2021 American Society of Hematology's 63rd Annual Meeting
Roche Analyst Audio Webcast

15 December, 2021

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Agenda

Welcome
Karl Mahler - Head of Investor Relations

Roche hematology strategy
Peter Ahnesorg - Franchise Head Hematology, Global Product Strategy

Key data presented at ASH: Hemlibra, mosunetuzumab, glofitamab, cevostamab, Venclexta
Charles Fuchs, MD, MPH - SVP, Global Head of Oncology and Hematology, Product Development

Key data presented at ASH: Polivy in 1L DLBCL (POLARIX)
Franck Morschhauser, MD, PhD - Professor of Hematology, University of Lille; President of LYSA, LYSARC

Q&A

Welcome

Karl Mahler | Head of Investor Relations

2021: Key late-stage news flow

	Compound	Indication	Milestone	
Regulatory	**Xofluza**	Healthy patients; High risk patients; Post exposure	EU approval	✔
	Evrysdi	SMA type 1/2/3	EU approval	✔
	faricimab	DME/nAMD	US/EU joint filing (DME+AMD)	✔
	Tecentriq	1L PDL1+ NSCLC	EU approval	✔
	Venclexta + azacitidine	1L unfit AML	EU approval	✔
	Ronapreve	SARS-CoV-2	EU approval	✔
	Susvimo	nAMD (continuous delivery)	US approval	✔
Phase III / pivotal readouts	**faricimab**	nAMD	Ph III TENAYA/LUCERNE	✔
	Ronapreve	SARS-CoV-2 Outpatient	Ph III Study 2067	✔
	Ronapreve	SARS-CoV-2 Post-exposure prophylaxis	Ph III Study 2069	✔
	Tecentriq	Adjuvant NSCLC	Ph III IMpower010	✔
	Evrysdi	SMA type 1/2/3 switching study	Ph II JEWELFISH	✔
	mosunetuzumab	3L+ FL	Ph Ib GO29781	✔
	Polivy + R-CHP	1L DLBCL	Ph III POLARIX	✔
	glofitamab	3L+ DLBCL	Ph Ib NP30179	✔
	Tecentriq + chemo	Adjuvant SCCHN	Ph III IMvoke010	**2022**

✔ **Angiogenesis**
faricimab in DME, nAMD

✔ **MDA**
Evrysdi SUNFISH part II

✔ **Diagnostics Investor Day**

✔ **ASCO**
Tecentriq IMpower010

✔ **Cure SMA**
Evrysdi JEWELFISH, RAINBOWFISH

✔ **Pharma Investor Day**

✔ **Digitalization along the value chain**

✔ **ESMO IO**
tiragolumab CITYSCAPE

✔ **ASH**
Polivy POLARIX, Hemlibra HAVEN 6, mosun/glofit

Roche hematology strategy

Peter Ahnesorg | Franchise Head Hematology, Global Product Strategy

Roche's approach to Hematology

Pharma Vision 2030: Providing more patient benefit at less cost to society

Building on our key areas of strength

- Polivy as potential new SOC in 1L DLBCL
- Focus on CD20XCD3 bispecifics
- Continued investment in Hemophilia
- Further expand in AML

Venture to new frontiers

- Serious efforts to establish footprint in Multiple Myeloma
- Enter Myelodysplastic Syndrome
- Expand in benign hematology

Innovate

- Leading developer of bispecific antibodies
- Developing beyond the drug solutions
- Driving combination therapies
- Exploring novel endpoints

SOC=standard of care; DLBCL=diffuse large B-cell lymphoma; AML= acute myeloid leukemia

Broadest portfolio in hematology

Rituxan Rituximab

	mAb	Small Molecule	ADC	Bispecific	Gene Therapy	Recombinant Protein
CLL	GAZYVA obinutuzumab injection ✓	VENCLEXTA venetoclax tablets ✓		mosunetuzumab		
iNHL/FL	GAZYVA obinutuzumab injection ✓		POLIVY polatuzumab vedotin	mosunetuzumab glofitamab		
DLBCL/MCL		VENCLEXTA venetoclax tablets	POLIVY polatuzumab vedotin ✓	mosunetuzumab glofitamab		
MM		VENCLEXTA venetoclax tablets		cevostamab GPRC5d x CD3		
AML		VENCLEXTA venetoclax tablets ✓				
MDS		VENCLEXTA venetoclax tablets				
Myelofibrosis						rhPTX-2
Non-Malignant	crovalimab			HEMLIBRA emicizumab-kxwh ✓	Spark SPK-8011 SPK-8016	

✓ = approved

Indications where Rituxan approved

Heme-onc indications where Rituxan not approved

Non-malignant

CLL=Chronic lymphoid leukemia; iNHL=Indolent Non-Hodgkin's lymphoma; FL=Follicular lymphoma; DLBCL=Diffuse large B-cell lymphoma; MCL=Mantle cell lymphoma; MM=Multiple myeloma; AML=Acute myeloid leukemia; MDS=Myelodysplastic syndrome; ADC=antibody drug conjugate; mAB=monoclonal antibody; Venclexta in collaboration with AbbVie

Roche's scientific expertise in hematology runs deep

Breaking boundaries in hematology

- 11 Breakthrough Therapy Designation by the FDA in hematology medicines
- RTOR for Venclexta in 1L CLL and 1L AML and AA for Polivy R/R DLBCL
- POLARIX PRIME designation in EU

Investing in early disease, presenting the opportunity for cure

Molecule	Indication	Ph 1	Ph 2	Ph 3
Polivy	1L DLBCL			*POLARIX* ✓
Venclexta	1L fit AML			*VIALE-M*
Glofit/Mosun	1L DLBCL	*Ph 1b*		

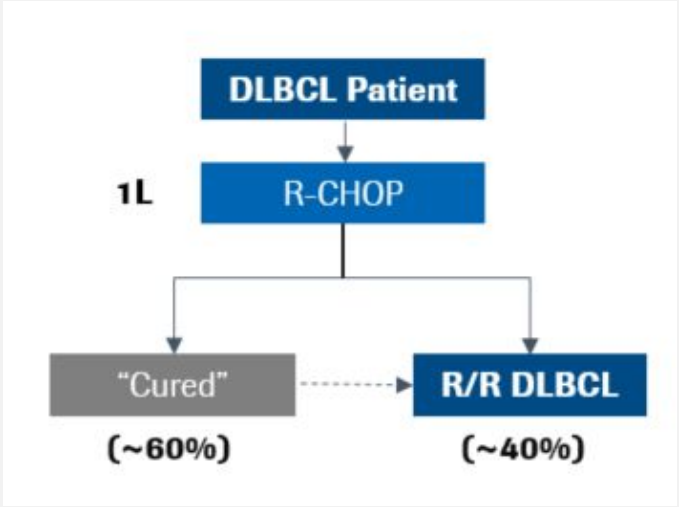
Remaining unmet needs

- Challenging the standard-of-care across malignant and non-malignant hematology
- Our broad portfolio and pipeline (>15 agents for >12 disease states) shows that we are here to stay

RTOR=real time oncology review; AA=accelerated approval; PRIME=Priority Medicines; R/R=relapsed/refractory; DLBCL= Diffuse large B-cell lymphoma; CLL=Chronic lymphoid leukemia; AML=Acute myeloid leukemia; Venclexta in collaboration with AbbVie

1L DLBCL can be curative, but high unmet need remains

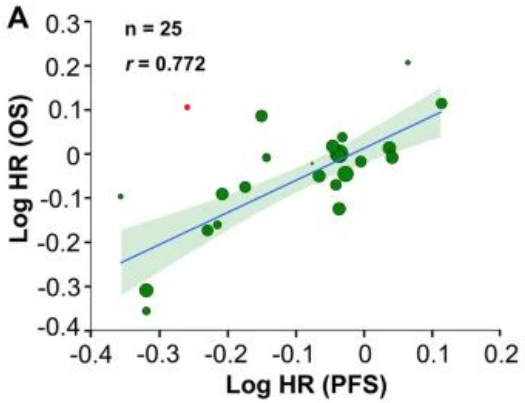
~40% of patients are not cured with R-CHOP



- For newly diagnosed patients, any clinically meaningful PFS benefit that a treatment can bring could have a significant positive impact for newly diagnosed patients
- Patients with R/R DLBCL have poor prognosis: mOS <2yrs

PFS is an appropriate primary end point in 1L DLBCL

Trial-level correlation between treatment effects on PFS and OS in RCTs



- PFS is a valid endpoint to demonstrate efficacy benefit in 1L DLBCL
- PFS as endpoint reduces the evaluation time for effective treatments to be delivered in clinical practice and prevents prolonged evaluation of ineffective treatments
- Treatment effects on PFS strongly predicts for treatment effects on OS[1]

1. Zhu, J., Yang, Y., Tao, J. *et al.* Association of progression-free or event-free survival with overall survival in diffuse large B-cell lymphoma after immunochemotherapy: a systematic review. *Leukemia* **34,** 2576–2591 (2020); RCT=randomized controlled trial; PFS=Progressive free survival; DLBCL=diffuse large B-cell lymphoma; R/R=relapsed/refractory; OS=overall survival; mOS=median overall survival; R-CHOP=Rituxan + cyclophosphamide + doxorubicin + vincristine + prednisone; HR=hazard ratio

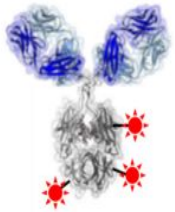
Polivy in DLBCL

First positive trial (POLARIX) in 1L DLBCL in >20 years

POLIVY® polatuzumab vedotin

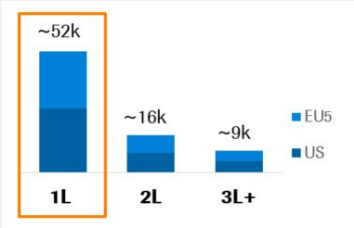
Polivy program

Anti-CD79b ADC



Combination	Indication	Ph1	Ph2	Ph3
Polivy+R+CHP	1L DLBCL			✓
Polivy+R+GemOx	R/R DLBCL			
Polivy+BR	R/R DLBCL/FL			✓
Polivy+mosun	R/R DLBCL			
Polivy+glofit	R/R NHL			
Polivy+mosun SC	1L unfit DLBCL			
Polivy+R-CHP+Ven	1L DLBCL			

Multibillion CHF market opportunity in 1L DLBCL



- No new 1L therapies approved since R-CHOP
- 3x more drug treated patients in 1L than 2L DLBCL
- No novel treatments expected in 1L DLBCL for >3.5 years

Physicians already have experience using Polivy in R/R setting

Off the shelf and fixed duration

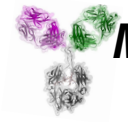
- Readily available; administered in any oncology facility, with no hospitalization required
- Administered for 6 cycles

Well tolerated safety profile

- No unique monitoring requirements
- Safety comparable with that of R-CHOP

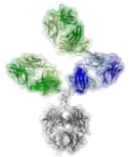
Polivy in collaboration with Seagen; ADC=antibody drug conjugate; R/R=relapsed/refractory; DLBCL=diffuse large B-cell lymphoma; R-CHOP=Rituxan + cyclophosphamide + doxorubicin + vincristine + prednisone; GemOx=gemcitabine + oxaliplatin; NHL=non-Hodgkin's lymphoma; FL=follicular lymphoma; R=Rituxan; B=bendamustine; SC=subcutaneous; Ven=Venclexta

Mosunetuzumab and glofitamab (CD20 x CD3 bispecifics) *Can be tailored to address diverse patient and customer needs with the potential to offer CAR-T like efficacy "off the shelf"*



Mosunetuzumab

- First-in-class bispecific in iNHL
- Promising as outpatient therapy for multiple settings



Glofitamab

- Designed for enhanced potency and combinability with aCD20
- Demonstrated strong efficacy in aNHL

Patients

- FL/DLBCL/MCL/other histologies
- 1L or R/R disease
- Patient characteristics, including risk/prognostic factors
- Single agent and combination

Providers

- Academic centers vs. community
- SC or IV administration
- Off-the shelf administration

Payer

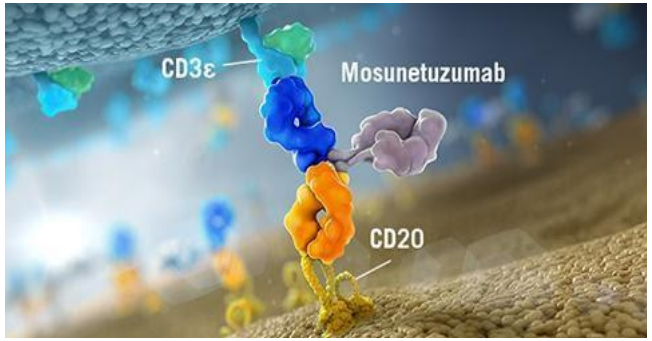
- Fixed duration vs. continuous
- Potential resource savings vs. CAR-T

iNHL=indolent Non-Hodgkin lymphoma; aNHL=aggressive Non-Hodgkin lymphoma; R/R=relapsed/refractory; DLBCL=diffuse large B-cell lymphoma; FL=follicular lymphoma; MCL= mantle cell lymphoma; SC=subcutaneous; IV=intravenous; CAR-T=chimeric antigen receptor T cell therapy

Mosunetuzumab and glofitamab development plans

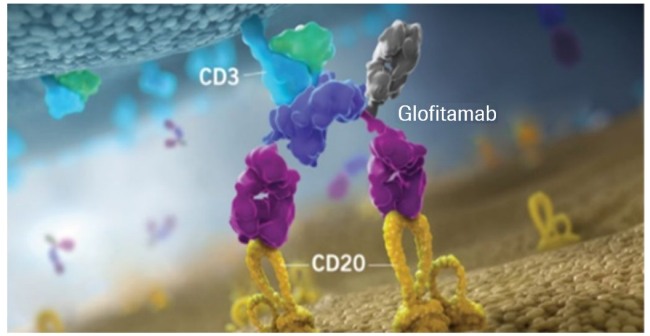
Moving into earlier lines of therapy in combination with SOC

