

Biespecíficos en Indolentes: ¿monodroga o combinado?

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Conflicto de Interés:

Speaker's Bureau: Janssen, Roche, Takeda, Abbvie, BMS,
Abbvie, Beigene, Knight, Lilly

Educational Support: Janssen, Takeda, Roche, Abbvie, Dr.
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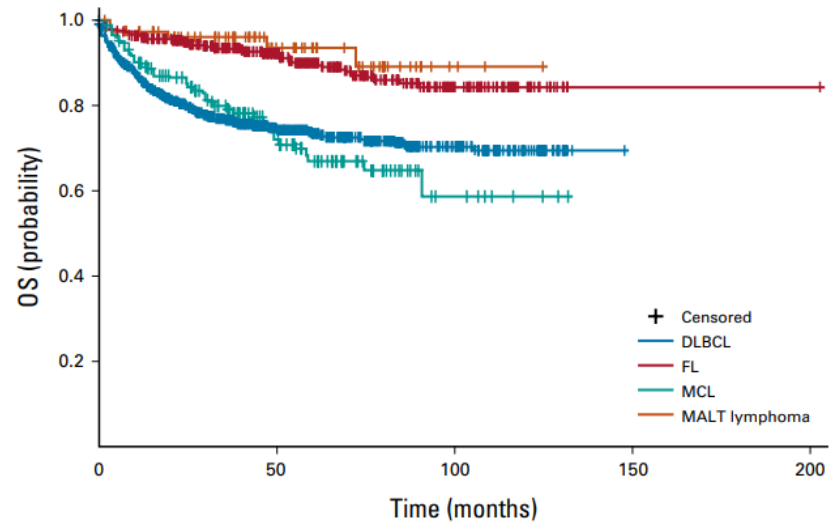
Advisory Board: Janssen, Abbvie, Astra Zeneca, Roche,
Abbvie, Beigene, Knight, Lilly

Research: Janssen, Millenium, Merck, Alnylam, BMS,
Beigene, Abbvie, Astra Zeneca, Lilly

Opinion Impopular (apesar que no fui invitado para esto)

- El Linfoma Folicular es un linfoma con altas tasas de cura (42% a 15 años)
- Hay un grupo pequeño de pacientes (18%-25%) con recaídas tempranas que necesitan terapias intensificadas y múltiples
- Mediana de edad en el diagnóstico: 64 años (SEER data)
- La mayoría de los pacientes van a llegar a una 2ª línea con >70 años, y estos pacientes están poco representados en estudios clínicos

LATAM data en LF



No. at risk:	0	50	100	150	200
DLBCL	1,387	497	100	0	
FL	544	284	65	1	1
MCL	172	70	8	0	
MALT lymphoma	77	34	3	0	

5-Year Survival Rate (%)	DLBCL	FL	MCL	MALT	Burkitt	Lymphoplasmacytic	B Lymphoblastic	T-cell	Other
Overall	69	87.6	57.1	90.8	55.7	65.9	35.1	49.3	83
Argentina	72.6	86.6	66.5	100	69.3	NA	NA	40.3	94
Brazil	50.8	71.3	35.4	92.3	57.1	52.6	0	37.5	76.7
Chile	81.7	87.3	38.1	75	NA	NA	NA	83.9	85.4
Colombia	62.1	96.1	75.1	91.7	47.6	100	60	49.2	63.5
Mexico	71.7	95.3	75.7	92.9	0	NA	NA	47.6	86.1
Panama and Guatemala	93.8	93.3	85.7	NA	NA	NA	NA	77.8	100

2960 Follicular Lymphoma in Latin America: Real-World Experience from 763 Patients

Program: Oral and Poster Abstracts

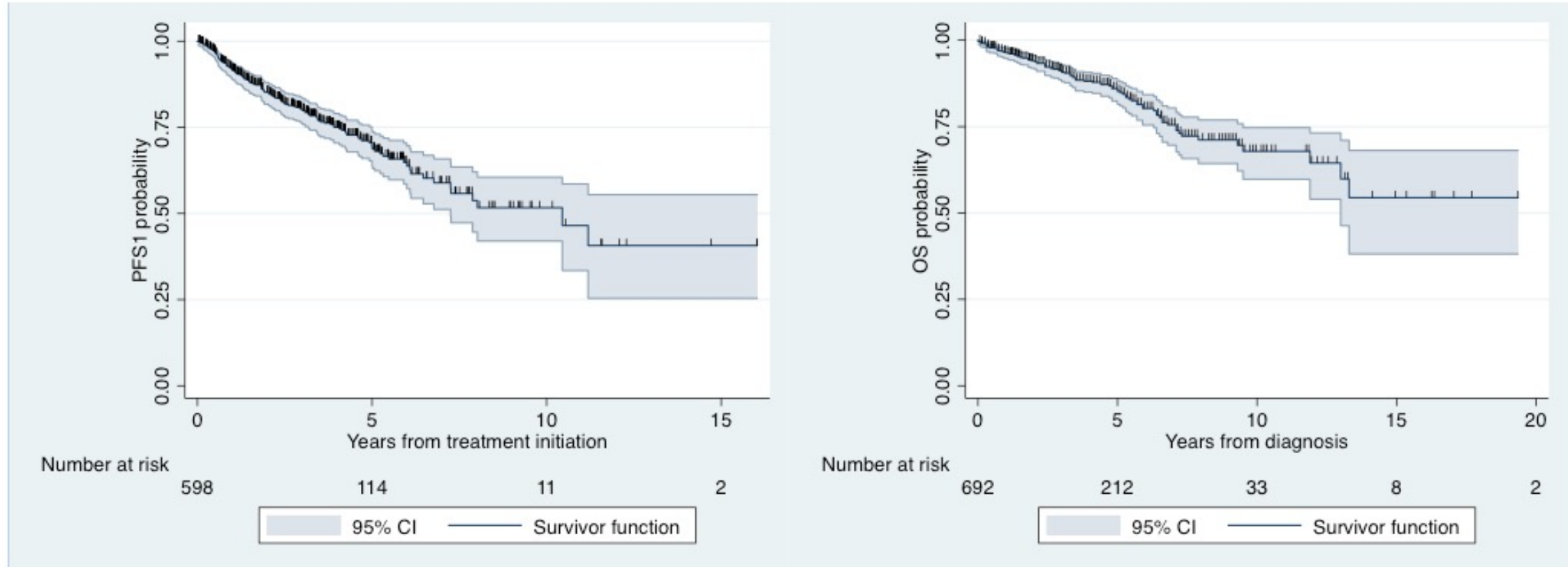
Session: 623. Mantle Cell, Follicular, and Other Indolent B-Cell Lymphoma—Clinical Studies: Poster III

Hematology Disease Topics & Pathways:

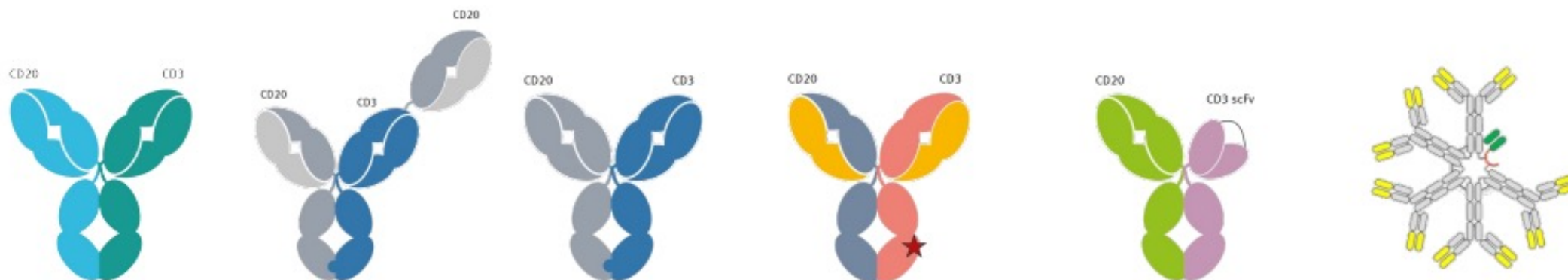
Follicular Lymphoma, Adult, Diseases, Therapies, Combinations, Non-Hodgkin Lymphoma, B-Cell Lymphoma, Cell Lineage, Lymphoid Malignancies, Study Population, Clinically relevant

Monday, December 7, 2020, 7:00 AM-3:30 PM

María Alejandra Torres Viera, MD^{1,2}, Brady E Beltran, MD^{3,4*}, Luis Villela Villela, MD, MC^{5,6*}, Denisse A. Castro, MD⁷, Victoria Otero, MD^{8*}, Lorena Fiad, MD^{9*}, Camila Peña, MD¹⁰, Henry Idrobo, MD^{11,12,13,14*}, Myrna Candelaria, MD, PharmD¹⁵, Alana Von Glasenapp, MD^{16*}, Ivan Perdomo, MD^{17*}, María Virginia Prates, MD⁹, Sally Rose Paredes, MD^{18*}, Fernando Pérez-Jacobo, MD¹⁹, Ana Ramírez-Ibarguen, MD^{20*}, Juan Alejandro Ospina Idarraga^{21,22*}, María Elena Cabrera, MD^{23*}, Claudia Gajardo, MD^{24*}, Macarena Alejandra Roa Salinas^{25*}, Catalina Díaz, MD^{26*}, Laura Silva Idárraga, MD^{27*}, Humberto Martínez Cordero, MD^{28*}, Melani Otañez, MD^{29*}, Fabiola Valvert, MD³⁰, Efree Montaña Figueroa, MD, PhD^{31*}, Marcos Di Stefano, MD^{32,33*}, Rosio Baena, MD^{34,35*}, Juan Antonio Choque, MD^{36*}, Virginia Abello, MD^{37*}, Cristaldo Nancy, MD^{38*}, Guilherme Fleury Perini^{39*}, Luis E Malpica Castillo, MD⁴⁰, Eduardo Sotomayor, MD⁴¹ and Jorge J. Castillo, MD^{42,43}*

