POST-ORLANDO 2025
Novità dal Meeting della Società Americana di Ematologia

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Torino
Centro Congressi Lingotto
19-21 febbraio 2026

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AbbVie						X	
Istituto Gentili						X	
BeiGene						X	
Incyte						X	
Novartis						X	

OUTLINE

- DLBCL (CAR T + something…., CAR T in PWH)
- PMBCL (anti PD1 therapy)
- Malattia di Waldenstrom (BRUIN, Rosewood)

OUTLINE

- DLBCL

American Society of Hematology
Helping hematologists conquer blood diseases worldwide

Phase II, single-arm, open-label, multicenter study: Efficacy of adjunctive Bruton's tyrosine kinase inhibitor (BTKi) zanubrutinib and chimeric antigen receptor T-cell therapy (CART) in aggressive B-cell non-Hodgkin lymphoma (aNHL)

Reem Karmali, Carlos Galvez, Jane N. Winter, Shuo Ma, Bin Zhang, Ping Xie, Yangruijue (Anna) MA, Ruohui Chen, Nirav Shah, Leo I. Gordon

23 patients

78% 2° line

61% primary refractory

Study Design: Single-Arm, Phase 2 Multi-Institutional Study

Key eligibility criteria

- Age ≥ 18 years
- R/R aNHL
- Commercially approved CD19 CART
- ≥ 1 prior line of systemic therapy, including anthracycline based therapy
- ECOG PS ≤ 1
- Adequate bone marrow, kidney, liver, cardiac function

*dose of 160 mg orally bid

Primary endpoint

- 6-month CR rate by Lugano 2014 criteria for efficacy-evaluable set (n=23)

**Historical benchmark of 44% derived from prior CART studies and RWE; null hypothesis rejected if ≥16/23 pts (69%) achieved a CR at D180 post CART

Secondary endpoints

- DOR, DOR if BOR is CR, PFS; OS; safety

Exploratory endpoints

- Changes in MRD status, immune cell subsets and cytokines with ZLI and ZM

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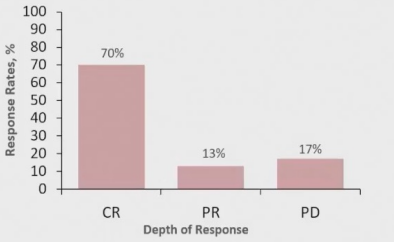
Response Rates and DOR on ZM (n=23)

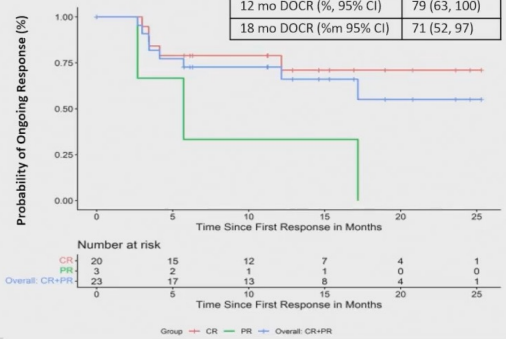
Response rates 6 months post CART (n=23)



Responses	Response D29 post CART (pre-ZM), n=30	Response D180 post CART (on ZM), n=23
CR, n (%)	16 (53%)	16 (70%)
PR, n (%)	7 (23%)	3 (13%) *3 converted to CR, 1 PD
PD, n (%)	7 (23%)	4 (17%) *3 CR and 1 PR at D29
MRD eval	Pending	Pending

DOR according to best overall response to CART (n=23)

Median DOR (mo)	Not reached
12 mo DOR (%, 95% CI)	73 (56,94)
12 mo DOCR (%, 95% CI)	79 (63, 100)
18 mo DOCR (%m 95% CI)	71 (52, 97)



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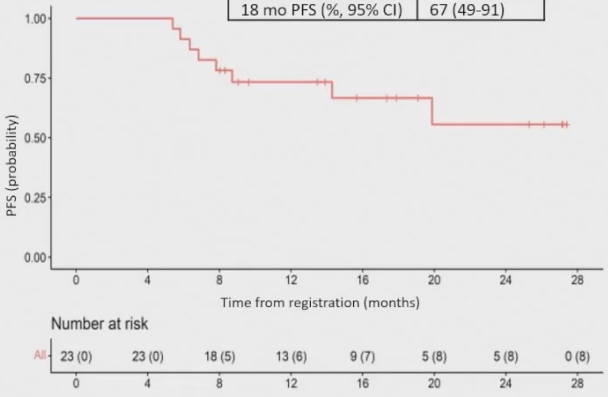
Progression Free and Overall Survival with ZM (n=23)

PFS

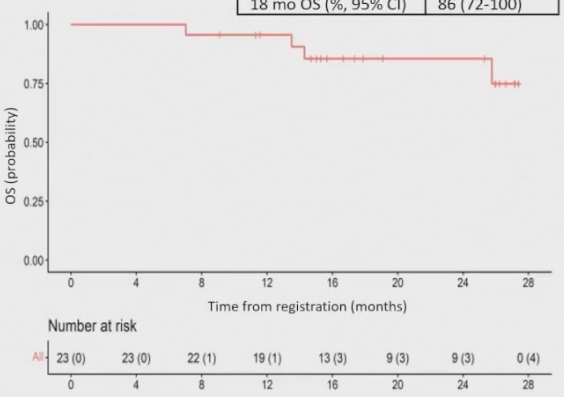
Median PFS (mo)	Not reached
6 mo PFS (%, 95% CI)	91 (81-100)
12 mo PFS (%, 95% CI)	73 (57-94)
18 mo PFS (%, 95% CI)	67 (49-91)



*12 mo PFS in ITT (n=30) – 61%

OS

Median OS (mo)	Not reached
6 mo OS (%, 95% CI)	100 (100-100)
12 mo OS (%, 95% CI)	96 (88-100)
18 mo OS (%, 95% CI)	86 (72-100)



*12 mo OS in ITT (n=30) – 84%

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Discussion

- Multicenter trial for novel combination of zanubrutinib and CD19 CART in aNHL
- ZLI prior to apheresis followed by ZM post CART achieved 6-mo sustained CR rate above historical rates reported for CART alone
  - Responses are durable 12 - 18 months post CART
- Safety profile of ZM predictable with low rates of G3 toxicities
- Changes in cytokines and immune subsets with ZLI predicted for sustained response
  - additional studies (including MRD evaluation) needed to clarify impact of zanubrutinib exposure post CART infusion on the TME and therapeutic effects of CART
- Our results support evaluation of this combination in a larger cohort of aNHL

Mosunetuzumab and Polatuzumab combined with Axicabtagene Ciloleucel induce high complete response rates at Day+90 in relapsed/refractory large B-cell lymphoma

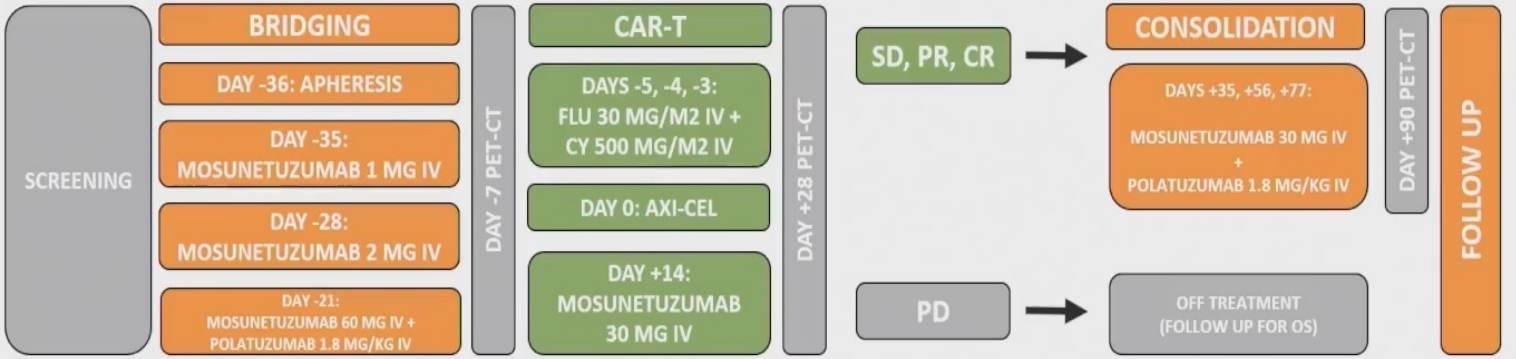
Jay Y. Spiegel, Juan P Alderuccio, Amer Beitinjaneh, Trent Wang, Noa Holtzman, Denise Pereira, Mark Goodman, Antonio Jimenez, Cara Benjamin, Alvaro Alencar, Georgios Pongas, Izidore S. Lossos, Joeseph Rosenblatt, Jonathan H Schatz, Michele Stanchina, Asaad Trabolsi, Juan Ramos, Craig Moskowitz, Robby Friedman, Keerthi Paladugu, Michelle Menard, Damian J. Green, Lazaros Lekakis