Mosunetuzumab program



Combination	Indication	Ph1	Ph2	Ph3
mosun+len	R/R FL			
mosun+CHOP	1L DLBCL			
mosun+CHP+Polivy	1L DLBCL			
mosun	R/R DLBCL/FL/MCL			
mosun	1L unfit DLBCL			
mosun SC+Polivy	1L unfit DLBCL			
mosun	3L+ DLBCL/FL			
mosun+Polivy	R/R DLBCL			
mosun+Tecentriq	R/R DLBCL/FL			
mosun SC	R/R DLBCL/FL			

Glofitamab program



Combination	Indication	Ph1	Ph2	Ph3
glofit+GemOx	2L+ DLBCL			
glofit	R/R DLBCL/FL			
glofit+Gazyva/R+CHOP	1L DLBCL			
glofit+Polivy+R-CHP	1L DLBCL			
glofit+Tecentriq	R/R DLBCL/FL			
glofit+Gazyva	R/R FL			
glofit+Polivy	R/R DLBCL			

Late line monotherapy

- Mosun in 3L+ FL filed in EU, FDA filing in coming weeks
- Glofit in 3L+ DLBCL, data readout. Results to be shared with health authorities and presented at upcoming congress

R/R NHL combinations

- Ph3 trials initiated with both mosun and glofit across R/R DLBCL and FL

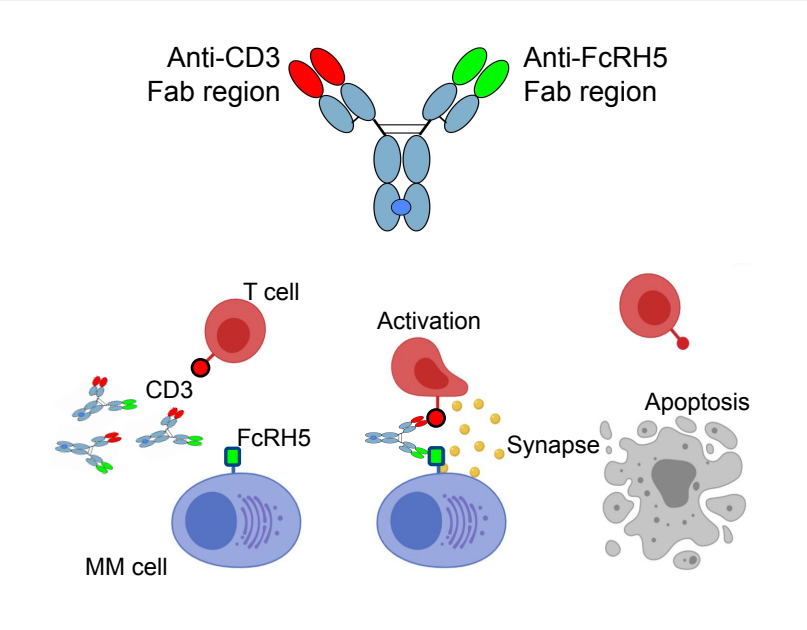
1L DLBCL

- Exploring combinations with Polivy

SOC=standard of care; NHL=non-Hodgkin's lymphoma; DLBCL=diffuse large B cell lymphoma; FL=follicular lymphoma; MCL=mantle cell lymphoma; CHOP=cyclophosphamide + doxorubicin + vincristine + prednisone; CHP=cyclophosphamide + doxorubicin + prednisone; GemOx=gemcitabine + oxaliplatin; R=Rituxan; R/R=relapsed/refractory; len=lenalidomide; SC=subcutaneous

Cevostamab (FcRH5 x CD3) in R/R MM
Promising activity in heavily pretreated patients

FcRH5 x CD3 bispecific antibody



- Humanized IgG-based T-cell-engaging bispecific ab
- Targets membrane-proximal domain of FcRH5 on myeloma cells and epsilon domain of CD3 on T cells[1]
- Dual binding results in T-cell directed killing of myeloma cells[1]

Fc receptor-homolog 5 (FcRH5)

- Expressed exclusively in B-cell lineage (myeloma cells > normal B cells)[1]
- Near ubiquitous expression on myeloma cells[1,2]
- Cevostamab is the only molecule in development that targets FcRH5

Program development

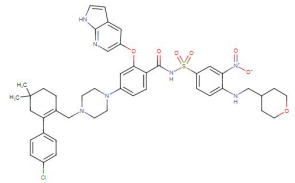
- Phase I dose escalation interim results update
- Investigating combination regimens with external partners and internal portfolio
- Exploring subcutaneous formulation
- Planning randomized studies

1. Li et al. Cancer Cell 2017;31:383–95; 2. Sumiyoshi et al. EHA 2021; 3. Cohen et al. ASH 2020; Ig=immunoglobulin; MM=multiple myeloma; ab=antibody

Venclexta in CLL, AML, MM, MDS
6th BTD for Venclexta in MDS obtained

Venclexta progam

Bcl-2 inhibitor



	Combination	Indication	Ph1	Ph2	Ph3
NHL	V+P+G/R	R/R DLBCL/FL			
CLL	V+G	1L unfit CLL			✓
	V+R	R/R CLL			✓
	V	R/R CLL 17p			✓
	V	R/R CLL after ibru/idel			
MM	V+G	1L fit CLL			
	V+dex	t(11;14) R/R MM			
	V+carfilzomib +dex	t(11;14) R/R MM			
AML	V+aza	1L unfit AML			✓
	V+LDAC	1L unfit AML			✓
	V+aza	1L fit AML maintenance			
	V+chemo	1L fit AML			
	V+AMG176	R/R AML			
	V+gilteritinib	R/R AML			
MDS	V+aza	1L MDS			
	V+/-aza	R/R MDS			

✔ **CLL**
- Venclexta + Gazyva approved in 1L CLL: fixed dose, chemo free regimen
- Ph III (CristaLLo) in 1L fit CLL initiated in Q2'20; primary endpoint: MRD-negativity

✔ **AML**
- US: Full approval in 1L unfit AML; >50% US market share; NCCN Category 1 listed
- Additional Ph III studies in AML initiated (1L maintenance, post-SCT maintenance)

Multiple Myeloma
- Ph III CANOVA trial data expected in 2022; ~15% of patients with t(11;14) translocation

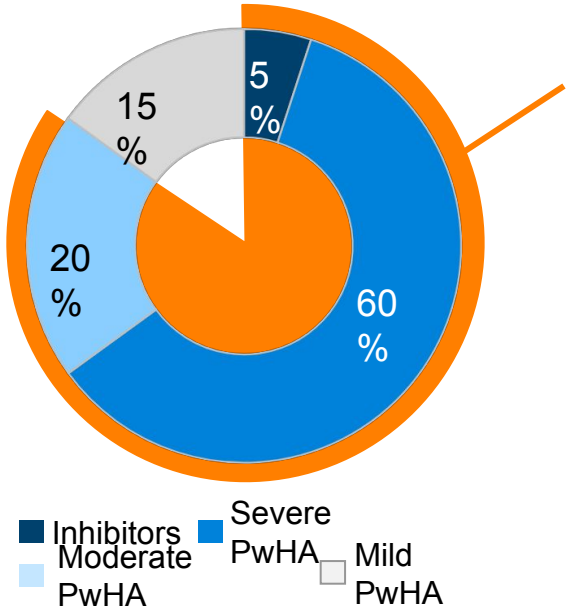
MDS
- Ph III VERONA trial in 1L MDS initiated Oct 2020, granted BTD in 2021

Venclexta in collaboration with AbbVie; BTD=breakthrough therapy; CLL=chronic lymphoid leukemia; AML=acute myeloid leukemia; MM=multiple myeloma; MDS=myelodysplastic syndrome; MRD=minimal residual disease; NCCN=National Comprehensive Cancer Network; SCT= stem cell transplant; V=Venclexta; P=Polivy; G=Gazyva; R=Rituxan; dex=dexamethasone; aza=azacitidine; LDAC=low dose cytarabine; R/R=relapsed/refractory; DLBCL=diffuse large B-cell lymphoma; FL=follicular lymphoma

Hemlibra

Transformational advance for Hemophilia A patients

HEMLIBRA emicizumab-kxwh



~85%
Hemlibra target population

- 32% patient share in the US (all severities)
- 30% share in the EU5 (severe patients only)

Continuing to gain market share in US and globally

- ~13,000 active patients on commercial Hemlibra
- Non-inhibitor approval in 98 countries, reimbursement in 42 countries to-date

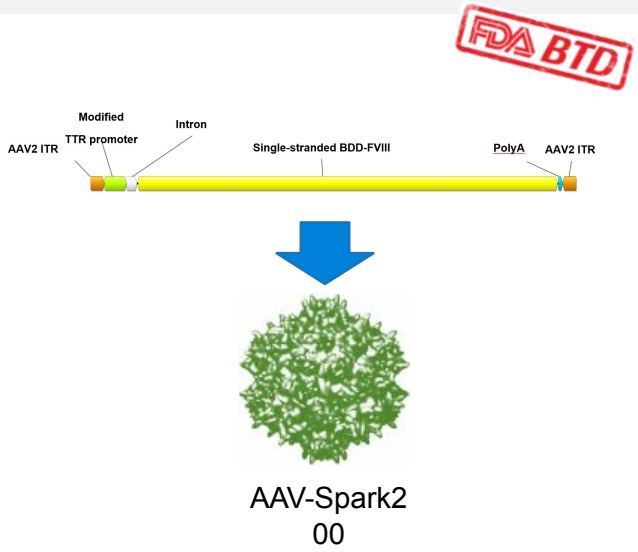
Demonstrated efficacy in moderate and mild patients: HAVEN6

- Up to 35% of hemophilia A patients have moderate or mild disease
- Filed in EU in mild/moderate patients in Q3'21

Source: Treated patients, Hemlibra Epidemiology models 2018; PWHA=People with Hemophilia A; EU=European Union

Non-malignant hematology: SPK-8011 in hem A
Efficacy and safety data up to 4 years

Hemophilia A gene therapy

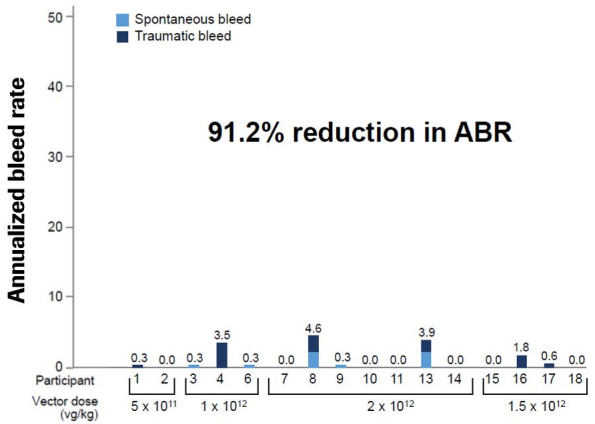


AAV-Spark200

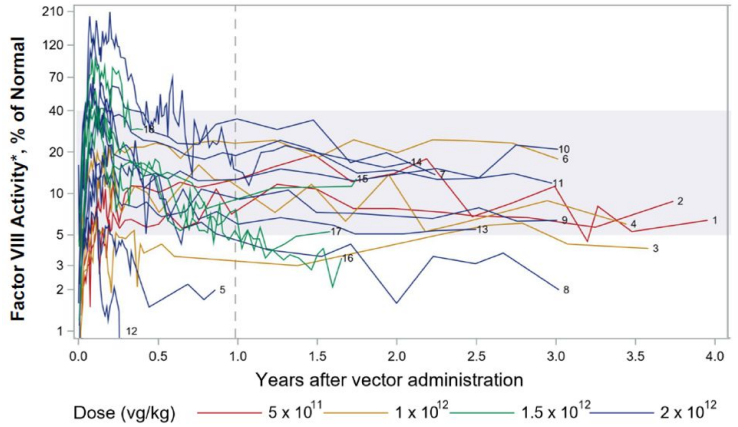
- Bio-engineered adeno-associated viral (AAV) vector utilizing the AAV-LK03 capsid (Spark200)
- Contains a codon-optimized human factor VIII gene under the control of a liver-specific promoter

Ph I/II results (SPK-8011-101)

ABR post vector administration of participants with sustained expression (n=16)*



Durable Factor VIII activity up to 4 years



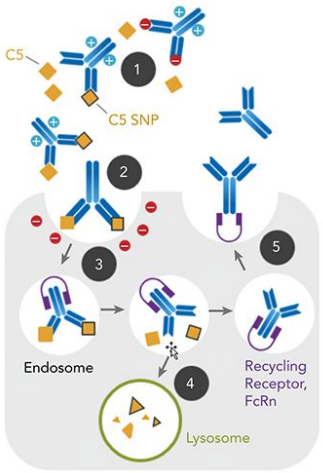
- 16 (out of 18) participants maintained expression with stable, durable Factor VIII activity and a 91.5% reduction in the ABR and 96.4% reduction in AIR (median follow up was 2.8 yrs)
- SPK-8011 shows acceptable safety in the ranges of doses studied: $5x10^{11}$–$2x10^{12}$ vg/kg
- Further dose optimization and selection of immunomodulatory regimen on-going
- Ph III (SPK-8011-302) start expected in coming months

George, L.A. et al, ISTH 2021; * Excludes 2 participants who lost expression; ABR=annualized bleed rate; AIR=annualized infusion rate