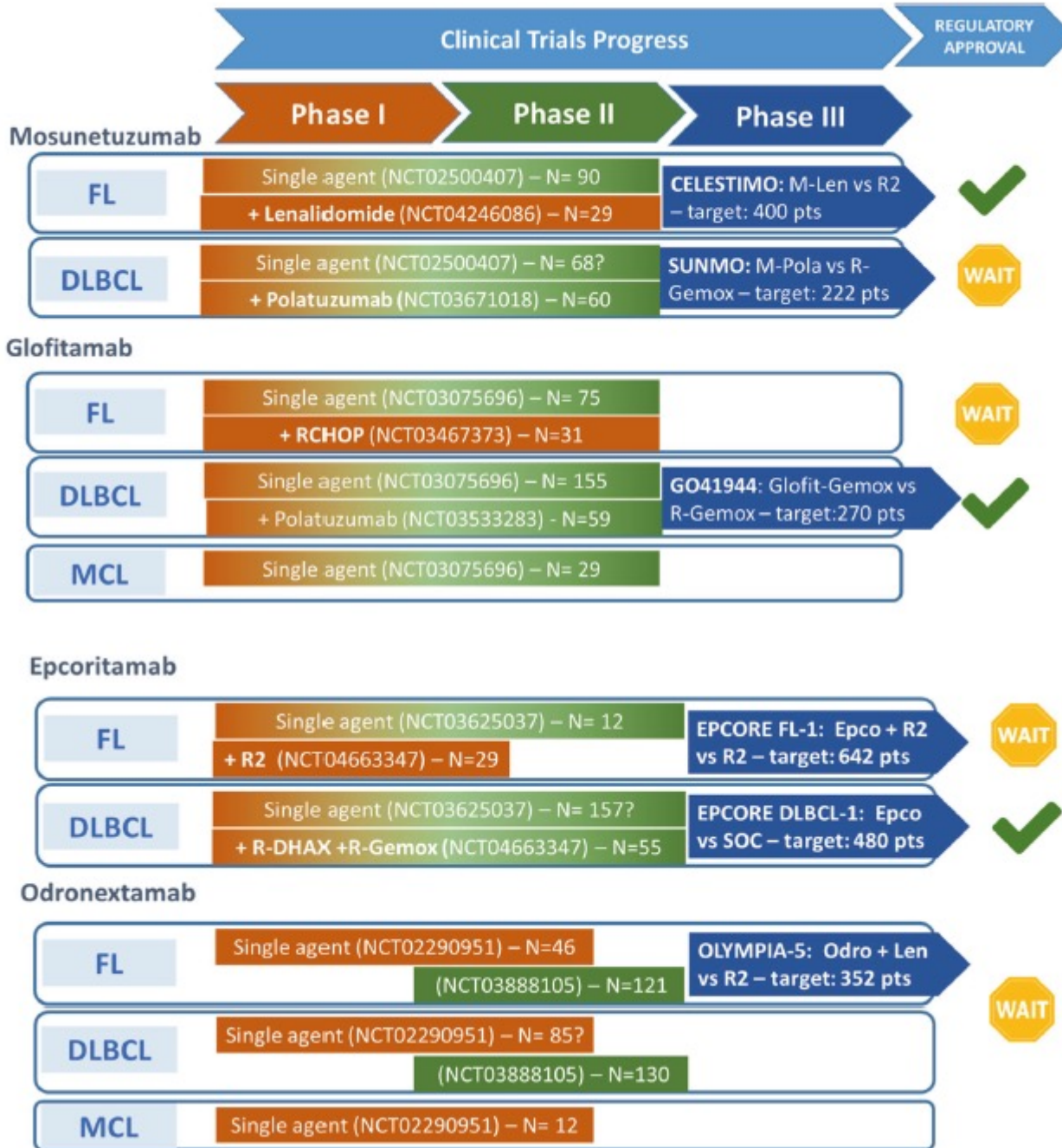


Overview of CD3xCD20 antibodies



Name of bispecific	Epcoritamab ¹	Glofitamab ^{2,3}	Mosunetuzumab ^{4,5}	Odronextamab ⁶	Plamotamab ⁷	IGM-2323 ⁸
Bispecific format	DuoBody IgG1	Fab-Fc x Fab-Fab-Fc Knob-into-hole (HC) XmAb (LC-HC)	Knob-into-hole (HC) IgG1	FcΔAdp IgG4	XmAb Fab-Fc x scFv-Fc	Proprietary IgM platform
CD3 Ab clone	huCACAO (SP34-der.) (CD3ε)	(SP34-der.) (CD3ε)	UCHT1v9 (CD3δε)	REG1250 (CD3δε)	α-CD3_H1.30 (SP34-der.) (CD3ε)	Not reported
CD20 Ab clone	7D8 (OFA epitope)	Obinutuzumab (Ritux epitope)	2H7 (Ritux epitope)	3B9-10 (OFA epitope)	C2B8_H1_L1 (Rituximab > Ritux epitope)	Not reported
Inert format	L234F,L235E,D265A (No FcγR,C1q binding)	IgG1-P329G-LALA (No FcγR binding)	N297G (No FcγR binding)	Modified IgG4 (No FcγRIII binding)	G236R, L328R (No FcγR binding)	IgM + modified J chain (10 CD-20 and 2 CD-3 binding domains)
Publications	Engelberts, et al. 2020	Bacac, et al. 2016 Bacac, et al. 2018	Sun, et al. 2015 Ferl, et al. 2018	Smith, et al. 2015	Patel, et al. ASH 2019 (abstract 4079)	Baliga, et al. ASH 2019 (abstract 1574)

1. Engelberts PJ, et al. *EBioMedicine* 2020; 52:10262; 2. Bacac M, et al. *Clin Cancer Res* 2016; 13:3286–97; 3. Bacac M, et al. *Clin Cancer Res* 2018; 19:4785–4797; 4. Sun LL, et al. *Sci Transl Med* 2015; 287:287ra70; 5. Ferl GZ, et al. *Clin Transl Sci* 2018; 3:296–304; 6. Smith EJ, et al. *Sci Rep* 2015; 5:17943; 7. Patel, et al. ASH 2019; Abstract 4079; 8. Baliga, et al. ASH 2019; Abstract 1574.



No tenemos estudios comparativos
Entre BsAs Monodroga x Combinado

Las aprobaciones regulatorias son
Diferentes:
Combinado: 2a línea
Monodroga: 3a línea

Mosunetuzumab Monotherapy Continues to Demonstrate Durable Responses in Patients with Relapsed and/or Refractory Follicular Lymphoma after ≥ 2 Prior Therapies: 3-Year Follow-Up from a Pivotal Phase II Study

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¹Lymphoma Program, Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA, USA; ²BC Cancer Centre for Lymphoid Cancer and The University of British Columbia, Vancouver, BC, Canada; ³Siteman Cancer Center, Washington University School of Medicine, St. Louis, MO, USA; ⁴Rutgers Cancer Institute of New Jersey, New Brunswick, NJ, USA; ⁵Jewish General Hospital, Montreal, QC, Canada; ⁶Royal Adelaide Hospital, Adelaide, Australia; ⁷Princess Margaret Cancer Centre, Toronto, ON, Canada; ⁸Fred Hutchinson Cancer Research Center and University of Washington, Seattle, WA, USA; ⁹Linear Clinical Research, Sir Charles Gairdner Hospital, Nedlands, Australia and The University of Western Australia, Perth, Australia; ¹⁰Universitat Heidelberg, Heidelberg, Germany; ¹¹St Vincent's Hospital and Royal North Shore Hospital, Sydney, Australia; ¹²St Vincent's Hospital, University of Melbourne, Melbourne, Australia; ¹³MD Anderson Cancer Center, Houston, TX, USA; ¹⁴Genentech, Inc., South San Francisco, CA, USA; ¹⁵City of Hope National Medical Center, Duarte, CA, USA

Study design

Pivotal, single-arm, Phase II expansion study in patients with R/R FL and ≥ 2 prior therapies (NCT02500407)

Key inclusion criteria

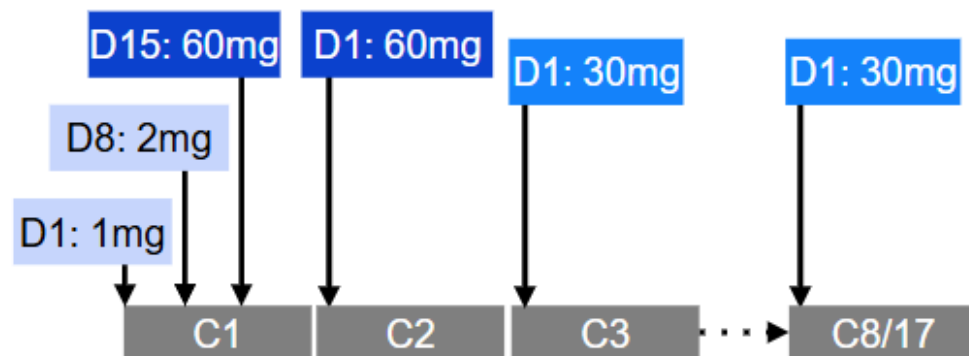
- FL Grade 1–3a
- ECOG PS 0–1
- ≥ 2 prior therapies including an anti-CD20 antibody and an alkylator

Data analysis

- Study met its primary endpoint: 60% CR rate versus 14% historic control ($p < 0.0001$)^{1,2}
- Updated efficacy and safety analysis with a median follow-up of 37.4 months

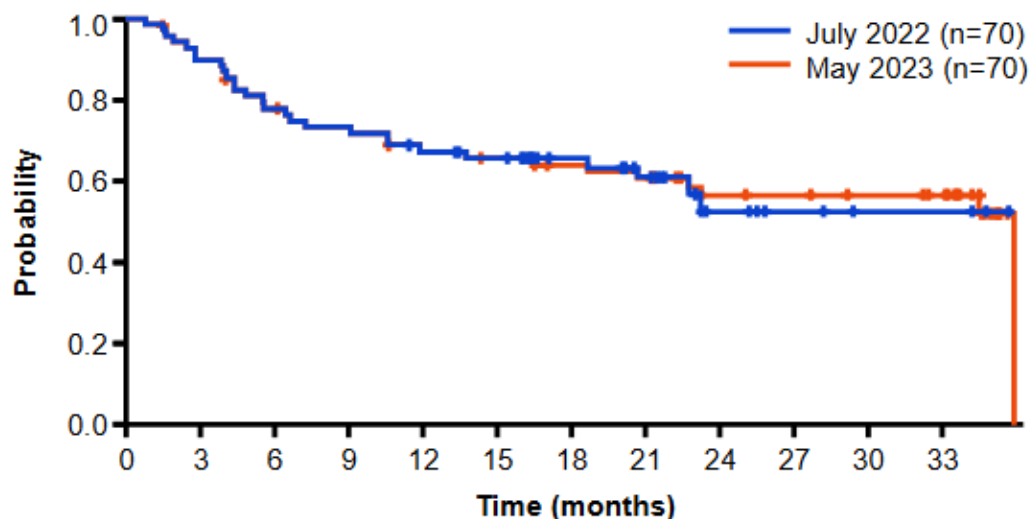
Mosunetuzumab administration

- IV mosunetuzumab administered in 21-day cycles with step-up dosing in C1
- Fixed-duration treatment: 8 cycles if CR after C8; 17 cycles if PR/SD after C8
- Retreatment with mosunetuzumab permitted at relapse for patients who achieved CR
- No mandatory hospitalization



Durability of responses

DOR (July 2022 vs May 2023 data cut-off)

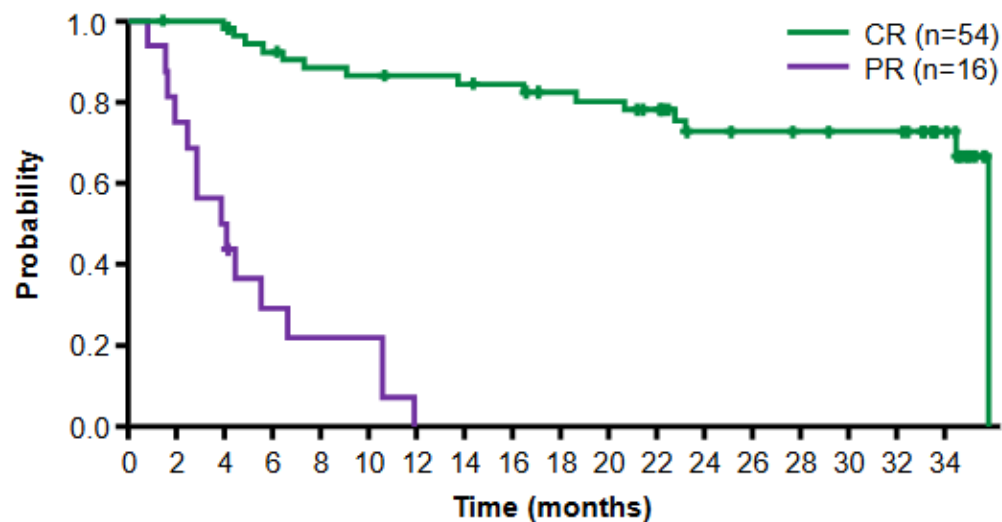


Patients at risk	
July 2022	70 62 52 48 42 38 30 25 9 5 3 3
May 2023	70 62 52 48 43 41 38 36 26 25 23 21

n=70

Median DOR, months (95% CI)*	35.9 (20.7–NE)
30-month DOR rate, % (95% CI)†	56.6% (44.2–68.9)

DOR for CR vs PR (May 2023 data cut-off)



Patients at risk	
CR	54 53 52 48 45 44 43 42 41 38 37 34 26 25 24 23 15
PR	16 12 8 4 3 3 NE NE NE NE NE NE NE NE NE NE

