ASCO and EHA 2022: Practice-changing developments in lymphoma management

Tuesday, September 13, 2022 | 17:00–18:30 (CEST)

Welcome and introductions

Chair: Professor Christian Buske

Disclosures

- **Honoraria:** AbbVie, BeiGene, Celltrion, Gilead, Janssen, Novartis, Pfizer, and Roche
- **Research funding:** AbbVie, Bayer, Celltrion, Janssen, MSD, and Roche

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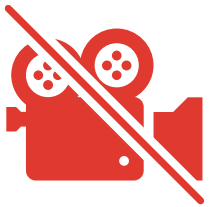
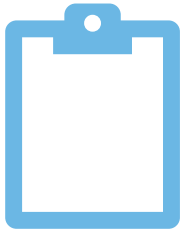
- Zanubrutinib is not approved for the treatment of CLL/SLL or follicular lymphoma.

CLL, chronic lymphocytic leukemia; SLL, small lymphocytic lymphoma.

Housekeeping



Please note that personal recording of this meeting is not permitted (a recording will be available to watch soon after the meeting)



A post-meeting survey will be shared at the end of the webinar; we would greatly appreciate your feedback

Introducing the panel

Christian Buske (Chair)
University Hospital Ulm, Germany

Wojciech Jurczak
Maria Skłodowska-Curie National Research Institute of Oncology, Poland

Véronique Leblond
Pitié-Salpêtrière Hospital, France

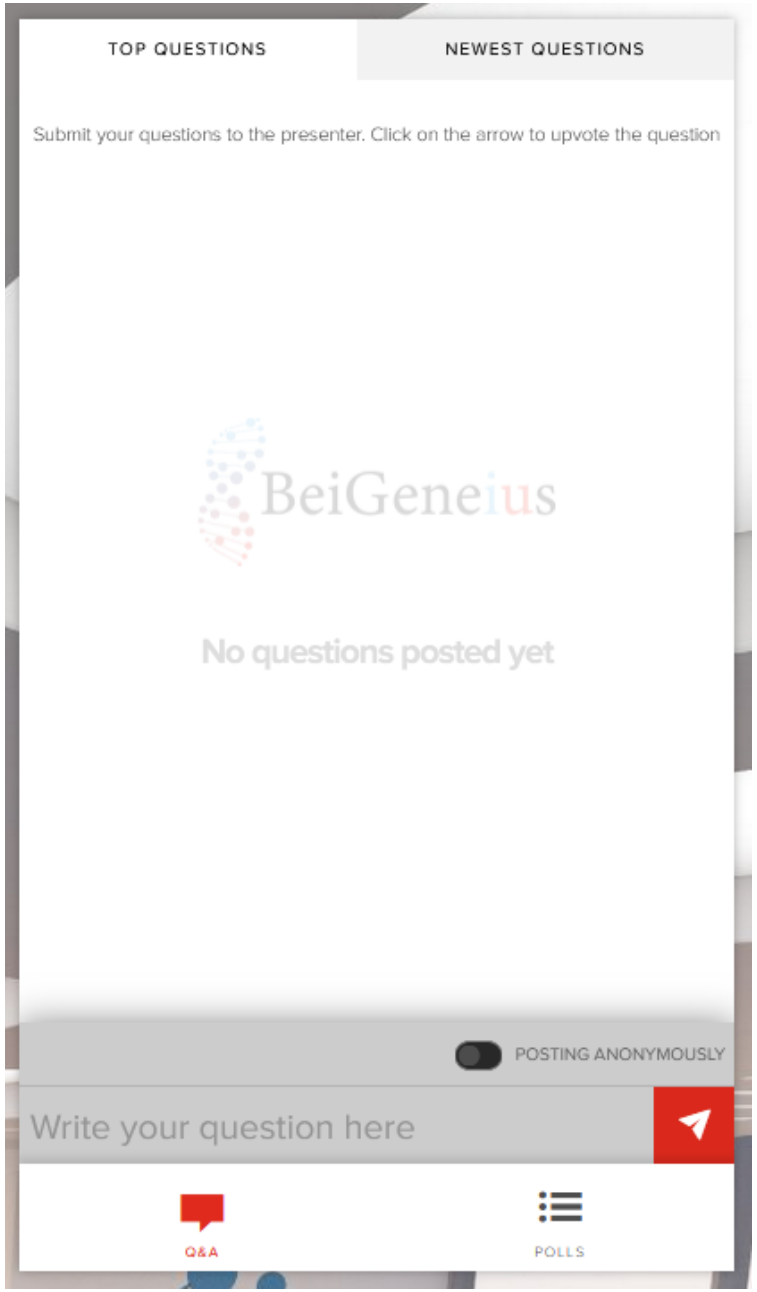
Pier Luigi Zinzani
University of Bologna, Italy

Agenda

17:00	**Welcome and introductions**	Christian Buske
17:05	**Highlights in aggressive lymphomas**	Pier Luigi Zinzani
17:20	**Highlights in indolent lymphomas**	Véronique Leblond
17:35	**Highlights in chronic lymphocytic leukemia**	Wojciech Jurczak
17:50	**Panel discussion**	**Panel:** All faculty
18:10	**Audience Q&A**	**Panel:** All faculty
18:25	**Summary and meeting close**	Christian Buske

Audience questions

- Please exit full-screen view and enter your question in the submission box for the panel to answer during the Q&A session
  - You can vote for the questions you would most like the panel to answer



2022 ASCO ANNUAL MEETING

June 3–7, 2022
McCormick Place | Chicago, IL
June 4–7: Exhibits
#ASCO22

EHA2022 HYBRID JUNE 9-17 VIENNA

Highlights in aggressive lymphomas

Professor Pier Luigi Zinzani
University of Bologna, Italy

Disclosures

- **Advisory boards**: ADC Therapeutics, BeiGene, BMS, Celltrion, Eusapharma, Gilead, Incyte, Janssen-Cilag, Kyowa Kirin, MSD, Novartis, Roche, Sandoz, Secura Bio, Servier, Takeda, and TG Therapeutics
- **Consultant**: Eusapharma, MSD, and Novartis
- **Speaker bureau**: BeiGene, BMS, Celltrion, Eusapharma, Gilead, Incyte, Janssen-Cilag, Kyowa Kirin, MSD, Novartis, Roche, Servier, Takeda, and TG Therapeutics

BMS, Bristol Myers Squibb; MSD, Merck Sharp & Dohme.

Glofitamab in patients with relapsed/refractory (R/R) diffuse large B-cell lymphoma (DLBCL) and ≥2 prior therapies: Pivotal Phase II expansion results

Michael Dickinson[1], Carmelo Carlo-Stella[2], Franck Morschhauser[3], Emmanuel Bachy[4], Paolo Corradini[5], Gloria Iacoboni[6], Cyrus Khan[7], Tomasz Wrobel[8], Fritz Offner[9], Marek Trneny[10], Shang-Ju Wu[11], Guillaume Cartron[12], Mark Hertzberg[13], Anna Sureda Balari[14], David Perez-Callejo[15], Linda Lundberg[15], James Relf[16], Emma Clark[16], Kathryn Humphrey[16], Martin Hutchings[17]

[1]Peter MacCallum Cancer Centre, Royal Melbourne Hospital and The University of Melbourne, Melbourne, VIC, Australia; [2]Humanitas University and IRCCS Humanitas Research Hospital, Milan, Italy; [3]Hôpital Claude Huriez and CHU de Lille, Lille, France; [4]Centre Hospitalier Lyon-Sud, Lyon, France; [5]Università degli Studi di Milano and Fondazione Istituti di Ricovero e Cura a Carattere Scientifico (IRCSS) Istituto Nazionale dei Tumori, Milan, Italy; [6]Vall d'Hebron University Hospital, Barcelona, Spain; [7]Allegheny Health Network, Pittsburgh, PA, USA; [8]Uniwersytet Medyczny we Wrocławiu, Wroclaw, Poland; [9]Universitair Ziekenhuis Gent, Ghent, Belgium; [10]Charles University Hospital, Prague, Czech Republic; [11]National Taiwan University Hospital, Taipei, Taiwan; [12]CHU de Montpellier, Montpellier, France; [13]Prince of Wales Hospital and University of New South Wales, Sydney, NSW, Australia; [14]Institut Català d'Oncologia Hospitalet, Barcelona, Spain; [15]F. Hoffmann-La Roche Ltd, Basel, Switzerland; [16]Roche Products Ltd, Welwyn Garden City, United Kingdom; [17]Rigshospitalet, Copenhagen, Denmark.

Dickinson M *et al*. Oral presentation at ASCO 2022; Chicago, IL, USA, June 3–7, 2022 (Abstract 7500).

Study overview

Pivotal Phase II expansion in patients with R/R DLBCL and ≥2 prior therapies (NP30179)

Key inclusion criteria

- DLBCL NOS, HGBCL, transformed FL, or PMBCL
- ECOG PS: 0–1
- ≥2 prior therapies including:
  - Anti-CD20 antibody
  - Anthracycline

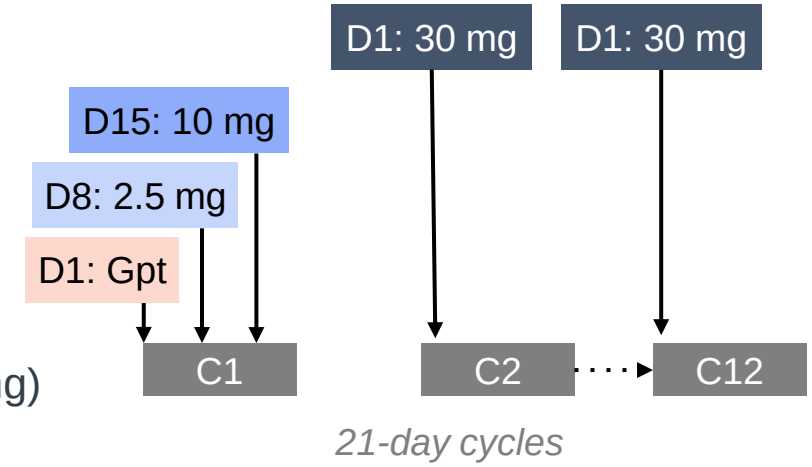
Glofitamab IV administration

Fixed-duration treatment

- Maximum 12 cycles

CRS mitigation:

- Gpt (1 × 1,000 mg)
- C1 step-up dosing
- Monitoring after first glofitamab dose (2.5 mg)



Endpoints

- **Primary: CR (best response) rate by IRC***
- **Key secondary:** ORR,† DoR, DoCR,† PFS, and OS

*By PET-CT (Lugano criteria). †By IRC and investigator.
C, Cycle; CD, cluster of differentiation; CR, complete response; CRS, cytokine release syndrome; D, Day; DLBCL, diffuse large B-cell lymphoma; DoCR, duration of complete response; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group Performance Status; FL, follicular lymphoma; Gpt, obinutuzumab pretreatment; HGBCL, high-grade B-cell lymphoma; IRC, independent review committee; IV, intravenous; NOS, not otherwise specified; ORR, overall response rate; OS, overall survival; PET-CT, positron emission tomography–computed tomography; PFS, progression-free survival; PMBCL, primary mediastinal large B-cell lymphoma; R/R, relapsed/refractory.
Dickinson M *et al*. Oral presentation at ASCO 2022; Chicago, IL, USA, June 3–7, 2022 (Abstract 7500).

Baseline characteristics

Heavily pretreated, highly refractory population

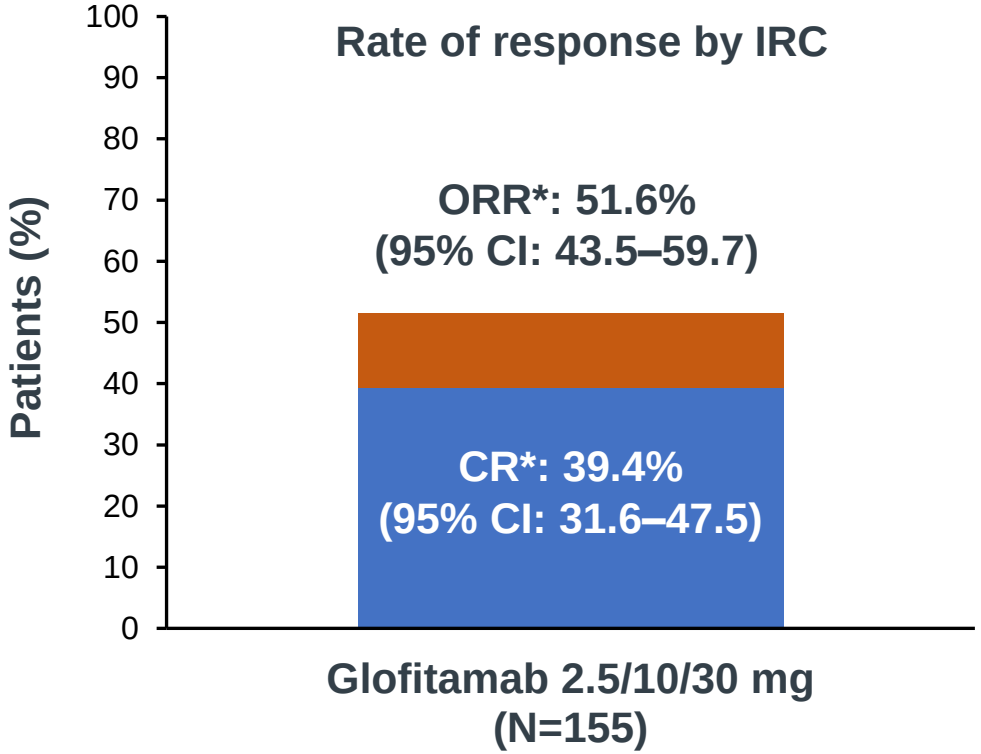
n (%)*		N=154†
Median (range) age, years		66.0 (21–90)
Male		100 (64.9)
ECOG PS‡	0	69 (44.8)
	1	84 (54.5)
Ann Arbor stage	I	10 (6.5)
	II	25 (16.2)
	III	31 (20.1)
	IV	85 (55.2)
NHL subtype	DLBCL	110 (71.4)
	trFL	27 (17.5)
	HGBCL	11 (7.1)
	PMBCL	6 (3.9)
Bulky disease	>6 cm	64 (41.6)
	>10 cm	18 (11.7)

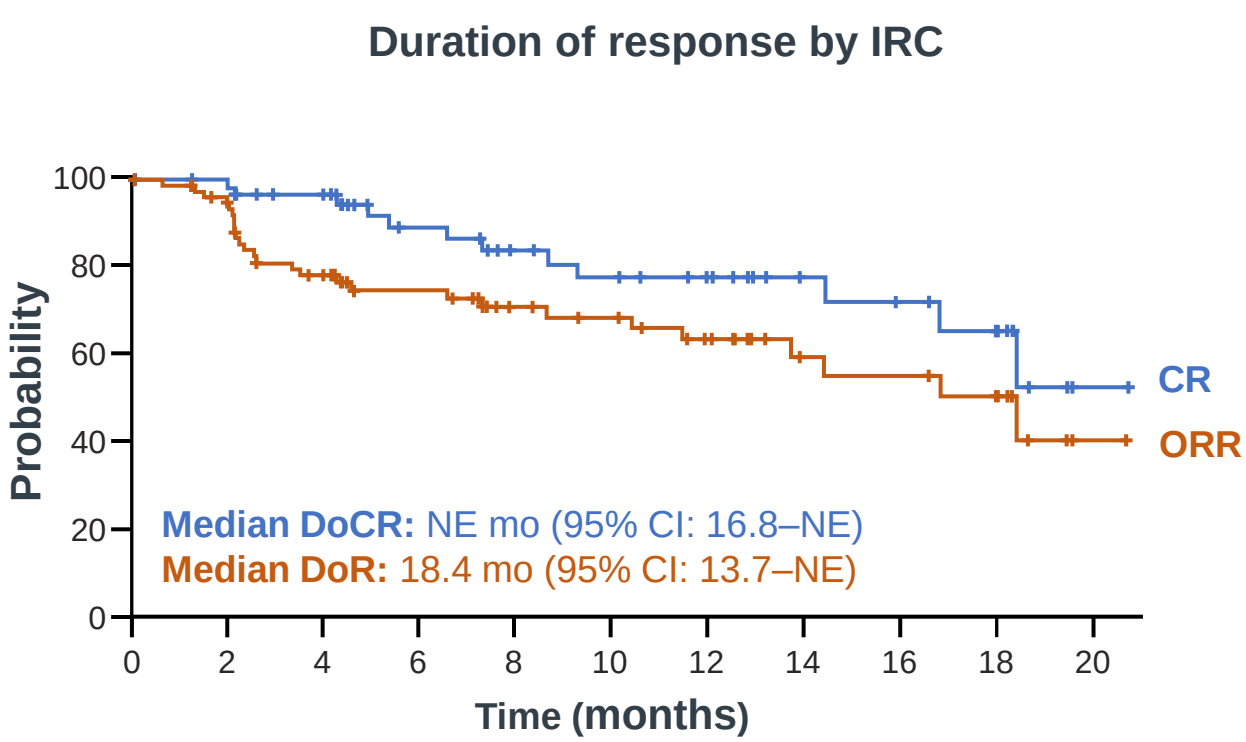
n (%)*	N=154†
Median (range) no. of prior lines, n	3 (2–7)
2 prior lines	62 (40.3)
≥3 prior lines	92 (59.7)
Prior anti-CD20 Ab therapy	154 (100.0)
Prior anthracycline therapy	149 (96.8)
Prior CAR-T therapy	51 (33.1)
Prior ASCT	28 (18.2)
Refractory to any prior therapy	139 (90.3)
Refractory to last prior therapy	132 (85.7)
Primary refractory	90 (58.4)
Refractory to prior CAR-T therapy	46 (29.9)
Refractory to any prior anti-CD20	128 (83.1)

Clinical cut-off date: March 14, 2022. *Unless otherwise specified. †Safety-evaluable population (all treated patients). ‡ECOG PS: 2, n=1 (0.6%).
Ab, antibody; ASCT, autologous stem cell transplant; CAR-T, chimeric antigen receptor T-cell; CD, cluster of differentiation; DLBCL, diffuse large B-cell lymphoma; ECOG PS, Eastern Cooperative Oncology Group Performance Status; HGBCL, high-grade B-cell lymphoma; NHL, non-Hodgkin lymphoma; PMBCL, primary mediastinal large B-cell lymphoma; trFL, transformed follicular lymphoma.
Dickinson M *et al*. Oral presentation at ASCO 2022; Chicago, IL, USA, June 3–7, 2022 (Abstract 7500).

Response rates

High CR/ORR rate and durable response after cessation of therapy





- At the time of the primary analysis, the primary endpoint was met in the primary efficacy population (n=108)†
  - 35.2% CR rate by IRC significantly greater (*P*<0.0001) than 20% historical control CR rate‡

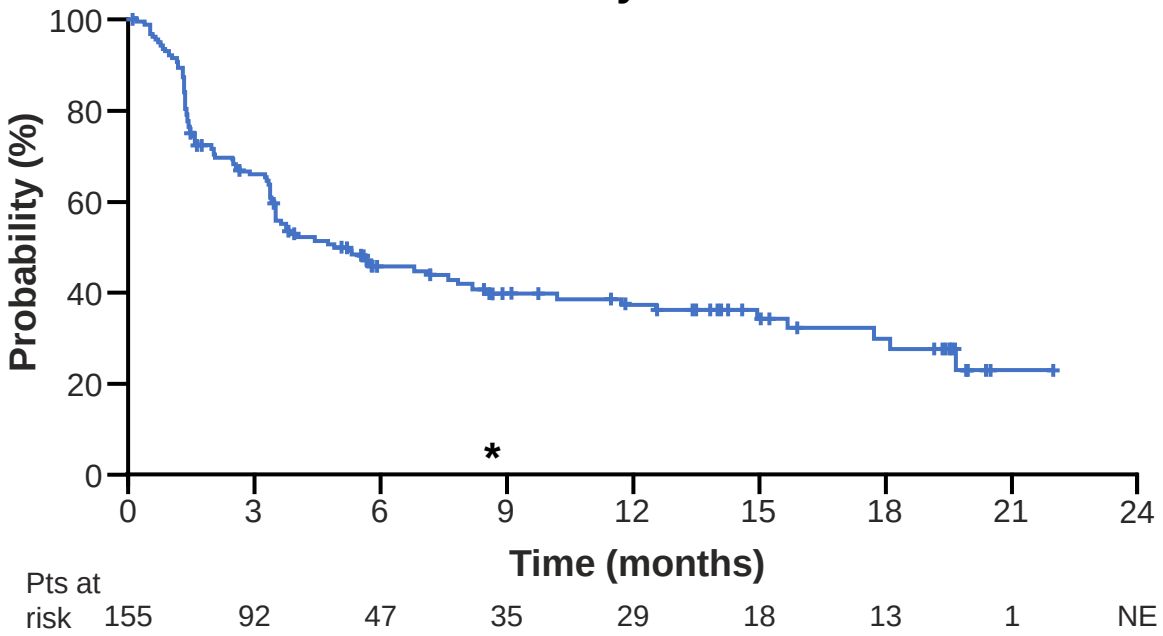
*Best response by intent-to-treat population; †the pivotal expansion cohort population; ‡the historical control CR rate was pre-specified based on a meta-analysis in patients with R/R DLBCL (where most [≥50%] had received ≥2 prior therapies) and compared with the CR rate in the primary efficacy-evaluable population using an exact binomial test (2-sided alpha level: 5%). CR, complete response; DoCR, duration of complete response; DoR, duration of response; IRC, Independent Review Committee; mo, months; NE, not estimable; ORR, overall response rate.