Crovalimab in PNH, aHUS, SCD

Recycling anti-C5 mAb for maximal complement

Anti-C5 mAb



1. High affinity binding
2. Preferential Ab uptake of antigen-bound Ab (PI engineering)
3. Acid-sensitive antigen release
4. C5 degradation in the endosome
5. Ab recycling by FcRn engineering, protecting Abs from degradation

- Chugai engineered, anti complement component 5 (C5) recycling mAb[1–6]
- Engineered to enable maximal, long-lasting neutralization of C5 in complement mediated diseases
- Convenient SC Q4W dosing at home

Paroxysmal Nocturnal Hemoglobinuria (PNH)

- Ph III COMMODORE 1/2 (switch & naïve, non-inferiority to eculizumab) achieved first-patient-in in H2 2020
- First PNH results expected in 2022

Atypical Hemolytic Uremic Syndrome (aHUS)

- Ph III in aHUS for adults (COMMUTE-a) initiated in Q2 2021
- Ph III for pediatrics (COMMUTE-p) started in Q4 2021

Sickle Cell Disease (SCD)

- Ph I for acute SCD (CROSSWALK-a) initiated
- Ph II in chronic SCD (CROSSWALK-c) to start in Q4 2021

Development in additional complement-mediated diseases is being explored

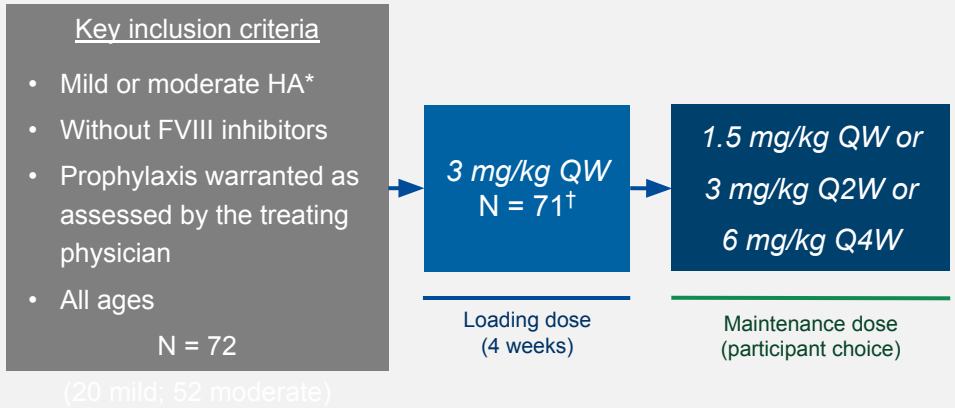
[1] Röth A et al. Blood 2020;135:912–20; [2] Fukuzawa T et al. Sci Rep 2017;7:1080; [3] Sampei Z et al. PLoS One 2018;13:e0209509; [4] Röth A, Nishimura J. Centro Congressi Federico II 2019; [5] Röth A et al. ASH 2018; [6] Sostelly A et al. ASH 2019; [7] Röth A et al. EHA 2019; [8] Peffault de la Tour, R. et al. EHA 2020; [7] Merle NS et al. JCI Insights 2018;3:e96910; [8] Roumenina LT et al. Am J Hematol. 2020;95:456; [9] Chudwin DS et al. Clin Immunol Immunopathol. 1994;71:199; [10] Vercellotti GM et al. Am J Hematol. 2019;94:327; mAb=monoclonal antibody; SC=subcutaneous; PNH=paroxysmal nocturnal hemoglobinuria; aHUS = Atypical Hemolytic Uremic Syndrome; SCD = sickle cell disease

Key data presented at ASH:
Hemlibra HAVEN6, mosunetuzumab, glofitamab, cevostamab, Venclexta

Charles Fuchs, MD, MPH | SVP - Global Head of Oncology and Hematology Product Development

Hemlibra HAVEN6: moderate to mild hemophilia A patients

HAVEN6 study design



Baseline Characteristics	Interim analysis population (N = 71)
Hemophilia severity,‡ n (%)	
Mild	20 (28.2)
Moderate	51 (71.8)
With target joints at baseline, n (%)	24 (33.8)
Number of bleeds in the past 24 wks: mean (SD)	3.4 (7.5)

Unmet need in moderate and mild hemophlia A

- Deficiency in FVIII levels may result in spontaneous bleeding, in particular into joints[1]
- Patients experience joint damage, leading to pain and impaired mobility, and reduced quality of life[1]

Participants reports for Hemlibra

- Improved treatment burden (CATCH raw score)
- 96% patients preferred Hemlibra to their previous treatment (Emipref questionnaire[2])
- Improved in joint health - Hemophilia joint health score (HJHS)

Negrier et al. ASH 2021; 1. Witkop M, et al., *Haemophilia*. 2021;27 Suppl 1:8–16; 2. Parnes et al. Haemophilia. 2021;1ePub ahead of print; doi:10.1111/hae.14421; *Mild HA (FVIII level >5%–<40%), moderate HA (FVIII level ≥1%–≤5%); †one participant with moderate HA was enrolled but withdrew prior to treatment ‡HA severity was defined based on the ISTH classification system where a FVIII level >5%–<40% of normal level is considered to be mild disease and ≥1%–≤5% of normal level is considered to be moderate disease; CATCH=comprehensive assessment tool of challenges in hemophilia

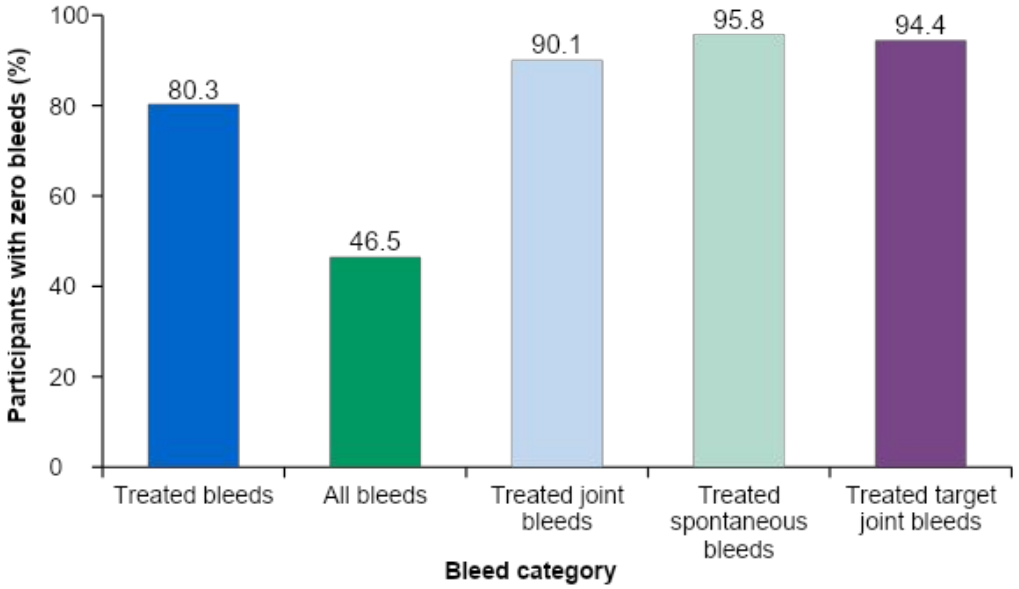
Hemlibra was efficacious for preventing bleeding events

Efficacy data consistent across all bleeding EPs and with other Haven studies

Model-based ABR* (95% CI)				
Treated bleeds	All bleeds	Treated joint bleeds	Treated spontaneous bleeds	Treated target joint bleeds
0.8 (0.41–1.46)	2.3 (1.63–3.10)	0.3 (0.12–0.65)	0.1 (0.02–0.23)	Not estimable

- Most median values for bleeding events were zero
- All model estimates showed ≤ 2.3 bleeds per year
- ABRs were consistent among mild and moderate subgroups†
- No new safety signals were identified and there were no thrombotic events, thrombotic microangiopathies, or deaths at the time of the interim analysis‡

Treated participants with zero bleeds



Hemlibra offers a favourable safety profile and an efficacious treatment option for people with moderate/mild HA while reducing treatment burden for those previously receiving either episodic or prophylactic FVIII treatment

*Model-based ABR was derived via negative binomial regression; †Subgroup analysis for treated bleeds, model-based ABR (95% CI), all treated patients, mild ABR 0.3 (0.10; 0.97), moderate ABR 0.9 (0.43; 1.89); ‡Median follow-up period of 27.5 weeks; ABR=annualized bleed rate; CI=confidence interval; EP=endpoint

Mosunetuzumab monotherapy in R/R FL

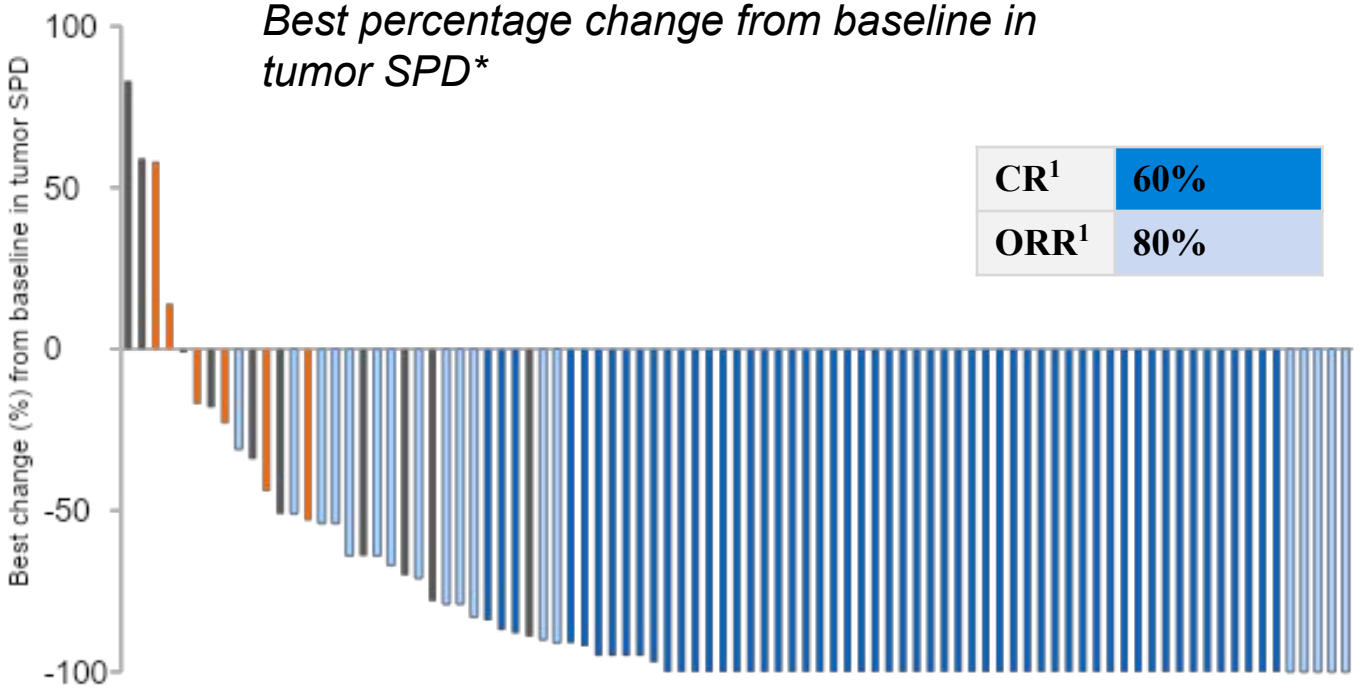
Primary endpoint met: CR rate greater than historical control

Pivotal phase II study (GO29781)

- Single-arm, pivotal Ph II expansion in patients with R/R FL and ≥2 prior therapies
- Q3IV dosing; C1 step-up dosing (CRS mitigation)
- **Fixed-duration treatment**
  - 8 cycles if CR after C8
  - 17 cycles if PR/SD after C8
- **No mandatory hospitalization**

Key baseline Characteristics	N=90
Median number of prior lines, n (range)	3 (2–10)
Refractory to any prior aCD20 therapy and alkylator therapy (double refractory)	48 (53.3%)
POD24	47 (52.2%)
Median duration of follow-up, months (range)	18.3 (2.0-27.5)
Number of cycles received‡	
<8 cycles	21 (23.3%)
8 cycles	53 (58.9%)

*Best percentage change from baseline in tumor SPD**



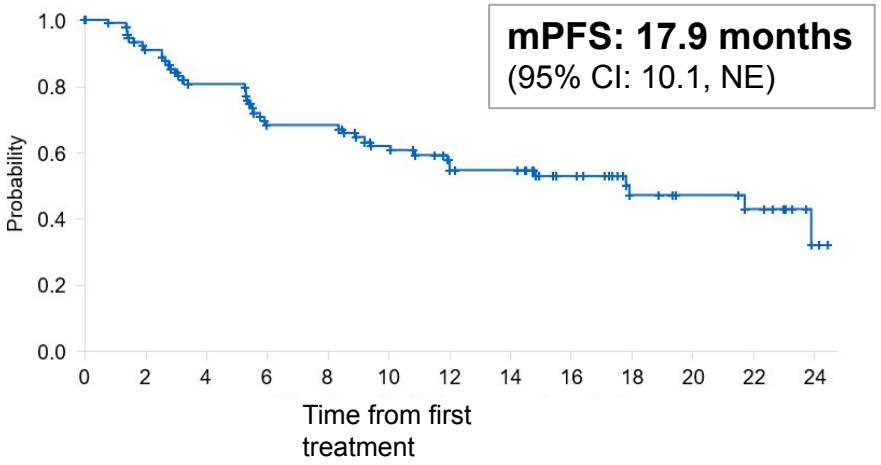
CR[1]	60%
ORR[1]	80%

60% CR rate significantly greater (p<0.0001)† than 14% historical control CR rate[2]