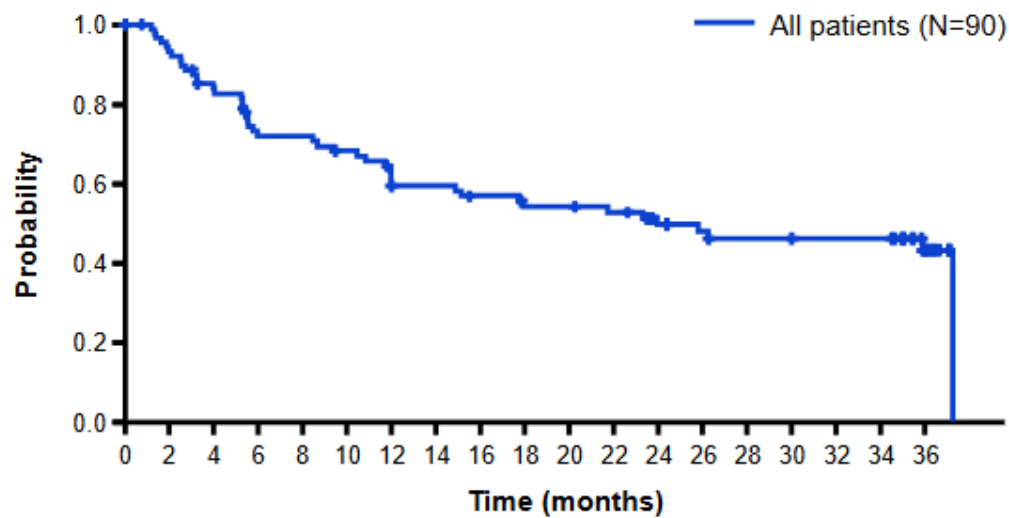
Median DOR in patients with CR, months (95% CI); n=54*	35.9 (NE–NE)
Median DOR in patients with PR, months (95% CI); n=16*	4.0 (2.5–6.7)

72.7% (95% CI: 60.8–86.8) of patients with a CR are estimated to remain alive and progression-free 30 months after their first response

*Responders per INV assessment. †36-month DOR data are not available as this analysis was conducted from the first response assessment, therefore the landmark analysis is shorter for the duration outputs.

PFS and OS; median follow-up >36 months

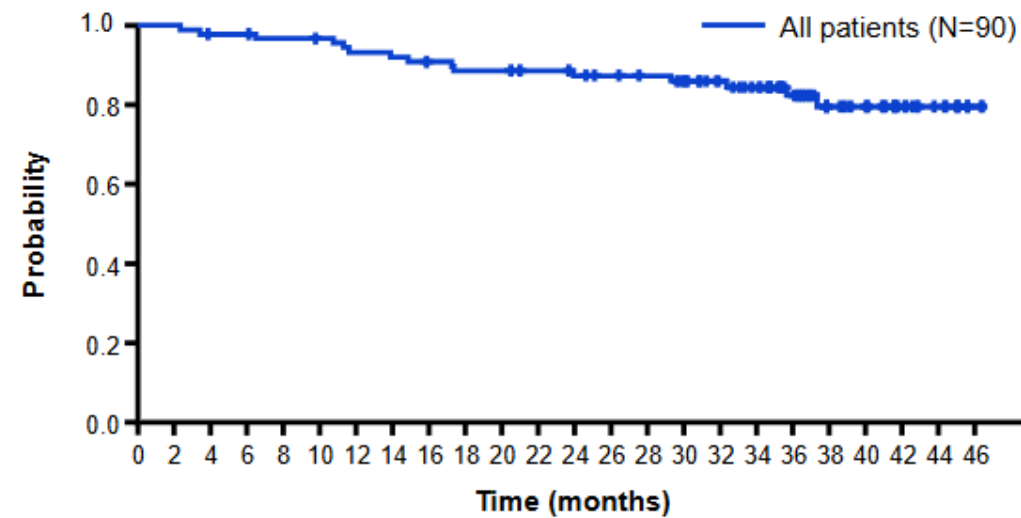
PFS



Patients at risk 90 81 72 60 59 55 47 46 43 40 40 38 30 27 25 25 24 24 13

N=90	
Median PFS, months (95% CI)	24.0 (12.0–NE)
36-month PFS, months (95% CI)	43.2% (31.3–55.2)

OS



Patients at risk 90 89 87 86 85 84 81 80 78 76 76 74 72 70 68 62 56 51 39 26 21 14 8 1

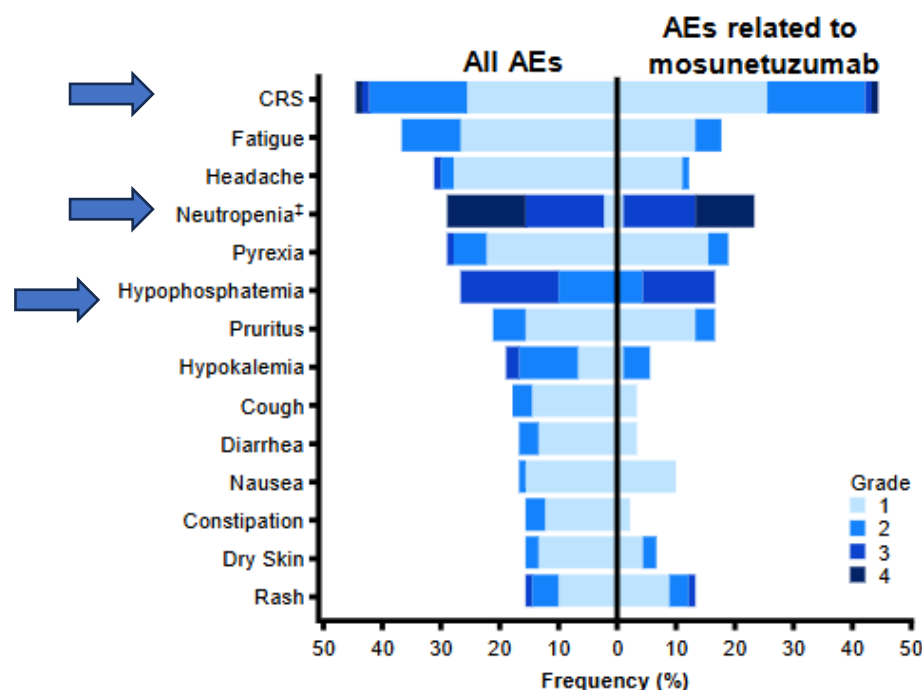
N=90	
Median OS, months (95% CI)	NR (NE–NE)
36-month OS, months (95% CI)	82.4% (73.8–91.0)

Robust and stable progression-free and overall survival rates at 3 years

Safety profile

Adverse events (AEs), n	N=90
AE	90 (100%)
Mosunetuzumab-related	83 (92%)
Grade 3/4 AE	63 (70%)
Mosunetuzumab-related	46 (51%)
Serious AE	42 (47%)
Mosunetuzumab-related	30 (33%)
Grade 5 (fatal) AE	2 (2%)*
Mosunetuzumab-related	0
AE leading to treatment discontinuation	4 (4%) [†]
Mosunetuzumab-related	2 (2%)

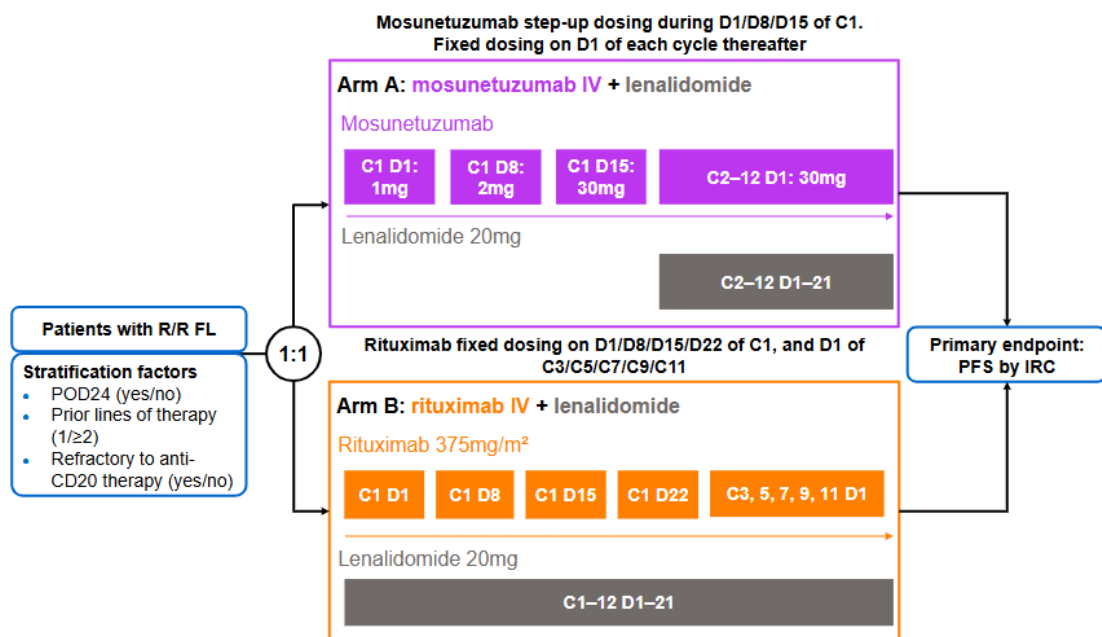
AEs (≥15%) by grade and relationship with mosunetuzumab



**No new AEs were reported since the previous data cut-off[§];
incidence of AEs and serious AEs remains unchanged with this extended follow-up**

*Malignant neoplasm progression (n=1, onset study D94) and unexplained death (n=1, onset study D60). [†]Mosunetuzumab related: CRS (n=2, onset study D15 and D22 [both recovered]); mosunetuzumab unrelated: Epstein-Barr viremia (n=1, onset study D11, recovered) and Hodgkin's disease (n=1, onset study D193, not recovered). [‡]Preferred terms neutropenia and neutrophil count decreased are combined. [§]One non-serious, unrelated AE was reported outside of the AE-reporting window and was subsequently inactivated.

Celestimo Trial (ASH 2025)



C, cycle; D, Day; FL, follicular lymphoma; IRC, independent review committee; IV, intravenous; PFS, progression-free survival; POD24, progression of disease within 24 months of first-line chemotherapy; R/R, relapsed/refractory

Table 3. Efficacy overview.

n (%)	2L+ FL US cohort (n=54)
ORR	52 (96.3)
CR	47 (87.0)
PR	5 (9.3)
Stable disease	0
Progressive disease	2 (3.7)

Celestimo Trial (ASH 2025)

Table 2. Baseline characteristics.

n (%), unless otherwise stated		2L+ FL US cohort (n=54)
Age, years	Median (range)	62.0 (37–82)
Sex	Male	32 (59.3)
Race	Asian	3 (5.6)
	Black or African American	2 (3.7)
	White	47 (87.0)
	Multiple*	1 (1.9)
	Unknown	1 (1.9)
Ethnicity	Hispanic or Latino	12 (22.2)
	Not Hispanic or Latino	42 (77.8)
ECOG PS	0	40 (74.1)
	1	13 (24.1)
	2	1 (1.9)
Ann Arbor stage	I/II	9 (16.7)
	III/IV	45 (83.3)
FLIPI score	0/1	n=52 [†] 13 (25.0)
	2	18 (34.6)
	3	17 (32.7)
	4	3 (5.8)
	5	1 (1.9)
FL grade	1/2	n=47 [†] 28 (59.6)
	3a	19 (40.4)
POD24	Yes	16 (29.6)
Number of prior lines of therapy	1	30 (55.6)
	≥2	24 (44.4)
Refractory to prior CD20 therapy	Yes	n=48 [†] 19 (39.6)
Relapsed after prior CD20 therapy	Yes	n=48 [†] 17 (35.4)
Double refractory	Yes	n=53 [†] 9 (17.0)

Table 4. Safety overview.