Dickinson M et al. Abstract 7500. Oral presentation at 2022 ASCO Annual Meeting; Chicago, Illinois, US. June 3–7. 2022.

Time-to-event endpoints

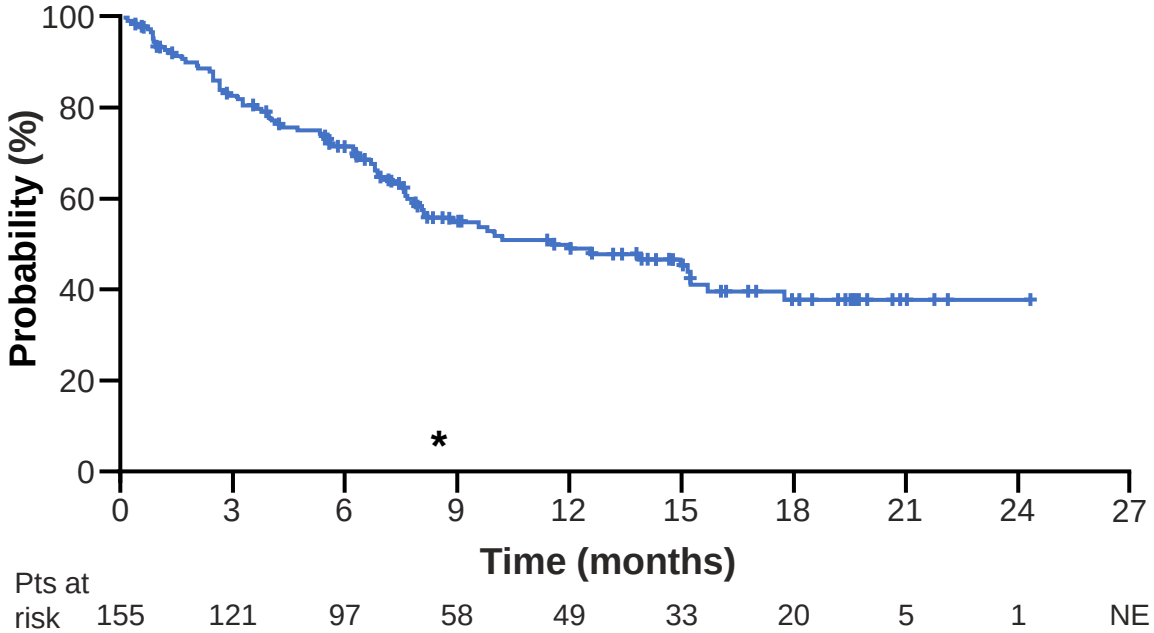
Clinically significant freedom from progression at 12 months and long-term OS

PFS by IRC



	N=155
Median PFS follow-up, months (range)	12.6 (0–22)
Median PFS, months (95% CI)‡	4.9 (3.4–8.1)
6-month event-free rate, % (95% CI)	45.5 (37.2–53.8)
12-month event-free rate, % (95% CI)	37.1 (28.5–45.8)

OS†



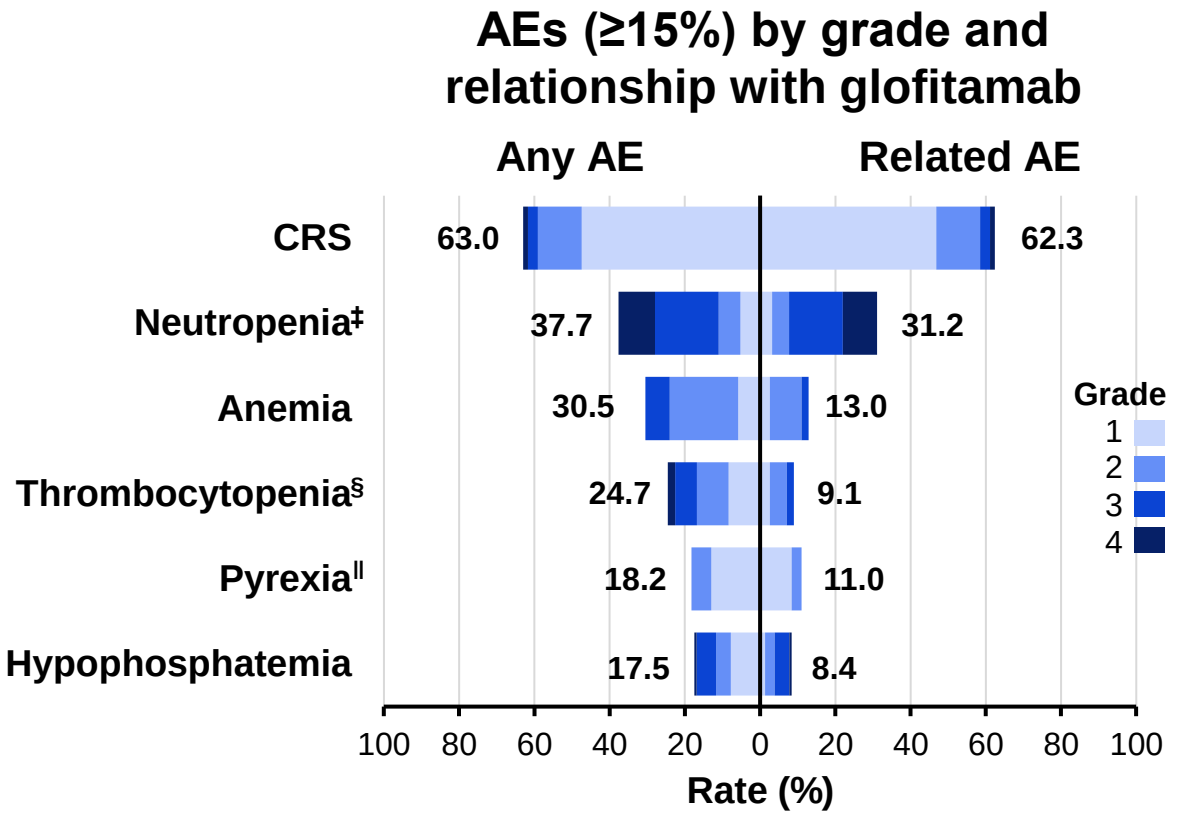
	N=155
Median OS, months (95% CI)‡	11.5 (7.9–15.7)
12-month OS rate, % (95% CI)	49.8 (41.1–58.5)

*Maximum treatment length. †Includes five deaths due to COVID-19. ‡Kaplan–Meier estimates.
CI, confidence interval; COVID-19, coronavirus disease 2019; IRC, independent review committee; NE, not estimable; OS, overall survival; PFS, progression-free survival; Pts, patients.
Dickinson M *et al*. Oral presentation at ASCO 2022; Chicago, IL, USA, June 3–7, 2022 (Abstract 7500).

Glofitamab safety profile

Glofitamab was well tolerated, with a manageable safety profile

n (%)*	N=154
Median no. of cycles received (range)	5 (1–13)
Median relative dose intensity, % (range)	100 (94–100)
AE Related AE	152 (98.7) 140 (90.9)
Grades 3–4 AE Related AE	87 (56.5) 64 (41.6)
Serious AE Related AE	73 (47.4) 46 (29.9)
Grade 5 (fatal AE) Related AEs	8 (5.2)† 0
AE leading to treatment discontinuation Related AE	14 (9.1) 5 (3.2)



CRS was mostly low grade, time of onset was predictable, and most events occurred during C1

*Unless otherwise specified. †COVID-19/COVID-19 pneumonia (n=5); sepsis (n=2); delirium (n=1). ‡Includes neutrophil count decreased. §Includes platelet count decreased. ‖Pyrexia events separate from CRS.
AE, adverse event; COVID-19, coronavirus disease 2019; CRS, cytokine release syndrome.
Dickinson M *et al*. Oral presentation at ASCO 2022; Chicago, IL, USA, June 3–7, 2022 (Abstract 7500).

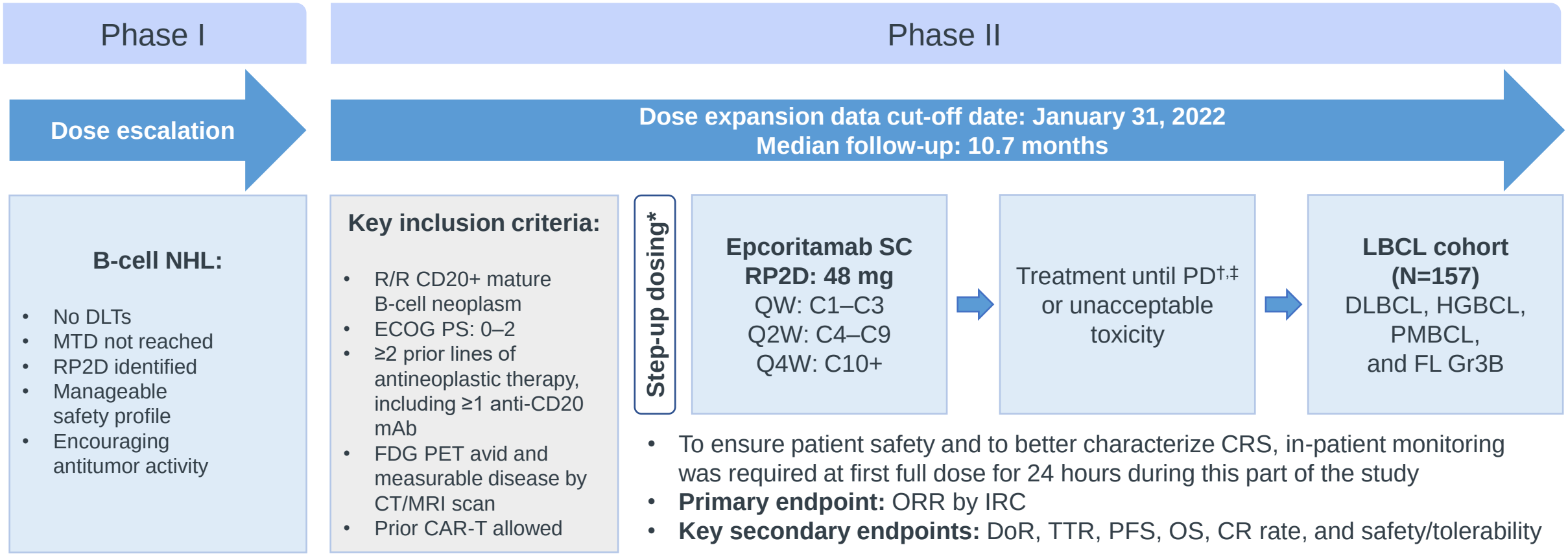
Subcutaneous epcoritamab in patients with relapsed or refractory large B-cell lymphoma (EPCORE NHL-1): Pivotal results from a Phase 2 study

Catherine Thieblemont[1], Tycel Phillips[2], Herve Ghesquieres[3], Chan Y. Cheah[4], Michael Roost Clausen[5], David Cunningham[6], Young Rok Do[7], Tatyana Feldman[8], Robin Gasiorowski[9], Wojciech Jurczak[10], Tae Min Kim[11], David John Lewis[12], Marjolein van der Poel[13], Michelle Limei Poon[14], Thomas Doerr[15], Nurgul Kilavuz[16], Menghui Chen[16], Mariana Sacchi[16], Brian Elliott[16], Martin Hutchings[17], Pieternella Lugtenburg[18]

[1]Assistance Publique & Hôpitaux de Paris (APHP), Hôpital Saint-Louis, Hémato-oncologie, Université de Paris, Paris, France; [2]University of Michigan Comprehensive Cancer Center, Ann Arbor, MI, USA; [3]Hospices Civils de Lyon, Centre Hospitalier Lyon Sud, Pierre-Bénite, France; [4]Sir Charles Gairdner Hospital, Nedlands, Australia; [5]Vejle Hospital, Vejle, Denmark; [6]The Royal Marsden NHS Foundation Trust, Sutton, UK; [7]Keimyung University Dongsan Medical Center, Daegu, Republic of Korea; [8]Hackensack Meridian Health Hackensack University Medical Center, Hackensack, NJ, USA; [9]Concord Hospital, University of Sydney, Sydney, Australia; [10]MSC National Research Institute of Oncology, Kraków, Poland; [11]Seoul National University Hospital, Seoul, Republic of Korea; [12]University Hospitals Plymouth NHS Trust, Derriford Hospital, Plymouth, UK; [13]On behalf of the Lunenburg Lymphoma Phase I/II Consortium-HOVON/LLPC, Maastricht, Department of Internal Medicine, Division of Hematology, GROW School for Oncology and Developmental Biology, Maastricht University Medical Center, Maastricht, Netherlands; [14]National University Hospital, Singapore; [15]AbbVie, North Chicago, IL, USA; [16]Genmab, Princeton, NJ, USA; [17]Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark; [18]On behalf of the Lunenburg Lymphoma Phase I/II Consortium-HOVON/LLPC, Erasmus MC Cancer Institute, University Medical Center, Department of Hematology, Rotterdam, Netherlands.

Thieblemont C *et al*. Oral presentation at EHA 2022; Vienna, Austria, June 9–17, 2022 (Abstract LB2364).

EPCORE NHL-1: LBCL expansion cohort



- To ensure patient safety and to better characterize CRS, in-patient monitoring was required at first full dose for 24 hours during this part of the study
- **Primary endpoint:** ORR by IRC
- **Key secondary endpoints:** DoR, TTR, PFS, OS, CR rate, and safety/tolerability

*Step-up dosing (priming 0.16 mg dosing and intermediate 0.8 mg dosing before first full dose) and corticosteroid prophylaxis were used to mitigate CRS. †Radiographic disease evaluation was performed every 6 weeks for the first 24 weeks (6, 12, 18, and 24 weeks), then every 12 weeks (36 and 48 weeks), and every 6 months thereafter. ‡Measurable disease with CT or MRI scan with involvement of ≥2 lesions/nodes with a long axis >1.5 cm and a short axis >1.0 cm (or 1 lesion/node with a long axis >2.0 cm and a short axis ≥1.0 cm) and FDG PET scan that demonstrated positive lesion(s) compatible with CT-defined (or MRI-defined) anatomic tumor sites for FDG-avid lymphomas. C, Cycle; CAR-T, chimeric antigen receptor T-cell; CD, cluster of differentiation; CR, complete response; CRS, cytokine release syndrome; CT, computed tomography; DLBCL, diffuse large B-cell lymphoma; DLT, dose-limiting toxicity; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group Performance Status; FDG, fluorodeoxyglucose; FL Gr3B, follicular lymphoma Grade 3B; HGBCL, high-grade B-cell lymphoma; IRC, independent review committee; LBCL, large B-cell lymphoma; mAb, monoclonal antibody; MRI, magnetic resonance imaging; MTD, maximum tolerated dose; NHL, non-Hodgkin lymphoma; ORR, overall response rate; OS, overall survival; PD, progressive disease; PET, positron emission tomography; PFS, progression-free survival; PMBCL, primary mediastinal large B-cell lymphoma; Q2W, every 2 weeks; Q4W, every 4 weeks; QW, once a week; RP2D, recommended Phase II dose; R/R, relapsed/refractory; SC, subcutaneous; TTR, time to response. ClinicalTrials.gov NCT03625037. Available at: https://clinicaltrials.gov/ct2/show/NCT03625037. Accessed September 2022. Thieblemont C *et al*. Oral presentation at EHA 2022; Vienna, Austria, June 9–17, 2022 (Abstract LB2364).

Patients were challenging to treat and highly refractory

Demographics	LBCL, N=157
Median age (range), years	64 (20–83)
<65, n (%)	80 (51)
65 to <75, n (%)	48 (31)
≥75, n (%)	29 (18)
ECOG PS, n (%)	
0	74 (47)
1	78 (50)
2	5 (3)

Disease characteristics*	LBCL, N=157
Disease type, n (%)	
DLBCL	139 (89)
De novo	97/139 (70)
Transformed	40/139 (29)
Unknown	2/139 (1)
HGBCL	9 (6)
PMBCL	4 (3)
FL Gr3B	5 (3)

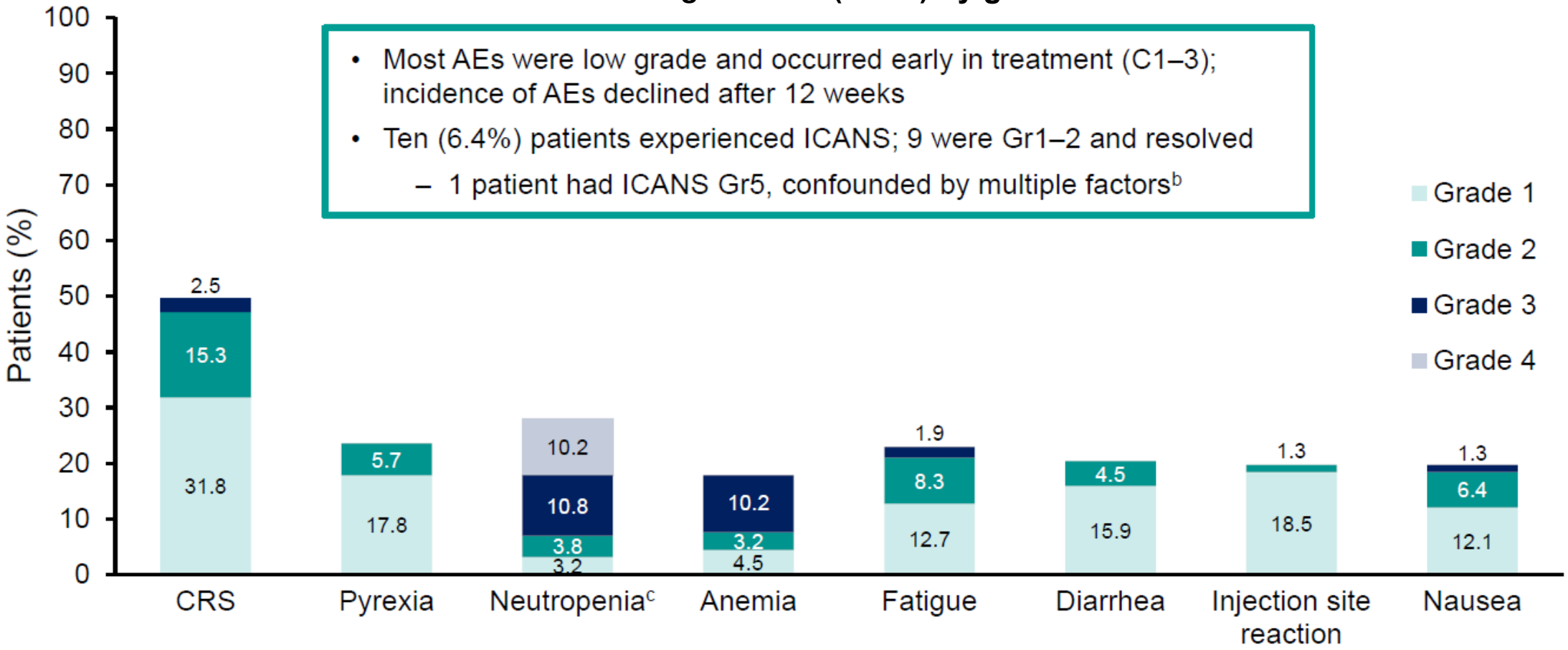
Prior treatments	LBCL, N=157
Median time from initial diagnosis to first dose, years	1.6
Median time from end of last therapy to first dose, months	2.4
Median no. of prior lines of therapy (range)	3 (2–11)
≥3 prior lines of therapy, n (%)	111 (71)
Primary refractory† disease, n (%)	96 (61)
Refractory† to last systemic therapy, n (%)	130 (83)
Refractory† to ≥2 consecutive lines of therapy, n (%)	119 (76)
Prior ASCT criteria, n (%)	31 (20)
Prior CAR-T therapy, n (%)	61 (39)
Progressed within 6 months of CAR-T therapy	46/61 (75)

*Double-/triple-hit patients included, many with responses. †Refractory disease is defined as disease that either progressed during therapy or progressed within <6 months of completion of therapy.
ASCT, autologous stem cell transplant; CAR-T, chimeric antigen receptor T-cell; DLBCL, diffuse large B-cell lymphoma; ECOG PS, Eastern Cooperative Oncology Group Performance Status; FL Gr3B, follicular lymphoma Grade 3B; HGBCL, high-grade B-cell lymphoma; LBCL, large B-cell lymphoma; PMBCL, primary mediastinal large B-cell lymphoma.
Thieblemont C *et al*. Oral presentation at EHA 2022; Vienna, Austria, June 9–17, 2022 (Abstract LB2364).

