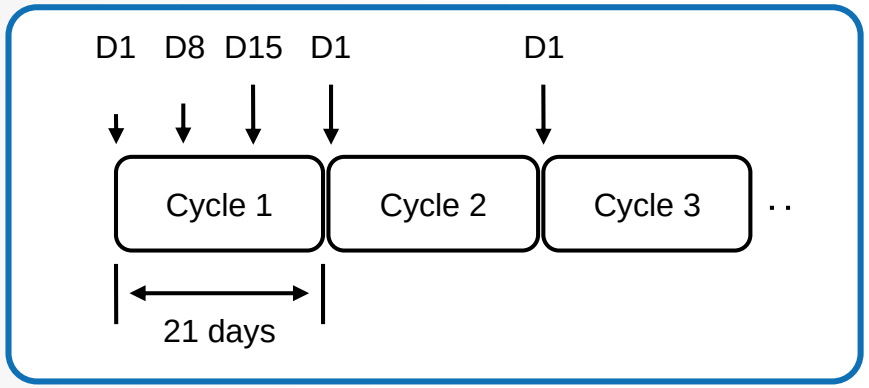


Bispecific Abs

Mosunetuzumab
GEN3013
REGN1979

Mosunetuzumab in aggressive NHL

Mosunetuzumab regimen



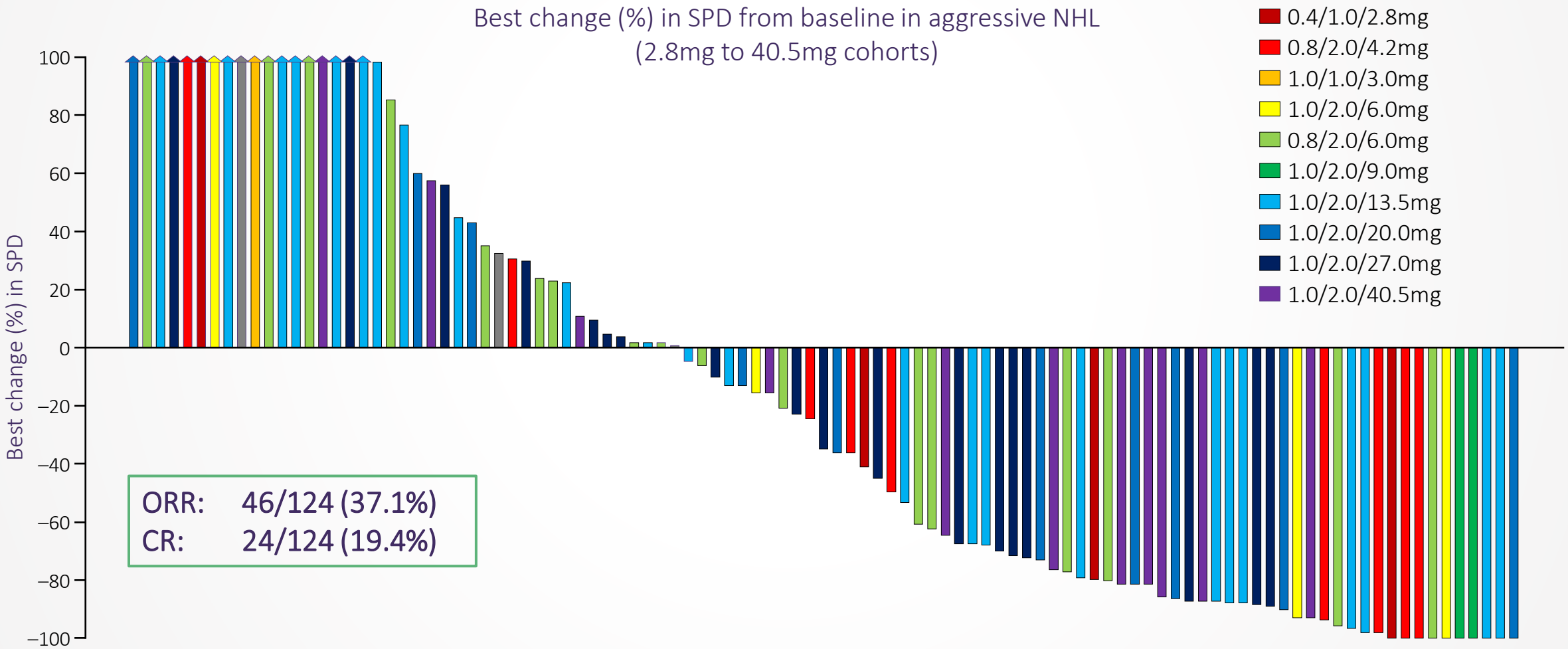
- IV administration in outpatient setting
- Cycle 1 step-up dosing then fixed dosing in subsequent cycles
- Initial treatment = 8 cycles; if CR achieved, treatment discontinued; if PR or SD, treatment continued for up to 17 cycles
- Retreatment allowed for CR patients who relapse after initial treatment