Budde et al. ASH 2021, 1. ORR by IRF; Cheson et al. J Clin Oncol 2007;25:579–86; 2. Dreyling et al. J Clin Oncol 2017;35:3898–905; CR=complete response; PR=partial response; SD=stable disease; CRS=cytokine release syndrome; POD24=progression of disease within 24m; ‡Cut-off date: August 27, 2021; †exact binomial test with two-sided alpha level of 5%; *in all patients with a baseline and ≥1 post-baseline SPD available; PD=progressive disease; SPD=sum of product diameters

Mosunetuzumab achieved deep and durable responses with favorable tolerability profile

Progression-free survival



mDoR: 22.8 months (95% CI 9.7, NE)

Managable CRS and saftey

N (%)	N=90
CRS (any Grade)*	40 (44.4%)
Grade 1	23 (25.6%)
Grade 2	15 (16.7%)
Grade 3	1 (1.1%)
Grade 4	1 (1.1%)†
AE leading to discontinuation of treatment	4 (4.4%)‡
Mosunetuzumab related§	2 (2.2%)‡

- CRS predominately low Grade and in Cycle 1
- Drug discontinuation is low
- Potential for use as outpatient therapy

First T-cell-engaging bispecific antibody to demonstrate clinically meaningful outcomes in pivotal Ph II in R/R

*assessed using ASTCT criteria; †patient with leukemic phase FL; §AE considered related to treatment by the investigator; ‡mosunetuzumab related: CRS (2 patients); mosunetuzumab unrelated: Esptein-Barr viremia and Hodgkin's disease (1 patient each); AE=adverse event; CRS=cytokine release syndrome; DoR=duration of response; CI=confidence interval; NE=not estimable; R/R=relapsed refractory; FL=follicular lymphoma

Mosun + Pola in R/R B-NHL dose-escalation and expansion
High response rates and manageable safety profile

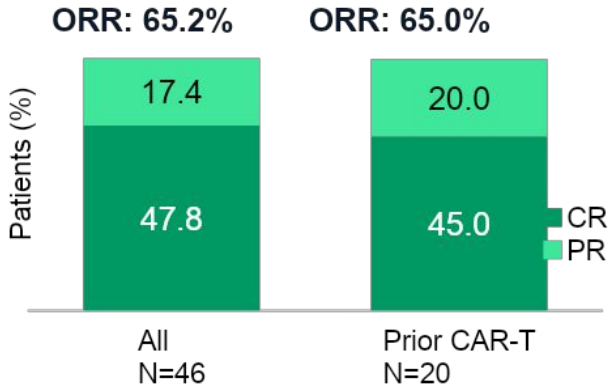
M-Pola phase II expansion (GO40516)

Mosunetuzumab
- Q3W IV infusions at RP2D up to 17 cycles
- No mandatory hospitalization

Polatuzumab vedotin
- Q3W intravenous infusions (1.8mg/kg) up to 6 cycles

Key baseline characteristics N (%) unless stated	All patients N=63
Median prior lines of therapy, range	3 (1–10)
Prior CAR-T therapy	25 (39.7)
Refractory to last prior therapy	48 (76.2)

Responses in all DLBCL patients at RP2D (N=46)



Cytokine release syndrome (n=63)

CRS (any Grade)*	**11 (17.5)**
Grade 1	10 (15.9)
Grade 2	1 (1.6)
Grade 3	0

- **PFS data are immature but early durability data are promising**
  - Of 29 patients who achieved CR, 28 remained in CR and 1 had PD
  - The patient with PD subsequently received retreatment and achieved a CR
- **CRS confined to C1 and gr 1-2**
  - All CRS events resolved without tocilizumab or vasopressors
- **Randomized phase III in 2L+ DLBCL for Mosun+Pola initiated**

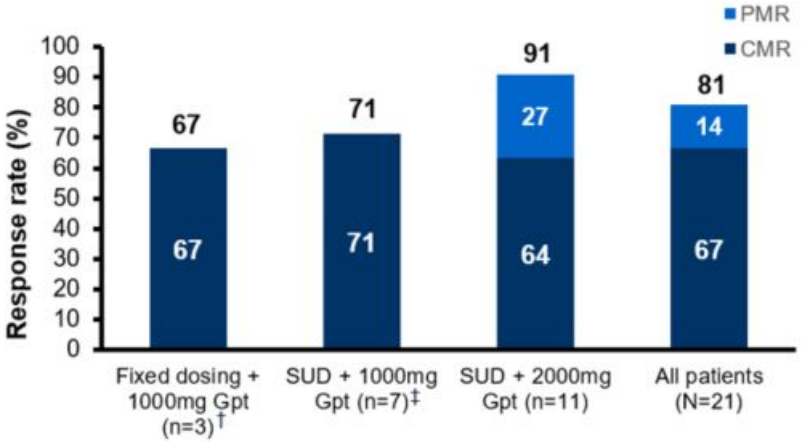
Budde et al. ASH 2021; *assessed using ASTCT criteria; NE=not estimable; RP2D=recommended phase II dose; ORR=overall response rate; PFS=progressive free disease; CRS=cytokine release syndrome; CAR-T=chimeric antigen receptor T cell; CR=complete response; PD=progressive disease; Pola=polatuzumab vedotin

Glofitamab step-up dosing in R/R MCL
High responses rates and manageable safety

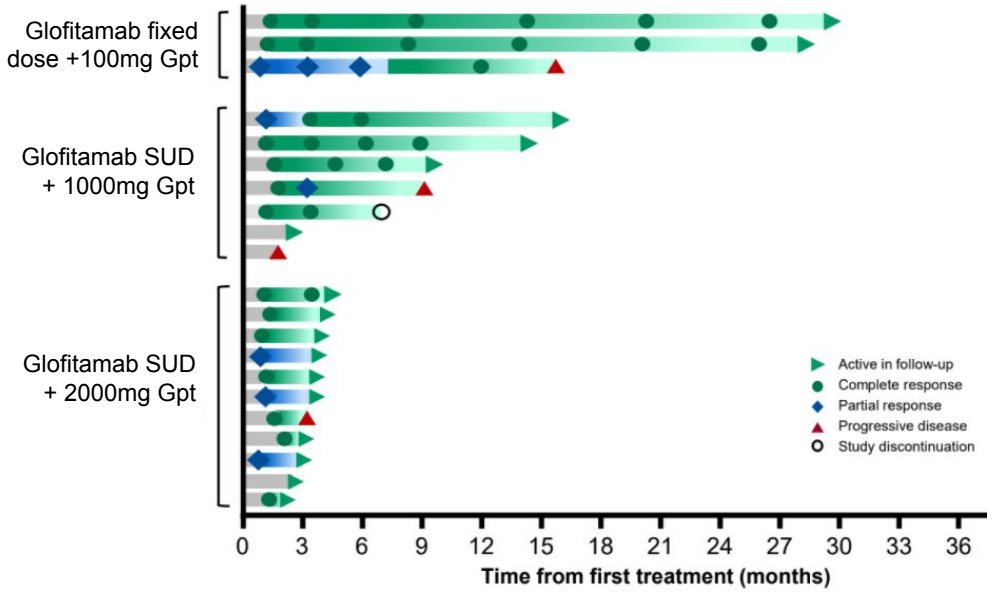
Ph I Dose Escalation in MCL (NP30179)

Key baseline Characteristics	N=29*
Prior lines of therapy, median (range)	3 (1-6)
Prior BTKi	20 (69.0)
Refractory to any prior therapy	26 (89.7)

Response rates[1] by glofitamab regimen§



Duration of response in efficacy-evaluable patients¤

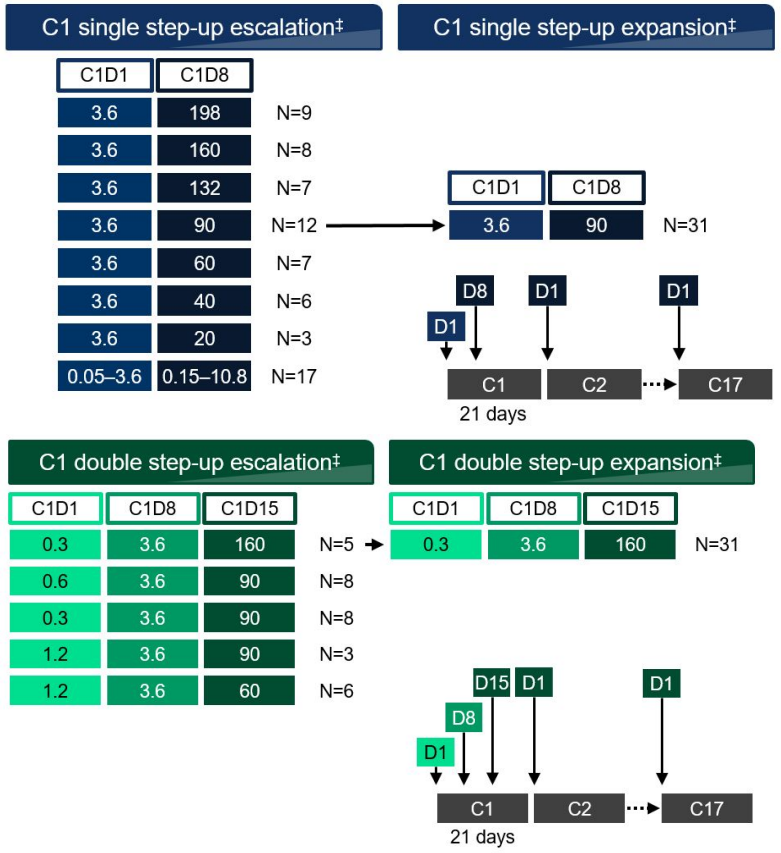


- Most patients had ongoing responses at the time of the data cut-off
- Most CRS events occurred during C1, were Grade 1 or 2 and resolved
- These results support a future confirmatory trial

Phillips et al. ASH 2021 *Three patients were treated with glofitamab in combination with obinutuzumab (G-combo); 1. Cheson, BD et al. J Clin Oncol 2014; §21/29 patients were efficacy-evaluable: the secondary efficacy-evaluable population includes all patients who had a response assessment performed (investigator-assessed), or who were still on treatment at the time of their first scheduled response assessment (Lugano 2014 criteria)[1]. †Due to a data issue, the response (CR) from one patient is reported as missing, and two patients treated with a combination of glofitamab and obinutuzumab (G-combo); ‡One patient treated with G-combo; ¤Secondary efficacy-evaluable population; MCL=mantle cell lymphoma; BTKi, Bruton's tyrosine kinase inhibitor; CMR= complete metabolic response; PMR=partial metabolic response; Gpt=obinutuzumab pretreatment; SUD=step-up dosing; CRS=cytokine release syndrome;

Cevostamab Ph 1 dose escalation in R/R MM

Patients were highly pretreated and highly refractory



Baseline characteristics

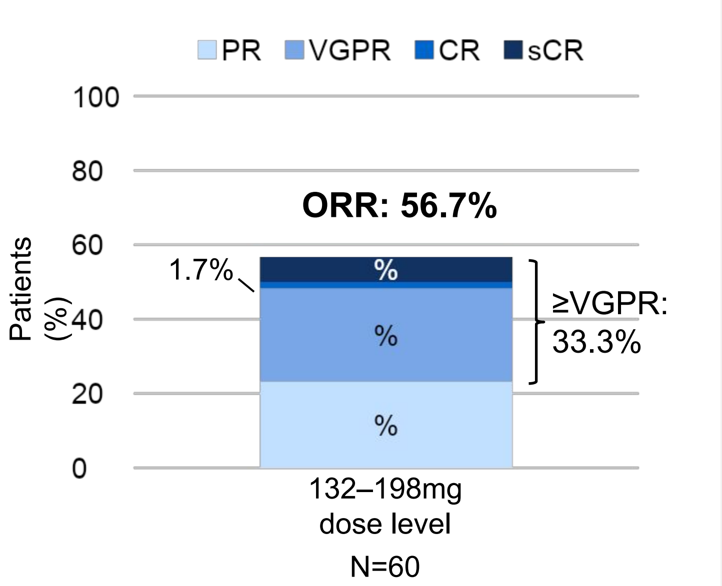
N (%) of patients unless stated	N=161
Number of lines of prior therapy, median (range)	6 (2–18)
Prior anti-CD38 antibody	142 (88.2)
Prior anti-BCMA	54 (33.5)
Prior CAR-T	28 (17.4)
Prior ADC	27 (16.8)
Prior bispecific antibody	13 (8.1)
Triple-class refractory†	136 (84.5)
Penta-drug refractory*	110 (68.3)
Refractory to last prior therapy	143 (88.8)

Trudel et al. ASH 2021; Cut-off date: August 25, 2021; ‡all doses in mg; ADC=antibody–drug conjugate; CAR-T=chimeric antigen receptor T-cell; C1D1= Cycle 1 Day 1; †≥1 IMiD, ≥1 PI, and ≥1 anti-CD38 antibody;
*≥2 IMiDs, ≥2 PIs and ≥1 anti-CD38 antibody; BCMA=B-cell maturation antigen