25 patients

60% 2° line
44% primary refractory

Total Therapy Approach: Mosun-Pola + Axi-cel

ClinicalTrials.gov: NCT05260957



KEY INCLUSION CRITERIA:
- **Age** ≥18
- **ELIGIBLE DIAGNOSES:** DLBCL (NOS), PMBCL, TFL, HGBL, FL grade 3B
- **DISEASE STATUS:** ≥ 1 lines of therapy
- **ECOG** PS 0-2; **CrCl** ≥30, **LVEF** ≥45%, **ANC** ≥1000, **Plt** ≥75k, **Hgb** ≥8

KEY EXCLUSION CRITERIA:
- **ACTIVE CNS INVOLVEMENT.** Prior CNS involvement allowed
- **PRIOR CD19 CAR-T THERAPY**

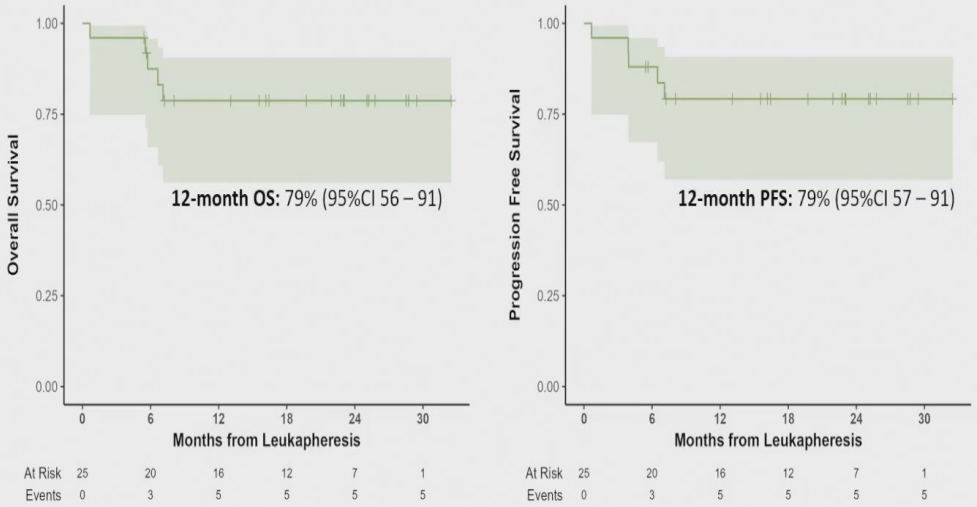
PRIMARY ENDPOINT:
- **CR at D90 post CAR-T infusion**

SECONDARY ENDPOINTS:
- **OS, PFS, DOR**
- **Safety**
- **ctDNA for MRD**

Mosun-Pola-Axi-cel Demonstrates High Durability

SYLVESTER COMPREHENSIVE CANCER CENTER
UNIVERSITY OF MIAMI HEALTH SYSTEM

Median follow-up: 22.7 months



Data cutoff November 1, 2025

Conclusions

SYLVESTER COMPREHENSIVE CANCER CENTER
UNIVERSITY OF MIAMI HEALTH SYSTEM

- Mosun-Pola-Axi-cel induced high response rates that are durable in 79% of patients at 1 year post axi-cel infusion
- Toxicities are consistent with prior studies of CAR-T therapies with potentially more prolonged neutropenia
- We plan to test this cohort in a randomized Phase II trial against SOC CAR-T approaches to better assess the efficacy of this combination

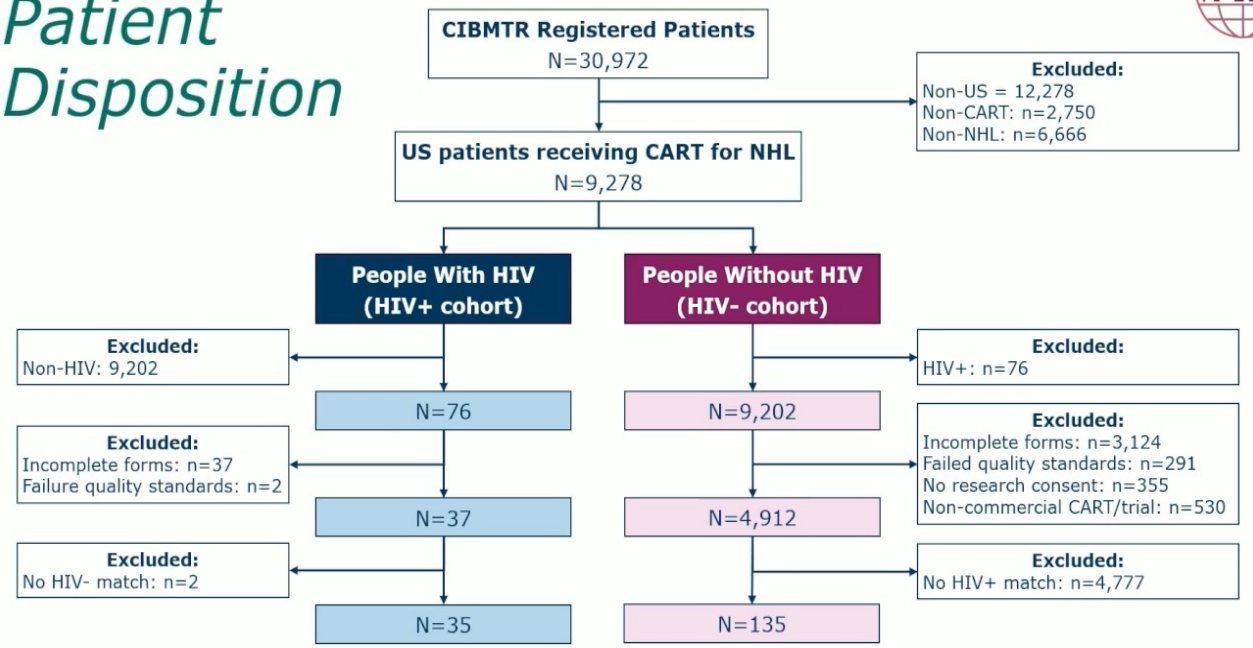
CONSORTIUM FOR Advancing Management and Prevention of Cancer in People with HIV

CIBMTR A RESEARCH COLLABORATION BETWEEN THE MEDICAL COLLEGE OF WISCONSIN AND NMDP

AMC-113: CD19-Directed CAR T-Cell Therapy for B-Cell Lymphoid Malignancies Is Safe and Effective in People Living with HIV (PWH) – A Matched Cohort Analysis by the Center for International Blood and Marrow Transplant Research (CIBMTR) and the AIDS Malignancy Consortium (AMC)

Stefan K. Barta, Ariela Noy, Kwang Woo Ahn, Jinalben Patel, Tiffany Hunt, Uroosa Ibrahim, Robert Biaocchi, Deukwoo Kwon, Marcelo C. Pasquini, Richard F. Ambinder