Patient characteristics	N=270	
Median age, years (range)	62	(19–96)
Male	172	(63.7%)
ECOG PS 1 at baseline	164	(61.2%)
Aggressive NHL	180	(66.7%)
DLBCL	117	(43.3%)
trFL	32	(11.9%)
MCL	23	(8.5%)
Other	8	(3.0%)
Indolent NHL	85	(31.5%)
FL	82	(30.4%)
Other	3	(1.1%)
Median prior systemic therapies, n (range)	3	(1–14)
Prior CAR-T therapy	30	(11.1%)
Prior autologous SCT	77	(28.5%)
Refractory to last prior therapy	194	(71.9%)
Refractory to prior anti-CD20 therapy	233	(86.3%)

Schuster SJ, et al. Abstract #6. ASH 2019.

CAR, chimeric antigen receptor; CR, complete response; DLBCL, diffuse large B-cell lymphoma; EGOG PS, Eastern Cooperative Oncology Group performance status; FL, follicular lymphoma; IV, intravenous; MCL, mantle cell lymphoma; NHL, non-Hodgkin lymphoma; PR, partial response; SCT, stem cell transplant; SD, stable disease; trFL, transformed FL.

Mosunetuzumab in aggressive NHL



Schuster SJ, et al. Abstract #6 ASH 2019.

CR, complete response; NHL, non-Hodgkin lymphoma; ORR, overall response rate; SPD, sum of the product of the diameters.

Back to the patient’s case…

Next therapy

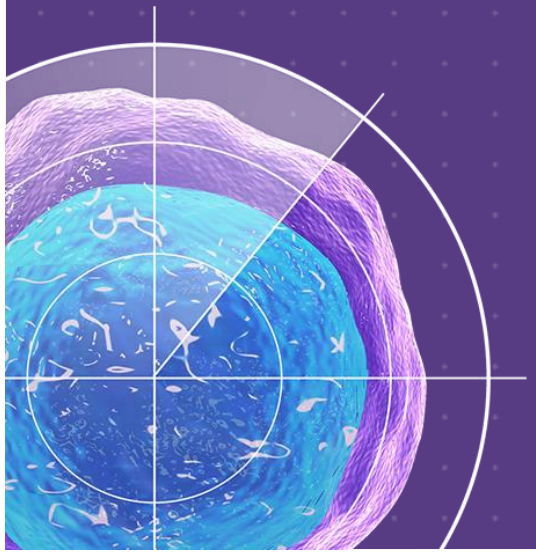
- Tafasitamab + lenalidomide
- Polatuzumab + BR
- Selinexor
- Loncastuximab tesirine
- Bispecific antibody
- Other approach

BR, bendamustine and rituximab.

Back to the patient’s case…

LymphomaHub

Thank you



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