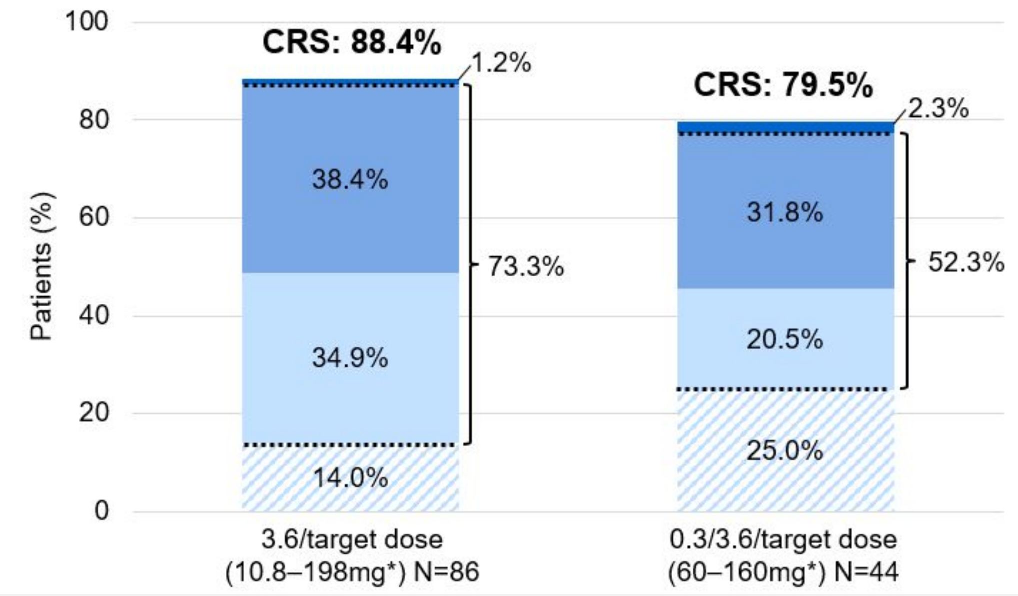
Cevostamab monotherapy has clinically meaningful activity and manageable safety in heavily pre-treated R/R MM

Roche

Response rate



CRS profile with C1 step-up dosing and C1 double step-up dosing



- C1 step-up dosing provided effective CRS mitigation.
- CRS was generally confined to C1 and was mostly low grade

Grade 3 CRS
Grade 2 CRS
Grade 1 CRS with symptoms in addition to fever
Grade 1 CRS with fever only

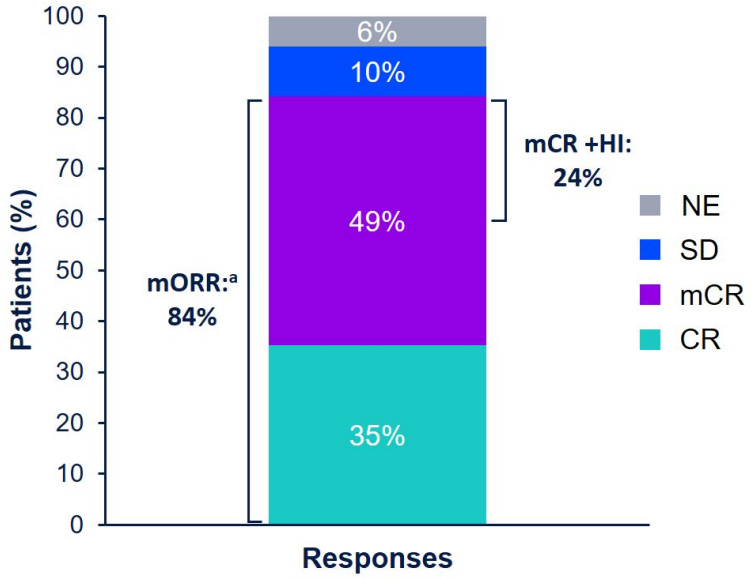
- MRD negativity by NGS ($<10^{-5}$) detected in 7/10 evaluable pts with ≥VGPR
- Cevostamab had a manageable safety profile; AEs leading to discontinuation were uncommon

Cevostamab may be a beneficial treatment option for pts in RRMM; clinical development program will expand in 2022

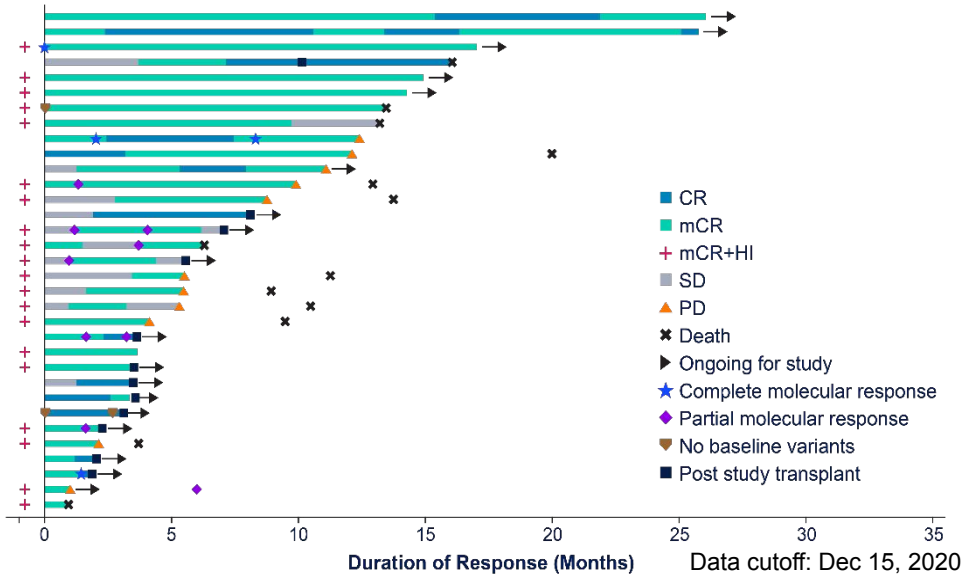
Trudel et al. ASH 2021; ORR=objective response rate; PR=partial response; sCR=stringent complete response; VGPR=very good partial response; NGS=next-generation sequencing; AE=adverse events; MRD=minimal residual disease; CRS=cytokine release syndrome; CI=confidence interval; *dose ranges represent all target dose levels evaluated in combination with the 3.6mg or 0.3/3.6mg step-up doses

Venclexta + Azacitidine in treatment-naive higher-risk MDS

Response rate (n=51)



Molecular responses in patients who recieved RP2D and achieved a clinical repsonse (n=33)*



Data cutoff: Dec 15, 2020

- 84% of patients who received RP2D Ven+Aza (N=51) responded to treatment
- Median time to response: 0.9 months (95% CI, 0.7-5.8)
- Median duration of response: 12.4 months (95% CI, 9.9-NR)
- Clinical and molecular responses were observed in patients with HR-MDS across the mutational spectrum

Garcia et al. ASH 2021; HR-MDS=higher-risk myelodysplastic syndrome; [a]mORR=CR+mCR+PR; PR, n=0; response rates based on IWG 2006 response criteria. mORR=modified overall response rate; CR=complete remission; mCR=marrow complete remission; HI= hematologic improvement; SD=stable disease; NE=not evaluable; RP2D, recommended phase 2 dose; CI=confidence interval; Aza=azacitidine; Ven=venetoclax; VAF=variant allele frequency; SCR=screnning; EOC=end of cycle; PD=progressive disease; PR, partial remission; *Includes patients who achieved a clinical response (CR, mCR, or mCR + HI) and had at least one molecular response assessed (BMA or PB). Complete molecular response = all gene VAF went below LOD at time of second molecular response assessment; partial molecular response = at least one gene VAF went below LOD at time of molecular assessment; if there is no molecular response symbol, that patient did not achieve a partial or complete molecular response.

Key data presented at ASH: POLARIX

Franck Morschhauser | MD, PhD, Professor of Hematology, University of Lille; President of LYSA, LYSARC

LBA-1

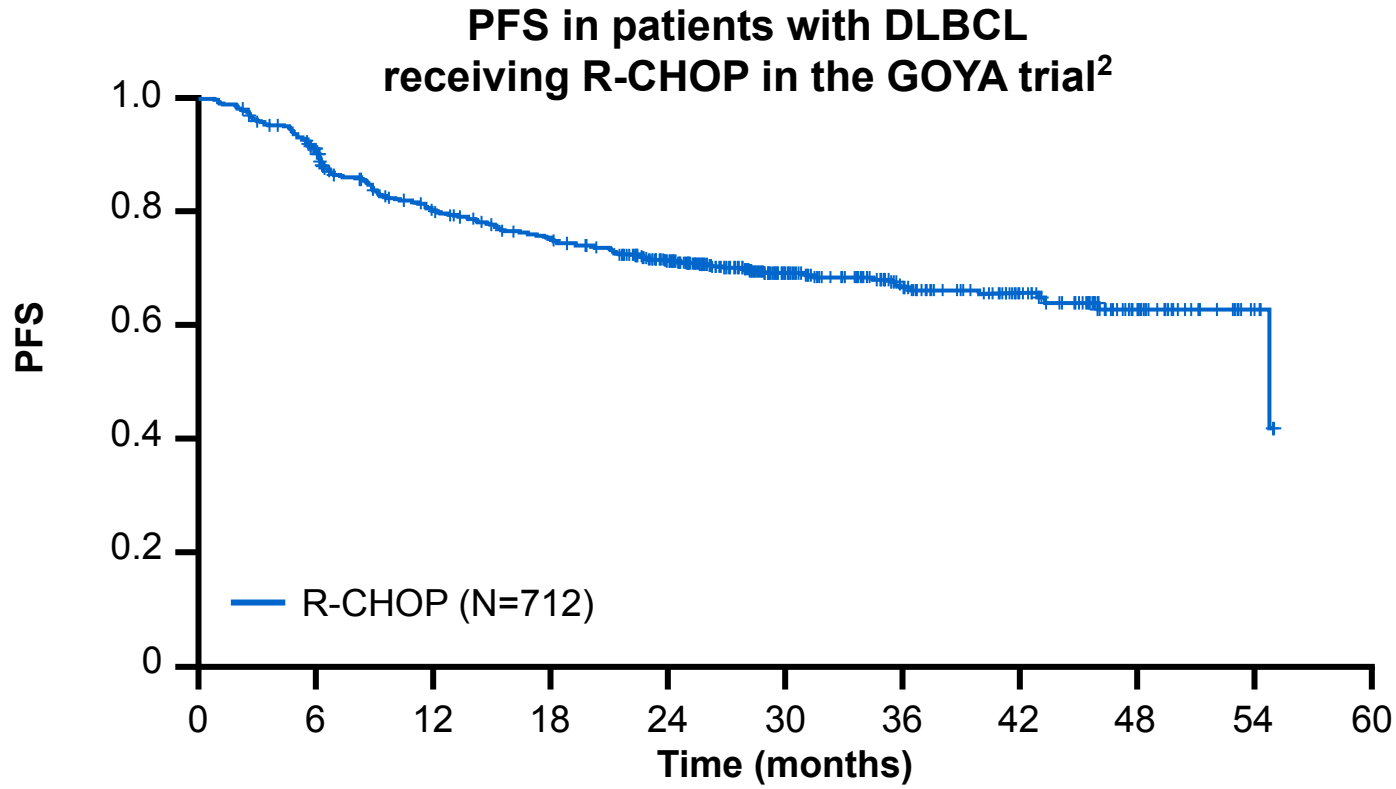
The POLARIX Study: Polatuzumab Vedotin with Rituximab, Cyclophosphamide, Doxorubicin, and Prednisone (Pola-R-CHP) Versus Rituximab, Cyclophosphamide, Doxorubicin, Vincristine and Prednisone (R-CHOP) Therapy in Patients with Previously Untreated Diffuse Large B-Cell Lymphoma

Hervé Tilly,[1] Franck Morschhauser,[2] Laurie H. Sehn,[3] Jonathan W. Friedberg,[4] Marek Trněný,[5] Jeff P. Sharman,[6] Charles Herbaux,[7] John M. Burke,[8] Matthew Matasar,[9] Shinya Rai,[10] Koji Izutsu,[11] Neha Mehta-Shah,[12] Lucie Oberic,[13] Adrien Chauchet,[14] Wojciech Jurczak,[15] Yuqin Song,[16] Richard Greil,[17] Larysa Mykhalska,[18] Juan Miguel Bergua Burgués,[19] Matthew C. Cheung,[20] Antonio Pinto,[21] Ho-Jin Shin,[22] Greg Hapgood,[23] Eduardo Munhoz,[24] Pau Abrisqueta,[25] Jyh-Pyng Gau,[26] Jamie Hirata,[27] Yanwen Jiang,[27] Mark Yan,[28] Calvin Lee,[27] Christopher Flowers,[29] Gilles Salles[30]

[1]Department of Hematology and U1245, Centre Henri Becquerel and University of Rouen, Rouen, France; [2]Univ. Lille, CHU Lille, ULR 7365 – GRITA – Group de Recherche sur les formes Injectables et les Technologies Associées, Lille, France; [3]BC Cancer Centre for Lymphoid Cancer and the University of British Columbia, Vancouver, Canada; [4]Wilmot Cancer Institute, University of Rochester, Rochester, NY, USA; [5]First Faculty of Medicine, Charles University, General Hospital, Prague, Czech Republic; [6]Willamette Valley Cancer Institute/US Oncology, Eugene, OR, USA; [7]CHU de Montpellier, Montpellier, France; [8]Rocky Mountain Cancer Centers/US Oncology, Aurora, CO, USA; [9]Memorial Sloan Kettering Cancer Center, New York City/Montvale, NY/NJ, USA; [10]Department of Hematology and Rheumatology, Kindai University, Faculty of Medicine, Osaka-Sayama City, Japan; [11]National Cancer Center Hospital, Tokyo, Japan; [12]Washington University in St. Louis, St. Louis, MO, USA; [13]Department of Hematology, Institut Universitaire du Cancer, Toulouse-Oncopole, Toulouse, France; [14]Department of Hematology, CHRU Besançon, Besançon, France; [15]Maria Sklodowska – Curie National Research Institute of Oncology, Kraków, Poland; [16]Peking University Cancer Hospital, Beijing, China; [17]3rd Medical Department, Paracelsus Medical University, Salzburg Cancer Research Institute-CCCIT and Cancer Cluster Salzburg, Salzburg, Austria; [18]Clinical Hospital Feofaniya, Kyiv, Ukraine; [19]Hospital San Pedro de Alcántara, Cáceres, Spain; [20]Odette Cancer Centre, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Canada; [21]Hematology-Oncology & Stem Cell Transplantation Unit, Istituto Nazionale Tumori, Fondazione 'G. Pascale', IRCCS, Naples, Italy; [22]Division of Hematology-Oncology, Department of Internal Medicine, Medical Research Institute, Pusan National University Hospital, Pusan National University School of Medicine, Busan, Korea; [23]Princess Alexandra Hospital, Brisbane, Australia; [24]Hospital Erasto Gaertner, Curitiba, Brazil; [25]Department of Hematology, Hospital Vall d'Hebron, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain; [26]Taipei Veterans General Hospital, Taipei, Taiwan; [27]Genentech, Inc., South San Francisco, CA, USA; [28]Hoffmann-La Roche Ltd, Mississauga, Canada; [29]MD Anderson Cancer Center, Houston, TX, USA; [30]Memorial Sloan Kettering Cancer Center, New York City, NY, USA.