Adverse events were primarily low grade

Treatment-emergent AEs[a] (≥15%) by grade

- Most AEs were low grade and occurred early in treatment (C1–3); incidence of AEs declined after 12 weeks
- Ten (6.4%) patients experienced ICANS; 9 were Gr1–2 and resolved
  - 1 patient had ICANS Gr5, confounded by multiple factors[b]



[a]COVID-19 incidence: 4.5%. [b]Patient experienced ICANS after intermediate dose with multiple confounders, including extensive opioid use for Gr3 pancreatitis, hyperammonemia, multifocal cerebral infarcts in the setting of possible microangiography, and tocilizumab administration. [c]Combined term includes neutropenia and decreased neutrophil count.

AE, adverse event; C, Cycle; COVID-19, coronavirus disease 2019; CRS, cytokine release syndrome; Gr, Grade; ICANS, immune effector cell–associated neurotoxicity syndrome.

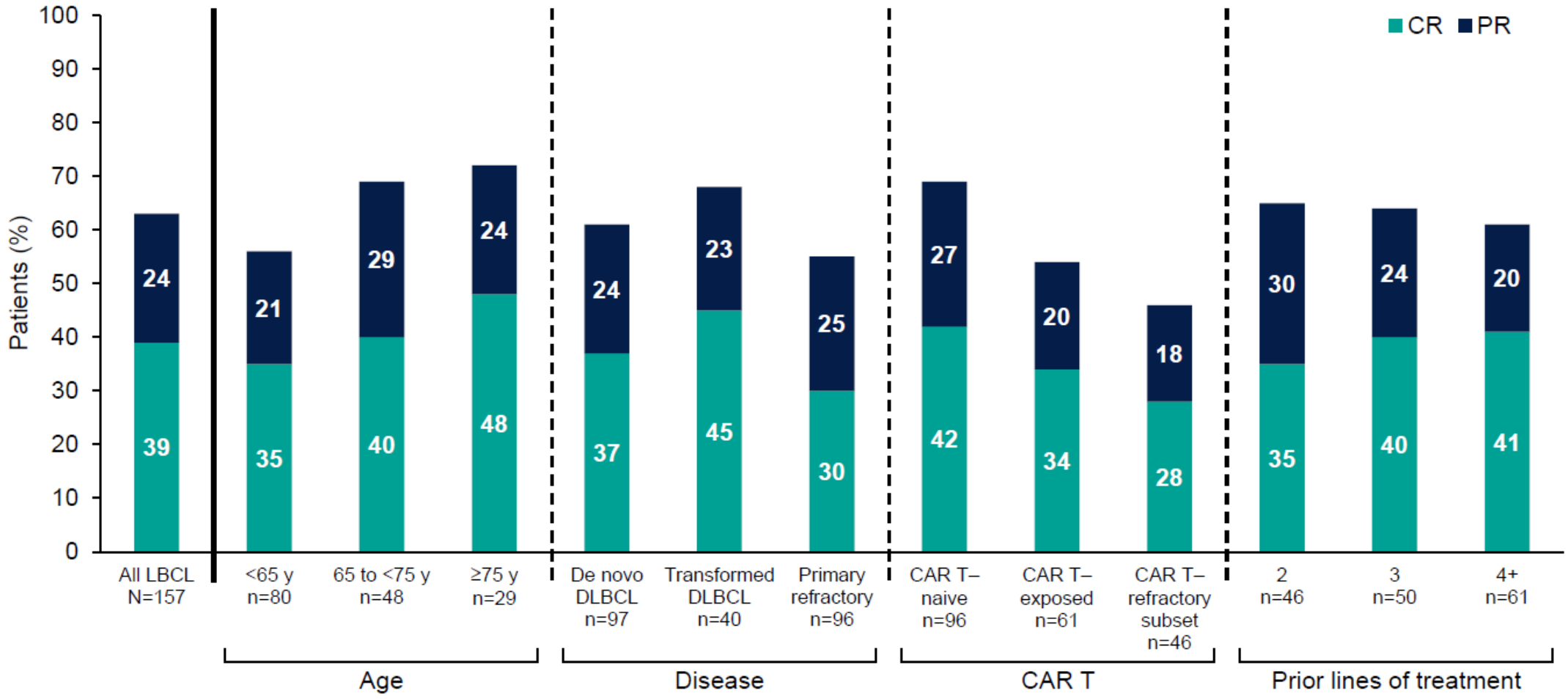
Thieblemont C *et al*. Oral presentation at EHA 2022; Vienna, Austria, June 9–17, 2022 (Abstract LB2364).

High response rates observed

Best overall response by IRC, n (%)*	LBCL, N=157
Overall response	**99 (63) [95% CI: 55–71]**
Complete response	**61 (39) [95% CI: 31–47]**
Partial response	38 (24)
Stable disease	5 (3)
Progressive disease	37 (24)

*Based on Lugano criteria.
CI, confidence interval; IRC, independent review committee; LBCL, large B-cell lymphoma.
Thieblemont C *et al*. Oral presentation at EHA 2022; Vienna, Austria, June 9–17, 2022 (Abstract LB2364).

Deep responses consistent across key subgroups



Based on IRC assessment and Lugano criteria.
CAR T, chimeric antigen receptor T-cell; CR, complete response; DLBCL, diffuse large B-cell lymphoma; IRC, independent review committee; LBCL, large B-cell lymphoma; PR, partial response.
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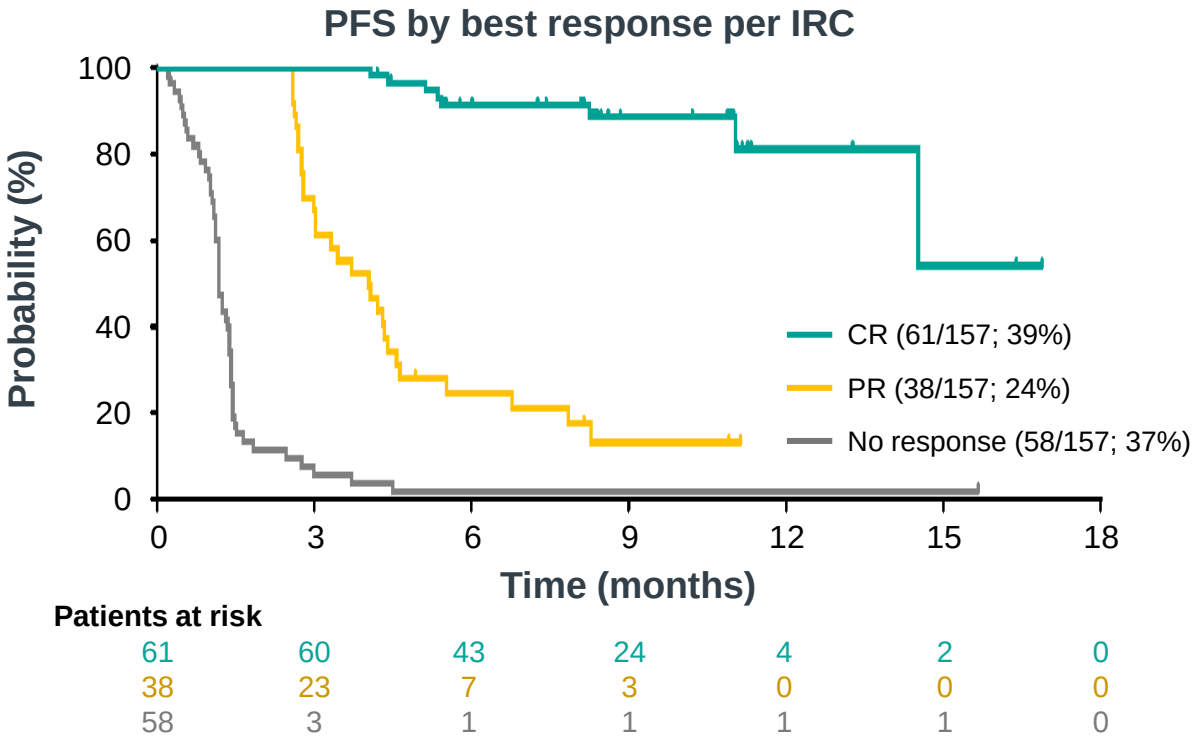
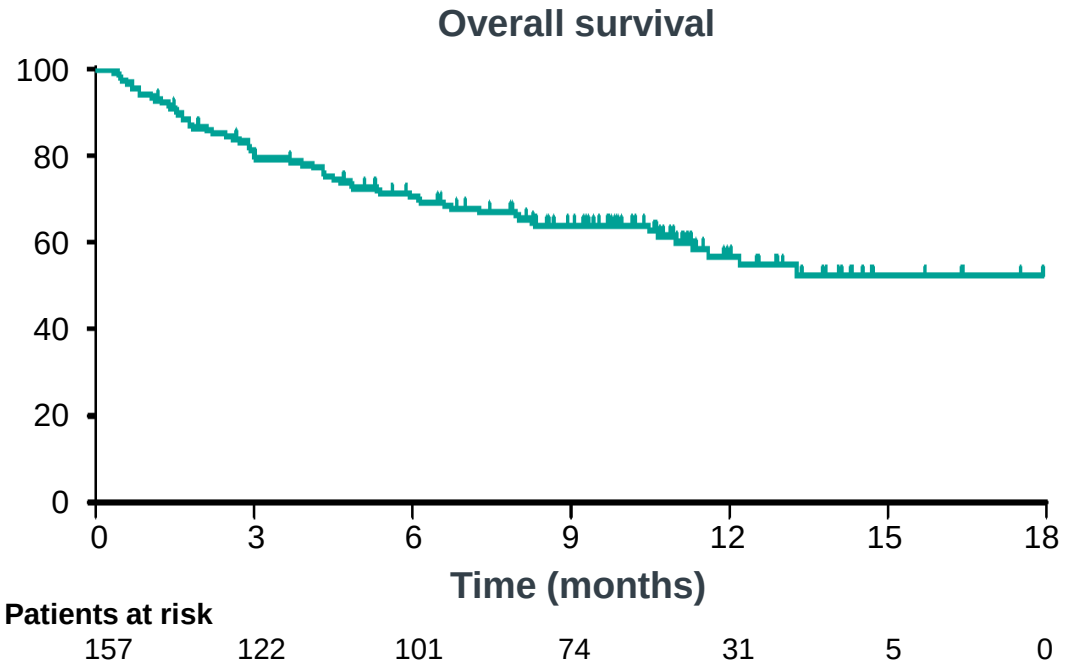
Survival outcomes





Kaplan-Meier estimate	
Median PFS for complete responders	Not reached
Complete responders remaining in CR at Month 9	89%
Median PFS, months (95% CI)	4.4 (3.0–7.9)
PFS rate at Month 6, % (95% CI)	43.9 (35.7–51.7)

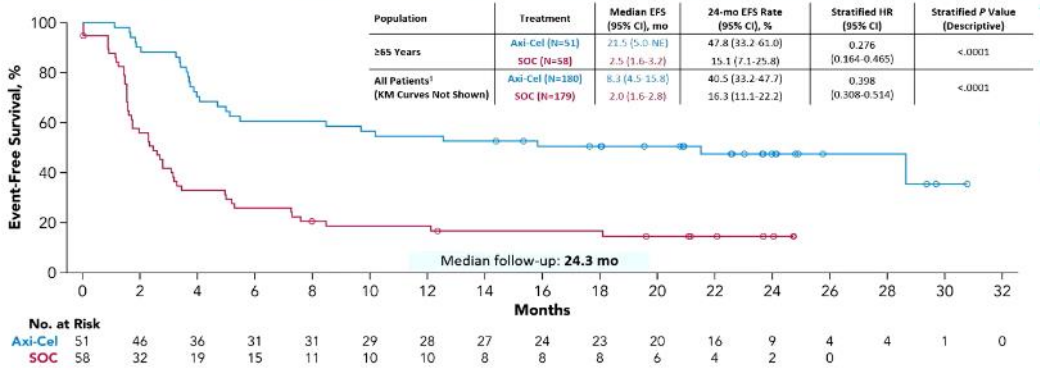
Kaplan-Meier estimate	
Median OS	Not reached
OS rate at Month 6, % (95% CI)	70.6 (62.7–77.2)
OS rate at Month 12, % (95% CI)	56.9 (47.3–65.4)

CI, confidence interval; CR, complete response; IRC, international review committee; PFS, progression free survival; OS, overall survival; PR, partial response.

Thieblemont C *et al*. Oral presentation at EHA 2022; Vienna, Austria, June 9–17, 2022 (Abstract LB2364).

Clinical and patient-reported outcomes in a Phase 3, randomized study evaluating axicabtagene ciloleucel (axi-cel) versus SoC therapy in elderly pts with R/R LBCL (ZUMA-7)

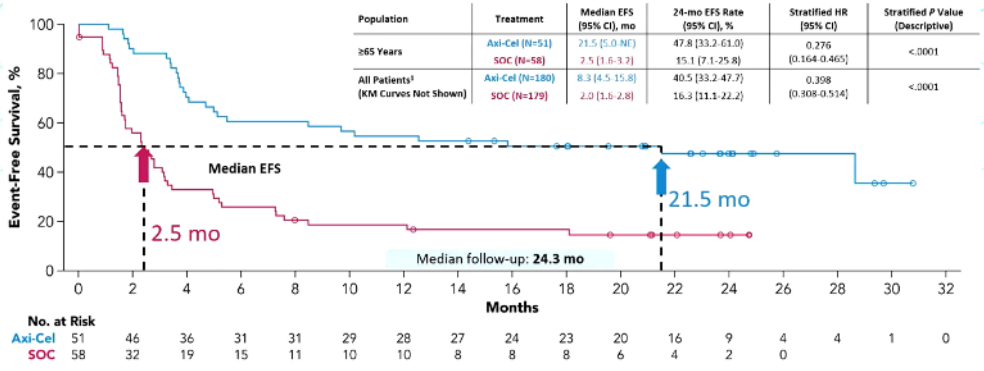
Primary Endpoint: Event-Free Survival per Blinded Central Review in Patients Aged ≥65 Years



Population	Treatment	Median EFS (95% CI), mo	24-mo EFS Rate (95% CI), %	Stratified HR (95% CI)	Stratified *P* Value (Descriptive)
≥65 Years	Axi-Cel (N=51)	21.5 (5.0-NE)	47.8 (33.2-61.0)	0.276 (0.164-0.465)	<.0001
	SOC (N=58)	2.5 (1.6-3.2)	15.1 (7.1-25.8)		
All Patients[1] (KM Curves Not Shown)	Axi-Cel (N=180)	8.3 (4.5-15.8)	40.5 (33.2-47.7)	0.398 (0.308-0.514)	<.0001
	SOC (N=179)	2.0 (1.6-2.8)	16.3 (11.1-22.2)		

- The primary endpoint of EFS showed that treatment with axi-cel was superior to SOC (HR, 0.276, descriptive *P*<.0001)

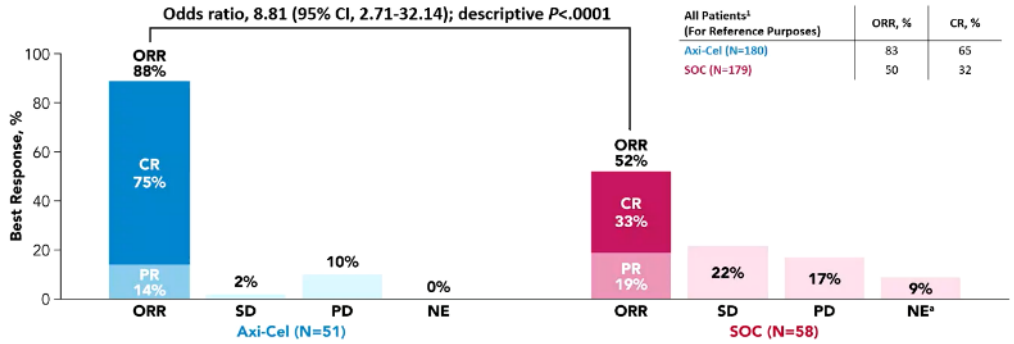
Primary Endpoint: Event-Free Survival per Blinded Central Review in Patients Aged ≥65 Years



Population	Treatment	Median EFS (95% CI), mo	24-mo EFS Rate (95% CI), %	Stratified HR (95% CI)	Stratified *P* Value (Descriptive)
≥65 Years	Axi-Cel (N=51)	21.5 (5.0-NE)	47.8 (33.2-61.0)	0.276 (0.164-0.465)	<.0001
	SOC (N=58)	2.5 (1.6-3.2)	15.1 (7.1-25.8)		
All Patients[1] (KM Curves Not Shown)	Axi-Cel (N=180)	8.3 (4.5-15.8)	40.5 (33.2-47.7)	0.398 (0.308-0.514)	<.0001
	SOC (N=179)	2.0 (1.6-2.8)	16.3 (11.1-22.2)		

- With 24.3-months median follow-up, median EFS was longer with axi-cel versus SOC (21.5 months [95% CI, 5.0-NE] vs 2.5 months [95% CI, 1.6-3.2], respectively) in patients aged 65 years or older

Objective Response Rate in Patients Aged ≥65 Years



All Patients[1] (For Reference Purposes)	ORR, %	CR, %
Axi-Cel (N=180)	83	65
SOC (N=179)	50	32

- ORR was higher with axi-cel versus SOC (descriptive *P*<.0001), and CR rate of the axi-cel arm was over double that of the SOC arm (75% vs 33%, respectively)

Safety Overview in Patients Aged ≥65 Years

Adverse Events, n (%)	Axi-Cel n=49		SOC n=55	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Any AE, n (%)[a,b]	**49 (100)**	**46 (94)**	**55 (100)**	**45 (82)**
Pyrexia	47 (96)	4 (8)	14 (25)	0 (0)
Neutropenia[c]	39 (80)	39 (80)	24 (44)	24 (44)
Nausea	23 (47)	1 (2)	37 (67)	3 (5)
Any serious AE, n (%)[d]	**29 (59)**	**25 (51)**	**26 (47)**	**23 (42)**
Reason for deaths, n (%)				
Progressive disease	19 (39)		20 (36)	
Grade 5 AEs during protocol-specified reporting period	1 (2)[e]		1 (2)[f]	
Definitive therapy–related mortality	0 (0)		1 (2)[f]	
Other[g]	1 (2)		5 (9)	

- Safety profile of axi-cel was manageable and consistent with previous studies in refractory LBCL[1]

Key results
(All patients: axi-cel n=180; SOC n=179)
Patients ≥65 years: axi-cel n=51; SOC n=58

- KM estimates of 24-month EFS rates: axi-cel 47.8% vs. SOC 15.1%
- CR: axi-cel 75% vs. SOC 33%
- Median OS: axi-cel 28.6 mo vs. SOC NR

Conclusions
Axi-cel demonstrated superiority over 2L SOC in patients ≥65 years with significantly improved EFS and a manageable safety profile

2L, second-line; AE, adverse event; axi-cel, axicabtagene ciloleucel; CI, confidence interval; CR, complete response; EFS, event-free survival; HR, hazard ratio; KM, Kaplan–Meier; LBCL, large B-cell lymphoma; mo, months; ORR, overall response rate; OS, overall survival; PD, progressive disease; PR, partial response; pts, patients; R/R, relapsed/refractory; SD, stable disease; SoC, standard of care.
Westin J *et al*. Oral presentation at ASCO 2022; Chicago, IL, USA, June 3–7, 2022 (Abstract 7548).