Patient Disposition



CIBMTR A RESEARCH COLLABORATION BETWEEN THE MEDICAL COLLEGE OF WISCONSIN AND NMDP

Adverse Events – CRS and ICANS

CART-Associated Toxicities among patients with follow up (n=19)													
	All Grades, n (%)		G1, n (%)		G2 n (%)		G3, n (%)		G4 n (%)		G5, n (%)		P-value
	HIV+	HIV-	HIV+	HIV-	HIV+	HIV-	HIV+	HIV-	HIV+	HIV-	HIV+	HIV-	
Cytokine Release Syndrome (CRS)	24 (69)	111(82)	17 (49)	70 (52)	5 (14)	36 (27)	0 (0)	3 (2)	0 (0)	1 (1)	**2 (6)***	0 (0)	**0.04**
Median time to onset, median (range):	**HIV+:** 5 days (1-10);				**HIV-:** 5 days (1-354)								0.12
Median time to resolution, median (range):	**HIV+:** 4 days (1-13);				**HIV-:** 5 days (1-22)								0.51
Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS)	8 (22)	60 (44)	0 (0)	16 (12)	1 (3)	12 (9)	3 (9)	19 (14)	3 (9)	5 (4)	0 (0)	2 (2)	**0.17**
Median time to onset, median (range):	**HIV+:** 8 days (4-11);				**HIV-:** 7 days (2-20)								0.82
Median time to resolution, median (range):	**HIV+:** 7 days (4-11);				**HIV-:** 4 days (1-27)								

** Concurrent G5 bacterial sepsis, n=1, and PD n=1*

Adverse Events – Infections & Hematologic

Infections by 100 days

	HIV+	HIV-	P-value
Bacterial infection, n(%)	10 (29)	14 (10)	<0.01
Fungal infection, n(%)	2 (6)	1 (1)	0.05
Viral infection, n(%)	6 (17)	26 (19)	0.78
Parasitic infection, n(%)	0 (0)	0 (0)	N/A
Other specified infection, n(%)	2 (6)	6 (4)	0.75

Hematological Toxicity

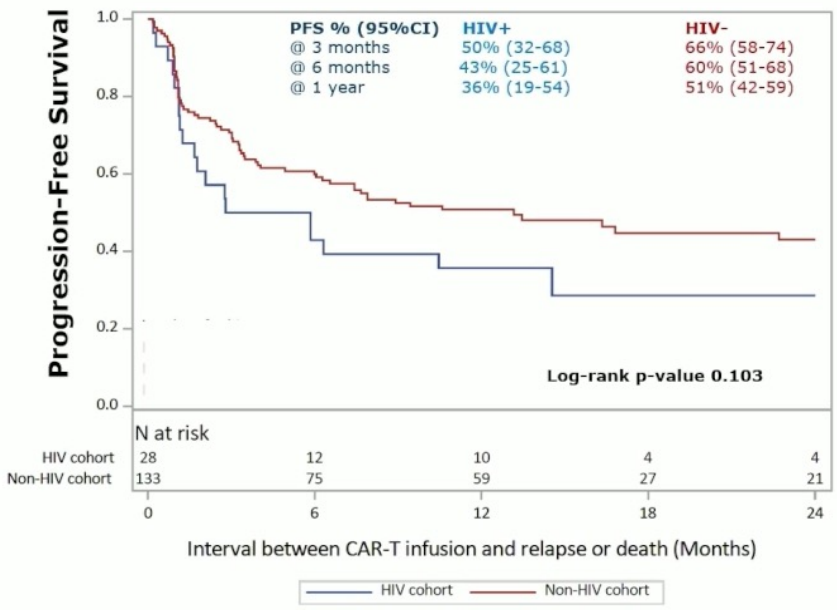
	HIV+	HIV-	P-value
Neutrophil recovery, n(%)	29 (83)	106 (79)	0.39
ANC≥ 500/mm³ x3			
@100 days, % (95%CI)	91 (78-99)	96 (92-99)	0.39
Platelet recovery, n(%) ≥ 20 × 10^9/L	27 (77)	122 (91)	0.13
@100 days, % (95%CI)	77 (61-90)	91 (85-95)	0.06

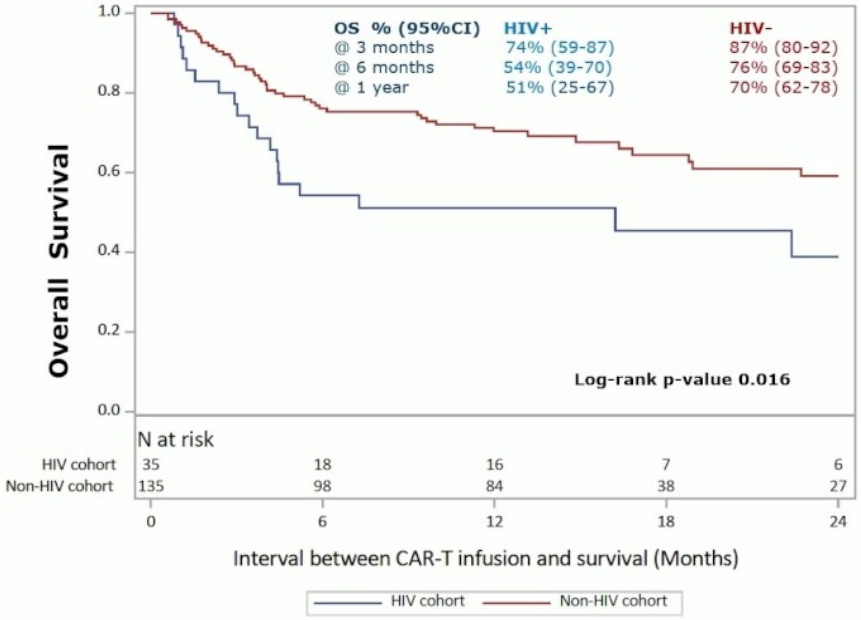
CIBMTR

Efficacy – Response

Response Rate		HIV+	HIV-	P-value
Best Response @ 100 days, n(%)				**0.003**
	CR	11 (32)	75 (56)	
	PR	3 (9)	14 (10)	
	SD	2 (6)	6 (4)	
	PD	16 (46)	32 (24)	
	Dead	2 (6)	4 (3)	
	Not assessed	1 (3)	4 (3)	
Best Response @ 6 months, n(%)				**0.003**
	CR	12 (34)	78 (58)	
	PR	2 (6)	13 (10)	
	SD	2 (6)	7 (5)	
	PD	16 (46)	31 (23)	
	Dead	3 (9)	4 (3)	
	Not assessed	0 (0)	2 (2)	
Best Response @ 1 year, n(%)				**0.003**
	CR	12 (34)	80 (59)	
	PR	2 (6)	13 (10)	
	SD	2 (6)	5 (4)	
	PD	16 (46)	33 (24)	
	Dead	3 (9)	4 (3)	

Outcomes - Survival





Summary and Conclusions

- **CART19 therapy** was **safely administered** in this large prospective cohort of **PWH** with **28.3% alive and in remission at 2 years** from therapy.
- Compared to a matched HIV- cohort, toxicities were mostly similar except for **less CRS but more infections in PWH**.
- The **lower OS for PWH was driven by worse lymphoma-control** rather than NRM, with lower response rates and a higher incidence of relapse.
- Possible explanations for this observed difference may include a more aggressive lymphoma behavior in PWH, a less potent CART product, or differences in bridging therapy, LD chemo and patient demographics.
- Notably, the HIV+ cohort contained a larger % of Black patients who are commonly underrepresented in clinical trials and may represent a clinically distinct entity with worse outcomes.[1]
- AMC-112 is currently enrolling onto a prospective CART19 study (NCT05077527)

1) Lee MJ, et al. *Cancer* 2020

OUTLINE

PMBCL (anti PD1 therapy)

Excellent Outcomes with Anti-PD1 Therapy in Relapsed/Refractory Primary Mediastinal Large B-Cell Lymphoma: Real-World Data from the LYSA group