n (%)	2L+ FL US cohort (n=54)
Any grade AE	54 (100)
Mosunetuzumab related	48 (88.9)
Lenalidomide related	50 (92.6)
AE leading to discontinuation of mosunetuzumab	6 (11.1)
AE leading to discontinuation of lenalidomide	10 (18.5)
Grade 3/4 AE	31 (57.4)
Grade 5*	1 (1.9)
Serious AE	15 (27.8)
Mosunetuzumab related	9 (16.7)
Lenalidomide related	4 (7.4)
CRS by ASTCT grading	15 (27.8)
Grade 1	12 (22.2)
Grade 2	2 (3.7)
Grade 3	1 (1.9)
Infections	31 (57.4)
Grade 1	2 (3.7)
Grade 2	24 (44.4)
Grade 3	3 (5.6)
Grade 4	1 (1.9)
Grade 5	1 (1.9)
Neutropenia/neutrophil count decreased	22 (40.7)
Grade 3/4	18 (33.3)
Febrile neutropenia (Grade 3)	2 (3.7)

Epcoritamab Induces Deep Responses in Relapsed or Refractory (R/R) Follicular Lymphoma (FL): Safety and Pooled Efficacy Data From EPCORE NHL-1 Pivotal and Cycle (C) 1 Optimization (OPT) FL Cohorts

Umberto Vitolo, MD,¹ Pieterella J. Lugtenburg, MD, PhD,² Martine E.D. Chamuleau, MD, PhD,³ Juan-Manuel Sancho, MD, PhD,⁴ Kim M. Linton, MBChB, PhD,⁵ Kristina Sonnevi, MD, PhD,⁶ David John Lewis, MD,⁷ Miguel A. Canales, MD, PhD,⁸ Julie M. Vose, MD, MBA,⁹ Julio C. Chavez, MD,¹⁰ Herve Ghesquieres, MD, PhD,¹¹ Catherine Thieblemont, MD, PhD,¹² Martin Hutchings, MD, PhD,¹³ Anna Sureda, MD, PhD,¹⁴ Tara Cochrane, MBBS, FRCPA, FRACP,¹⁵ Michael Roost Clausen, MD, PhD,¹⁶ Sirpa Leppä, MD, PhD,¹⁷ Emmanuel Gyan, MD, PhD,¹⁸ Elena Favaro, MD, PhD,¹⁹ Daniela Hoehn, MD, PhD,²⁰ Işıl Altıntaş, PhD,²¹ Christopher Morehouse, MS,²⁰ Zhu Li, MS, PhD,²⁰ Rebekah Conlon, BN,²² Wojciech Jurczak, MD, PhD²³

¹Candiolo Cancer Institute, FPO-IRCCS, Candiolo (Turin), Italy; ²On behalf of the Lunenburg Lymphoma Phase I/II Consortium-HOVON/LLPC, Erasmus MC Cancer Institute, University Medical Center, Department of Hematology, Rotterdam, Netherlands; ³On behalf of the Lunenburg Lymphoma Phase I/II Consortium-HOVON/LLPC, Amsterdam UMC, VU University Medical Center, Amsterdam, Netherlands; ⁴Catalan Institute of Oncology (ICO), ICO Hospital Germans Trias i Pujol, Badalona, Spain; ⁵The Christie NHS Foundation Trust, Manchester Cancer Research Centre, and Division of Cancer Sciences, University of Manchester, Manchester, UK; ⁶Karolinska Institutet, Stockholm, Sweden; ⁷University Hospitals Plymouth NHS Trust, Derriford Hospital, Plymouth, UK; ⁸Clínica Universidad de Navarra, Pamplona, Spain; ⁹University of Nebraska Medical Center, Omaha, NE, USA; ¹⁰Moffitt Cancer Center, Tampa, FL, USA; ¹¹Hospices Civils de Lyon, Centre Hospitalier Lyon Sud, Pierre-Bénite, France; ¹²Assistance Publique & Hôpitaux de Paris (APHP), Hôpital Saint-Louis, Hémato-oncologie, Université de Paris, Paris, France; ¹³Rigshospitalet and University of Copenhagen, Copenhagen, Denmark; ¹⁴Clinical Hematology Department, Institut Català d'Oncologia – L'Hospitalet, IDIBELL, Universitat de Barcelona, Barcelona, Spain; ¹⁵Gold Coast University Hospital, Southport, Queensland, Australia; ¹⁶Vejle Hospital, Vejle, Denmark; ¹⁷University of Helsinki and Helsinki University Hospital Comprehensive Cancer Center, Helsinki, Finland; ¹⁸Service d'Hématologie et Thérapie Cellulaire, Centre Hospitalier Universitaire de Tours, CIC INSERM U1415, Tours, France; ¹⁹Genmab, Copenhagen, Denmark; ²⁰Genmab, Plainsboro, NJ, USA; ²¹Genmab, Utrecht, Netherlands; ²²AbbVie, North Chicago, IL, USA; ²³MSC National Research Institute of Oncology, Kraków, Poland

Baseline Characteristics Consistent Across Cohorts

Demographics	Pivotal Cohort N=128	C1 OPT N=86
Median age, y (range)	65 (39–84)	63.5 (33–90)
Male, n (%)	79 (62)	49 (57)
Ann Arbor stage, n (%) ^a		
III–IV	109 (85)	79 (92)
FLIPI, n (%) ^b		
3–5	78 (61)	44 (51)

Treatment History	Pivotal Cohort N=128	C1 OPT N=86
Median number of prior lines of therapy (range)	3 (2–9)	2 (2–9)
≥3 prior lines, n (%)	81 (63)	41 (48)
≥4 prior lines, n (%)	40 (31)	17 (20)
POD24 (any 1L), ^c n (%)	67 (52)	42 (49)
Double refractory, ^{d,e} n (%)	90 (70)	54 (63)
Primary refractory, ^d n (%)	69 (54)	38 (44)
Refractory ^d to last prior systemic therapy, n (%)	88 (69)	49 (57)

- Both cohorts included patients from a high-risk R/R FL population with a high unmet need
- Prior treatments included alkylating agents (98%), anthracyclines (76%), bendamustine (60%), nucleotides (38%), lenalidomide (35%), topoisomerase inhibitors (33%), autologous stem cell transplant (22%), PI3K inhibitors (13%), and CAR T-cell therapy (7%)

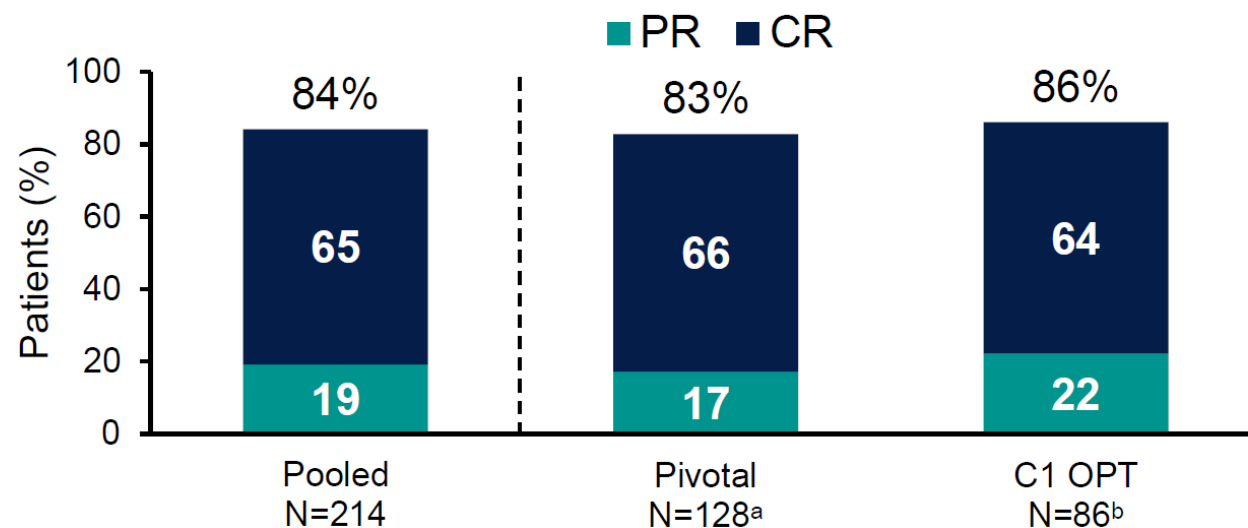
1L, first-line. ^aAnn Arbor stage was I–II in 19 patients in the pivotal cohort and 7 patients in C1 OPT. ^bFLIPI was 0–2 in 48 patients in the pivotal cohort (not available in 2 patients) and 42 patients in C1 OPT. FLIPI was prior to first dose on study. ^cProgression within 2 y of initiating any 1L therapy. ^dRefractory: No response or relapse within 6 mo after therapy. ^eDouble refractory: Refractory to both anti-CD20 and an alkylating agent.

Treatment Exposure and Follow-Up

	Pivotal Cohort N=128	C1 OPT N=86
Median follow-up, mo (range)	17.4 (0.2+ to 30.1)	5.7 (0.4–11.8)
Epcoritamab treatment exposure		
SUD 2, n (%)	127 (99)	85 (99)
SUD 3, n (%)	NA	82 (95)
First full dose, n (%)	126 (98)	82 (95)
Median number of treatment cycles initiated (range)	8 (1–33)	5 (1–12)
Median duration of treatment, mo (range)	8.3 (0.03–30)	3.8 (0.3–11.8)
Ongoing treatment, n (%)	47 (37)	64 (74)
Discontinued treatment, n (%)		
PD	44 (34)	17 (20)
AE	24 (19)	3 (3) ^a
Other ^b	13 (10)	2 (2)

AE, adverse event; NA, not applicable; PD, progressive disease. ^aAEs included bronchopulmonary aspergillosis (grade 2; n=1) and pneumonitis (grade 2; n=2); all were considered related to treatment. ^bReasons included transplant (n=4), withdrawal (n=3), and other reasons (n=6) in the pivotal cohort. Reasons included noncompliance (n=1) and investigator decision (n=1) in the C1 OPT cohort.