Late-Breaking Abstract Accepted as an Oral Presentation at the 63rd ASH Annual Meeting and Exposition, 11–14 December 2021

R-CHOP has been the standard of care in first-line DLBCL for over 20 years



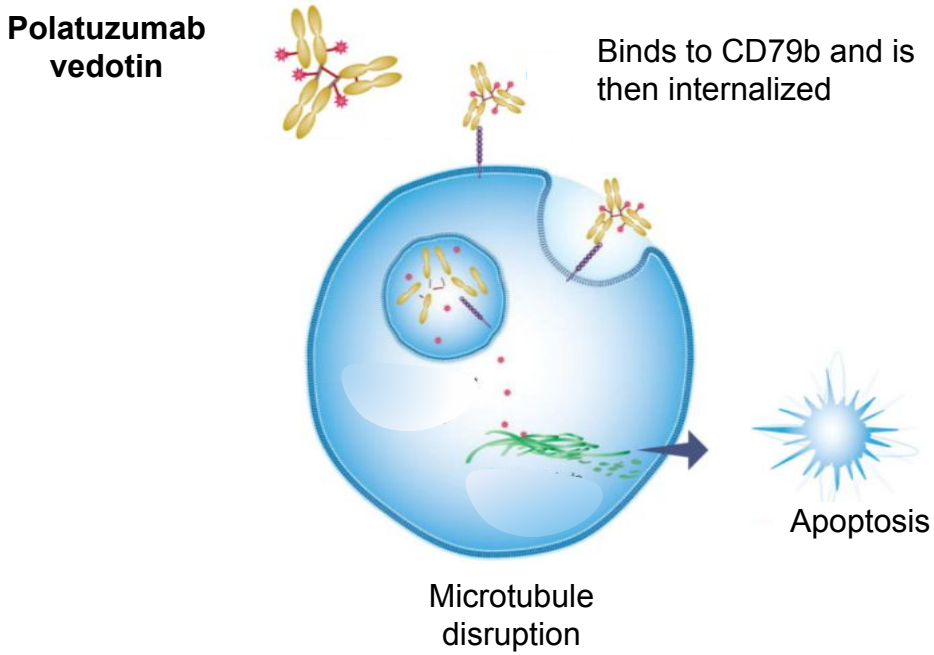
- Only 60–70% of patients are cured with R-CHOP[1,2]
- An unmet need remains for patients with previously untreated DLBCL

PFS, progression-free survival.

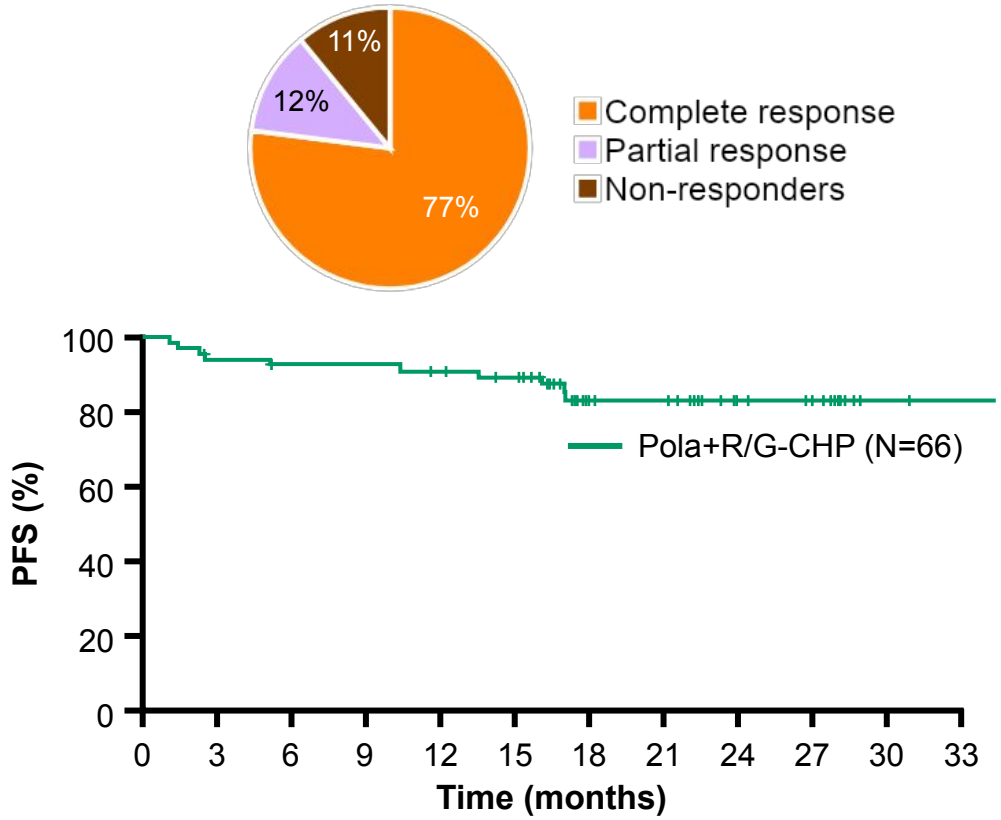
1. Sehn LH and Salles G. N Engl J Med 2021;384(9):842–8;
2. Vitolo U, et al. J Clin Oncol 2017;35:3529–37.

Polatuzumab vedotin is an ADC targeting CD79b

CD79b is ubiquitously expressed on DLBCL cells[1–3]



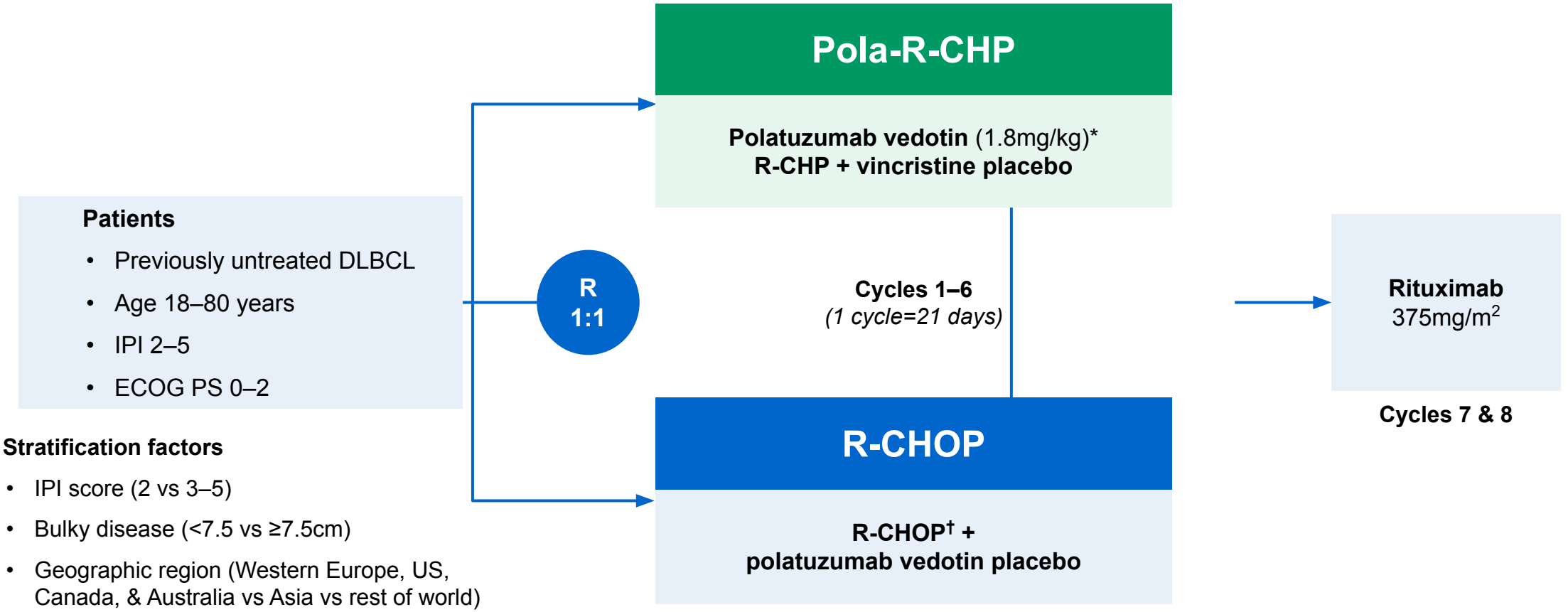
Pola+R/G-CHP demonstrated activity in first-line DLBCL[4]



ADC, antibody–drug conjugate; G, obinutuzumab.

1. Dornan D, et al. Blood 2009;114:2721–9; 2. Polson AG, et al. Expert Opin Invest Drugs 2011;20:75–85; 3. Doronina SO, et al. Nat Biotechnol 2003;21:778–84; 4. Tilly H, et al. Lancet Oncol 2019;20:998–1010.

POLARIX: A randomized double-blinded study



*IV on Day 1; †R-CHOP: IV rituximab 375mg/m^2, cyclophosphamide 750mg/m^2, doxorubicin 50mg/m^2, and vincristine 1.4mg/m^2 (max. 2mg) on Day 1, plus oral prednisone 100mg once daily on Days 1–5.
IPI, International prognostic index; ECOG PS, Eastern Cooperative Oncology Group performance status; R, randomized.

POLARIX: Key endpoints and analysis timing

Key endpoints	
Primary endpoint	**Progression-free survival (Investigator-assessed)**
Secondary endpoints	Event-free survival Complete response rate at end of treatment (PET/CT, IRC-assessed) Disease-free survival Overall survival
Safety endpoints	Incidence, nature, and severity of adverse events

Statistical design and timing of primary analysis:

- 875 patients, all on study for ≥24 months with approximately 228 PFS events, were required for the primary analysis. This occurred on June 28, 2021 (clinical cut-off date)
- Median follow up at the primary analysis was 28.2 months

IRC, Independent Review Committee.