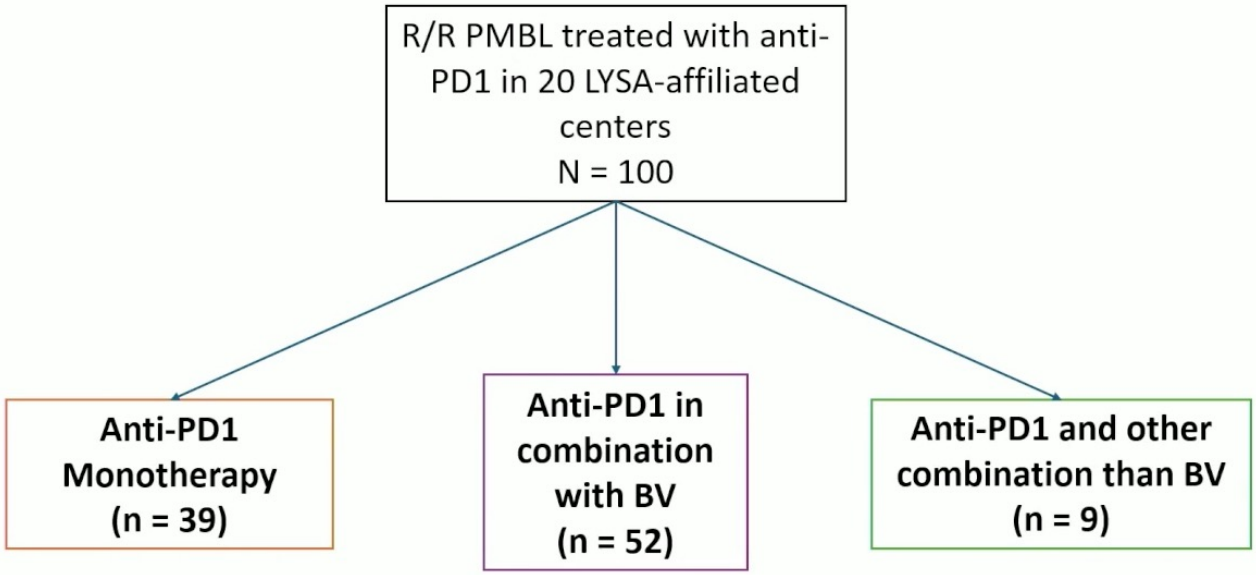
(PMBL-SIGN study)

Loïc Renaud[1], Florian Chevillon[2], Emilie Lévêque[3], Arnaud Pages[1], Justine Decroocq[2], Robin Noel[4], Eric Durot[5], Denis Coulomb[6], Charles Herbaux[6], Fabien Claves[7], Hiba Ghannoum[1], Jean Galtier[8], Cedric Rossi[9], Doriane Cavalieri[10], Arnaud Campidelli[11], Roch Houot[12], Jerome Cornillon[13], Maya Belhadj[14], François Lemonnier[15], Antoine Bonnet[16], Pierre Sesques[17], **Vincent Camus[3].**

(1) Gustave Roussy Cancer Campus, Villejuif, France; (2) AP-HP, Hôpitaux Universitaires Paris Nord, Paris, France; (3) Centre Henri Becquerel, Rouen, France; (4) Institut Paoli-Calmettes, Marseille, France; (5) CHU de Reims, Reims, France; (6) CHU de Montpellier, Montpellier, France; (7) CHU Grenoble Alpes, Grenoble, France; (8) CHU Bordeaux, Bordeaux, France; (9) CHU Dijon, Dijon, France; (10) CHU de Lille, Lille, France; (11) CHRU de Nancy, Nancy, France; (12) CHU de Rennes, Rennes, France; (13) CHU de Saint-Étienne, Saint-Étienne, France; (14) CHU de La Réunion, La Réunion, France; (15) Hôpital Henri Mondor, Lymphoid Hematology Department, AP-HP, Créteil, France; (16) Centre Hospitalier Bretagne Atlantique, Vannes, France; (17) Hôpital Lyon Sud, Hospices Civils de Lyon, Pierre-Bénite, France.

Abstract Number 1019. *Session 629. Aggressive Lymphomas, Immunotherapy including Bispecific Antibodies: Improving Outcomes in Rare Large Cell Lymphomas; December 8*

Flow chart

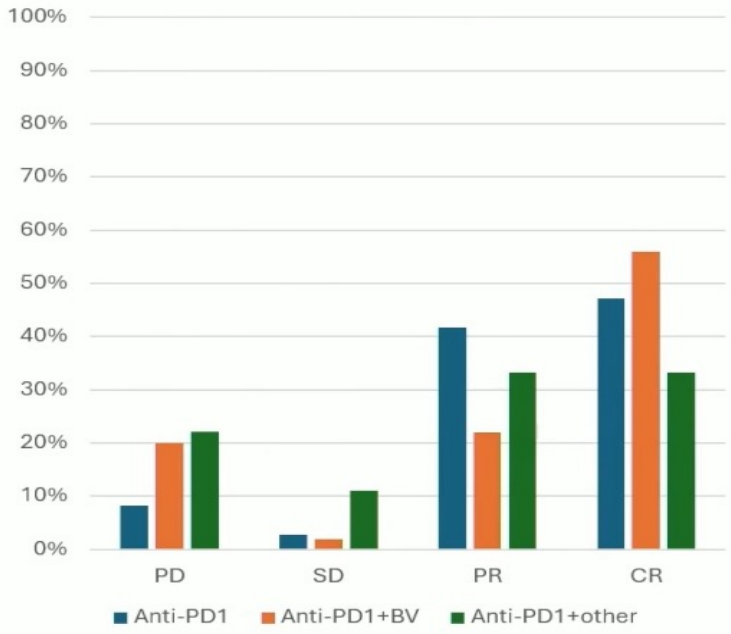


BV: brentuximab-vedotin

Renaud L, ..., Camus V, ASH 2025

Response rates

Outcome	Anti-PD1 single-agent	Anti-PD1 + Brentuximab-vedotin	Anti-PD1 + other agents
Patients evaluated (N)	36	50	9
Best response			
– PD	3 (8.3%)	10 (20%)	2 (22.2%)
– SD	1 (2.8%)	1 (2%)	1 (11.1%)
– PR	15 (41.7%)	11 (22%)	3 (33.3%)
– CR	17 (47.2%)	28 (56%)	3 (33.3%)
Time to best response (months)			
Median [Q1–Q3]	**2.9 [2–6]**	**2.2 [1–3]**	**2.9 [1–3]**



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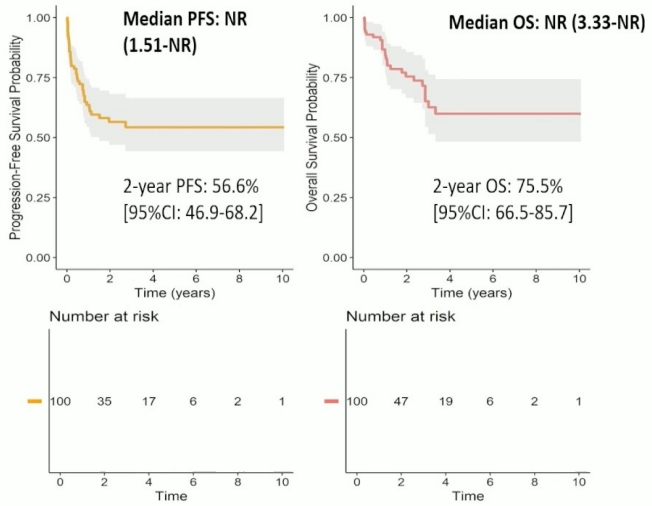
Outcomes



Follow up time (IQR) : 31.8 (11.93;51.75) months

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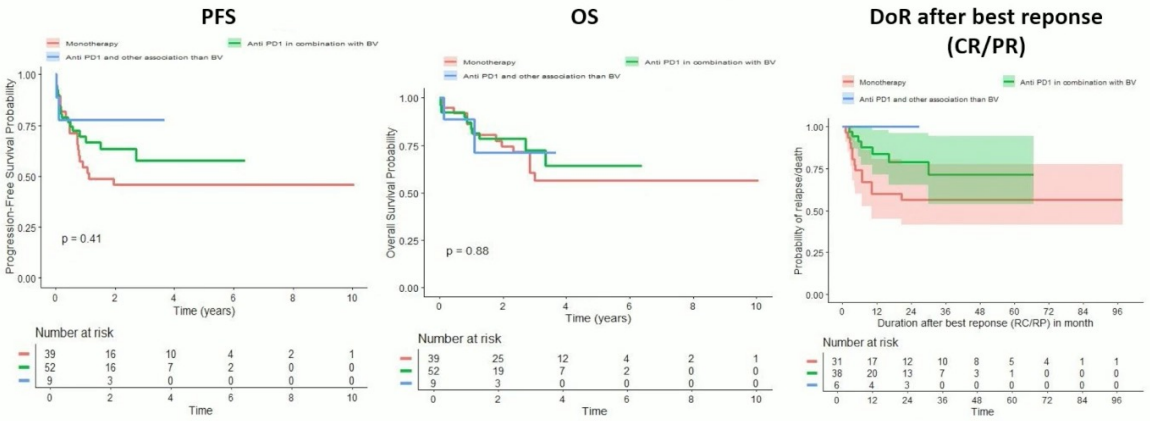
Outcomes according to treatment