High Rates of Complete Response and MRD Negativity



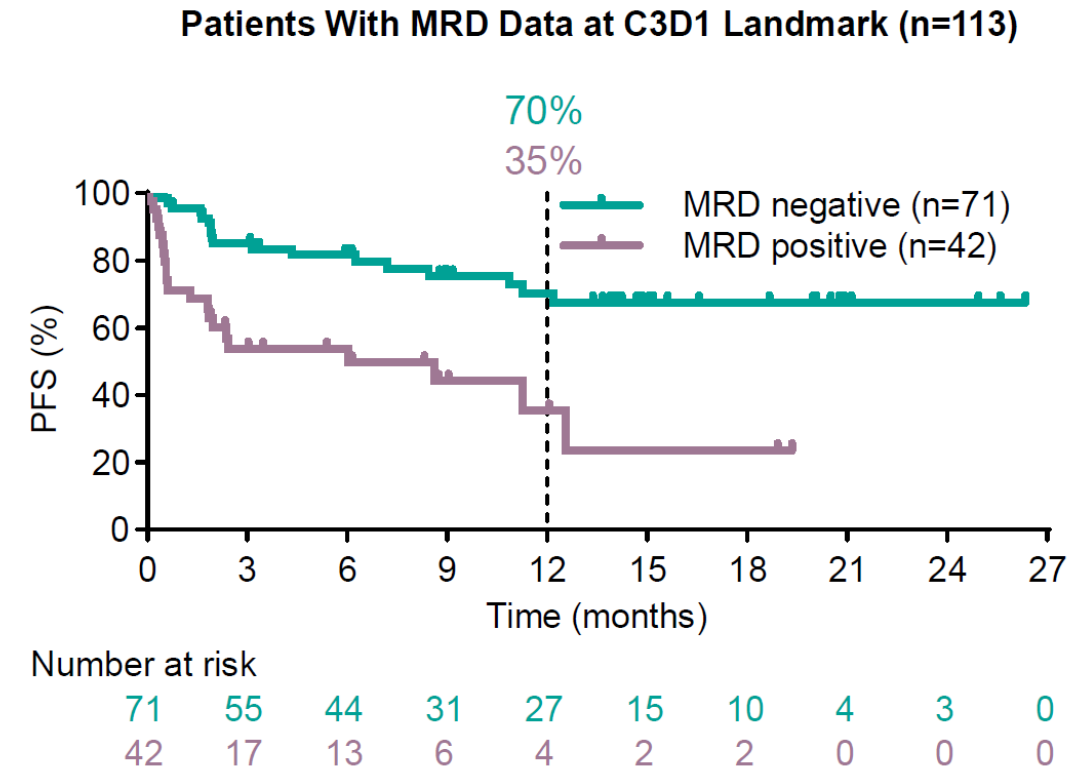
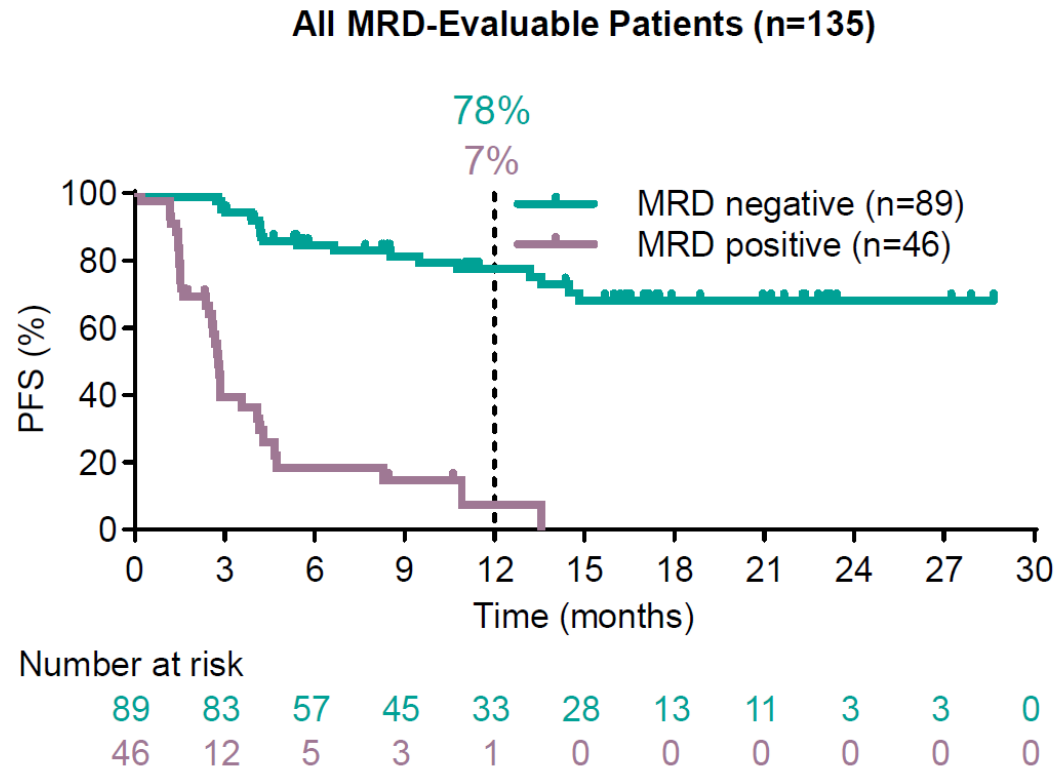
MRD-Negativity Rate	n (%)
Pooled (n=135)	89 (66)
Pivotal (n=91)	61 (67)
C1 OPT (n=44)	28 (64)

Based on MRD-evaluable population per clonoSEQ[®] PBMC assay with 10⁻⁶ cutoff.

- No impact on time to response in C1 OPT
 - Median time to response was 1.4 mo in both cohorts^c
 - Median time to complete response was 1.5 mo in both cohorts^d

CR was complete metabolic response (ie, PET negativity). CR, complete response; PBMC, peripheral blood mononuclear cell; PR, partial response. ^aThree patients (2%) were not evaluable. ^bFive patients (6%) were not evaluable. ^cRange: 1.2–4.4 in C1 OPT, 1.0–3.0 in pivotal. ^dRange: 1.2–4.7 in C1 OPT, 1.2–11.1 in pivotal.

Overall and C3D1 MRD Negativity Associated With Favorable PFS



Median follow-up: 17.4 mo for pivotal cohort and 5.7 mo for C1 OPT cohort. PFS assessed by investigator. MRD was assessed in peripheral blood using the clonoSEQ® next-generation sequencing assay with 10^{-6} cutoff. MRD negative was defined as having MRD negativity at any time point (left graph) or at any time point up to C3D1 (right graph).

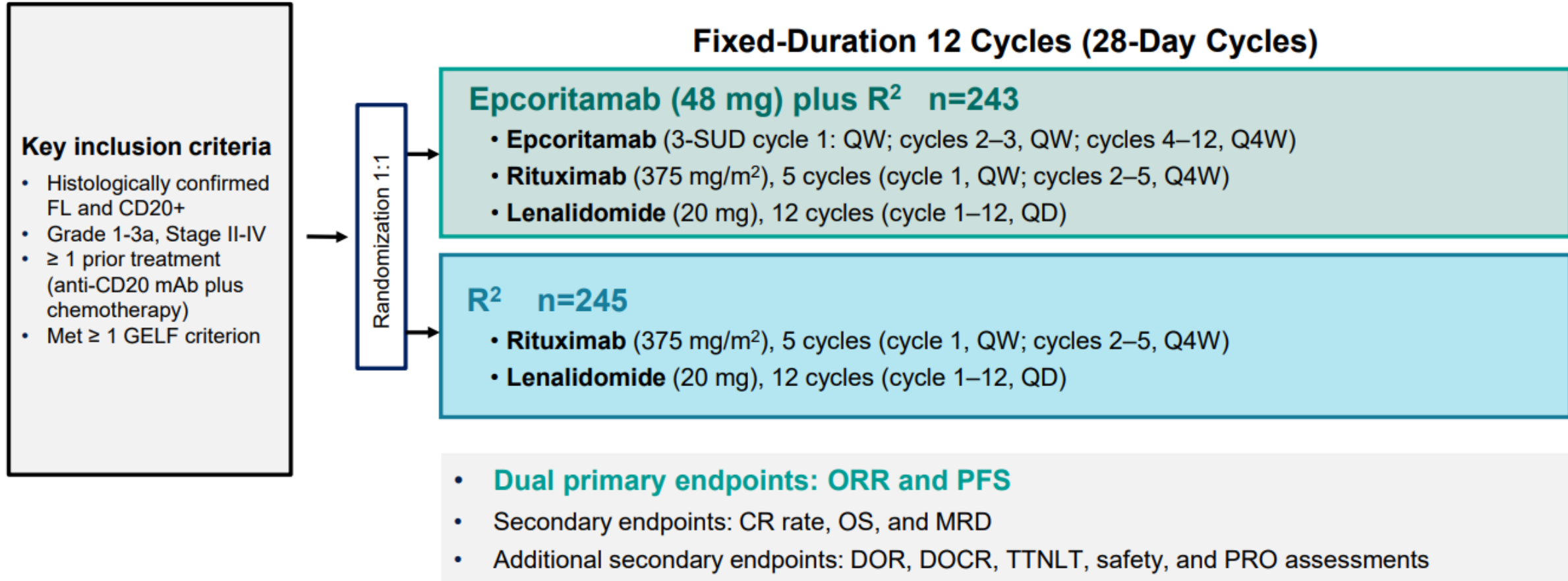
Primary Phase 3 Results From the EPCORE FL-1 Trial of Epcoritamab With Rituximab and Lenalidomide (R²) Versus R² for Relapsed or Refractory Follicular Lymphoma

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EPCORE FL-1: Global Randomized Phase 3 Study