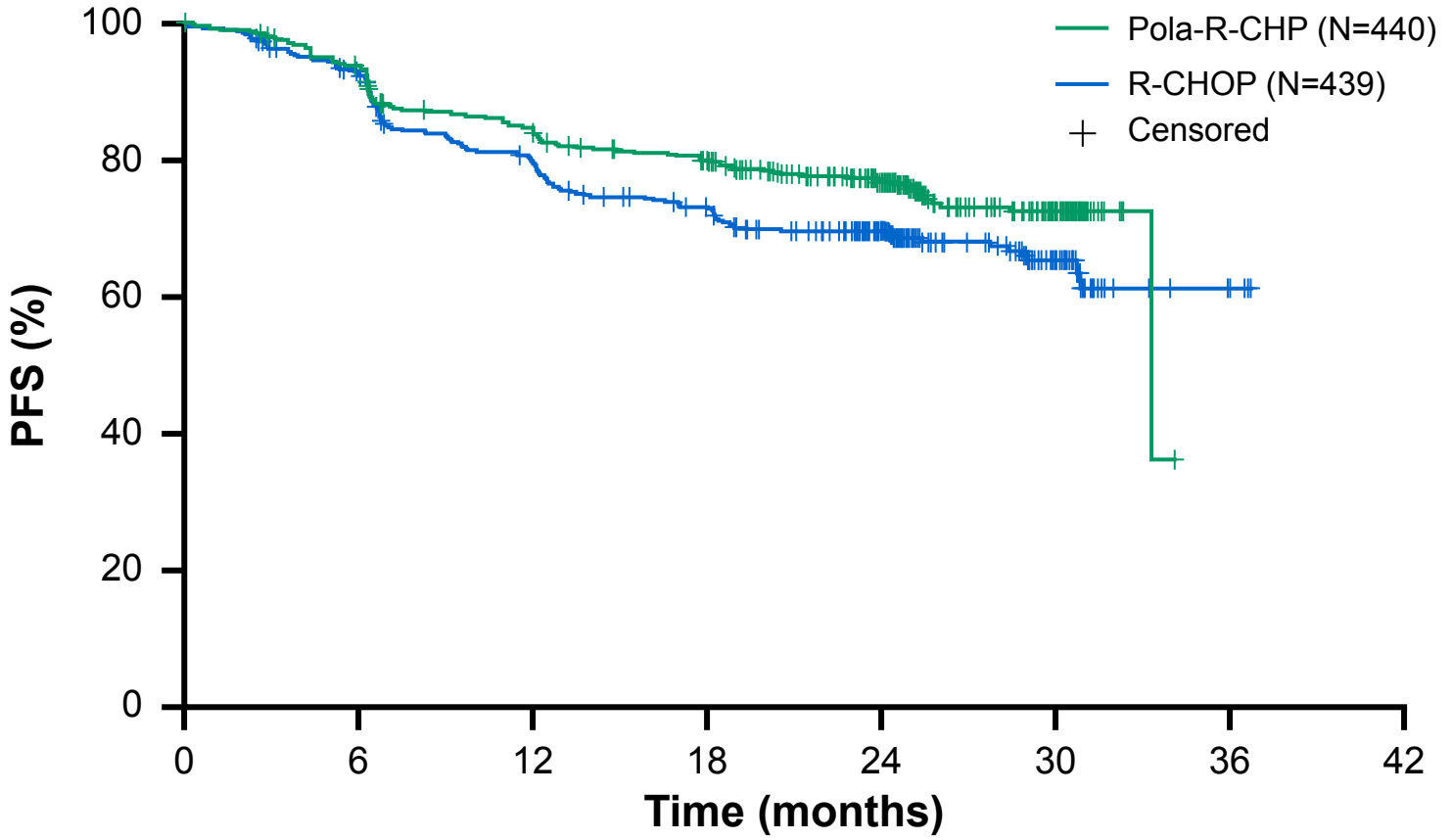
Baseline characteristics

ITT population		Pola-R-CHP (N=440)	R-CHOP (N=439)
Age	Median (range), years	65.0 (19–80)	66.0 (19–80)
Sex, n (%)	Male	239 (54)	234 (53)
ECOG PS, n (%)	0–1	374 (85)	363 (83)
	2	66 (15)	75 (17)
Bulky disease (≥7.5cm), n (%)	Present	193 (44)	192 (44)
Elevated LDH, n (%)	Yes	291 (66)	284 (65)
Time from diagnosis to treatment initiation	Median, days	26	27
Ann Arbor Stage, n (%)	III–IV	393 (89)	387 (88)
Extranodal sites, n (%)	≥2	213 (48)	213 (49)
IPI score, n (%)	2	167 (38)	167 (38)
	3–5	273 (62)	272 (62)
Cell-of-origin, (%)*	ABC	102 (31)	119 (35)
	GCB	184 (56)	168 (50)
	Unclassified	44 (13)	51 (15)
MYC/BCL2 expression, n (%)*	Double expression	139 (38)	151 (41)
MYC/BCL2/BCL6 rearrangement, n (%)*	Double-/triple-hit	26 (8)	19 (6)

*In the Pola-R-CHP and R-CHOP groups, respectively, the numbers of patients evaluable for cell-of-origin were 330 and 338, with IHC for MYC/BCL2 expression were 362 and 366, and with FISH for *MYC/BCL2/BCL6* rearrangements were 331 and 334.
ABC, activated B-cell; FISH, fluorescence in situ hybridization; GCB, germinal center B-cell; LDH, lactate dehydrogenase.

Primary endpoint: Progression-free survival

Pola-R-CHP significantly improved PFS versus R-CHOP



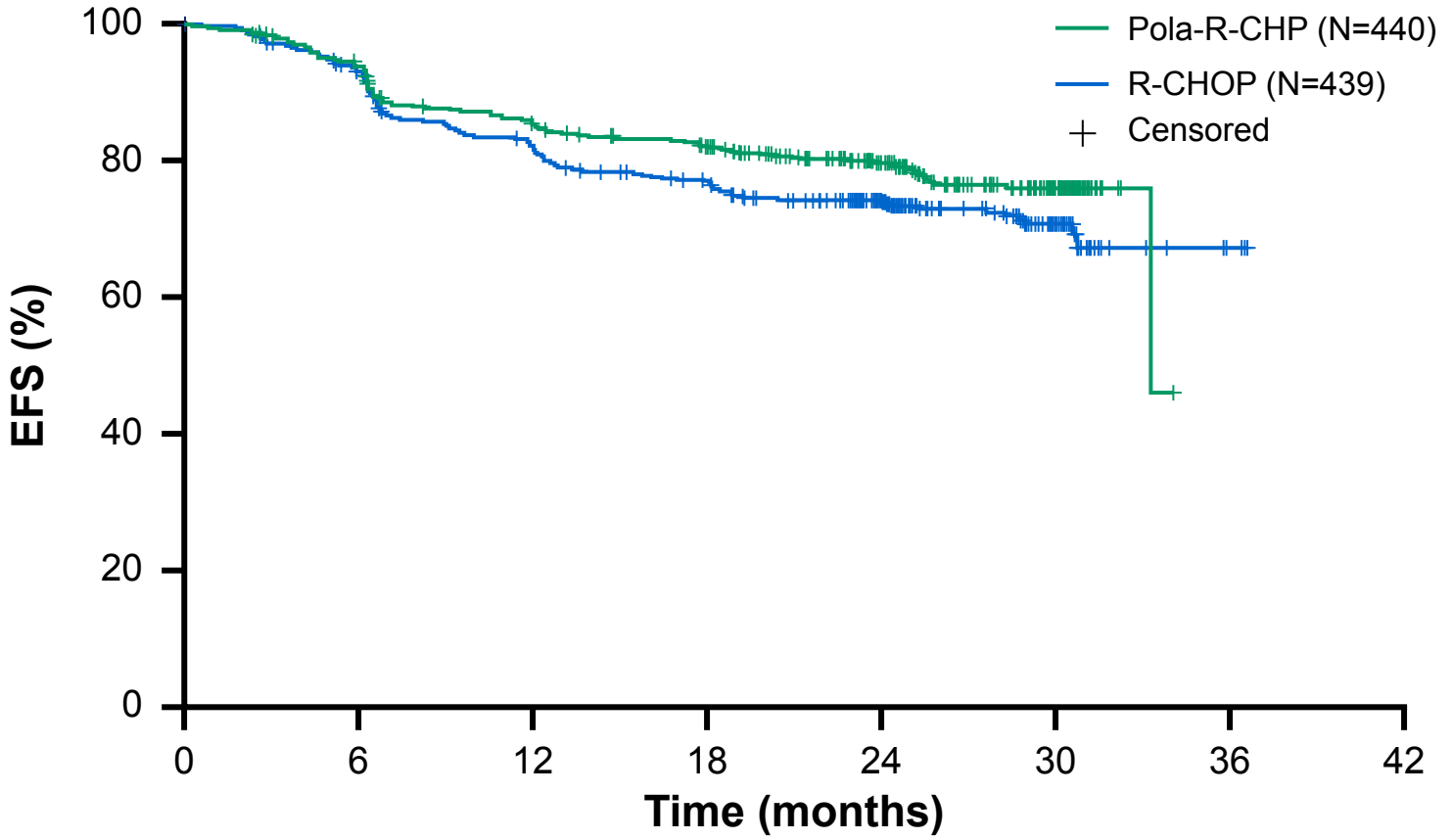
No. of patients at risk								
Pola-R-CHP	440	404	353	327	246	78	NE	NE
R-CHOP	439	389	330	296	220	78	3	NE

HR 0.73 **(P<0.02)**
95% CI: 0.57, 0.95

- Pola-R-CHP demonstrated a **27% reduction in the relative risk of disease progression, relapse, or death** versus R-CHOP
- **24-month PFS:**
  76.7% with Pola-R-CHP versus
  70.2% with R-CHOP (Δ**=6.5%**)

ITT population. Data cut-off: June 28, 2021; median 28.2 months' follow-up.
NE, not evaluable.

Event-free survival

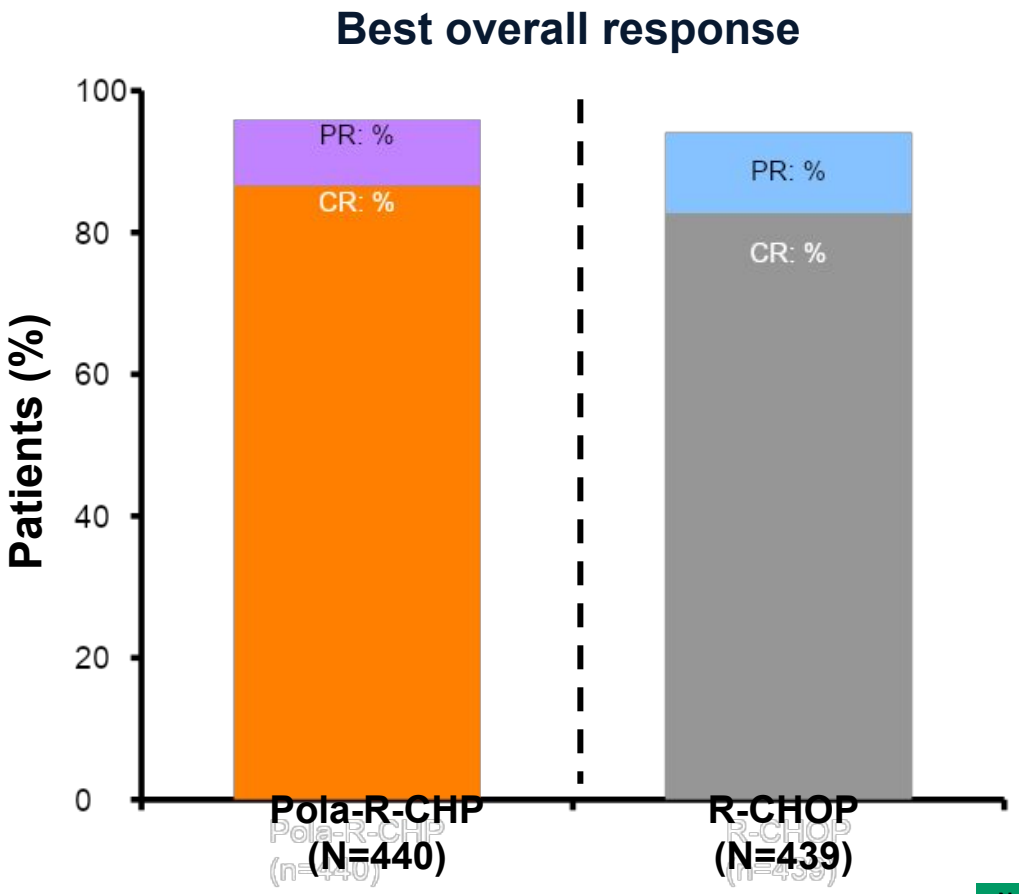


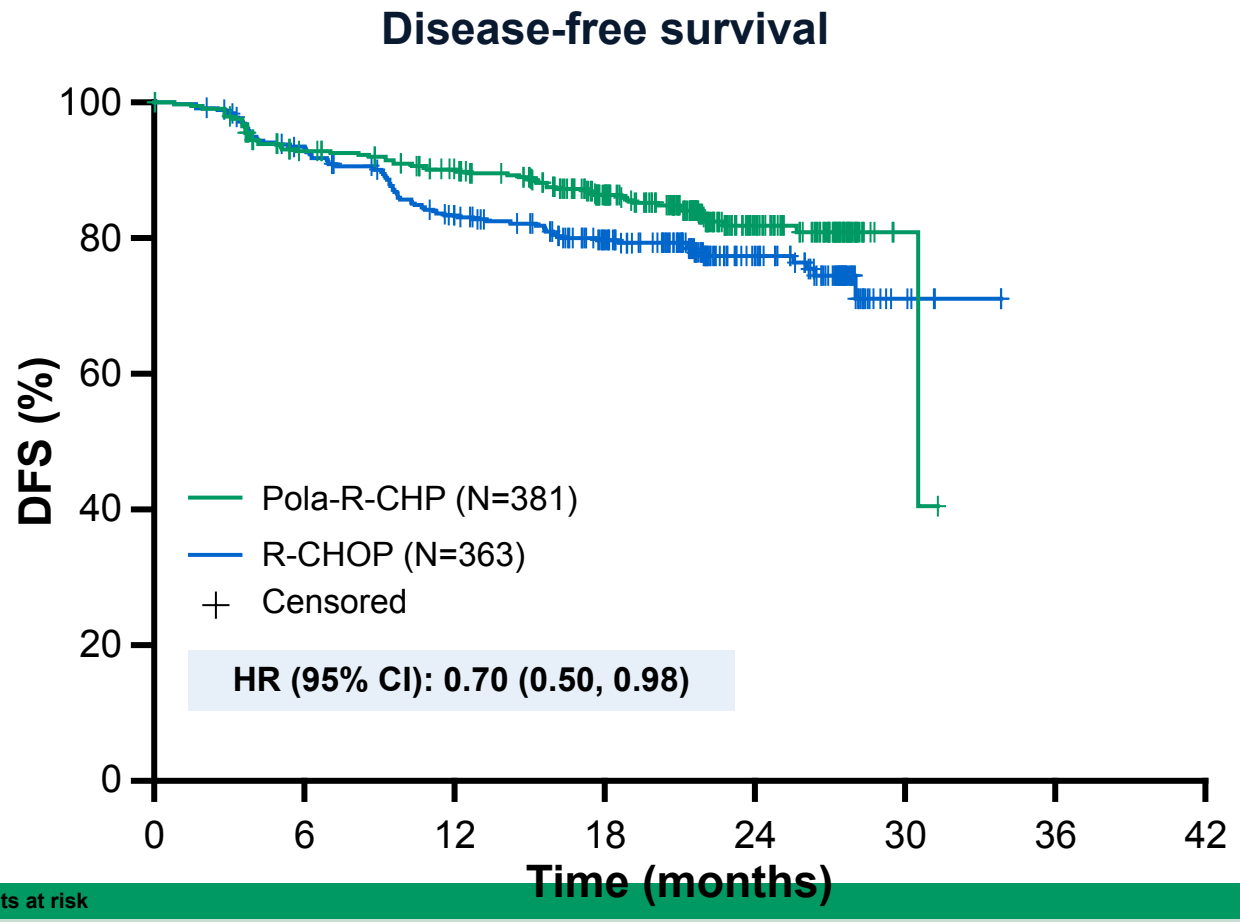
HR 0.75 (P=0.02)
95% CI: 0.58, 0.96

No. of patients at risk								
Pola-R-CHP	440	402	348	323	243	78	NE	NE
R-CHOP	439	386	327	294	218	78	3	NE

ITT population. Data cut-off: June 28, 2021; median 28.2 months' follow-up.
EFS, event-free survival.