Primary results from the double-blind, placebo-controlled, Phase III SHINE study of ibrutinib in combination with bendamustine-rituximab and rituximab maintenance as a first-line treatment for older patients with mantle cell lymphoma

Michael Wang[1], Wojciech Jurczak[2], Mats Jerkeman[3], Judith Trotman[4], Pier Luigi Zinzani[5], Jan Andrzej Walewski[6], Jun Zhu[7], Stephen Spurgeon[8], Andre Goy[9], Paul A. Hamlin[10], David Belada[11], Muhit Ozcan[12], John Storring[13], David John Lewis[14], Jose Angel Hernandez Rivas[15], Todd Henninger[16], Sanjay Deshpande[16], Rui Qin[16], Steven Le Gouill[17], Martin H. Dreyling[18]

[1]The University of Texas MD Anderson Cancer Center, Houston, TX; [2]Maria Sklodowska-Curie National Research Institute of Oncology, Krakow, Poland; [3]Skane University Hospital and Lund University, Lund, Sweden; [4]Concord Repatriation General Hospital, University of Sydney, Sydney, NSW, Australia; [5]Institute of Hematology "Seragnoli" University of Bologna, Bologna, Italy; [6]Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland; [7]Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education), Department of Lymphoma, Peking University Cancer Hospital & Institute (Beijing Cancer Hospital), Beijing, China; [8]Division of Hematology and Medical Oncology, Oregon Health & Science University, Portland, OR; [9]John Theurer Cancer Center, Hackensack, NJ; [10]Memorial Sloan Kettering Cancer Center, New York, NY; [11]4th Department of Internal Medicine - Haematology, Charles University, Hospital and Faculty of Medicine, Hradec Kralove, Czech Republic; [12]Ankara University School of Medicine, Ankara, Turkey; [13]The Research Institute of the McGill University Health Centre, McGill University, Montreal, QC, Canada; [14]University Hospitals Plymouth NHS Trust, Plymouth, United Kingdom; [15]Department of Hematology, Hospital Universitario Infanta Leonor, Universidad Complutense, Madrid, Spain; [16]Janssen Research & Development, Raritan, NJ; [17]Institut Curie comprehensive cancer center, Paris, France; Hospitalier Universitaire de Nantes, Centre de Recherche en Cancérologie et Immunologie Nantes Angers, INSERM, Université de Nantes, Nantes, France; [18]Klinikum der Universität München, LMU, Munich, Germany

Wang M *et al*. Oral presentation at ASCO 2022; Chicago, IL, USA, June 3–7, 2022 (Abstract LBA7502).

Study overview

Phase III study in older patients with MCL

Key inclusion criteria

- Previously untreated MCL
- ≥65 years of age
- Stage II–IV disease
- No planned stem cell transplant

Stratification factor

- Simplified MIPI score (low vs. intermediate vs. high)

N=523

R 1:1

BR induction for 6 cycles → If CR or PR → **Rituximab** maintenance every 8 weeks for 12 cycles

Ibrutinib 560 mg (4 capsules daily) until PD or unacceptable toxicity

BR induction for 6 cycles → If CR or PR → **Rituximab** maintenance every 8 weeks for 12 cycles

Placebo (4 capsules daily) until PD or unacceptable toxicity

Enrollment

Enrolled between May 2013 and November 2014 at 183 sites

Endpoints

- **Primary endpoint:** PFS (investigator-assessed) in the ITT population
- **Key secondary endpoints:** Response rate, TTNT, OS, safety

BR, bendamustine and rituximab; CR, complete response; ITT, intention-to-treat; MCL, mantle cell lymphoma; MIPI, Mantle Cell Lymphoma International Prognostic Index; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; R, randomized; TTNT, time to next treatment.

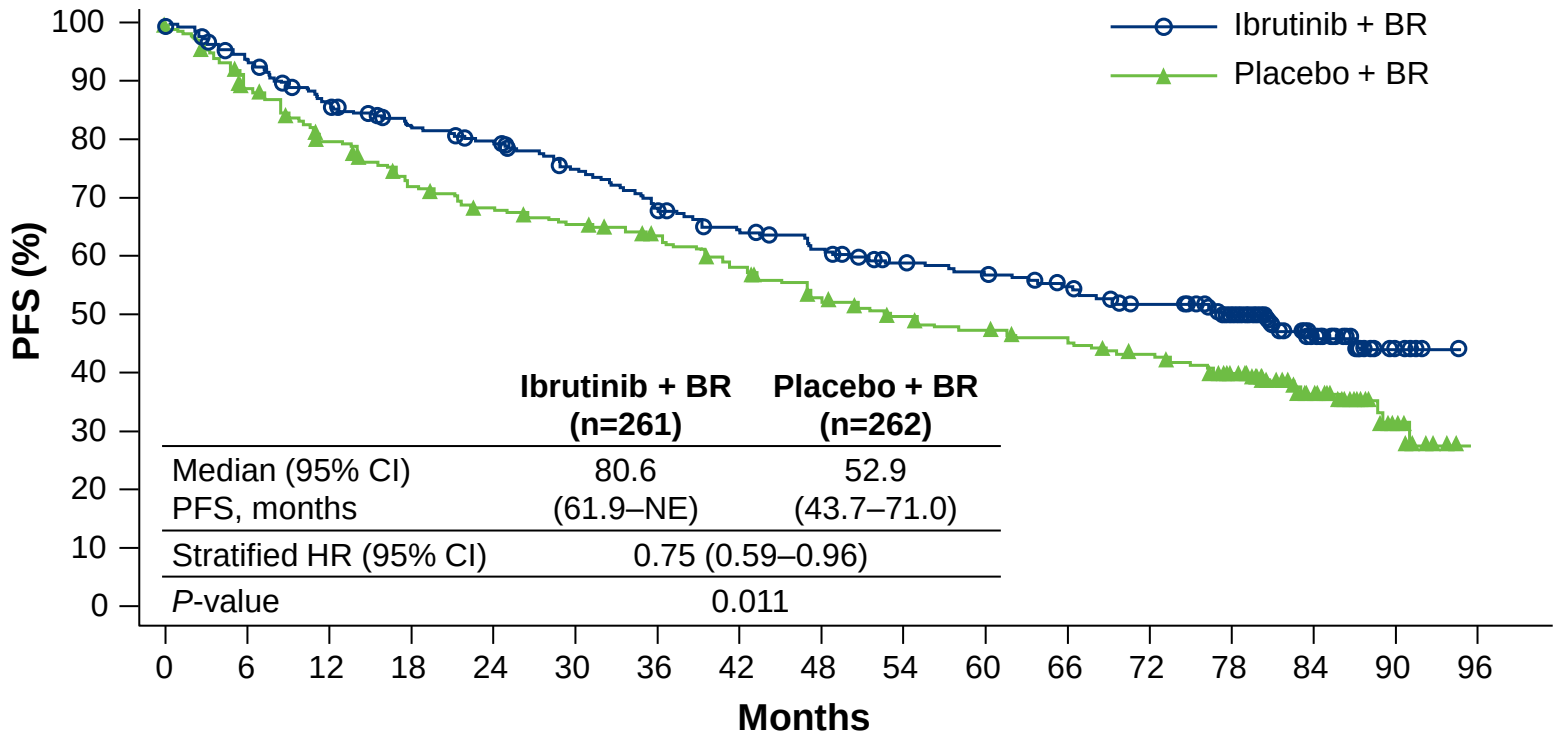
Wang M *et al*. Oral presentation at ASCO 2022; Chicago, IL, USA, June 3–7, 2022 (Abstract LBA7502).

Patient characteristics

	Ibrutinib + BR (n=261)	Placebo + BR (n=262)
Median (range) age, years	71 (65–86)	71 (65–87)
≥75 years, n (%)	74 (28.4)	82 (31.3)
Male, n (%)	178 (68.2)	186 (71.0)
ECOG PS 1, n (%)	127 (48.7)	118 (45.0)
Simplified MIPI, n (%)		
Low risk	44 (16.9)	46 (17.6)
Intermediate risk	124 (47.5)	129 (49.2)
High risk	93 (35.6)	87 (33.2)
Bone marrow involvement, n (%)	198 (75.9)	200 (76.3)
Blastoid/pleomorphic histology, n (%)	19 (7.3)	26 (9.9)
Extranodal, n (%)	234 (89.7)	226 (86.3)
Bulky (≥5 cm), n (%)	95 (36.4)	98 (37.4)
***TP53* mutated, n (%)**	26 (10.0)	24 (9.2)
***TP53* mutation status unknown, n (%)**	121 (46.4)	133 (50.8)

BR, bendamustine and rituximab; ECOG PS, Eastern Cooperative Oncology Group Performance Status; MIPI, Mantle Cell Lymphoma International Prognostic Index.
Wang M *et al*. Oral presentation at ASCO 2022; Chicago, IL, USA, June 3–7, 2022 (Abstract LBA7502).

Progression-free survival (all patients)



	Ibrutinib + BR (n=261)	Placebo + BR (n=262)
Median (95% CI) PFS, months	80.6 (61.9–NE)	52.9 (43.7–71.0)
Stratified HR (95% CI)	0.75 (0.59–0.96)	
P-value	0.011	

Patients at risk

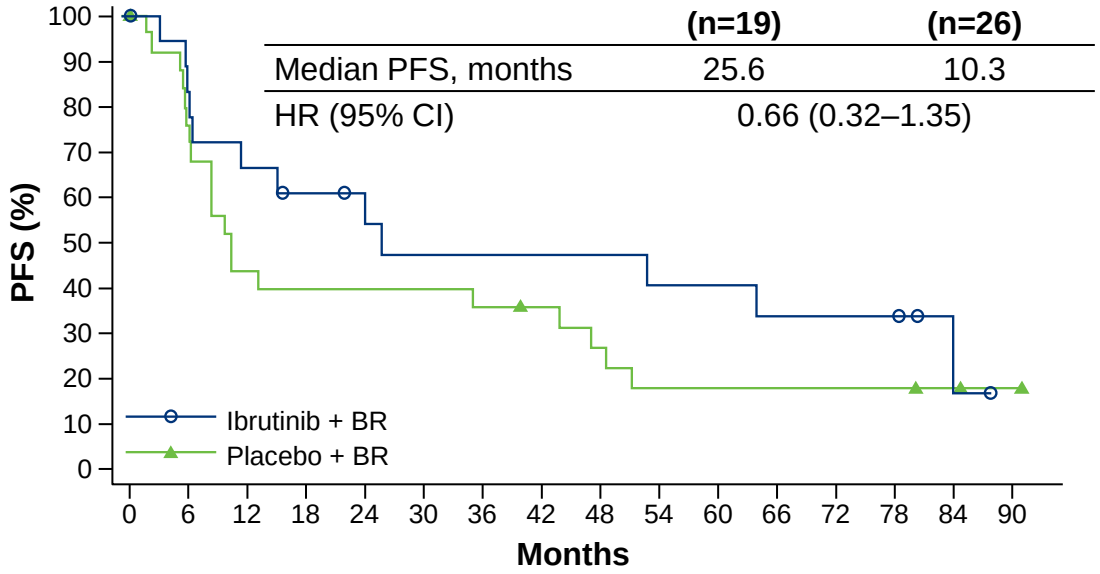
Ibrutinib + BR	261	228	207	191	182	167	152	139	130	120	115	106	95	78	39	11	0
Placebo + BR	262	226	199	177	166	158	148	135	119	109	103	98	90	78	41	11	0

- Ibrutinib + BR associated with a 25% reduction in risk of PD or death vs. placebo + BR
- Median PFS was 2.3 years longer with ibrutinib + BR vs. placebo + BR
  - 6.7 vs. 4.4 years; *P*=0.011

BR, bendamustine and rituximab; CI, confidence interval; HR, hazard ratio; NE, not evaluable; PD, progressive disease; PFS, progression-free survival.
Wang M *et al*. Oral presentation at ASCO 2022; Chicago, IL, USA, June 3–7, 2022 (Abstract LBA7502).

Progression-free survival (high-risk subgroups)

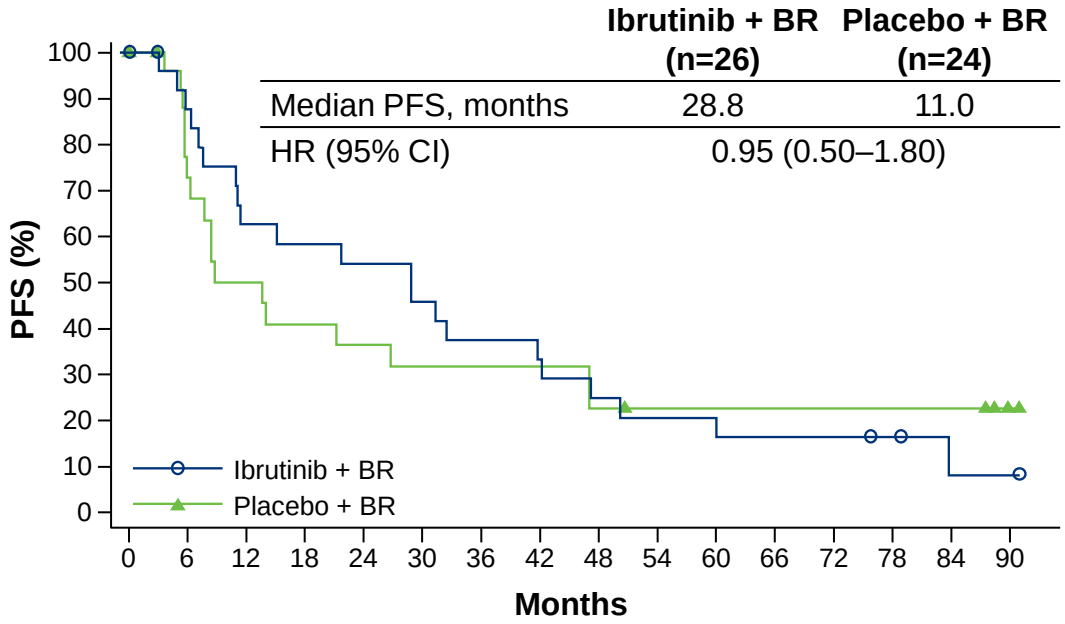
Blastoid/pleomorphic histology



Patients at risk

Ibrutinib + BR	19	14	12	10	8	7	7	7	7	6	6	5	5	5	1	0
Placebo + BR	26	19	11	10	10	10	9	8	6	4	4	4	4	4	3	1

TP53 mutation present

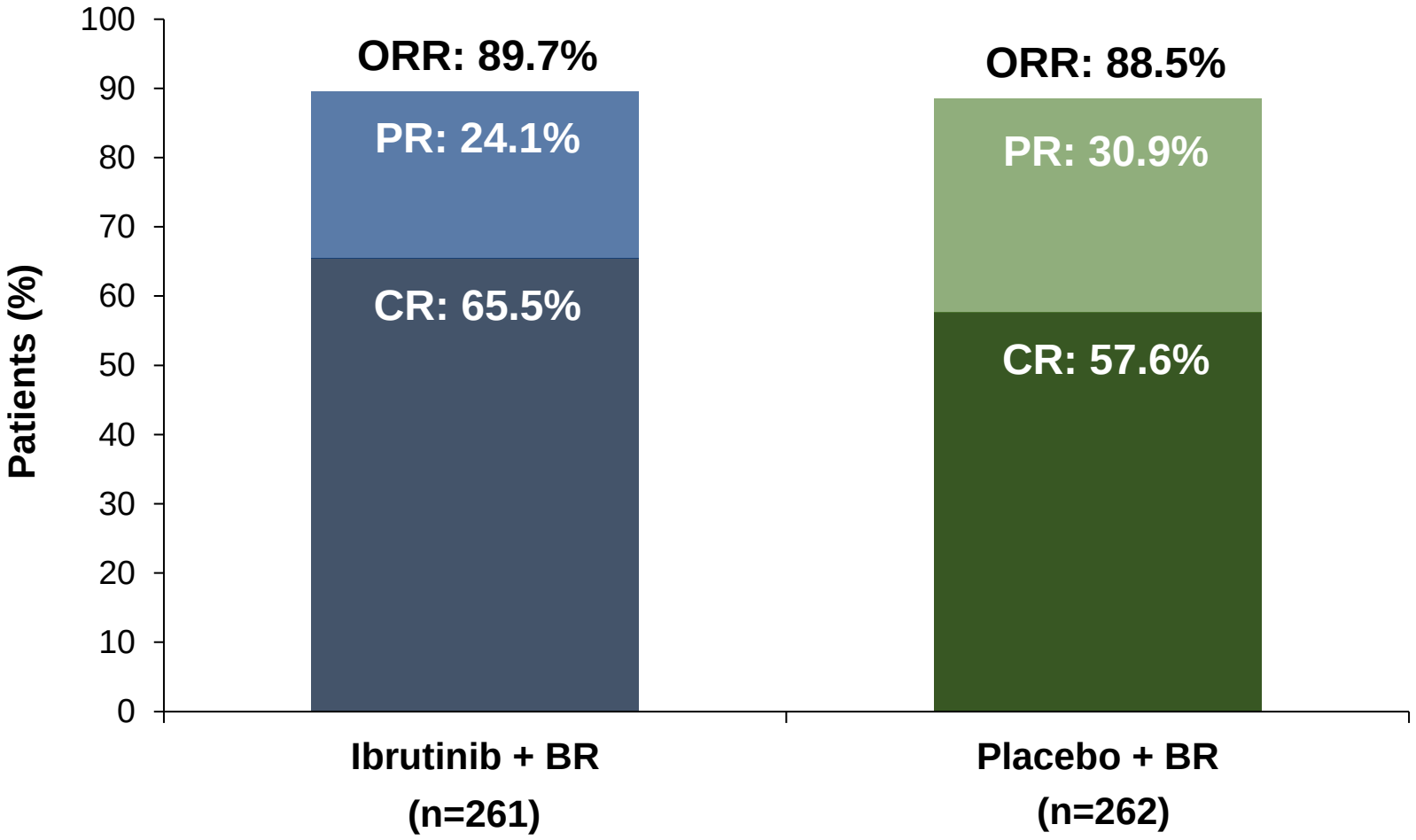


Patients at risk

Ibrutinib + BR	26	21	15	14	13	11	9	7	6	5	4	4	4	3	1	1
Placebo + BR	24	16	11	9	8	7	7	7	5	4	4	4	4	4	4	1

BR, bendamustine and rituximab; CI, confidence interval; HR, hazard ratio; PFS, progression-free survival.
Wang M *et al*. Oral presentation at ASCO 2022; Chicago, IL, USA, June 3–7, 2022 (Abstract LBA7502).

Response rates according to treatment arm



CR rate was numerically higher in the ibrutinib + BR arm vs. the placebo + BR arm (65.5% vs. 57.6%; *P*=0.057)

Best ORR.
BR, bendamustine and rituximab; CR, complete response; ORR, overall response rate; PR, partial response.
Wang M *et al*. Oral presentation at ASCO 2022; Chicago, IL, USA, June 3–7, 2022 (Abstract LBA7502).