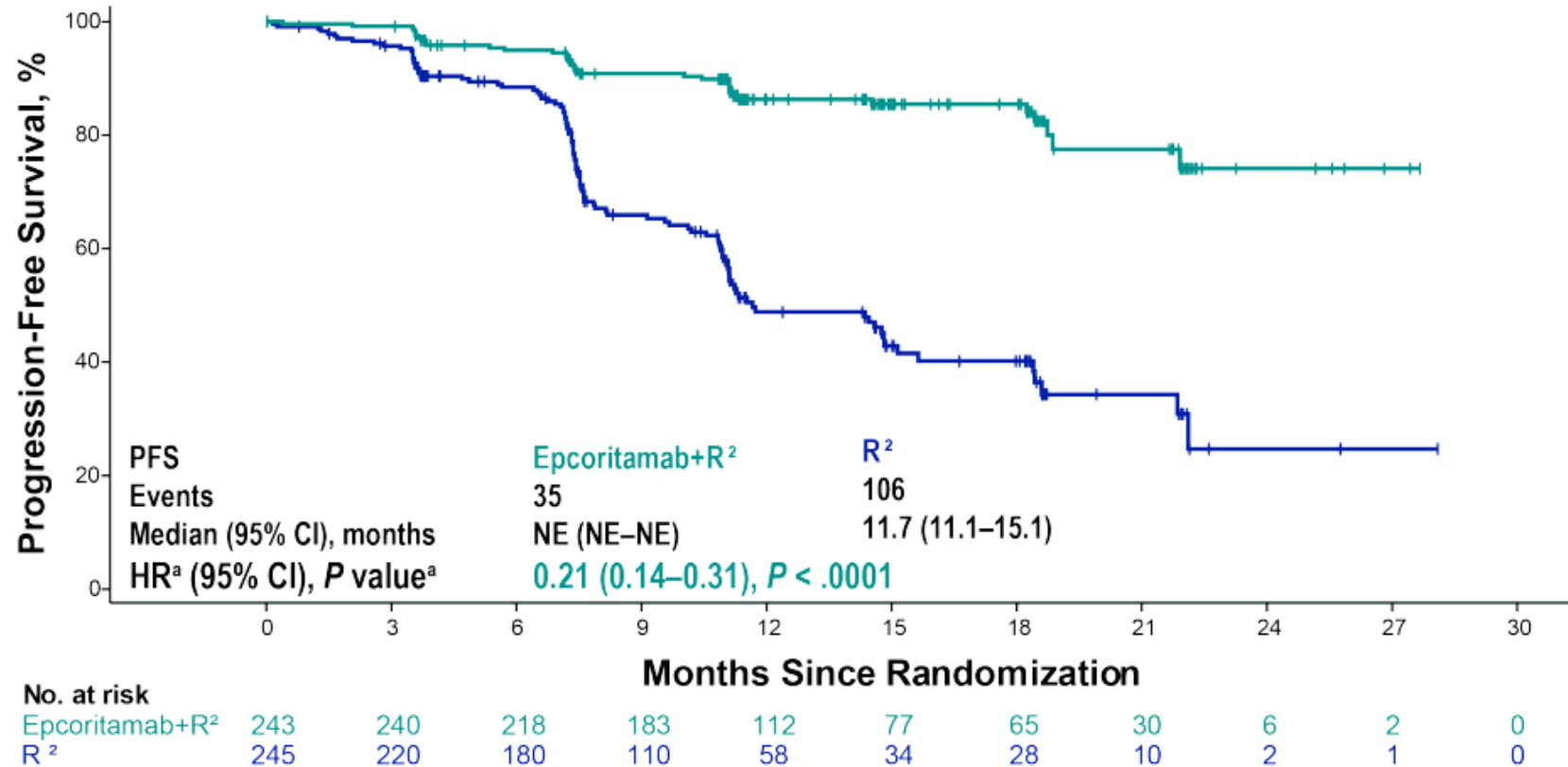
Median follow-up: 14.8 months

Enrollment period: October 2022 - January 2025

Baseline Demographics Were Balanced

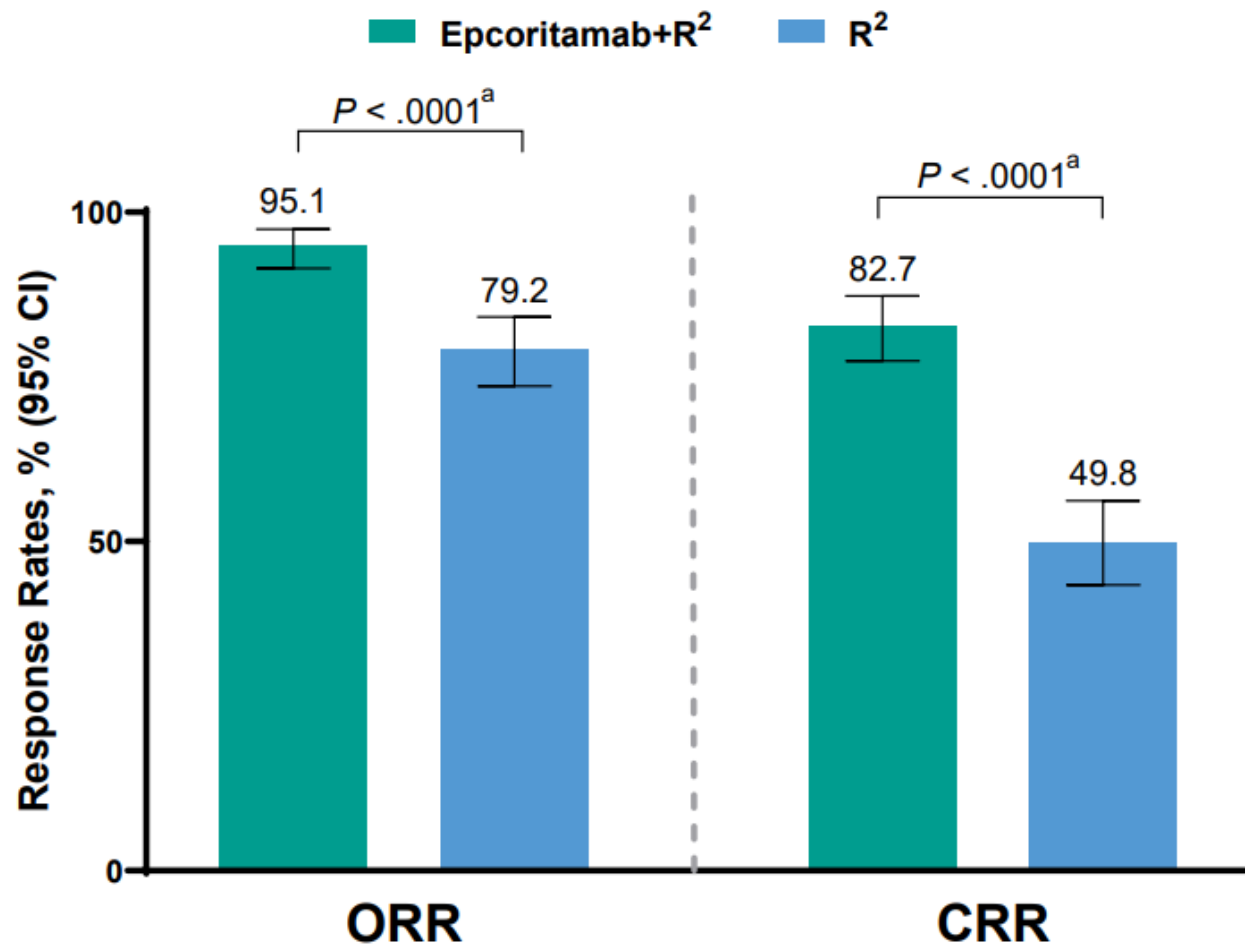
Characteristic	Epcoritamab+R ² (N = 243)	R ² (N = 245)	Overall (N = 488)
Median age, y (range)	60 (30, 84)	63 (24, 89)	61 (24, 89)
ECOG, n (%)			
0	166 (68)	170 (69)	336 (69)
1-2	77 (32)	75 (31)	152 (31)
Ann Arbor stage, n (%)			
II	37 (15)	44 (18)	81 (17)
III-IV	206 (85)	201 (82)	407 (83)
FLIPI score, n (%)			
0-1	63 (26)	56 (23)	119 (24)
2	79 (33)	76 (31)	155 (32)
3-5	100 (41)	113 (46)	213 (44)
Bulky disease (≥ 7 cm), n (%)	47 (19)	61 (25)	108 (22)
Number of prior lines of therapy, median (range)	1 (1, 7)	1 (1, 6)	1 (1, 7)
1, n (%)	145 (60)	141 (58)	286 (59)
Prior anti-CD20 antibody, n (%)	243 (100)	245 (100)	488 (100)
POD24, n (%)	106 (44)	93 (38)	199 (41)
Refractory to 1L therapy, n (%)	86 (35)	81 (33)	167 (34)
Double refractory	91 (37)	91 (37)	182 (37)

Superior PFS With 79% Risk Reduction



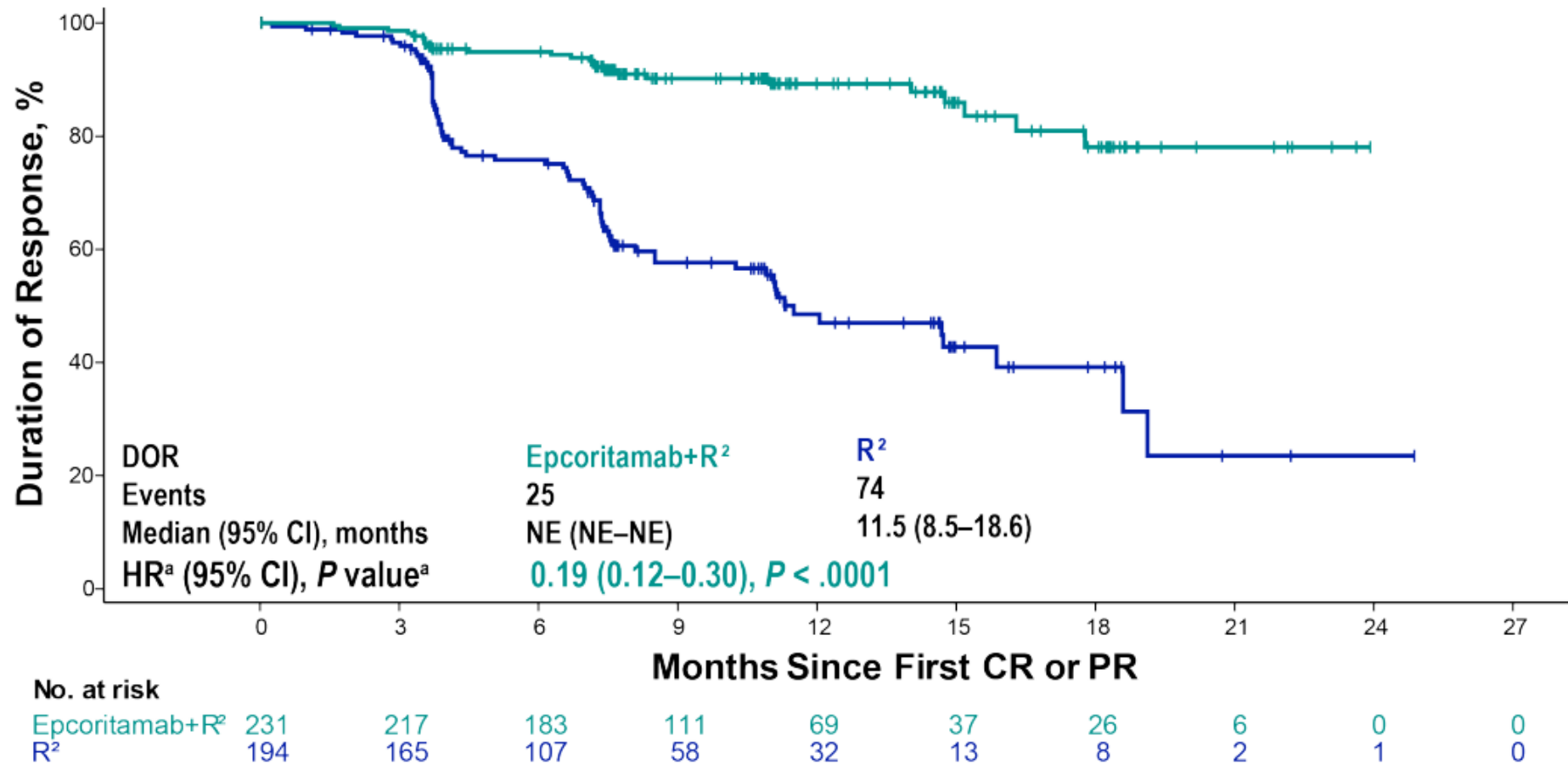
- Across pre-specified subgroups, epcoritamab+R² demonstrated favorable PFS in a broad R/R FL population

Higher Response Rates



	Epcoritamab+R ² (N = 243)	R ² (N = 245)
ORR	95%	79%
CRR	83%	50%
PR, n (%)	12%	29%
SD/PD, n (%)	3%	13%
NE, ^b n (%)	4 (2)	18 (7)

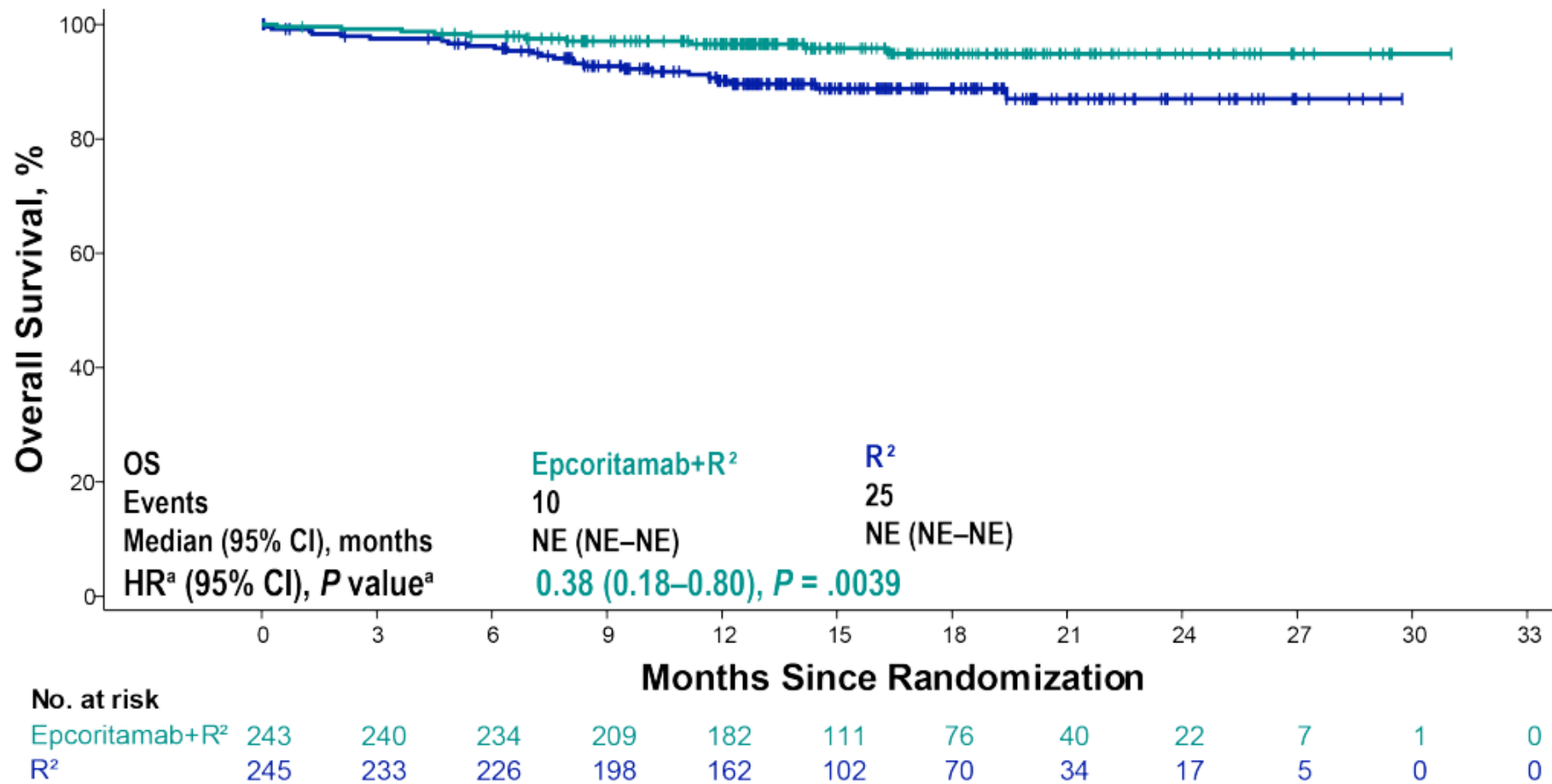
Deep and Durable Responses



Median follow-up for DOR: epcoritamab+R² (10.6m), R² (10.6m).