Follow up time (IQR) : 31.8 (11.93;51.75) months

Renaud L, ..., Camus V, ASH 2025

Anti-PD1 treatment discontinuations

Anti-PD1 Monotherapy (n = 39)

Reasons for discontinuation of anti-PD1	
Planned number of cycles reached	36 (38.3%)
CR	7 (7.4%)
Progression	23 (24.5%)
Toxicity	**6 (6.4%)**
Patient's decision	1 (1.1%)
other reason : mainly **go to consolidation with CAR-T or RT or ASCT**	21 **(22.3%)**

Anti-PD1 in combination with BV (n = 52)

Reasons for discontinuation of Bv	
Planned number of cycles reached	23 (44.2%)
CR	3 (5.8%)
Progression	8 (15.4%)
Toxicity	**5 (9.6%)**
Patient's decision	1 (1.9%)
other reason : mainly **go to consolidation with CAR-T or RT or ASCT**	12 **(23.1%)**

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Conclusions

- Anti–PD-1 therapy, either as a single agent or in combination with BV, shows **high efficacy** and durable responses in R/R PMBL in **real-world settings** in France with no new safety signal.
- **2-year OS: 75.5%** and **2-year PFS: 56.6%** confirm a clinically meaningful benefit beyond what has been shown in clinical trials.
- **Patients achieving CR (~51%) did so quickly (median : 3 months) and had a favorable prognosis (relapse and death rates: 6%).**
- **CNS-IPI** is the **strongest independent prognostic factor** for both OS and PFS.
- Further work is **ongoing to identify** patients who may truly benefit from **post–anti-PD1 consolidation** (CAR-T cells, radiotherapy, SCT) and to elucidate the underlying **biological factors driving anti-PD1 response**.
- **Results confirm a favorable benefit–risk profile for the routine use of CPIs in R/R PMBL.**

Renaud L, ..., Camus V, ASH 2025

OUTLINE

- Malattia di Waldenstrom

American Society of Hematology 2025; Orlando, USA; 6-9 December 2025 226

Pirtobrutinib in Relapsed/Refractory (R/R) Waldenström Macroglobulinemia (WM): Up to 5 Years of Follow-Up From the Phase 1/2 BRUIN Study

Chan Y. Cheah[1], Manish R. Patel[2], Toby A. Eyre[3], Wojciech Jurczak[4], David Lewis[5], Thomas Gastinne[6], Shuo Ma[7], Jonathon B. Cohen[8], Krish Patel[8,10], Jennifer R. Brown[11], Lydia Scarfò[12,13], Talha Munir[14], Ewa Lech-Maranda[15], Marc S. Hoffmann[16], Chaitra Ujjani[17], Bita Fakhri[18], Michael Wang[19], Koji Izutsu[20], Hirokazu Nagai[21], Constantine S. Tam[22], Joanna M. Rhodes[23], Julie Vose[24], Matthew McKinney[25], James N. Gerson[26], Minal A. Barve[27], Bryone J. Kuss[28], Youngil Koh[29], Aisling Barrett[30], Steven P. Treon[30], Jorge J. Castillo[30], John F. Seymour[31], Amy S. Ruppert[32], Samuel C. McNeely[32], Richard A. Walgren[32], Donald E. Tsai[32], Katherine Bao[32], Binoj Nair[32], Jennifer Woyach[33], M. Lia Palomba[34]

[1]Linear Clinical Research, Sir Charles Gairdner Hospital and University of Western Australia, Perth, Australia, [2]Florida Cancer Specialists/Sarah Cannon Research Institute, Sarasota, USA, [3]Oxford University Hospitals NHS Foundation Trust, Churchill Cancer Center, Oxford, UK, [4]Maria Sklodowska-Curie National Research Institute of Oncology, Krakow, Poland, [5]University Hospitals Plymouth NHS, Plymouth, UK, [6]Centre Hospitalier Universitaire de Nantes, Nantes, France, [7]Robert H. Lurie Comprehensive Cancer Center of Northwestern University, Chicago, USA, [8]Winship Cancer Institute, Emory University, Atlanta, USA, [9]Swedish Cancer Institute, Seattle, USA, [10]Sarah Cannon Research Institute, Nashville, USA, [11]Dana-Farber Cancer Institute, Harvard Medical School, Boston, USA, [12]Università Vita-Salute San Raffaele, Milano, Italy, [13]IRCCS Ospedale San Raffaele, Milano, Italy, [14]St. James's University Hospital, Leeds, UK, [15]Institute of Hematology and Transfusion Medicine, Warsaw, Poland, [16]The University of Kansas Cancer Center, Kansas City, USA, [17]Fred Hutchinson Cancer Research Center, Seattle, USA, [18]Stanford University School of Medicine, Stanford, USA, [19]UT MD Anderson Cancer Center, Houston, USA, [20]National Cancer Center Hospital, Tokyo, Japan, [21]National Hospital Organization Nagoya Medical Center, Aichi, Japan, [22]Alfred Hospital and Monash University, Melbourne, Australia, [23]Rutgers Cancer Institute, New Brunswick, USA, [24]University of Nebraska Medical Center, Omaha, USA, [25]Duke Cancer Institute, Durham, USA, [26]University of Vermont Larner College of Medicine, Burlington, USA, [27]Mary Crowley Cancer Research, Dallas, USA, [28]Flinders University Medical Centre, South Australia, Australia, [29]Seoul National University Hospital, Seoul, Korea, [30]Bing Center for Waldenström Macroglobulinemia, Dana-Farber Cancer Institute, Harvard Medical School, Boston, USA, [31]Royal Melbourne Hospital, Peter MacCallum Cancer Centre and University of Melbourne, Melbourne, Australia, [32]Eli Lilly and Company, Indianapolis, USA, [33]The Ohio State University Comprehensive Cancer Center, Columbus, USA, [34]Memorial Sloan Kettering Cancer Center, New York, USA

Sponsored by Eli Lilly and Company

Efficacy in Patients with WM Treated with Pirtobrutinib

Response Rates

Response Evaluable in Patients With WM	All Patients (N=80)	Prior cBTKi (n=63)	cBTKi Naïve (n=17)
CR + VGPR rate,[a] % (95% CI)	27.5 (18.1, 38.6)	25.4 (15.3, 37.9)	35.3 (14.2, 61.7)
Major response rate,[b] % (95% CI)	72.5 (61.4, 81.9)	68.3 (55.3, 79.4)	88.2 (63.6, 98.5)
ORR[c], n (%)	66 (82.5)	51 (81.0)	15 (88.2)
Best response, n (%)			
CR	1 (1.3)	1 (1.6)	0
VGPR	21 (26.3)	15 (23.8)	6 (35.3)
PR	36 (45.0)	27 (42.9)	9 (52.9)
MR	8 (10.0)	8 (12.7)	0
SD	11 (13.8)	9 (14.3)	2 (11.8)
PD	3 (3.8)	3 (4.8)	0