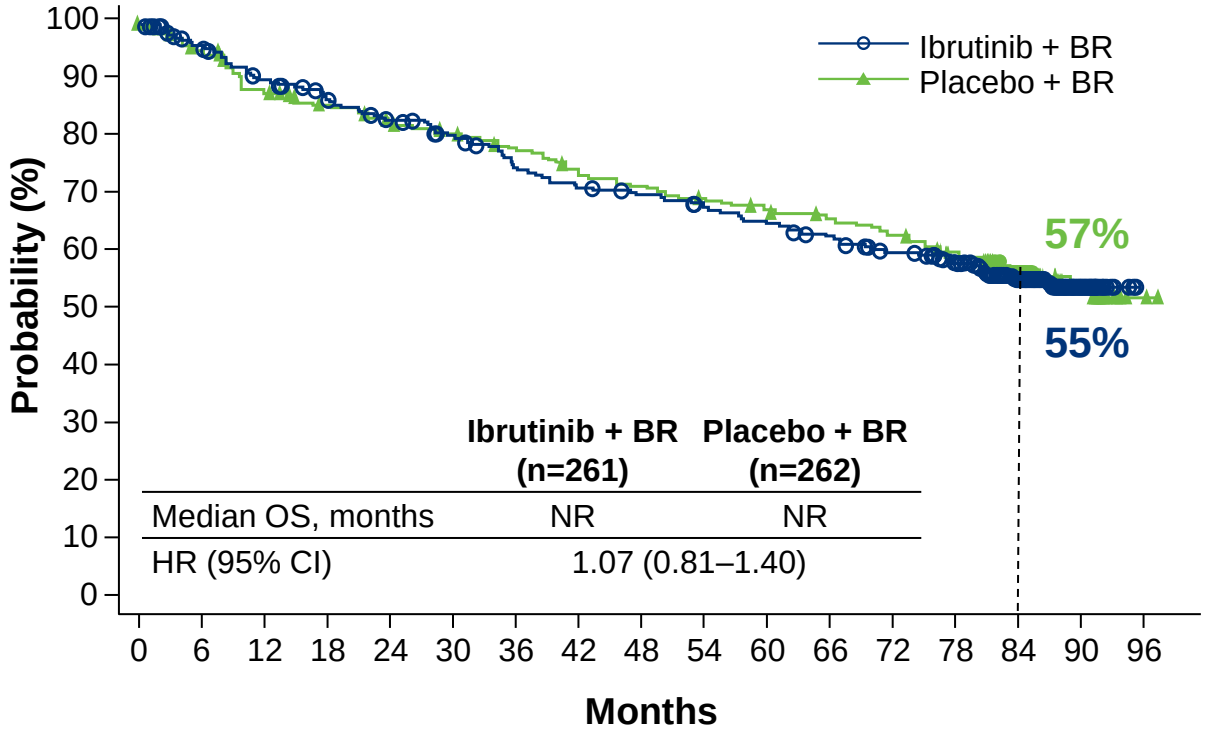
Treatment-emergent adverse events

- These adverse events were generally not treatment-limiting
- During the entire study period, second primary malignancies (including skin cancers) occurred in 21% of patients in the ibrutinib arm and in 19% of patients in the placebo arm
  - MDS or AML occurred in 2 patients in the ibrutinib arm and 3 patients in placebo arm

	Ibrutinib + BR (n=259)		Placebo + BR (n=260)	
	Any grade	Grades 3 or 4	Any grade	Grades 3 or 4
Any bleeding, %	42.9	3.5	21.5	1.5
Major bleeding, %	5.8	–	4.2	–
Atrial fibrillation, %	13.9	3.9	6.5	0.8
Hypertension, %	13.5	8.5	11.2	5.8
Arthralgia, %	17.4	1.2	16.9	0

AML, acute myeloid leukemia; BR, bendamustine and rituximab; MDS, myelodysplastic syndrome.
Wang M *et al*. Oral presentation at ASCO 2022; Chicago, IL, USA, June 3–7, 2022 (Abstract LBA7502).

Overall survival and safety profile



Patients at risk

Ibrutinib + BR	261	239	221	208	197	187	171	163	158	152	145	138	128	118	70	25	0
Placebo + BR	262	244	223	212	203	197	188	177	171	165	159	154	147	137	90	31	2

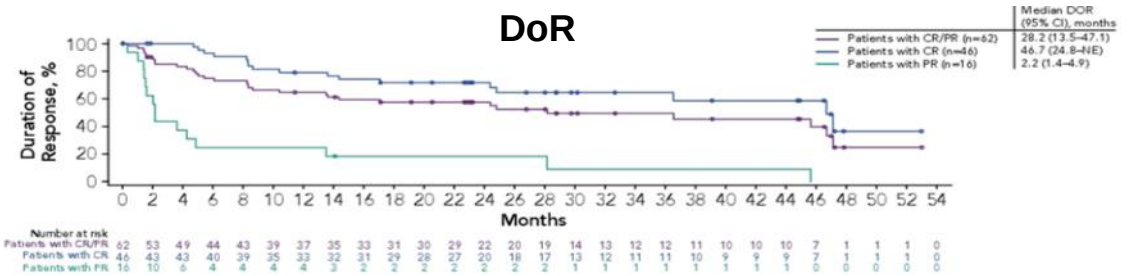
Cause of death, n (%)	Ibrutinib + BR (n=261)	Placebo + BR (n=262)
Death due to PD and TEAEs	58 (22.2)	70 (26.7)
Death due to PD	30 (11.5)	54 (20.6)
Death due to TEAEs	28 (10.7)	16 (6.1)
Death during post-treatment follow-up period excluding PD	46 (17.6)	37 (14.1)
Total deaths	104 (39.8)	107 (40.8)

- Death due to COVID-19 occurred in 3 patients in the ibrutinib arm during the TEAE period and in 2 patients in the placebo arm after the TEAE period.
- The most common Grade 5 TEAE was infections in the ibrutinib and placebo arms: 9 vs. 5 patients, respectively. Grade 5 TEAE of cardiac disorders occurred in 3 vs. 5 patients, respectively.
- **Exploratory analysis of cause-specific survival including only deaths due to PD or TEAEs showed an HR of 0.88.**

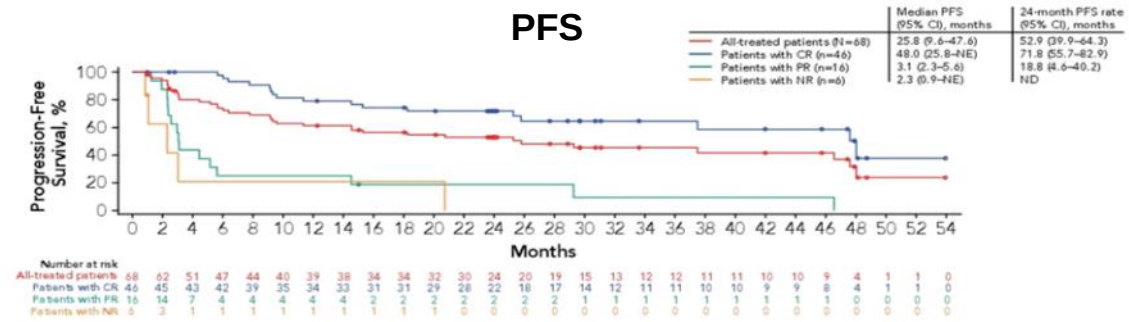
BR, bendamustine and rituximab; CI, confidence interval; COVID-19, coronavirus disease 2019; HR, hazard ratio; NR, not reached; OS, overall survival; PD, progressive disease; TEAE, treatment-emergent adverse event.
Wang M *et al*. Oral presentation at ASCO 2022; Chicago, IL, USA, June 3–7, 2022 (Abstract LBA7502).

3-year follow-up of outcomes with KTE-X19 in patients with R/R MCL in ZUMA-2

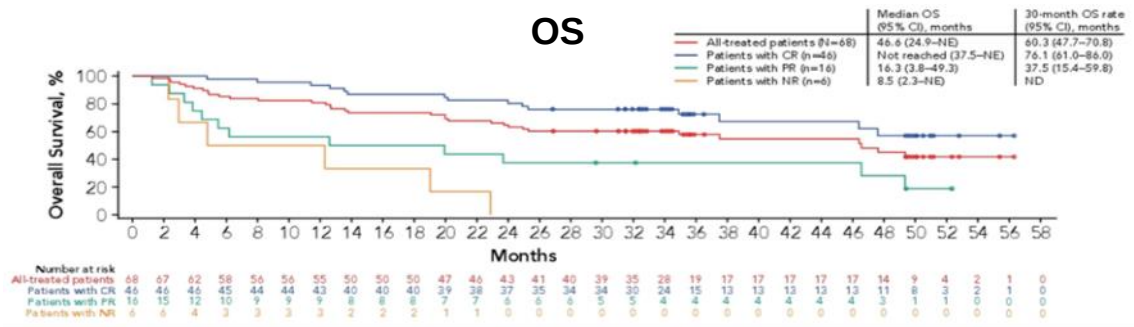
DoR



PFS



OS

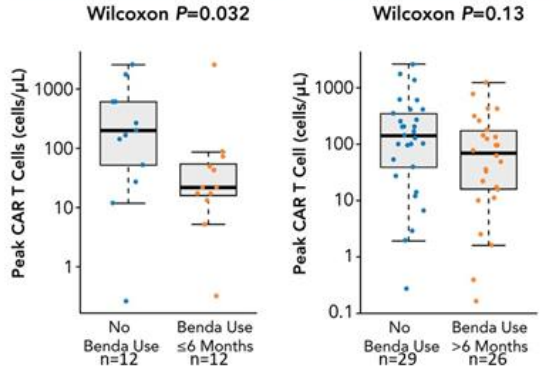


DoR, duration of response; OS, overall survival; PFS, progression-free survival.
Wang M *et al*. Oral presentation at ASCO 2022; Chicago, IL, USA, June 3–7, 2022 (Abstract 7518).

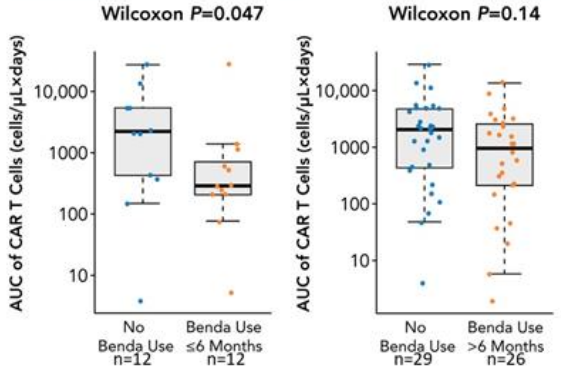
Efficacy and durability outcomes in patients by MRD status

	N	ORR, n (%)	CR, n (%)	PR, n (%)	SD, n (%)	PD, n (%)	mDOR, mo (95% CI) [n]	mPFS, mo (95% CI) [n]	mOS, mo (95% CI) [n]
MRD status at Month 6									
Positive	4	3 (75)	2 (50)	1 (25)	0 (0)	1 (25)	6.1 (5.4–NE) [3]	7.1 (0.9–NE) [4]	27.0 (13.5–NE) [4]
Negative	15	15 (100)	14 (93)	1 (7)	0	0	NR (10.4–NE) [15]	NR (11.3–NE) [15]	NR (46.4–NE) [15]

Peak CAR T-cell Levels



Area Under the Curve CAR T-cell Levels



- Long-term safety was manageable, with only 3% of AEs of interest occurring during this longer follow-up, few late-onset events, and no new CRS
- DOR, PFS, and OS were not reached in patients with MRD-negativity at 6 months, suggesting MRD-negativity may predict for a longer response duration, although sample size of this exploratory analysis was limited and further investigation is warranted
- Results of an exploratory post hoc analysis suggest that bendamustine use shortly before leukapheresis requires careful consideration due to its potential effects on patient T-cell fitness and CAR T-cell expansion
  - Although a majority of patients (54%) in the overall ZUMA-2 population had prior bendamustine, it may be advantageous to consider administering the potentially curative therapy KTE-X19 after an extended period following bendamustine exposure, in order to obtain a quality immune response and maximize the benefit of KTE-X19

Summary

- Promising data for bispecific antibodies (anti-CD20×CD3) was reported from two Phase 2 trials
  - Fixed-duration glofitamab induced durable CRs in patients with heavily pre-treated and refractory DLBCL[1]
  - Epcoritamab demonstrated clinically meaningful efficacy in a highly refractory LBCL patient population[2]
- Axi-Cel demonstrated superior efficacy versus second-line SoC in elderly patients with R/R LBCL[3]
- In the Phase III SHINE study, ibrutinib plus BR and R maintenance significantly improved PFS rates compared with standard chemoimmunotherapy in older patients with TN MCL[4]
- KTE-X19 induced durable long-term responses with a manageable safety and low late relapse potential in R/R MCL[5]

axi-cel, axicabtagene ciloleucel; BR, bendamustine and rituximab; CAR-T, chimeric antigen receptor T-cell; CD, cluster of differentiation; DLBCL, diffuse large B-cell lymphoma; LBCL, large B-cell lymphoma; MCL, mantle cell lymphoma; PFS, progression-free survival; R/R, relapsed/refractory; SoC, standard of care.

1. Dickinson M *et al*. Oral presentation at ASCO 2022; Chicago, IL, USA, June 3–7, 2022 (Abstract 7500). 2. Thieblemont C *et al*. Oral presentation at EHA 2022; Vienna, Austria, June 9–17, 2022 (Abstract LB2364).
3. Westin J *et al*. Oral presentation at ASCO 2022; Chicago, IL, USA, June 3–7, 2022 (Abstract 7548). 4. Wang M *et al*. Oral presentation at ASCO 2022; Chicago, IL, USA, June 3–7, 2022 (Abstract LBA7502).
5. Wang M *et al*. Oral presentation at ASCO 2022; Chicago, IL, USA, June 3–7, 2022 (Abstract 7518).

Highlights in indolent lymphomas

Professor Véronique Leblond
Pitié-Salpêtrière Hospital and Sorbonne University, France

September 2022 | 0822-BGB-3111-MRC-025

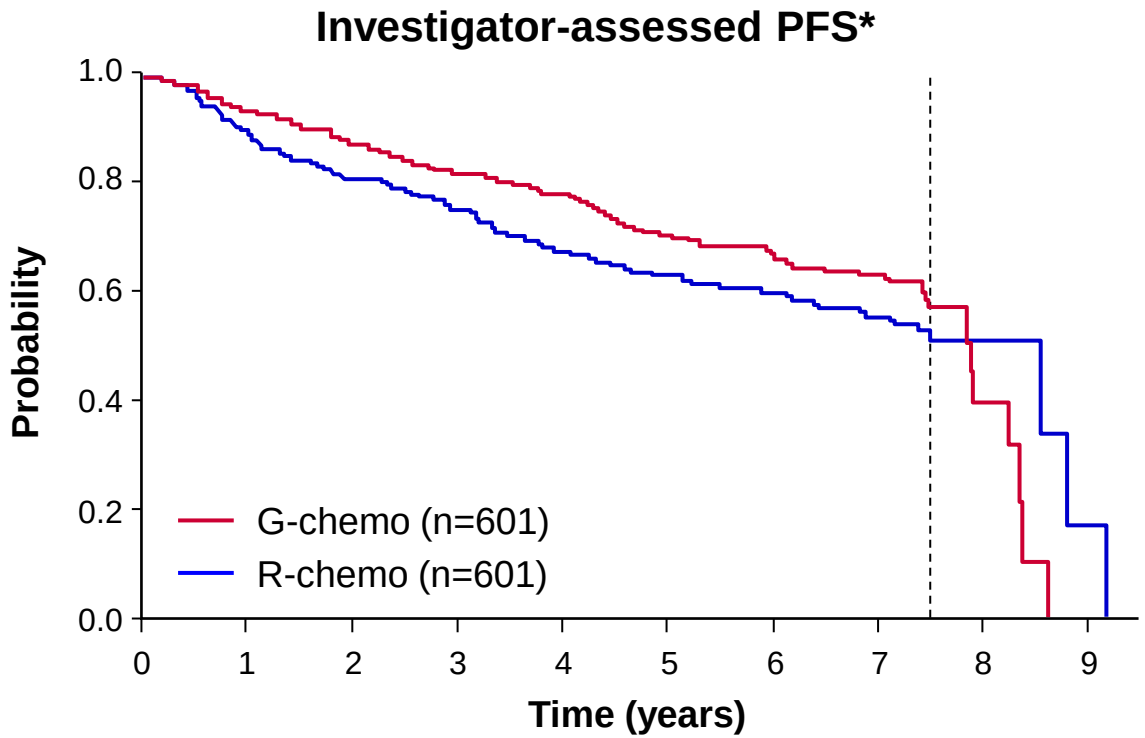
Disclosures

- **Speakers bureau**: AbbVie, BeiGene, Gilead, Janssen, and Roche
- **Board**: AbbVie, AstraZeneca, Gilead, Janssen-Cilag, MSD, and Roche
- **Honoraria**: AbbVie, Amgen, AstraZeneca, BeiGene, Gilead, Janssen-Cilag, Lilly, MSD, and Roche

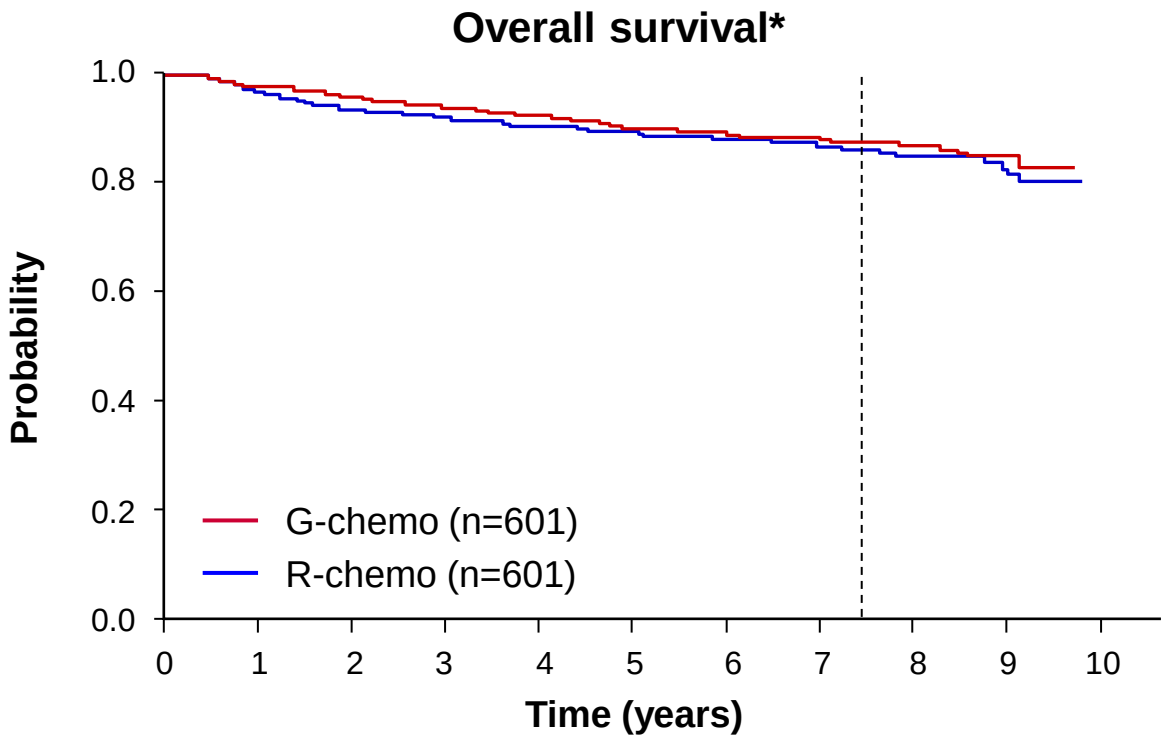
MSD, Merck Sharp and Dohme.