^aNominal P value is based on stratified log-rank test. Hazard ratio is estimated using stratified Cox proportional hazards model.

Positive Trend for OS With Epcoritamab+R²

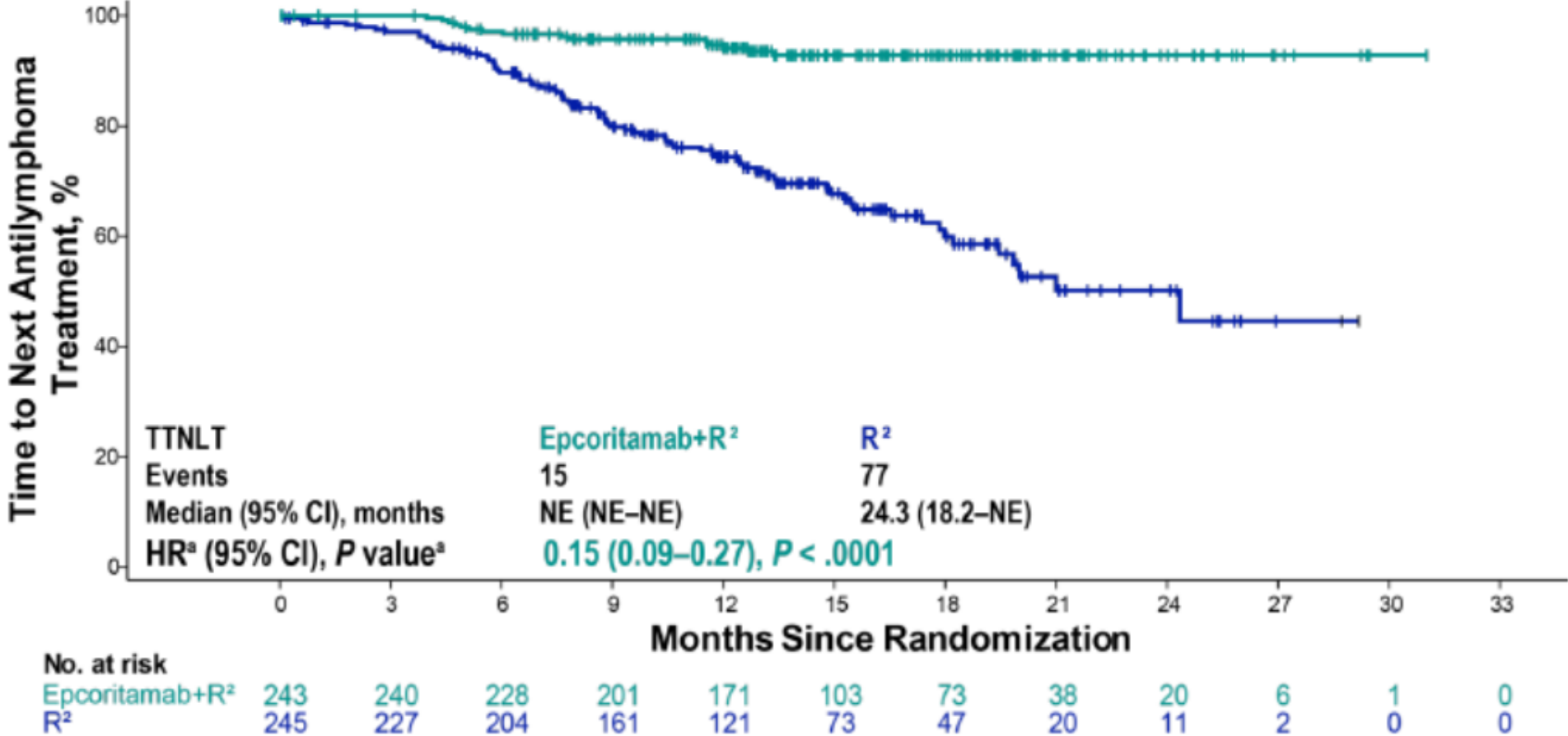


The 16-month estimate for OS was 95.8% with epcoritamab+R² and 88.8% with R²

Median follow-up for OS: epcoritamab+R² (14.8m), R² (14.6m).

^aP value is based on stratified log-rank test with 1-sided significance level of 0.000005. Hazard ratio is estimated using stratified Cox proportional hazards model.

Epcoritamab+R² Extended Time to Next Treatment



- At 16 months, 92.8% of patients treated with epcoritamab+R² remained free from new antilymphoma treatment compared with 64.9% of patients treated with R²

Median follow-up for TTNLT: epcoritamab+R² (14.6m), R² (14.1m). TTNLT results are for descriptive purposes only.
^aNominal P value is based on stratified log-rank test. Hazard ratio is estimated using stratified Cox proportional hazards model.

Manageable Safety, No New Signals

Adverse Event, n (%)	Epcoritamab+R ² (N = 243)		R ² (N = 238)	
	Any Grade	Grade ≥ 3	Any Grade	Grade ≥ 3
Any adverse event	242 (100)	219 (90)	235 (99)	161 (68)
Serious adverse event	135 (56)	-	69 (29)	-
Adverse event leading to treatment discontinuation	46 (19)	-	29 (12)	-
<i>Epcoritamab</i>	21 (9)	-	-	-
<i>Rituximab</i>	7 (3)	-	12 (5)	-
<i>Lenalidomide</i>	45 (19)	-	29 (12)	-
Adverse event of clinical interest > 20% ^{a,b}				
Infections ^c	188 (77)	81 (33)	125 (53)	37 (16)
Neutropenia	180 (74)	167 (69)	123 (52)	100 (42)
Cytokine release syndrome	85 (35)	-	1 (< 1)	-
Anemia	68 (28)	19 (8)	41 (17)	11 (5)
Thrombocytopenia	67 (28)	23 (9)	44 (18)	15 (6)
Pyrexia	58 (24)	1 (< 1)	33 (14)	3 (1)
Rash	58 (24)	19 (8)	53 (22)	9 (4)
COVID-19	54 (22)	7 (3)	32 (13)	4 (2)

- CRS was all low-grade and resolved
- Neutropenia and infections were manageable, few patients discontinued therapy due to these AEs
- Fatal adverse events were low; epcoritamab +R², 1.6%; R², 3.8%
- Median relative dose intensity ≥ 90% for epcor+R²
- Quality of Life (QOL) was preserved

^aNeutropenia, anemia, pyrexia, rash and COVID-19 are grouped terms comprising multiple clinically related Preferred Terms. ^bThis includes the AESI of CRS. ^cEvents were in the MedDRA system organ class "Infections and Infestations." No grade 5 infections were reported.

Conclusiones

- BsAs son terapias increíblemente eficaces en 3a línea como monodroga
 - Mosun terapia fija o Epcó continuo
 - Tolerables, incluso en pacientes en líneas avanzadas
 - Pocos datos a largo plazo, pero los datos de 3 años de Mosun son muy interesantes!
- La combinación con R2 trae los BsAs a 2a línea, y esto es genial
 - Los datos son impresionantes
 - Con epcó, una terapia finita mejora los costos también!
 - Pero hay un incremento significativo de la toxicidad
 - 33% de infecciones grado 3 es malo
 - Follow up es muy corto aún (<15 meses)

Conclusiones

- Sin embargo, estamos empezando a utilizar BsAs y es muy importante alguna experiencia con los efectos secundarios
 - CRS, neutropenia, hipogamma
- No mate a su paciente con Linfoma Folicular en líneas tempranas!
 - No es posible desmorir!
 - Tenemos muchas otras terapias disponibles
 - La expectativa de supervivencia en LF es >30 años

Current Epcoritamab Plus Rituximab and Lenalidomide Perceptions for Patients With Relapsed/Refractory Follicular Lymphoma

Authors: Emily Levine, MPH; Danielle Gentile, PhD; Scott Swain PhD, MPH¹; Robert N. Bone, PhD; Luke Jennings-Zhang, PharmD, BCPS; Yolaine Jeune-Smith, PhD; Bruce Feinberg, DO*

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Poster code: HSD88

Figure 1: Previous Familiarity with Epcoritamab

Question: How familiar are you with the bispecific CD20-CD3 T cell-engager therapy epcoritamab?

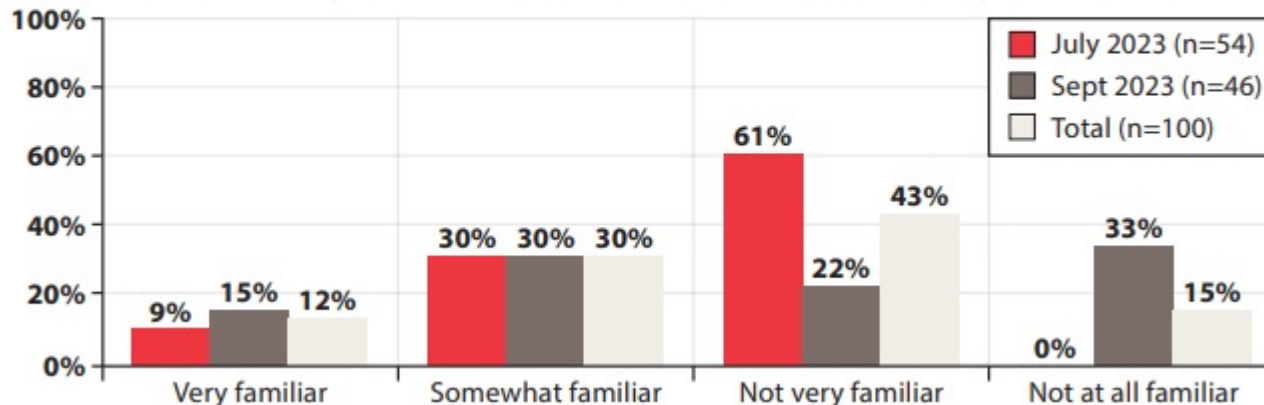
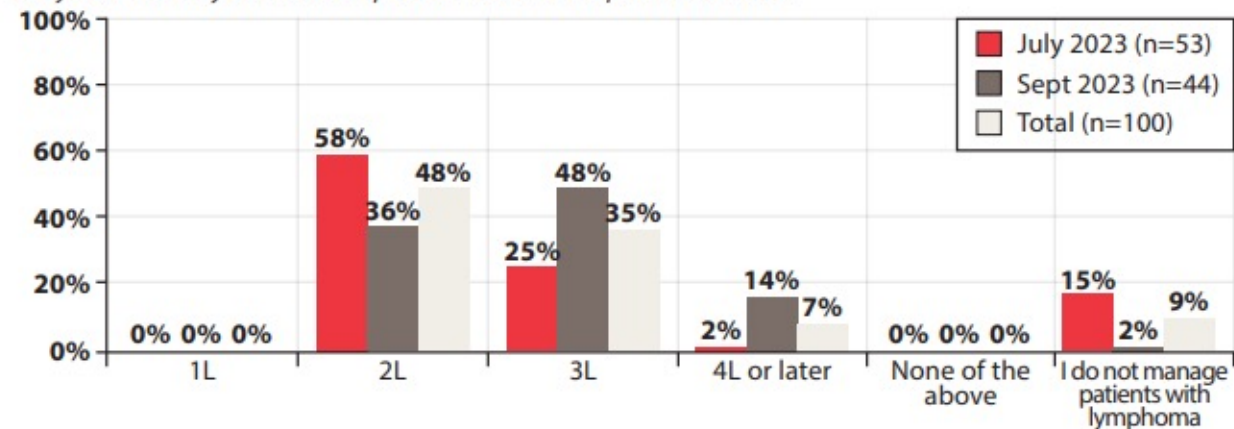