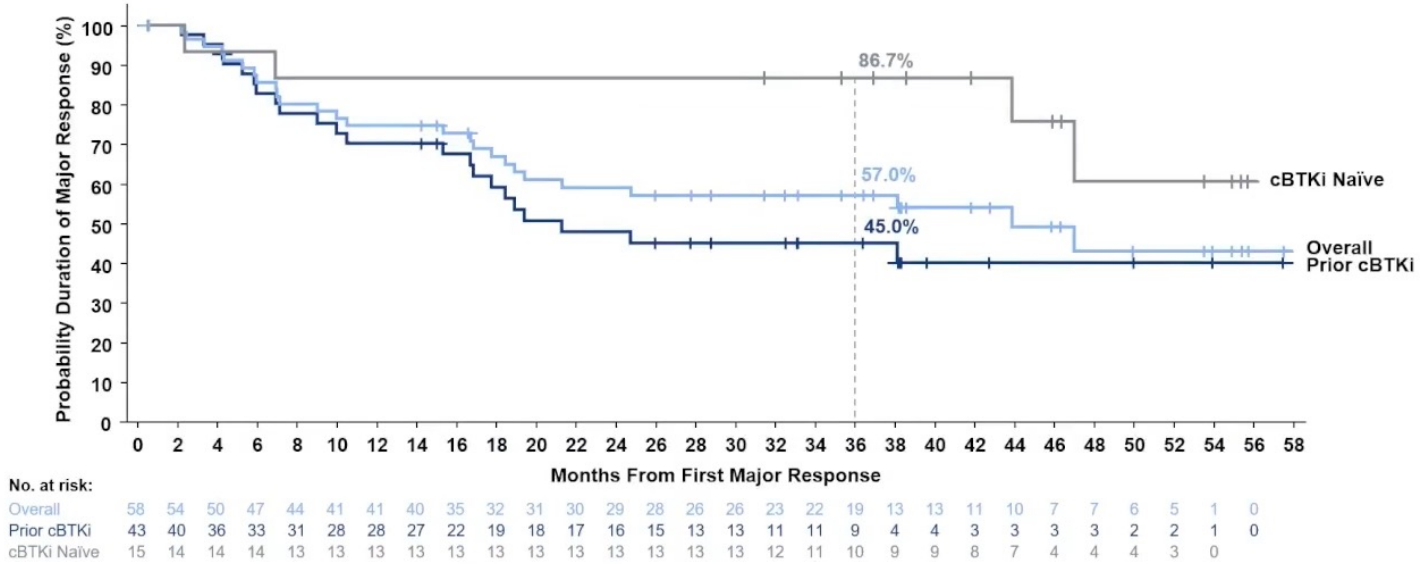
Median study follow-up: 35.0 months (range, 2.7-62.9)

[a]The CR/VGPR rate in patients who previously discontinued cBTKi due to progressive disease was 22.0% (9/41). [b]Major response includes patients with a best response of CR, VGPR, or PR. [c]Includes patients with a best response of CR, VGPR, PR or MR.

Note: Response as assessed by investigator based on Modified IWWM6 (Owen's) criteria. Under modified IWWM6 criteria, a PR is upgraded to VGPR if corresponding IgM is in normal range or has at least 90% reduction from baseline.

Abbreviations: BTKi, Bruton tyrosine kinase inhibitor; cBTKi, covalent BTKi; CI, confidence interval; CR, complete response; IWWM6, International Workshop on Waldenstrom's Macroglobulinemia; MR, minor response; ORR, overall response rate; PD; progressive disease; PR, partial response; SD, stable disease; VGPR, very good partial response; WM, Waldenström macroglobulinemia.

Duration of Major Response in Patients with WM Treated with Pirtobrutinib



No. at risk:

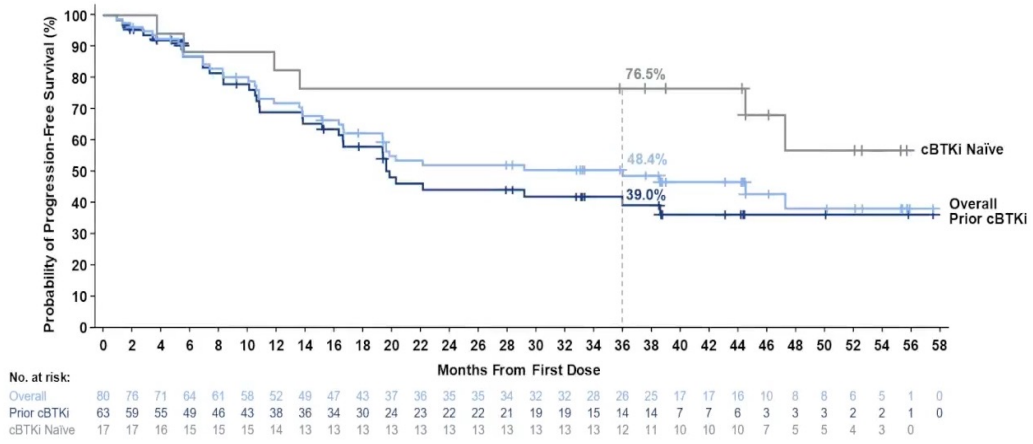
Overall	58	54	50	47	44	41	41	40	35	32	31	30	29	28	26	26	23	22	19	13	13	11	10	7	7	6	5	1	0
Prior cBTKi	43	40	36	33	31	28	28	27	22	19	18	17	16	15	13	13	11	11	9	4	4	3	3	3	3	2	2	1	0
cBTKi Naïve	15	14	14	14	13	13	13	13	13	13	13	13	13	13	13	13	12	11	10	9	9	8	7	4	4	4	3	0	

The median DOR (95% CI) was:

- **42.3 months (17.9, NE) in all patients with WM** (Events/total: 26/58)
- **20.3 months (15.8, NE) in patients with prior cBTKi therapy** (Events/total: 22/43)
- **NR (42.3, NE) in cBTKi-naïve patients** (Events/total: 4/15)

Abbreviations: cBTKi, covalent Bruton tyrosine kinase inhibitor; CI, confidence interval; DOR, duration of response; NE, not estimable; NR, not reached; WM, Waldenström macroglobulinemia.

Progression-Free Survival[a] in Patients with WM



No. at risk:

Overall	80	76	71	64	61	58	52	49	47	43	37	36	35	35	34	32	32	28	26	25	17	17	16	10	8	8	6	5	1	0
Prior cBTKi	63	59	55	49	46	43	38	36	34	30	24	23	22	22	21	19	19	15	14	14	7	7	6	3	3	3	2	2	1	0
cBTKi Naïve	17	17	16	15	15	15	14	13	13	13	13	13	13	13	13	13	13	13	12	11	10	10	10	7	5	5	4	3	0	

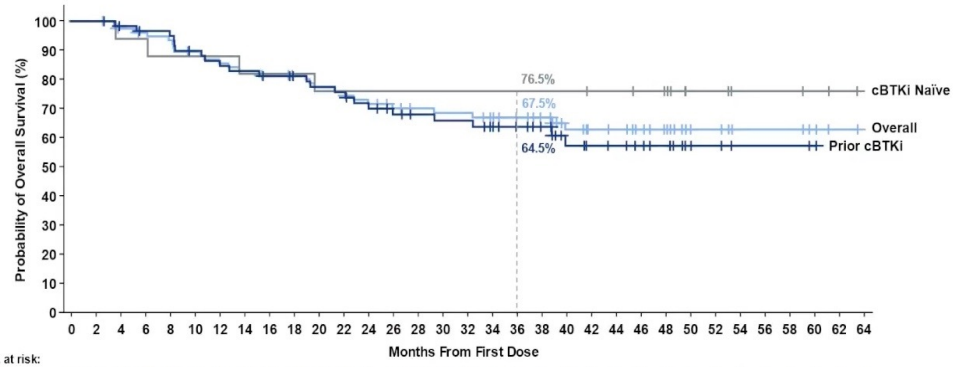
The median PFS (95% CI) was:

- **35.9 months (19.3, NE) in all patients with major response** (Events/total: 40/80)
- **19.6 months (15.1, 38.5) in patients with prior cBTKi therapy** (Events/total: 34/63)
- **NR (13.6, NE) in cBTKi-naïve patients** (Events/total: 6/17)

[a]Investigator-assessed.

Abbreviations: cBTKi, covalent Bruton tyrosine kinase inhibitor; CI, confidence interval; mPFS, median PFS; NE, not estimable; NR, not reached; PD, progressive disease; PFS, progression-free survival; Tx, toxicity; WM, Waldenström macroglobulinemia.