Response rates and disease-free survival

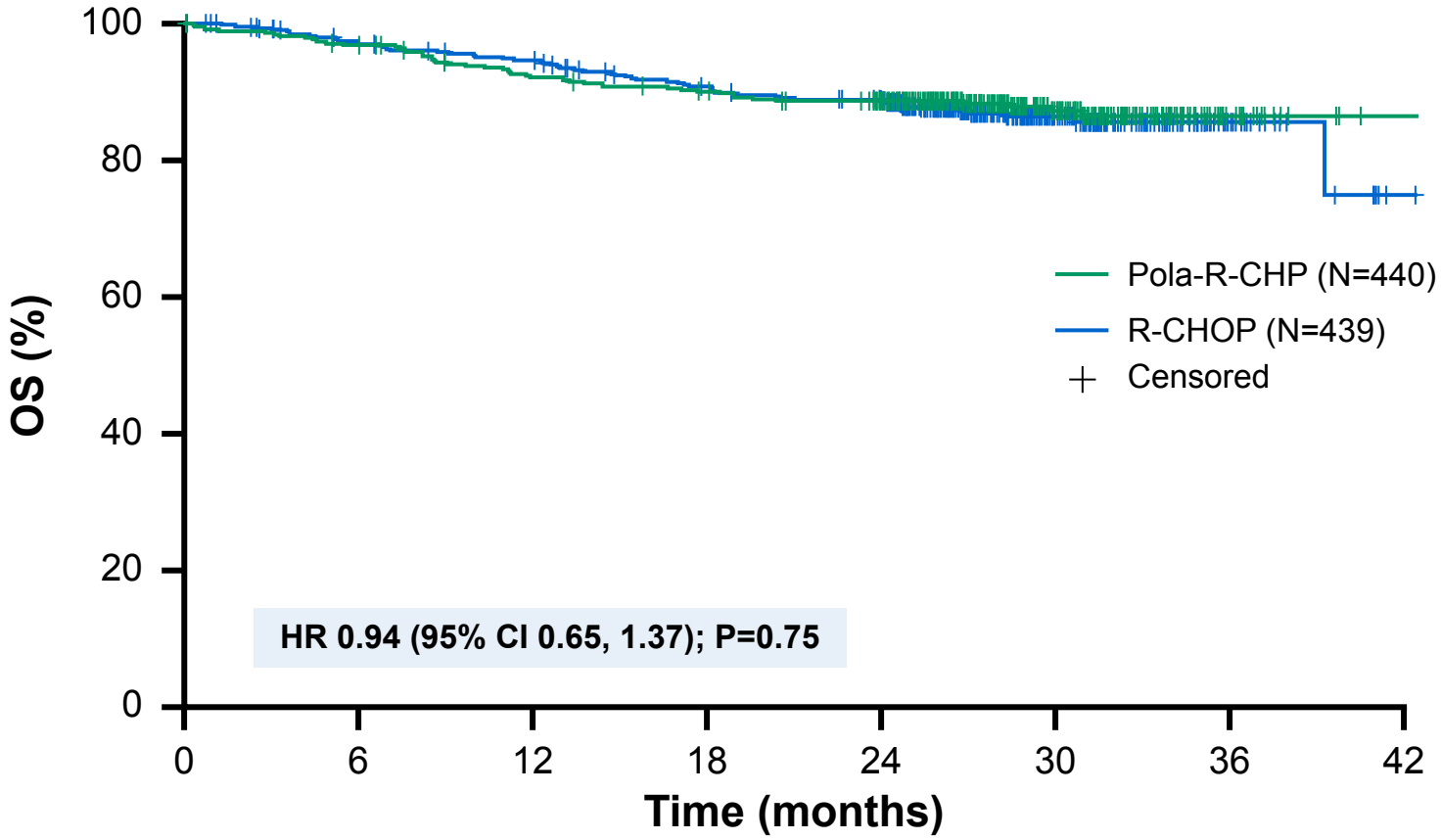




No. of patients at risk								
Pola-R-CHP	381	342	322	266	106	2	NE	NE
R-CHOP	363	326	282	238	96	5	NE	NE

ITT population. Data cut-off: June 28, 2021; median 28.2 months' follow-up. Disease-free survival (DFS) defined as the time from the date of the first occurrence of a documented complete response to the date of progression, relapse, or death from any cause for the subgroup of patients with a best overall response of CR.

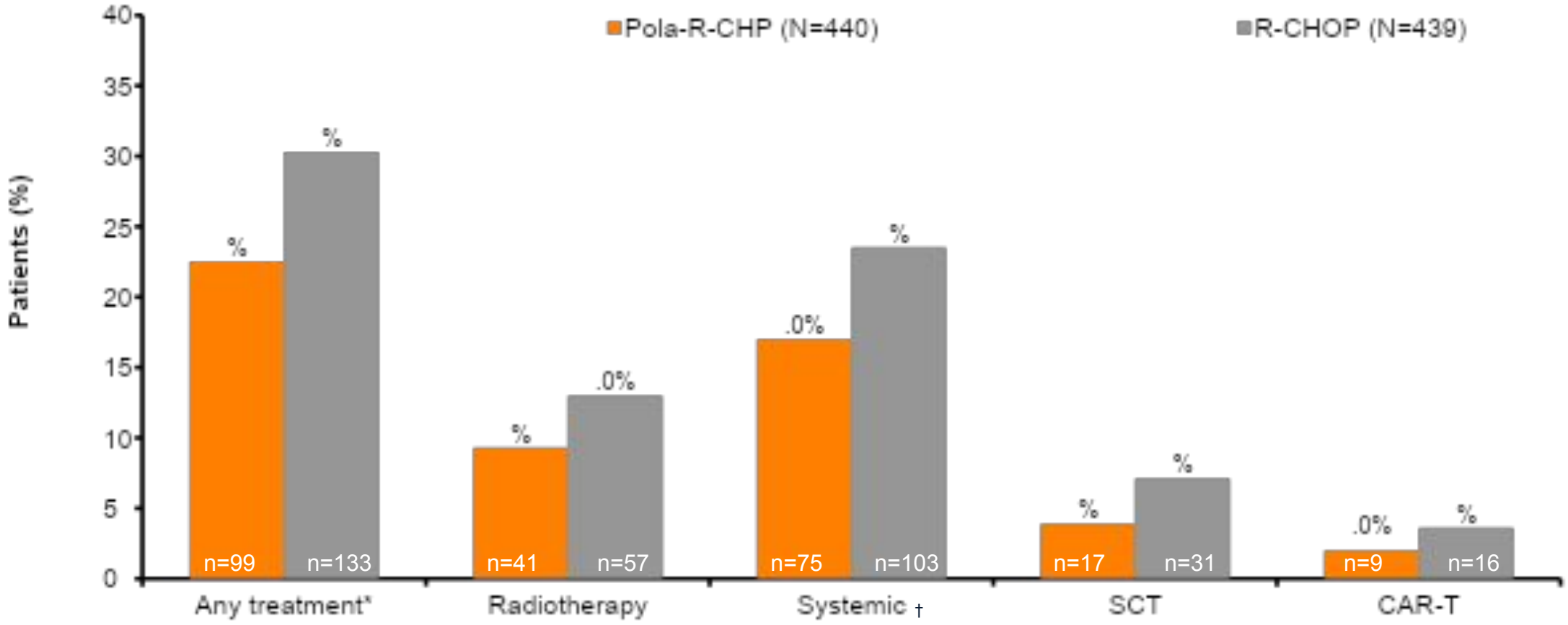
Overall survival



No. of patients at risk								
Pola-R-CHP	440	423	397	384	362	140	15	1
R-CHOP	439	414	401	376	355	132	20	1

ITT population. Data cut-off: June 28, 2021; median 28.2 months' follow-up.

Patients receiving subsequent treatments



Data cut-off: June 28, 2021. *Subsequent lymphoma treatment was defined as non-protocol anti-lymphoma therapy; †Includes any monotherapy, multi-drug, or cell-based regimen.
CAR-T, chimeric antigen receptor T-cell therapy; SCT, stem cell transplant.

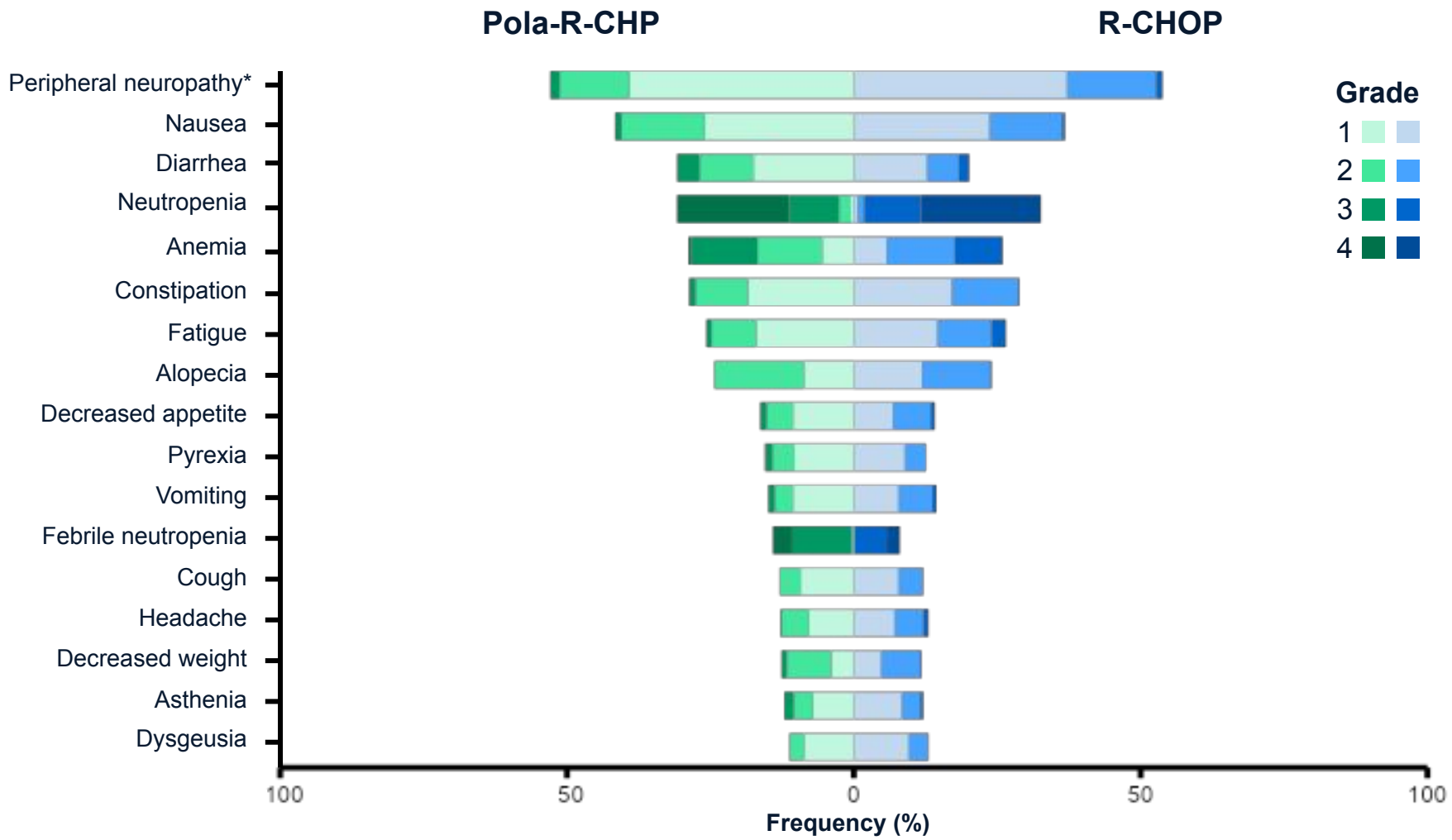
Safety summary

Safety profiles were similar with Pola-R-CHP and R-CHOP

n (%)	Pola-R-CHP (N=435)	R-CHOP (N=438)
Any-grade adverse events	426 (97.9)	431 (98.4)
Grade 3–4	251 (57.7)	252 (57.5)
Grade 5	13 (3.0)	10 (2.3)
Serious adverse events	148 (34.0)	134 (30.6)
Adverse events leading to:		
Discontinuation of any study drug	27 (6.2)	29 (6.6)
Polatuzumab vedotin / vincristine	19 (4.4)	22 (5.0)
Dose reduction of any study drug	40 (9.2)	57 (13.0)

Data cut-off: June 28, 2021.

Common adverse events



Data cut-off: June 28, 2021. Adverse events are Medical Dictionary for Regulatory Activities version 24.0 preferred terms; shown are all-grade adverse events occurring in ≥12% of patients in any treatment arm. *Peripheral neuropathy is defined by standard organ class group of preferred terms.

Conclusions

Pola-R-CHP significantly prolongs PFS compared with R-CHOP (HR 0.73) in patients with intermediate- and high-risk previously untreated DLBCL

The **safety profiles** of Pola-R-CHP and R-CHOP were **comparable**

Exploratory analyses are ongoing with regards to various subgroups and other prognostic classification systems

These results **support the use of Pola-R-CHP** in the initial management of patients with DLBCL

Doing now what patients need next