Figure 4: Treatment Line Consideration of Epcoritamab + R2 for R/R FL

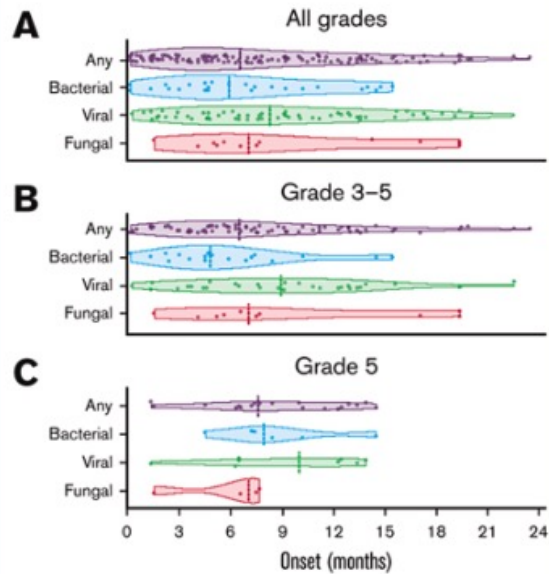
Question: After reviewing the EPCORE NHL-2 trial and assuming FDA approval, for which line therapy are you most likely to consider epcoritamab + R2 for patients with FL?



Infecciones con BsAs

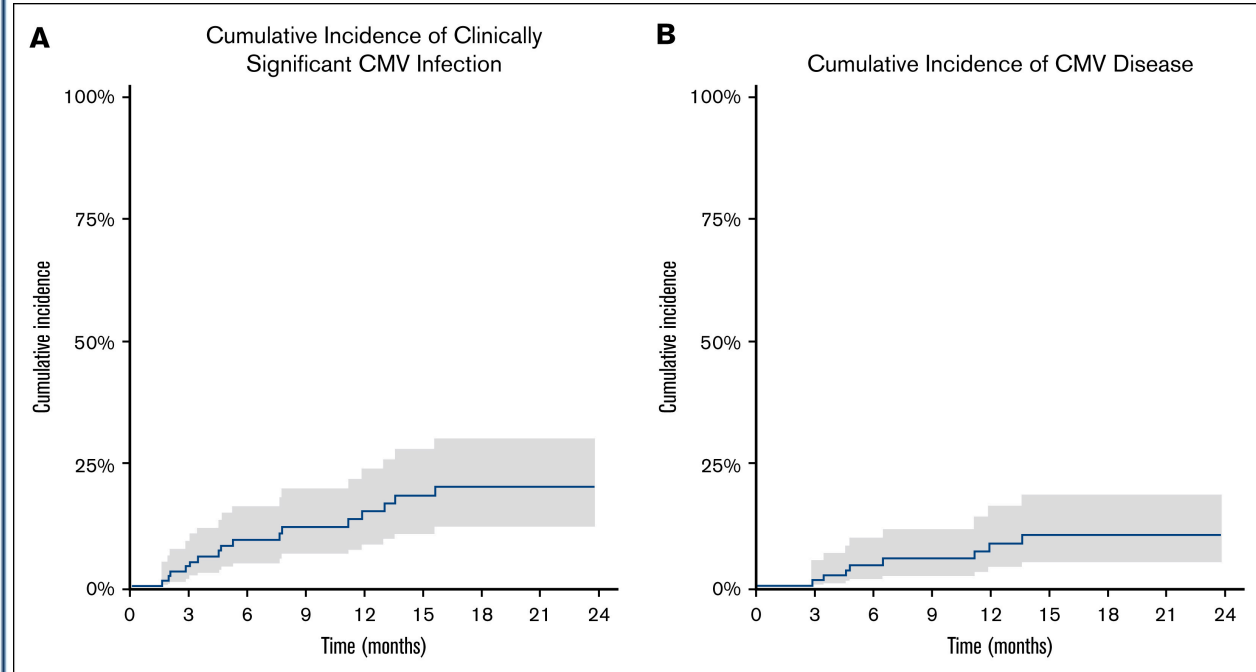
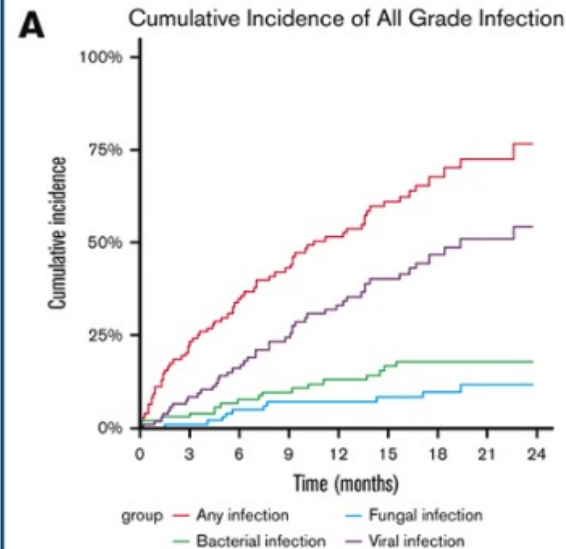
Infection Characteristics:

- Of all infections, 61.2% were grade ≥ 3 .
- The median time to infection was 6.6 months, with bacterial infections occurring earliest.
- Viral infections were most frequent, with SARS-CoV-2 being the leading cause.



Infection Incidence:

- Infections occurred in 62.4%, with 37.6% being grade ≥ 3 .
- Cumulative infection incidence reached 76.4% at 24 months.
- Neutropenia and hypogammaglobulinemia were associated with a higher risk of infection.



Un Cuento

- ¿Será la lena probar combin



ia en LF

fármaco para

SYMPHONY-1:

SYMPHONY-1 is an ongoing Ph 3 study (confirmatory study in Tazemetostat + R² vs. R² in 2L+ all-comers FL patients (mutant

Population	Patients with relapsed / refractory FL who have been systemic therapy, including patients who are rituximab	
Key Objectives	Phase 1b (safety run-in) Safety, pharmacokinetics, antitumor activity, RP3D	Phase 3 (efficacy) Primary: PFS as determined by IRC, respo Secondary: PFS by IRC, respo QOL, safety
Safety Run-in	Phase 3 Randomization (12 months)	
All-comers	MT/WT EZH2 enrichment based on Cobas® EZH2 mutation test	
Tazemetostat + rituximab + lenalidomide (N=40)	Tazemetostat + rituximab + lenalidomide (n=250, mPFS, 36 mo)	Placebo + rituximab + lenalidomide (n=250, mPFS, 25 mo)
	Stratification for randomized portion by EZH2 mutation status: treatment-sensitive vs refractory to prior rituximab-containing regimen, patients treated with 1 prior vs ≥2 prior systemic therapies	

Material exclusivo para treinamento



-1 Investigator,

information regarding tazemetostat in patients with follicular lymphoma in the ongoing study; **immediate discontinuation of tazemetostat/ placebo dosing following emerging** **logic secondary malignancies and immediate cessation of patient enrolment.**

-1 Investigator,

of an important safety update concerning tazemetostat in patients enrolled in the ongoing clinical study evaluating tazemetostat in combination with lenalidomide and rituximab in refractory follicular lymphoma.

n ad hoc review of emerging safety data by the Independent Data Monitoring Committee ented an immediate stop to study treatment and further patient enrolment as part of an (IM). As such please, with immediate effect, stop any patient tazemetostat/ placebo dosing

and patient enrollment in the EZH-302/SYMPHONY 1 study.

¿Hay otras combinaciones?

- Mithic-FL II

Multicenter Phase 2 Study Overview

Eligibility:

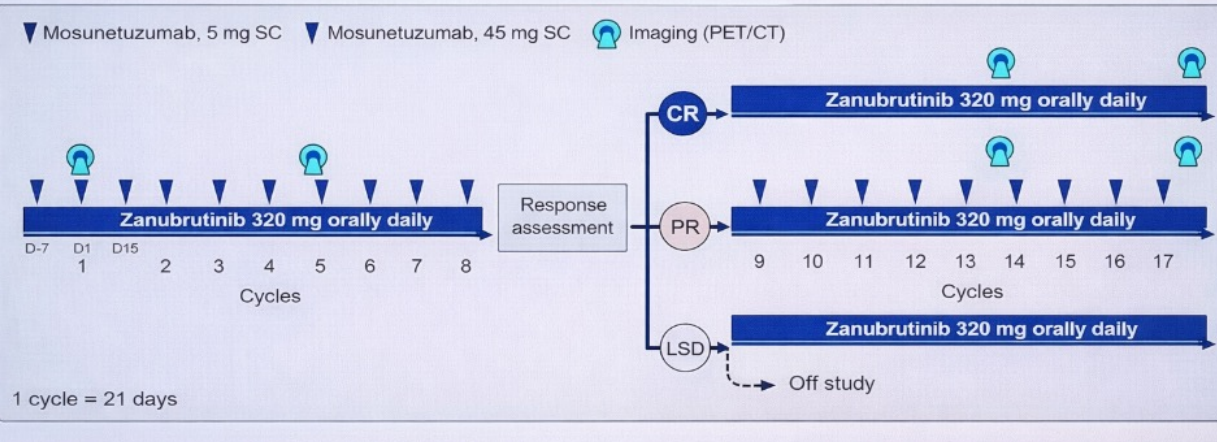
- ≥18 years; ECOG PS 0-2
- CD20+ previously untreated FL
- G1-3A, stage II-IV
- In need of therapy per GELF criteria

Endpoints:

- **Primary:** CR per Lugano
- **Secondary:** ORR, safety, PFS, DOR, TTNT, OS
- **Exploratory:** PD, ctDNA monitoring

Outpatient administration:

- Administration: Zanubrutinib PO; mosunetuzumab SC
- Prophylaxis: Dexamethasone, antihistamine H2 blocker, acetaminophen in C1 (and C2 if prior CRS)
- VZV and PJP prophylaxis and GCSF support per treating physician



At median follow-up of 6.5 months, overall response rate (ORR) was 92% and CR rate was 82%, with 10% of patients achieving a partial response (PR).

The predominant AEs were injection site reaction (67%), cytokine release syndrome (CRS) (61%), and dry skin (58%); all Grade 1/2.

My take en Combinaciones vs Monodroga

- Combinación:

- Pacientes jóvenes, en donde necesito una respuesta profunda y duradora
- Bajar la dosis/sacar Lena si neutropenia prolongada
- Este atento a infecciones, incluso reactivación de CMV
- Reemplazar Inmunoglobulina en algunos casos (\$\$\$)
- Pacientes frágiles en 2^a línea – Mejor con TafaR2?

My take en Combinaciones vs Monodroga

- Monodroga
 - Pacientes mayores, con comorbilidades (que en verdad son casi todos)
 - Pacientes ya expuestos o con contraindicación a Lena
 - Pacientes con >3 líneas
- Para todos:
 - Vacunación
 - Manejar agresivamente las infecciones
 - Atento a reactivación de CMV (casi 25% en datos del mundo real)
 - Si posible, reemplazar Igs en pacientes con hipogamma

LatAm: Siempre Combinado!



Nos vemos en LEx 2027!

Gracias!

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