Overall Survival in Patients with WM Treated with Pirtobrutinib



No. at risk:

Overall	80	80	76	74	72	68	65	63	61	59	56	55	51	48	46	45	45	41	39	36	30	27	26	22	19	9	9	5	5	5	2	1	0
Prior cBTKi	63	63	60	58	57	53	50	49	47	45	43	42	38	35	33	32	32	28	26	23	17	15	14	11	10	4	4	2	2	2	0		
cBTKi Naïve	17	17	16	16	15	15	15	14	14	14	13	13	13	13	13	13	13	13	13	13	13	12	12	11	9	5	5	3	3	3	2	1	0

The median OS (95% CI) was:

- **NR (NE, NE) in all patients with major response** (Events/total: 26/80)
- **NR (38.5, NE) in patients with prior cBTKi therapy** (Events/total: 22/63)
- **NR (19.6, NE) in cBTKi-naïve patients** (Events/total: 4/17)

Abbreviations: cBTKi, covalent Bruton tyrosine kinase inhibitor; CI, confidence interval; mOS, median OS; NE, not estimable; NR, not reached; OS, overall survival; WM, Waldenström macroglobulinemia.

Conclusions

- These extended 5-year follow-up results demonstrate durable benefit of pirtobrutinib in patients with WM, including in patients previously exposed to cBTKi therapy, addressing a key unmet need
  - With more mature follow-up, the 36-month DOR and OS rates were 57.0% and 67.5%, respectively, in all patients with WM
  - Pirtobrutinib was also active in high-risk patients with either *CXCR4* mutations or *MYD88*-WT disease
  - The depth of response observed, as demonstrated by over 25% of patients achieving a CR+VGPR, is noteworthy in the subset of patients who received prior cBTKi therapy
- The safety profile remained in line with previous findings[1], with low rates of treatment discontinuation and dose reduction due to treatment-related adverse events, and low rates of atrial fibrillation, with longer follow-up
- Pirtobrutinib may provide a valuable therapeutic option for patients with WM who have limited options after cBTKi therapy

1. Palomba ML, et al. *Blood*. 2022;140(S1):557-560.

Abbreviations: cBTKi, covalent Bruton tyrosine kinase inhibitor; CR, complete response; CXCR4, C-X-C chemokine receptor type 4; DOR, duration of response; MYD88, myeloid differentiation primary response gene 88; OS, overall survival; VGPR, very good partial response; WM, Waldenström macroglobulinemia; WT, wild-type.

Final Analysis of the Randomized Phase 2 ROSEWOOD Study of Zanubrutinib + Obinutuzumab vs Obinutuzumab Monotherapy in Patients With Relapsed/Refractory Follicular Lymphoma

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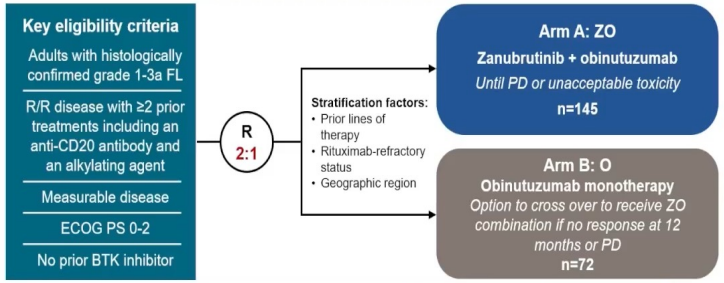
[1]Institute of Hematology "Seràgnoli," University of Bologna, Bologna, Italy; [2]Masaryk University and University Hospital, Brno, Czech Republic; [3]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [4]Institut Bergonié, Bordeaux, France; [5]Institut Català d'Oncologia (ICO) - Hospital Duran i Reynals, Barcelona, Spain; [6]Peking University Cancer Hospital and Institute, Beijing, China; [7]Harbin Medical University Cancer Hospital, Harbin, China; [8]Hematology, University Hospital "Ospedale di Circolo e Fondazione Macchi" - ASST Sette Laghi, University of Insubria, Varese, Italy; [9]Hôpital Haut-Lévêque, CHU Bordeaux, Pessac, France; [10]Department of Haematology, Christchurch Hospital, Christchurch, New Zealand; [11]Tianjin Medical University Cancer Institute & Hospital, Tianjin, China; [12]Calvary Mater Newcastle, Waratah, NSW, Australia; [13]Charles University, General Hospital, Prague, Czech Republic; [14]St Bartholomew's Hospital, Barts Health NHS Trust, London, UK; [15]BeOne Medicines, Ltd, Shanghai, China; [16]BeOne Medicines, Ltd, San Carlos, CA, USA; [17]Department of Hematology, Concord Repatriation General Hospital, Sydney, NSW, Australia

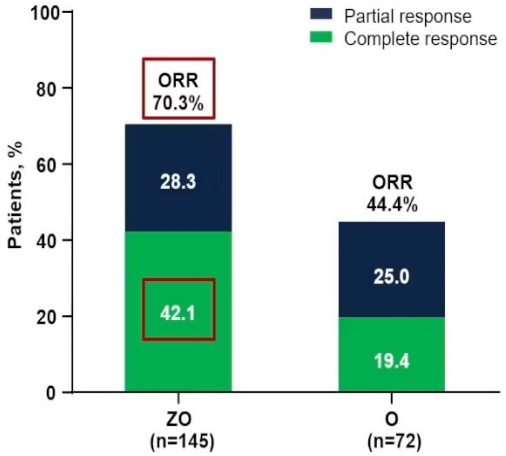
ROSEWOOD: A Global, Randomized, Open-Label, Phase 2 Study



BTK, Bruton tyrosine kinase; CD, cluster of differentiation; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; FL, follicular lymphoma; INV, investigator; IRC, independent review committee; NCI CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events; O, obinutuzumab; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; R, randomized; R/R, relapsed/refractory; ZO, zanubrutinib + obinutuzumab.

1. Cheson BD, et al. *J Clin Oncol.* 2014;32(27):3059-3068.

ORR per IRC With ZO Was Higher Compared With O

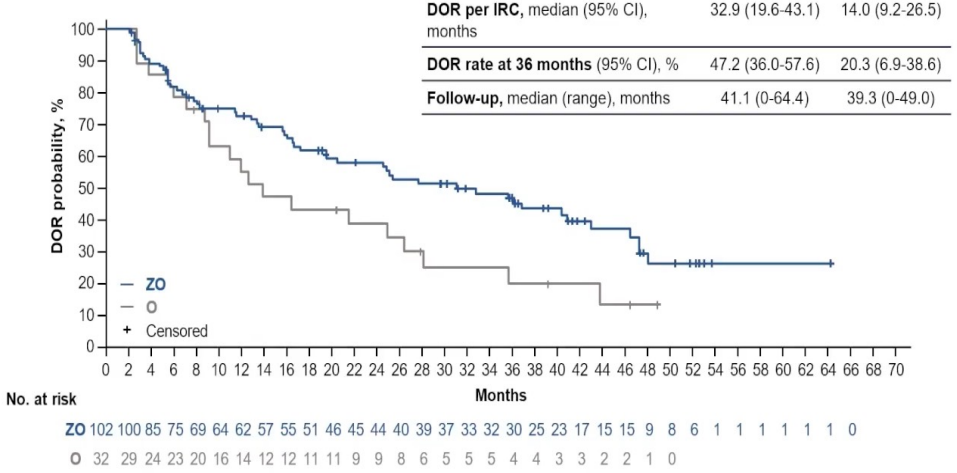


- ORRs per INV were similar to ORRs per IRC (ZO, 68.3%; O, 43.1%)

	ZO (n=145)	O (n=72)
Overall response rate, n (%)	102 (**70.3**)	32 (**44.4**)
95% CI	62.2-77.6	32.7-56.6
Risk difference (95% CI), %	25.5 (11.8-39.3)	
2-sided *P* value[a]	.0003	
Complete response rate, n (%)	61 (**42.1**)	14 (**19.4**)
95% CI	33.9-50.5	11.1-30.5
2-sided *P* value[a]	.0009	
Other responses, n (%)		
Stable disease	21 (14.5)	14 (19.4)
Indeterminate due to zanubrutinib hold	1 (0.7)	0
Non-progressive disease[b]	6 (4.1)	9 (12.5)
Progressive disease	13 (9.0)	16 (22.2)
Discontinued prior to first assessment/NE	2 (1.4)	1 (1.4)

[a]*P* value is descriptive. [b]Defined as PET assessment missing or not evaluable, and CT assessment showed no progressive disease.
CT, computed tomography; INV, investigator; IRC, independent review committee; O, obinutuzumab; ORR, overall response rate; PET, positron emission tomography; ZO, zanubrutinib + obinutuzumab.