Follicular lymphoma

The GALLIUM study: Obinutuzumab plus chemotherapy vs. rituximab plus chemotherapy in untreated FL



	7-year PFS
G-chemo	63.4%
R-chemo	55.7%

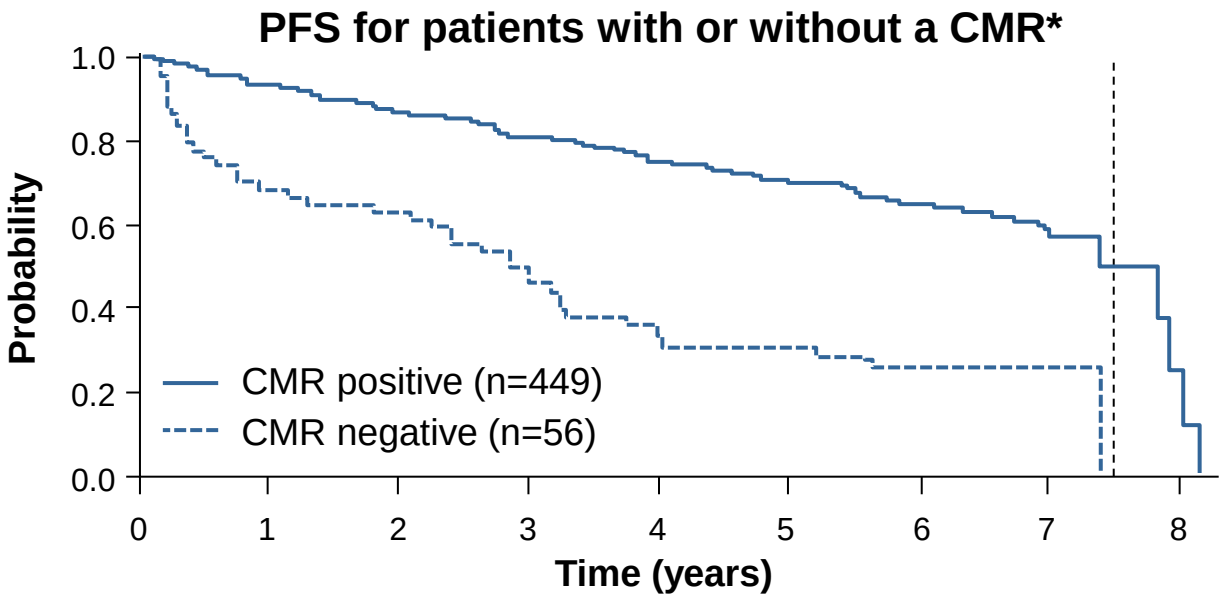


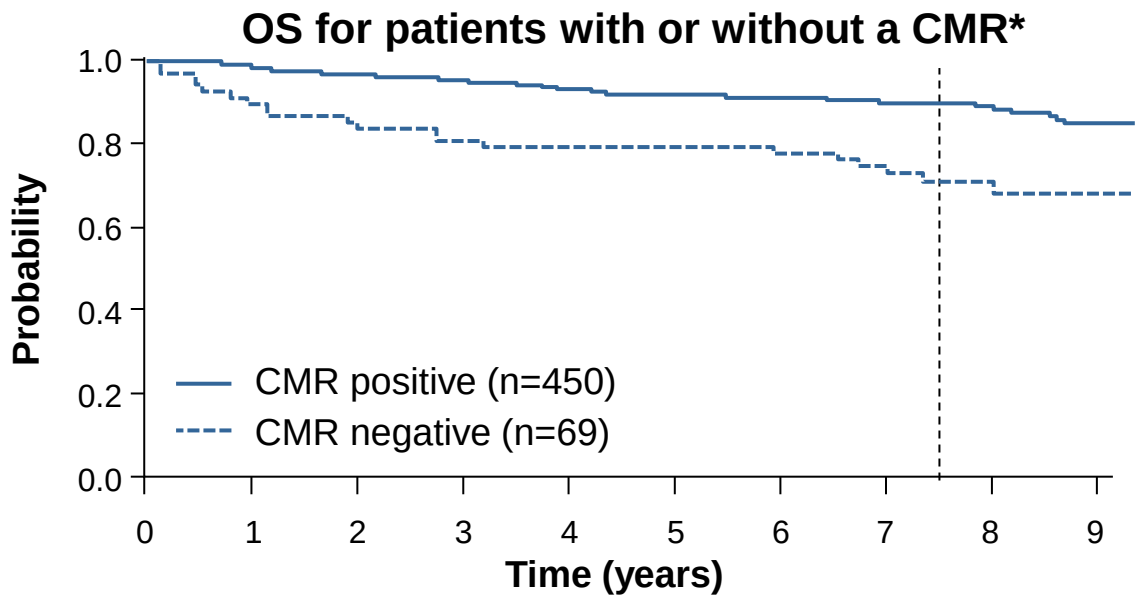
	7-year OS
G-chemo	88.5%
R-chemo	87.2%

*Event-free probabilities became unreliable after 7 years because only 10%–20% of patients remained in follow-up.
chemo, chemotherapy; FL, follicular lymphoma; G, obinutuzumab; OS, overall survival; PFS, progression-free survival; R, rituximab.
Townsend W *et al*. Oral presentation at EHA 2022; Vienna, Austria, June 9–17, 2022 (Abstract S206).

The GALLIUM study: The importance of a complete metabolic response

- Patients from both treatment groups with a PET scan at EOI were retrospectively assessed for response





	7-year PFS
CMR positive	57.2%
CMR negative	26.5%

	7-year OS
CMR positive	90.2%
CMR negative	73.2%

*Event-free probabilities became unreliable after 7 years because only 10%–20% of patients remained in follow-up.
CMR, complete metabolic response; EOI, end of induction; OS, overall survival; PET, positron emission tomography; PFS, progression-free survival.
Townsend W *et al*. Oral presentation at EHA 2022; Vienna, Austria, June 9–17, 2022 (Abstract S206).

The GALLIUM study: Tolerability

Mortality by chemotherapy combination:

- G-CHOP: 2.6%; R-CHOP: 2.5%
- G-CVP: 1.7%; R-CVP: 1.8%
- **G-Benda: 5.9%; R-Benda: 6.2%**

Second cancers:

- G-chemo: 13.1%
- R-chemo: 9.9%

	Induction period		Maintenance period		Post-treatment follow-up period	
	G-chemo	R-chemo	G-chemo	R-chemo	G-chemo	R-chemo
Neutropenia (Grade ≥3), %	40.5	37.4	18.5	12.0	3.5	1.7
Infections (Grade ≥3), %	7.6	7.5	12	10.3	8.7	5.8
Infusion-related reactions (Grade ≥3), %	12.1	7.2	0.7	0.4	0	0
All toxicities (Grade ≥3), %	61.8	58.6	40	33.1	21.3	15.7

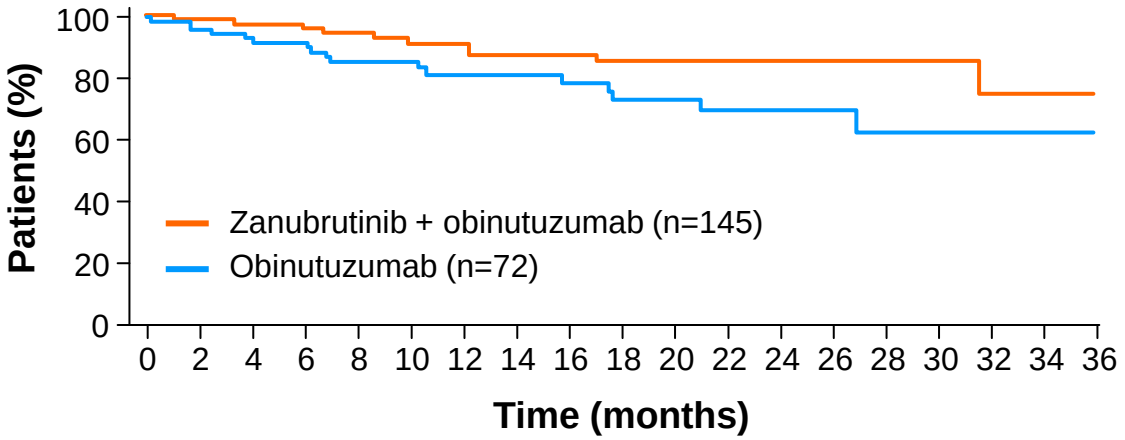
Benda, bendamustine; chemo, chemotherapy; CHOP, cyclophosphamide, doxorubicin, vincristine, and prednisolone; CVP, cyclophosphamide, vincristine, and prednisolone; G, obinutuzumab; R, rituximab.
Townsend W *et al*. Oral presentation at EHA 2022; Vienna, Austria, June 9–17, 2022 (Abstract S206).

The ROSEWOOD study

Zanubrutinib plus obinutuzumab vs. obinutuzumab in R/R FL

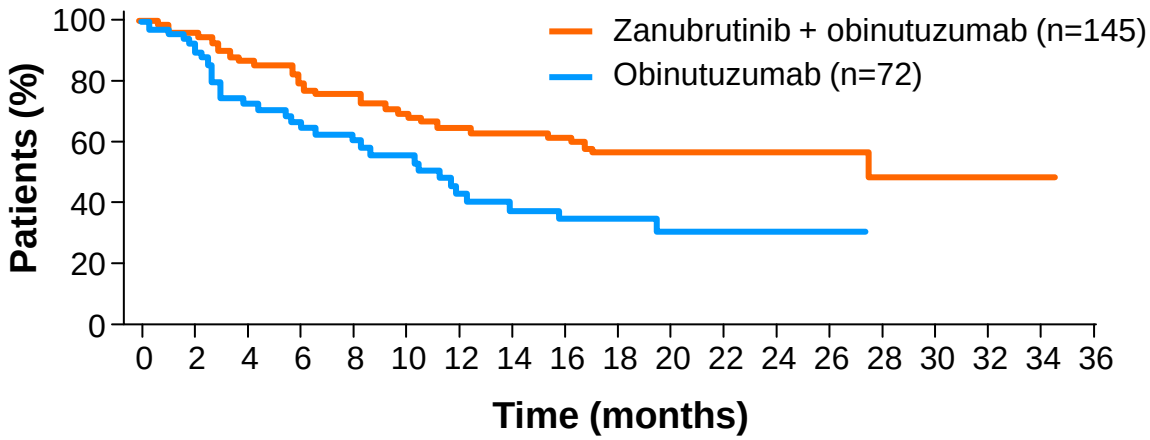
- The primary endpoint of a superior ORR was met:
  - ORR = 68.3% with zanubrutinib plus obinutuzumab vs. 45.8% with obinutuzumab

OS



	Zanubrutinib + obinutuzumab	Obinutuzumab
Median (95% CI)	NE (31.4–NE)	NE (26.8–NE)
HR (95% CI)	0.44 (0.22–0.88); *P*=0.0177	

PFS



	Zanubrutinib + obinutuzumab	Obinutuzumab
Median (95% CI)	27.4 (16.1–NE)	11.2 (6.5–15.7)
HR (95% CI)	0.51 (0.32–0.81); *P*=0.0040	

CI, confidence interval; FL, follicular lymphoma; HR, hazard ratio; NE, not evaluable; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; R/R, relapsed/refractory.
Zinzani PL *et al*. Oral presentation at EHA 2022; Vienna, Austria, June 9–17, 2022 (Abstract S205). Zanubrutinib is not approved for this condition.

The ROSEWOOD study: Tolerability

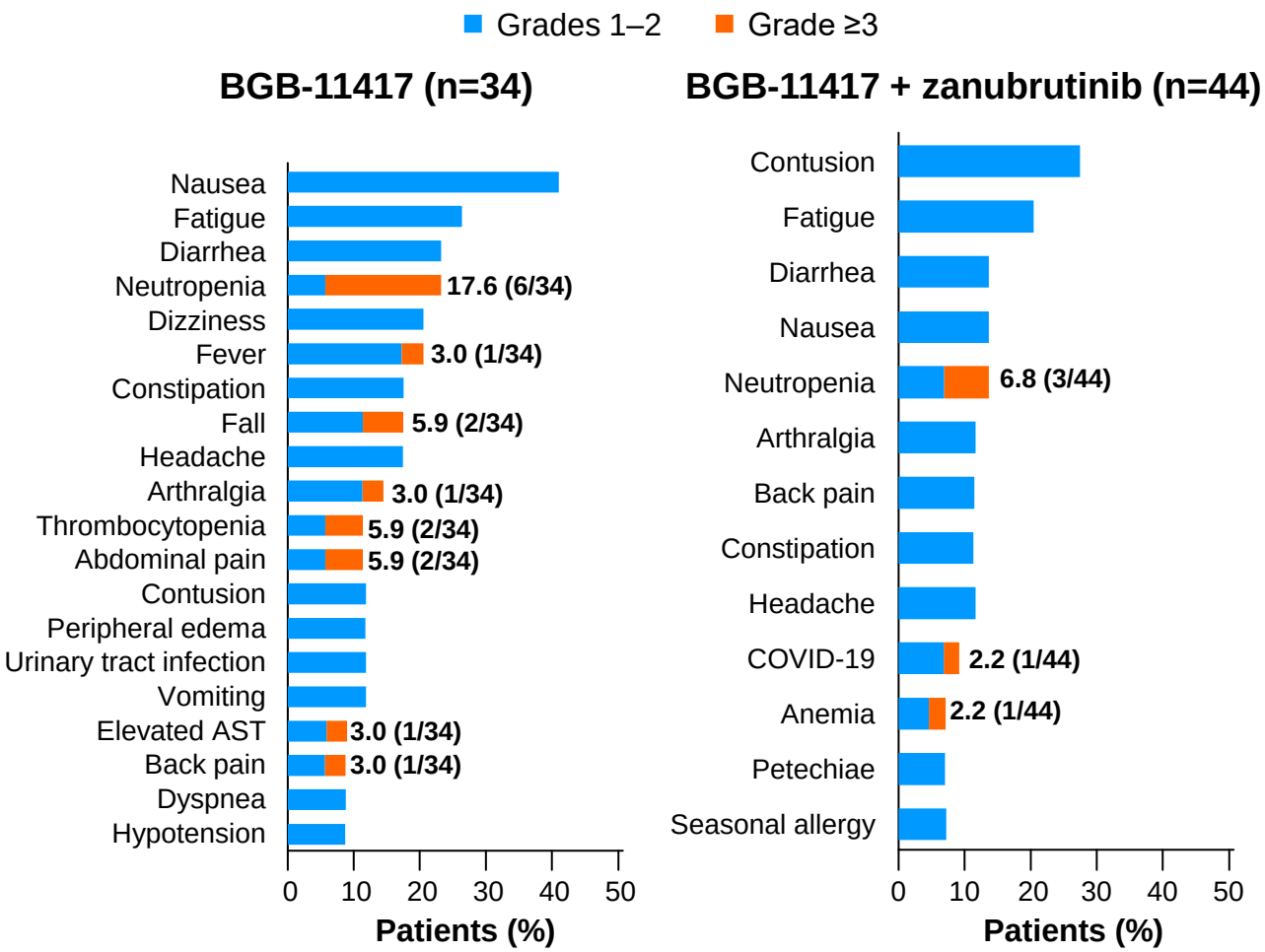
	Zanubrutinib plus obinutuzumab (n=143)		Obinutuzumab (n=71)	
	All grades	Grade ≥3	All grades	Grade ≥3
Patients with TEAE, %	92.3	53.8	88.7	47.9
Thrombocytopenia	34.3	14.0	23.9	7.0
Neutropenia	27.3	22.4	25.4	19.7
Diarrhea	16.1	2.8	16.9	0.0
Fatigue	14.0	1.4	11.3	0.0
Constipation	13.3	0.0	7.0	0.0
Cough	11.9	0.0	11.3	0.0
Fever	11.2	0.0	19.7	0.0
Dyspnea	10.5	1.4	9.9	0.0
Anemia	9.1	4.2	9.9	5.6
Nausea	8.4	0.0	12.7	0.0
Pruritus	7.0	0.0	9.9	0.0
Infusion-related reactions	2.8	0.7	9.9	4.2
AEs of specific interest, %				
Fibrillation/flutter	2.1	0.7	1.4	0.0
Hypertension	3.5	0.7	4.2	1.4
Hemorrhage	26.6	1.4	8.5	0.0
Major hemorrhage	1.4	1.4	1.4	0.0
Infections	47.6	18.9	36.6	12.7
Secondary cancers	6.3	3.5	2.8	0.0

AE, adverse event; TEAE, treatment-emergent adverse event.

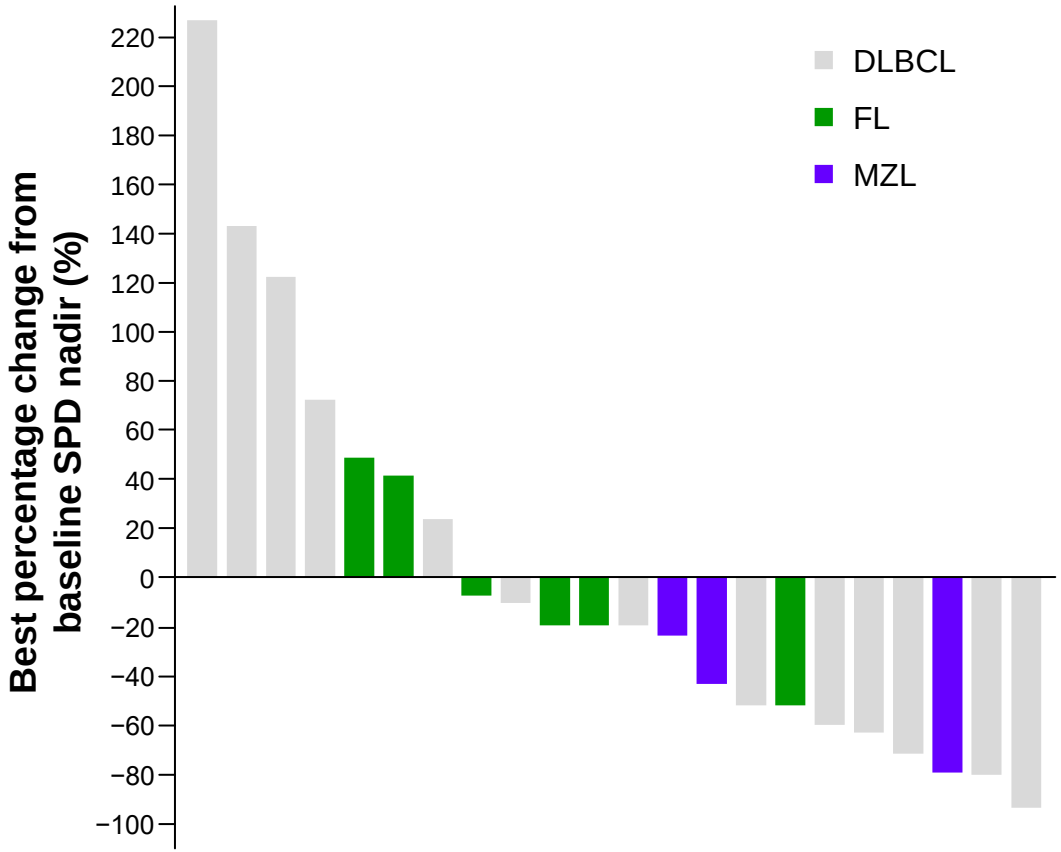
Zinzani PL *et al*. Oral presentation at EHA 2022; Vienna, Austria, June 9–17, 2022 (Abstract S205).