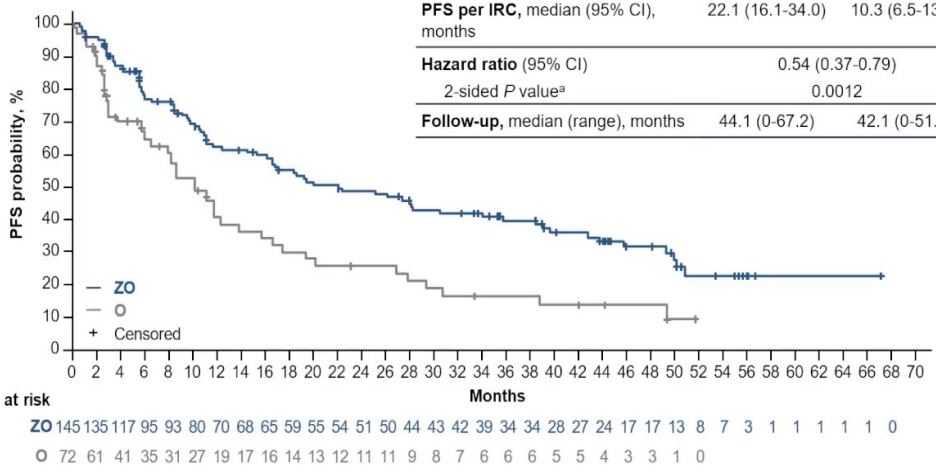
Duration of Response Was Longer in the ZO Arm



	ZO	O
DOR per IRC, median (95% CI), months	32.9 (19.6-43.1)	14.0 (9.2-26.5)
DOR rate at 36 months (95% CI), %	47.2 (36.0-57.6)	20.3 (6.9-38.6)
Follow-up, median (range), months	41.1 (0-64.4)	39.3 (0-49.0)

DOR, duration of response; IRC, independent review committee; O, obinutuzumab; ZO, zanubrutinib + obinutuzumab.

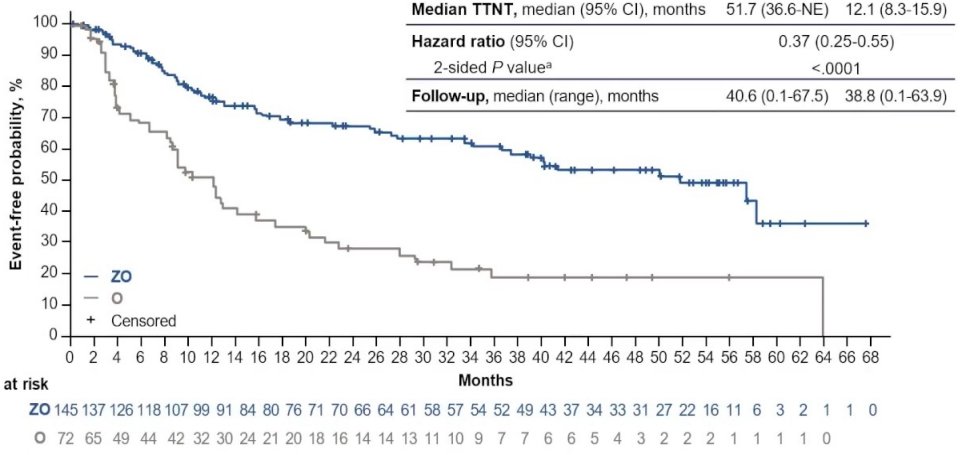
PFS per IRC Was Longer in the ZO Arm



	ZO	O
PFS per IRC, median (95% CI), months	22.1 (16.1-34.0)	10.3 (6.5-13.8)
Hazard ratio (95% CI)	0.54 (0.37-0.79)	
2-sided *P* value[a]	0.0012	
Follow-up, median (range), months	44.1 (0-67.2)	42.1 (0-51.8)

[a]*P* value is descriptive.
IRC, independent review committee; O, obinutuzumab; PFS, progression-free survival; ZO, zanubrutinib + obinutuzumab.

Time to New Anticancer Therapy Was Longer in the ZO Arm vs the O Arm



	ZO	O
Median TTNT, median (95% CI), months	51.7 (36.6-NE)	12.1 (8.3-15.9)
Hazard ratio (95% CI)	0.37 (0.25-0.55)	
2-sided *P* value[a]	<.0001	
Follow-up, median (range), months	40.6 (0.1-67.5)	38.8 (0.1-63.9)

[a]*P* value is descriptive.
TTNT, time to new anticancer therapy or crossover; NE, not estimable; O, obinutuzumab; ZO, zanubrutinib + obinutuzumab.

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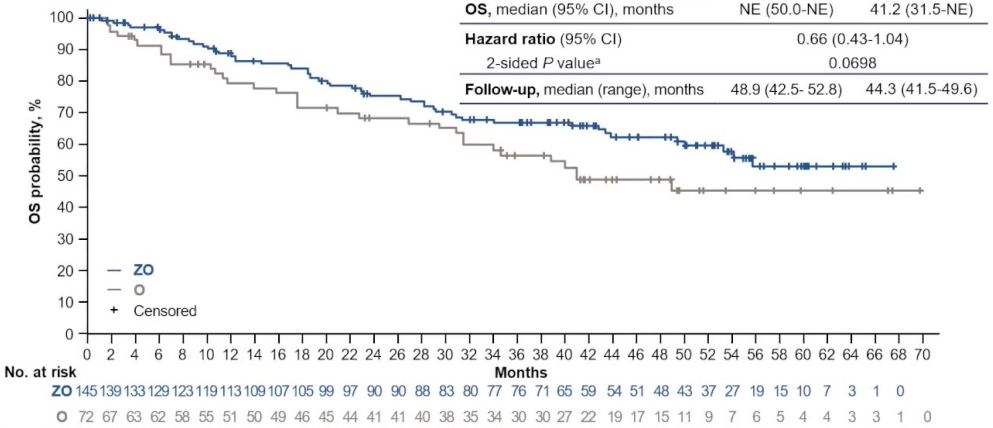
Overall Survival



	ZO	O
OS, median (95% CI), months	NE (50.0-NE)	41.2 (31.5-NE)
Hazard ratio (95% CI)	0.66 (0.43-1.04)	
2-sided *P* value[a]	0.0698	
Follow-up, median (range), months	48.9 (42.5- 52.8)	44.3 (41.5-49.6)

[a]*P* value is descriptive.
NE, not estimable; O, obinutuzumab; OS, overall survival; ZO, zanubrutinib + obinutuzumab.

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Final Analysis of ROSEWOOD: Conclusions

- The favorable risk-benefit profile of ZO in heavily pretreated patients with R/R FL was sustained
- Compared with O monotherapy, combination treatment with ZO demonstrated substantially
  - higher ORR and CR rate
  - longer DOR and PFS
- ZO had a manageable, consistent safety profile, with no new safety signals
- With a long median follow-up (34.6 months), these data support the potential benefit of ZO as a novel combination therapy for patients with R/R FL
- To further evaluate ZO in patients with R/R FL with ≥1 prior line of therapy, the phase 3 MAHOGANY study (NCT05100862) comparing ZO vs lenalidomide + rituximab is ongoing

CR, complete response; DOR, duration of response; FL, follicular lymphoma; O, obinutuzumab; ORR, overall response rate; PFS, progression-free survival; R/R, relapsed/refractory; Z, zanubrutinib; ZO, zanubrutinib + obinutuzumab.

GRAZIE PER L'ATTENZIONE