Phase I preliminary data for the BCL2 inhibitor BGB-11417 vs. BGB-11417 plus zanubrutinib in patients with B-cell malignancies

Tolerability



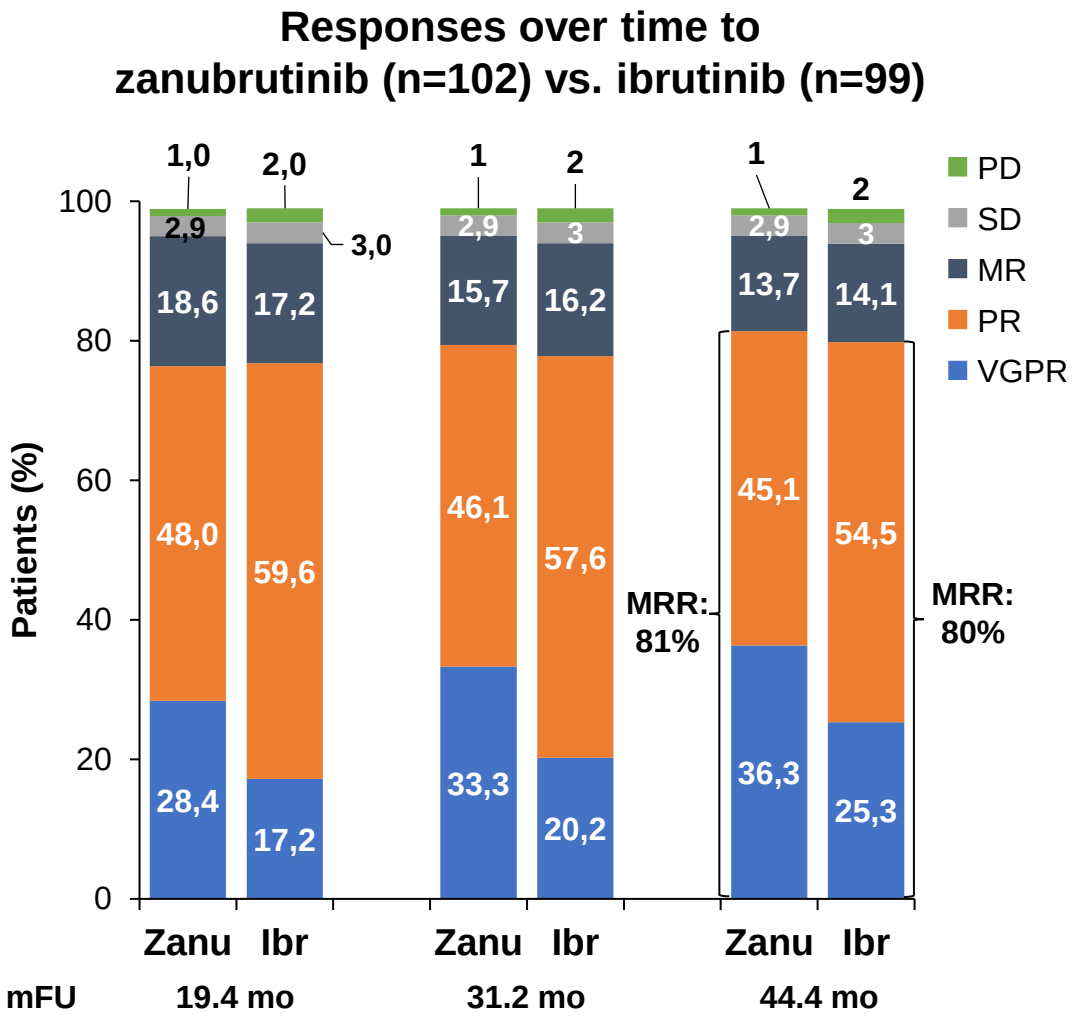
Tumor response in patients with NHL receiving BGB-11417 monotherapy

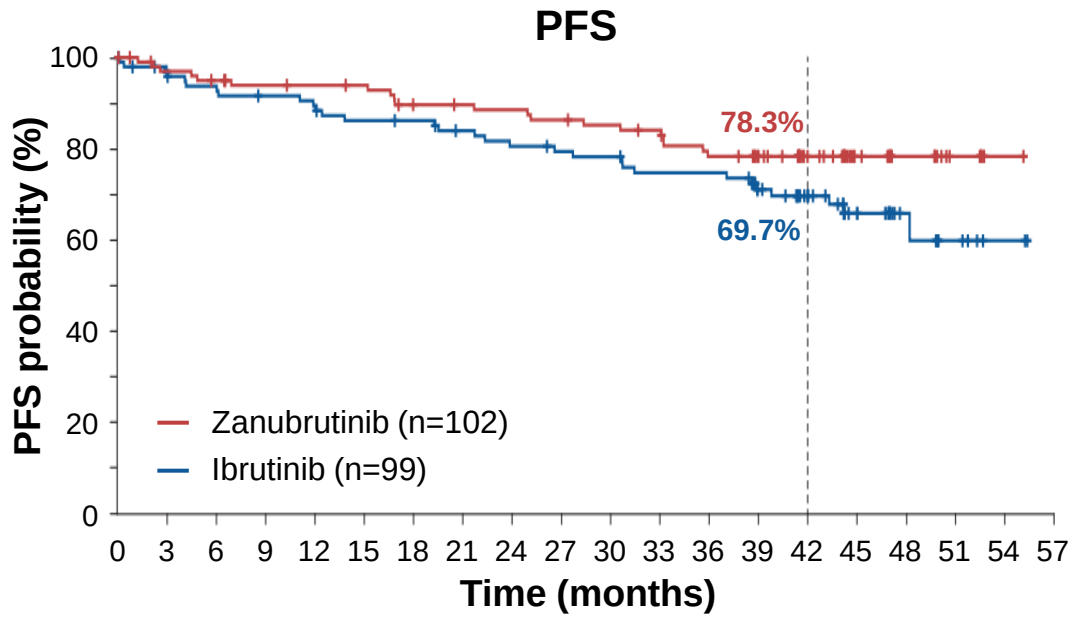


AST, aspartate aminotransferase; BCL, B-cell lymphoma; COVID-19, coronavirus disease 2019; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; MZL, marginal zone lymphoma; NHL, non-Hodgkin lymphoma; SPD, sum of the products of diameters. Opat S *et al*. Poster P687 presented at EHA 2022; Vienna, Austria, June 9–17, 2022.

Waldenström’s macroglobulinemia

ASPEN: Long-term follow-up of zanubrutinib vs. ibrutinib in patients with WM





	Zanubrutinib	Ibrutinib
CR + VGPR, %	36.6	25.3
Median time to CR + VGPR, mo	6.7	16.6
42-month OS, %	87.5	85.2

CR, complete response; Ibr, ibrutinib; mFU, median follow-up; mo, months; MR, minimal response; MRR, major response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; SD, stable disease; VGPR, very good partial response; WM, Waldenström's macroglobulinemia; Zanu, zanubrutinib.

Dimopoulos M *et al*. Poster P1161 presented at EHA 2022; Vienna, Austria, June 9–17, 2022.

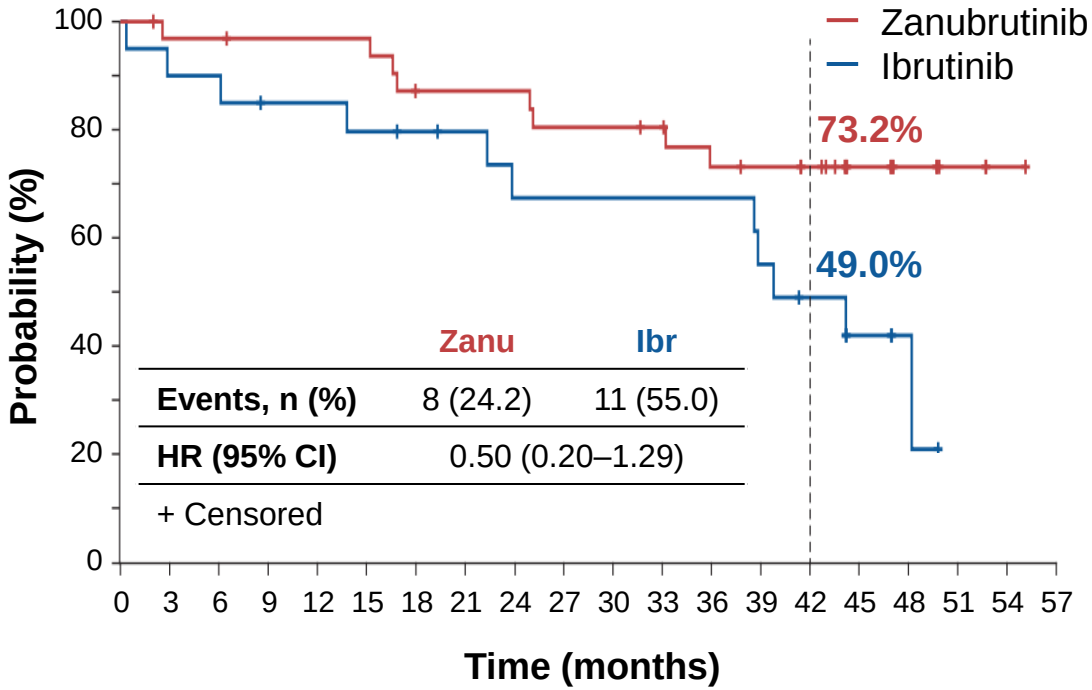
ASPEN: Outcomes according to *CXCR4* mutational status

Responses according to *CXCR4* status

	CXCR4^{MUT}*		*CXCR4*^{WT}*	
	Zanu (n=33)	**Ibr (n=20)**	**Zanu (n=65)**	**Ibr (n=72)**
VGPR or better, n (%)	**7 (21.2)**	2 (10.0)	**29 (44.6)**	22 (30.6)
Major response, n (%)	**26 (78.8)**	13 (65.0)	54 (83.1)	61 (84.7)
Overall response, n (%)	30 (90.9)	19 (95.0)	63 (96.9)	68 (94.4)
Median time to major response, months	3.4	6.6	2.8	2.8
Median time to VGPR, months	11.1	31.3	6.5	11.3

Bold blue text indicates >10% difference between arms.
Data cut-off: October 31, 2021.

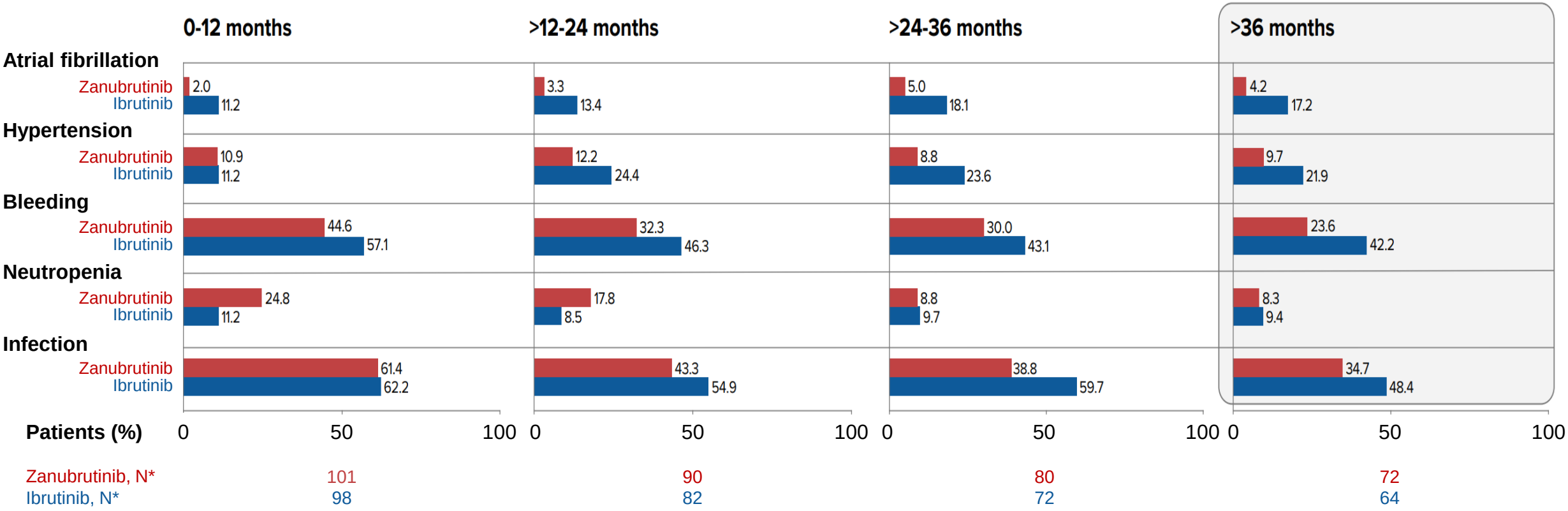
PFS in patients with *CXCR4*^{MUT}



**CXCR4* mutation determined by NGS; 92 ibrutinib-treated and 98 zanubrutinib-treated patients had NGS results available.
CI, confidence interval; HR, hazard ratio; Ibr, ibrutinib; MUT, mutant; NGS, next-generation sequencing; PFS, progression-free survival; VGPR, very good partial response; WT, wild-type; Zanu, zanubrutinib.
Dimopoulos M *et al*. Poster P1161 presented at EHA 2022; Vienna, Austria, June 9–17, 2022.

ASPEN: Long-term safety data

Long-term safety and tolerability: AEs of interest



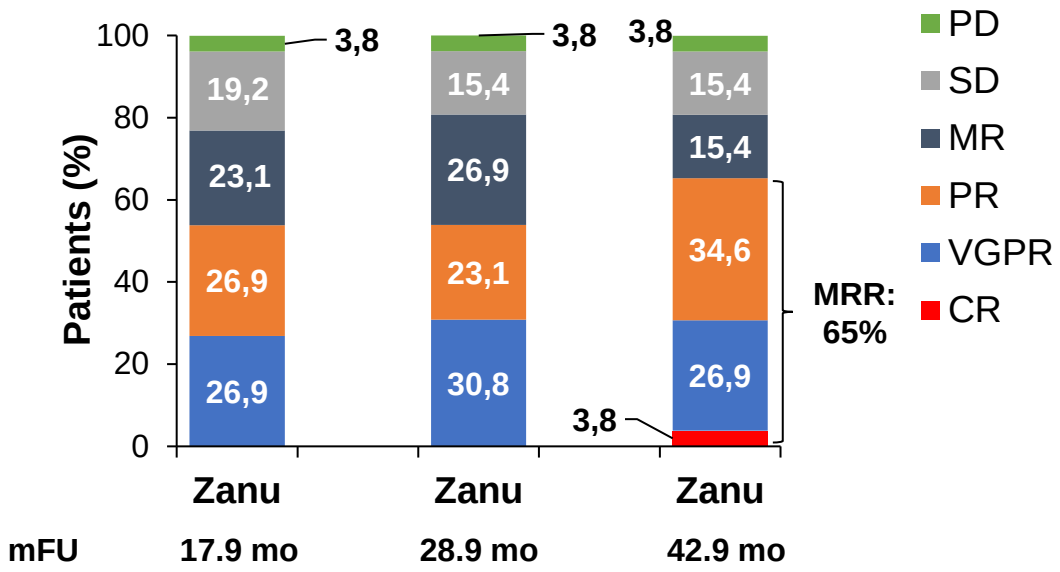
Zanubrutinib, N*	101	90	80	72
Ibrutinib, N*	98	82	72	64

Data cut-off: October 31, 2021.
*N is the number of patients who are on treatment in each time interval or who discontinued treatment, but the time from the first dose date to the earliest date (last dose date +30 days, initiation of new anticancer therapy, end of study, death, or cut-off date) is within the time interval.
AE, adverse event.
Dimopoulos M *et al*. Poster P1161 presented at EHA 2022; Vienna, Austria, June 9–17, 2022.

ASPEN: Long-term follow-up of zanubrutinib in *MYD88*^{WT} WM

Outcomes: Cohort 2 *MYD88*^{WT} (n=28)

Responses over time



At 42 months:

- PFS: 53.8% (95% CI: 33.3–70.6)
- OS: 83.9% (95% CI: 62.6–93.7)

Overall safety summary

Category, n (%)	Cohort 2 Zanubrutinib
Patients with ≥1 AE	26 (92.9)
Grade ≥3	20 (71.4)
Serious	14 (50.0)
AE leading to death	3 (10.7)
AE leading to treatment discontinuation	6 (21.4)
AE leading to dose reduction	2 (7.1)
AE leading to dose held	18 (64.3)
AE related to COVID-19	2 (7.1)

AE, adverse event; CI, confidence interval; COVID-19, coronavirus disease 2019; CR, complete response; mFU, median follow-up; mo, months; MR, minimal response; MRR, major response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; SD, stable disease; VGPR, very good partial response; WM, Waldenström's macroglobulinemia; WT, wild-type; Zanu, zanubrutinib.
Dimopoulos M *et al*. Poster P1161 presented at EHA 2022; Vienna, Austria, June 9–17, 2022.

Acalabrutinib in WM:* 5-year follow-up of a Phase II, single-arm study

Acalabrutinib monotherapy

	Follow-up	
	27.4 months	63.7 months
ORR TN	93%	93%
MRR TN	79%	79%
ORR R/R	93%	95%
MRR R/R	78%	82%

***Median follow-up: 63.7* months**

- ✓ **Median PFS**
  - **TN: Not reached**
  - **R/R: 68 months**
- ✓ **Estimated 66-month PFS**
  - **TN: 84%**
  - **R/R: 52%**
- ✓ **Estimated 66-month OS**
  - **TN: 91%**
  - **R/R: 71%**

106 patients: 14 TN, 92 R/R; median prior therapies: 2 (range 1–7)

At 63.7 months:

- **TN patients on treatment: 50% (discontinuation for AEs: 29%; PD: 7%)**
- **R/R patients on treatment: 47% (discontinuation for AEs: 16%; PD: 22%)**

	TN (n=14)		R/R (n=92)	
	Any grade	Grades 3–4	Any grade	Grades 3–4
Common AEs (≥30% of patients), n (%)				
Headache	5 (36)	0	39 (42)	0
Diarrhea	6 (43)	0	35 (38)	2 (2)
Fatigue	3 (21)	0	29 (31)	2 (2)
Arthralgia	5 (36)	0	29 (31)	1 (1)
Nausea	5 (36)	0	21 (23)	2 (2)
Dizziness	5 (36)	0	23 (25)	0
Selected ECI, n (%)				
Atrial fibrillation/flutter	1 (7)	0	11 (12)	2 (2)
Hemorrhage	10 (71)	0	56 (61)	6 (6)
Hypertension	0	0	7 (8)	4 (4)

*Acalabrutinib is not approved for the treatment of WM.

AE, adverse event; ECI, event of clinical interest; MRR, major response rate; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; R/R, relapsed/refractory; TN, treatment-naive; WM, Waldenström's macroglobulinemia.

Owen RG *et al*. *Lancet Haematol* 2020; 7 (2): e112–e121. Owen R *et al*. Poster P1130 presented at EHA 2022; Vienna, Austria, June 9–17, 2022.

Bispecific antibodies across indications

Bispecific CD20×CD3 antibodies

Molecule	Structure	Drug delivery	Clinical development
Mosunetuzumab	Full-length, humanized IgG1 **CD20:CD3 (1:1)**	IV or SC every 21 days	• **Phase I/II** mosunetuzumab ± atezolizumab in R/R B-cell NHL and CLL (NCT02500407) • **Phase II** SC mosunetuzumab in R/R B-cell NHL (NCT05207670) • **Phase III** mosunetuzumab + lenalidomide vs. R^2 in R/R FL (CELESTIMO; NCT04712097)
Epcoritamab	Full-length, humanized IgG1 **CD20:CD3 (1:1)**	SC every 28 days	• **Phase I/II** epcoritamab in R/R B-cell NHL (EPCORE NHL-1; NCT03625037) • **Phase I/II** epcoritamab + combinations in R/R B-cell NHL (EPCORE NHL-2; NCT04663347) • **Phase III** epcoritamab + R^2 vs. R^2 in R/R FL (EPCORE FL-1; NCT05409066)
Odronextamab	Hinge-stabilized, humanized IgG4 **CD20:CD3 (1:1)**	IV or SC weekly, then maintenance every 15 days	• **Phase I** odronextamab in R/R B-cell NHL (ELM-1; NCT02290951) • **Phase II** odronextamab in R/R B-cell NHL (ELM-2; NCT03888105)
Glofitamab	Full-length, humanized IgG1 **CD20:CD3 (2:1)**	IV every 21 days	• **Phase I/II** glofitamab ± obinutuzumab in R/R B-cell NHL (NCT03075696) • **Phase Ib/II** glofitamab + polatuzumab vedotin or atezolizumab in R/R B-cell NHL (NCT03533283)

CLL, chronic lymphocytic leukemia; FL, follicular lymphoma; IgG, immunoglobulin G; IV, intravenous; NHL, non-Hodgkin lymphoma; R^2, rituximab and lenalidomide; R/R, relapsed/refractory; SC, subcutaneous.

Bispecific CD20×CD3 antibodies

Outcomes in subsets of patients with indolent lymphomas

Molecule	Description	Patients, n	No. of previous therapies	ORR, n (%)	CR/CMR, n (%)	Median DoR, mo
Mosunetuzumab[1]	Phase I/II study of the safety and efficacy of mosunetuzumab in patients with R/R B-cell NHL (NCT02500407)	68	≥1	45 (66)	CR: 33 (49)	16.8
Epcoritamab[2]	Phase I/II study of epcoritamab in patients with R/R B-cell NHL (EPCORE NHL-1; NCT03625037)	10	≥2	9 (90)	CR: 5 (50)	–
Odronextamab[3]	Phase I dose-escalation and dose-expansion study of odronextamab in patients with R/R B-cell NHL (ELM-1; NCT02290951)	32	≥2	29 (91)	CMR: 23 (72)	15.8
Glofitamab[4]	Phase I/II study of glofitamab in patients with R/R B-cell NHL (NCT03075696)	53	≥1	43 (81)	CMR: 37 (70)	10.8

Data in the table are sourced from different studies; the limitations of cross-study comparisons apply.

CMR, complete metabolic response; CR, complete response; DoR, duration of response; mo, months; NHL, non-Hodgkin lymphoma; ORR, overall response rate; R/R, relapsed/refractory.

1. Budde LE *et al*. *J Clin Oncol* 2022; 40 (5): 481–491. 2. Thieblemont C *et al*. Oral presentation at EHA 2022; Vienna, Austria, June 9–17, 2022 (Abstract LB2364). 3. Bannerji R *et al*. *Lancet Haematol* 2022; 9 (5): e327–e339. 4. Morschhauser F *et al.* Oral presentation at the 63rd ASH Annual Meeting and Exposition; Atlanta, Georgia, USA. December 11–14, 2021 (Abstract 623).

Summary

- Obinutuzumab plus chemotherapy demonstrated a long-term benefit over rituximab plus chemotherapy in patients with previously untreated FL in the GALLIUM study[1]
- Obinutuzumab plus zanubrutinib demonstrated superior efficacy to obinutuzumab monotherapy in R/R FL in the ROSEWOOD study[2]
- Promising Phase I preliminary data have been reported for the BCL2 inhibitor BGB-11417 in patients with indolent B-cell malignancies[3]
- In the long-term follow-up of the ASPEN trial of zanubrutinib vs. ibrutinib:[4]
  - There was a trend toward a deeper response with zanubrutinib in all patients and in the subset of patients with *CXCR4* mutations
  - 30.7% of patients with *MYD88*^{WT} achieved a VGPR or CR with zanubrutinib treatment in the single-arm substudy
- There were durable responses and a favorable safety profile with acalabrutinib in patients with TN or R/R WM[5,6]
- Encouraging clinical data for bispecific CD20×CD3 antibodies have been reported from several ongoing trials for patients with R/R B-cell NHL[7–10]

BCL, B-cell lymphoma; CR, complete response; FL, follicular lymphoma; NHL, non-Hodgkin lymphoma; R/R, relapsed/refractory; TN, treatment-naive; VGPR, very good partial response; WM, Waldenström's macroglobulinemia; WT, wild-type.

1. Townsend W *et al*. Oral presentation at EHA 2022; Vienna, Austria, June 9–17, 2022 (Abstract S206). 2. Zinzani PL *et al*. Oral presentation at EHA 2022; Vienna, Austria, June 9–17, 2022 (Abstract S205). 3. Opat S *et al*. Poster P687 presented at EHA 2022; Vienna, Austria, June 9–17, 2022. 4. Dimopoulos M *et al*. Poster P1161 presented at EHA 2022; Vienna, Austria, June 9–17, 2022. 5. Owen RG *et al*. *Lancet Haematol* 2020; 7 (2): e112–e121. 6. Owen R *et al*. Poster P1130 presented at EHA 2022; Vienna, Austria, June 9–17, 2022. 7. Budde LE et al. J Clin Oncol 2022; 40 (5): 481–491. 8. Thieblemont C et al. Oral presentation at EHA 2022; Vienna, Austria, June 9–17, 2022 (Abstract LB2364). 9. Bannerji R et al. Lancet Haematol 2022; 9 (5): e327–e339. 10. Dickinson M et al. Oral presentation at EHA 2022; Vienna, Austria, June 9–17, 2022 (Abstract 7500).

Highlights in CLL

Professor Wojciech Jurczak
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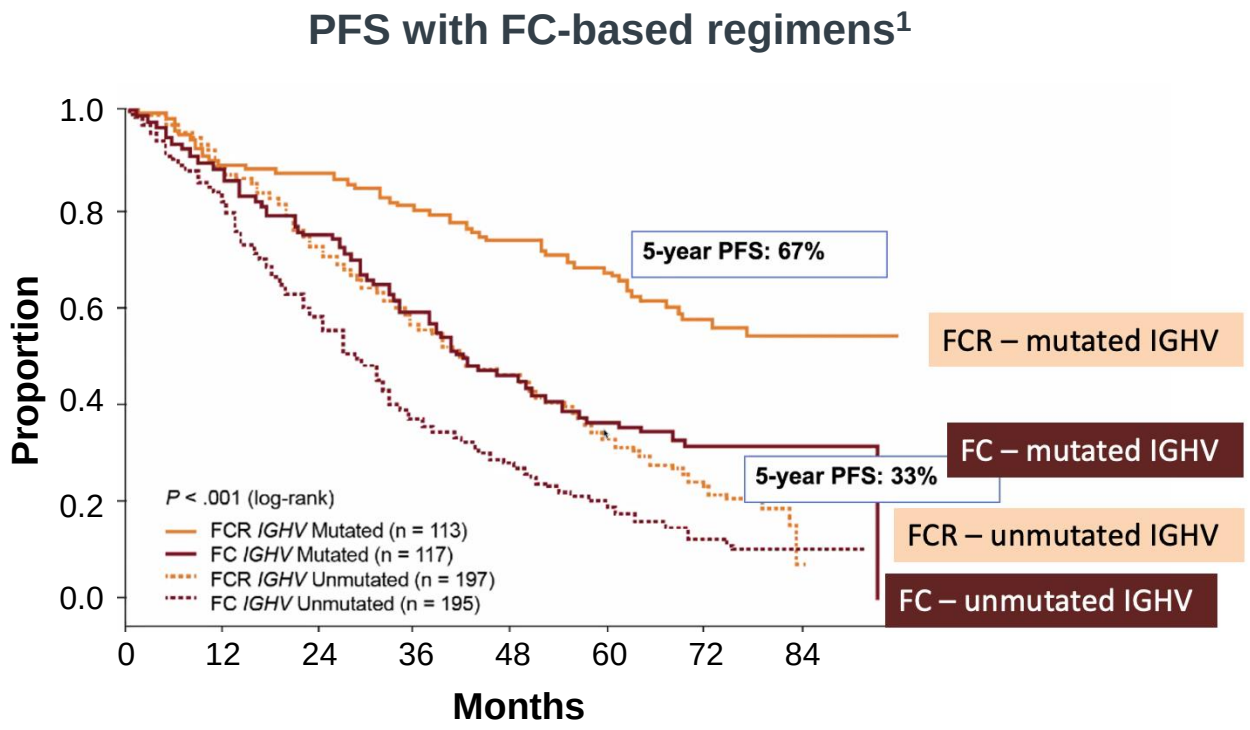
Disclosures

- **Advisory boards:** AstraZeneca, Beigene, Janssen, Loxo, and Meipharma
- **Research Funding:** AbbVie, AstraZeneca, Bayer, Beigene, Celgene, Gilead Sciences, Janssen, Loxo, Merck, MSD, Meipharma, Roche, Takeda, and TG Therapeutics,

FCR in patients with low-risk CLL

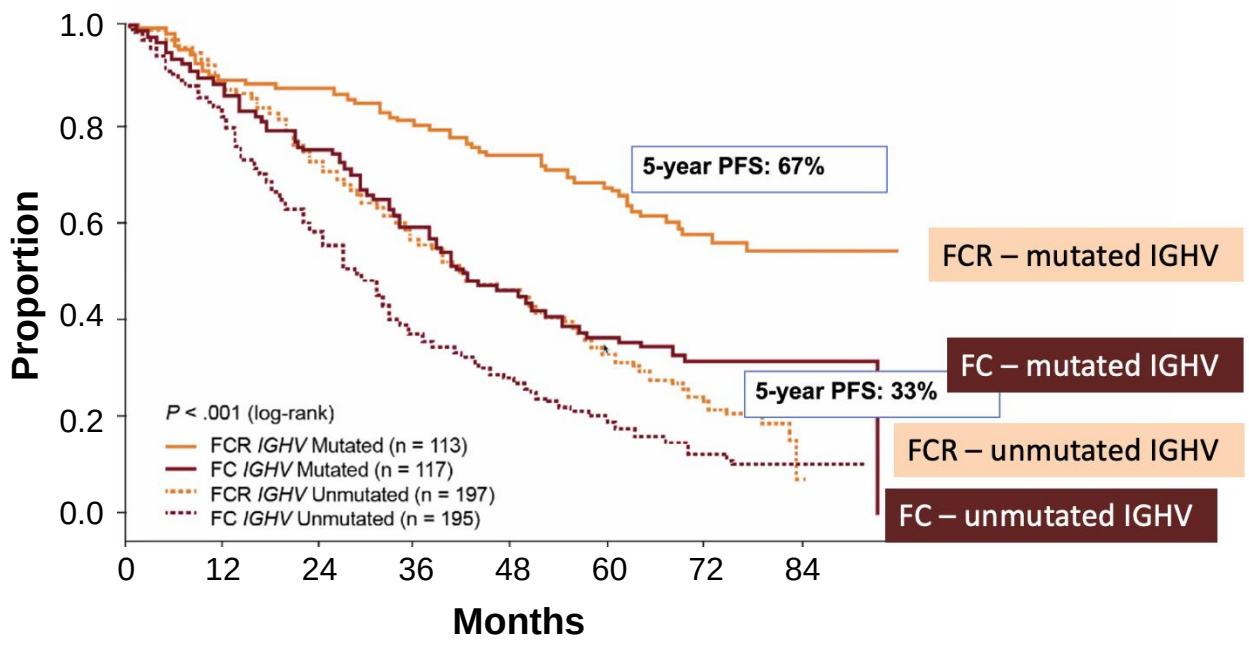


BM, bone marrow; FC, fludarabine and cyclophosphamide; FCR, FC and rituximab; PFS, progression-free survival; U-MRD, undetectable minimal residual disease.

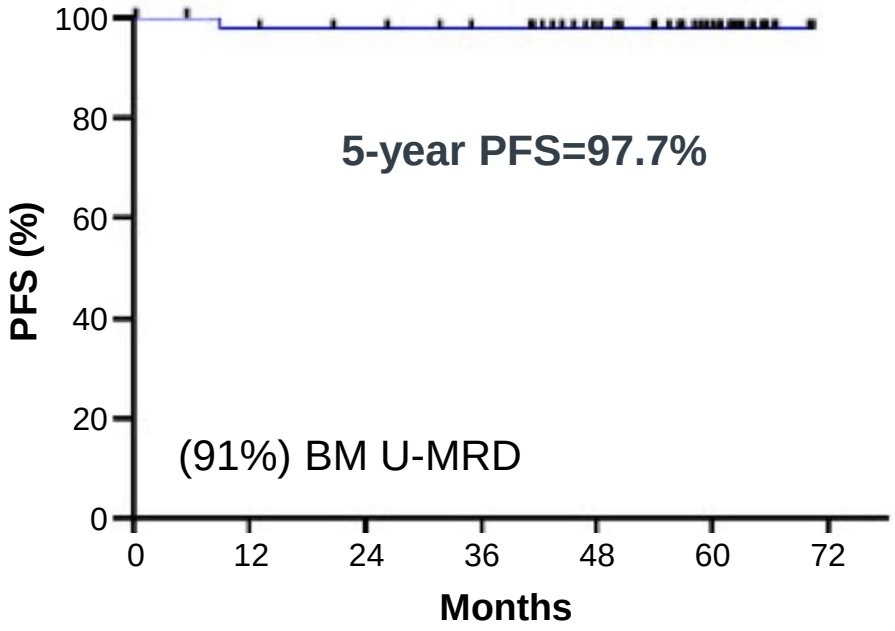
1. Fischer K *et al*. *Blood*; 127 (2): 208–215. 2. Jain N *et al*. Oral presentation at EHA 2022; Vienna, Austria, June 9–17, 2022 (Abstract S149).

FCR in patients with low-risk CLL

PFS with FC-based regimens[1]



PFS with iFCG* (N=45)[2]



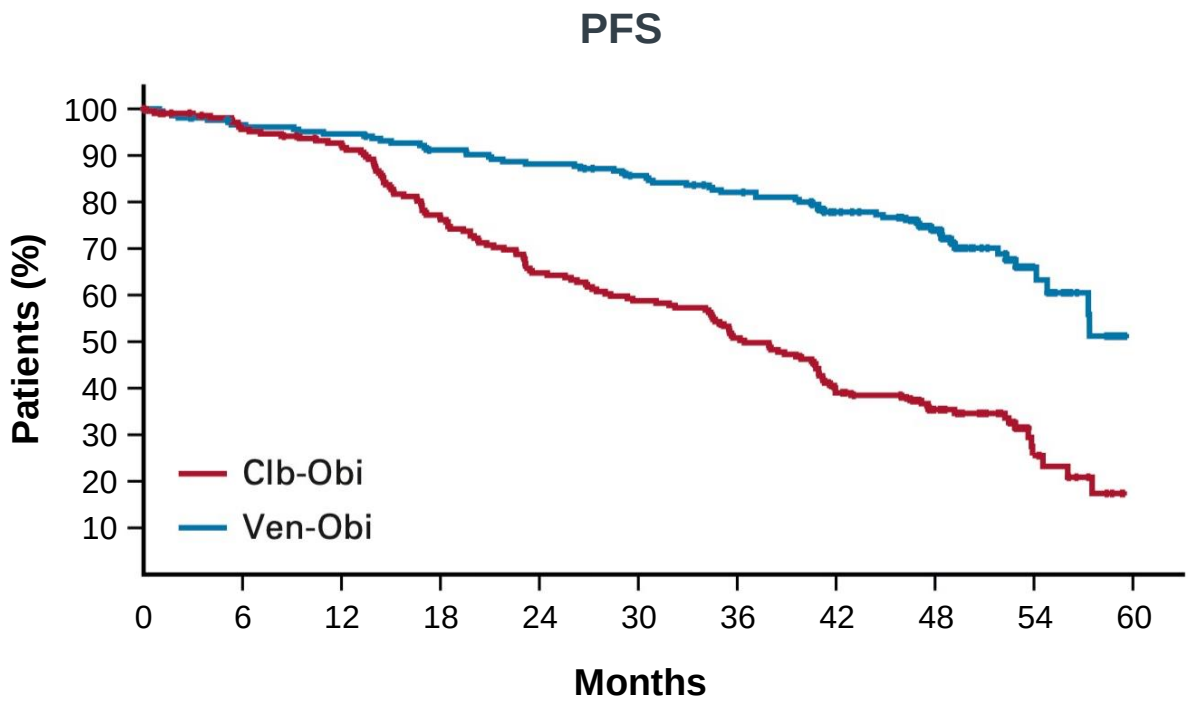
*Ibrutinib, fludarabine, cyclophosphamide, and obinutuzumab (iFCG) for 3 cycles, followed by iG for 3 cycles, followed by ibrutinib monotherapy or iG for 6 months.
BM, bone marrow; FC, fludarabine and cyclophosphamide; FCR, FC and rituximab; PFS, progression-free survival; U-MRD, undetectable minimal residual disease.
1. Fischer K *et al*. *Blood*; 127 (2): 208–215. 2. Jain N *et al*. Oral presentation at EHA 2022; Vienna, Austria, June 9–17, 2022 (Abstract S149).

CLL14 study: Venetoclax plus obinutuzumab for untreated CLL

Outcomes

- >60% of patients who had received 1-year fixed-duration Ven-Obi have remained in remission 4 years after end of therapy

- 1-year Ven-Obi regimen continues to be an effective fixed-duration option for patients with CLL and co-existing conditions

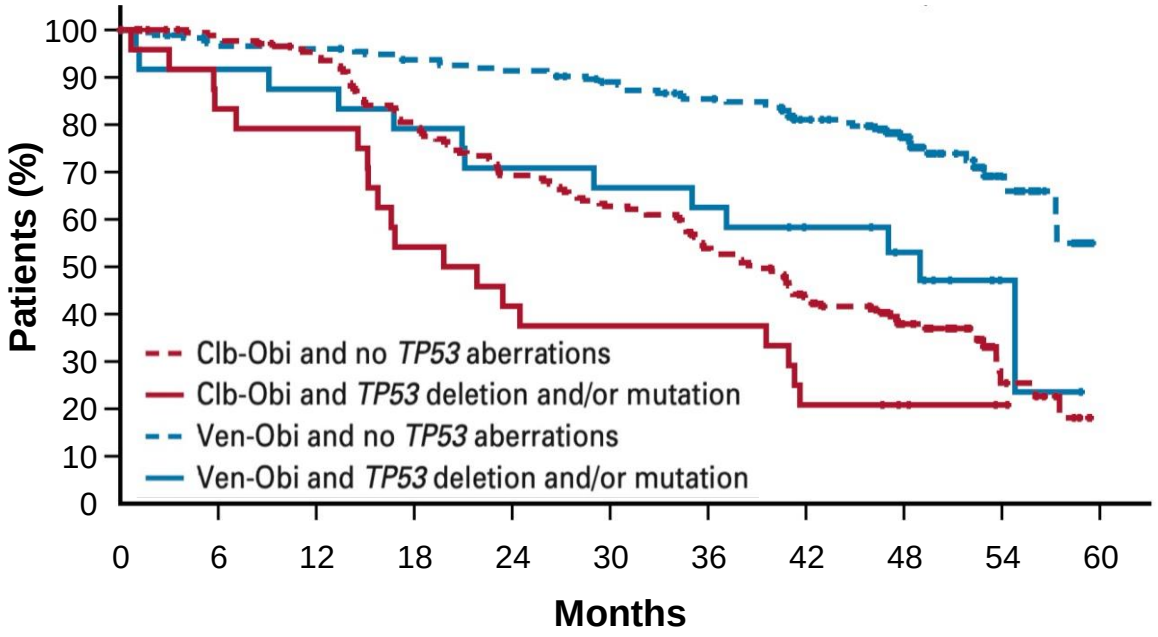


Clb, chlorambucil; CLL, chronic lymphocytic leukemia; Obi, obinutuzumab; PFS, progression-free survival; Ven, venetoclax.
Al-Savaf O *et al*. Oral presentation at EHA 2022; Vienna, Austria, June 9–17, 2022 (Abstract S148).

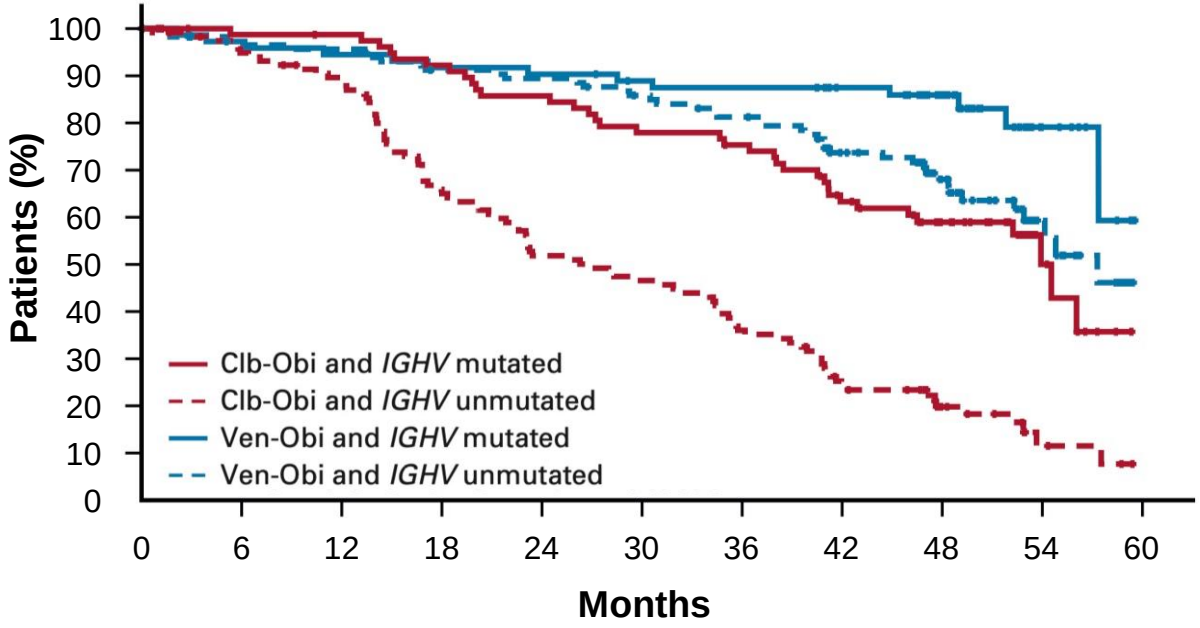
Venetoclax plus obinutuzumab for untreated CLL

5-year results of the randomized CLL14 study

PFS according to *TP53* status



PFS according to IGHV status



Clb, chlorambucil; CLL, chronic lymphocytic leukemia; Obi, obinutuzumab; PFS, progression-free survival; Ven, venetoclax.

Al-Savaf O *et al*. Oral presentation at EHA 2022; Vienna, Austria, June 9–17, 2022 (Abstract S148).

Zanubrutinib versus BR in untreated CLL

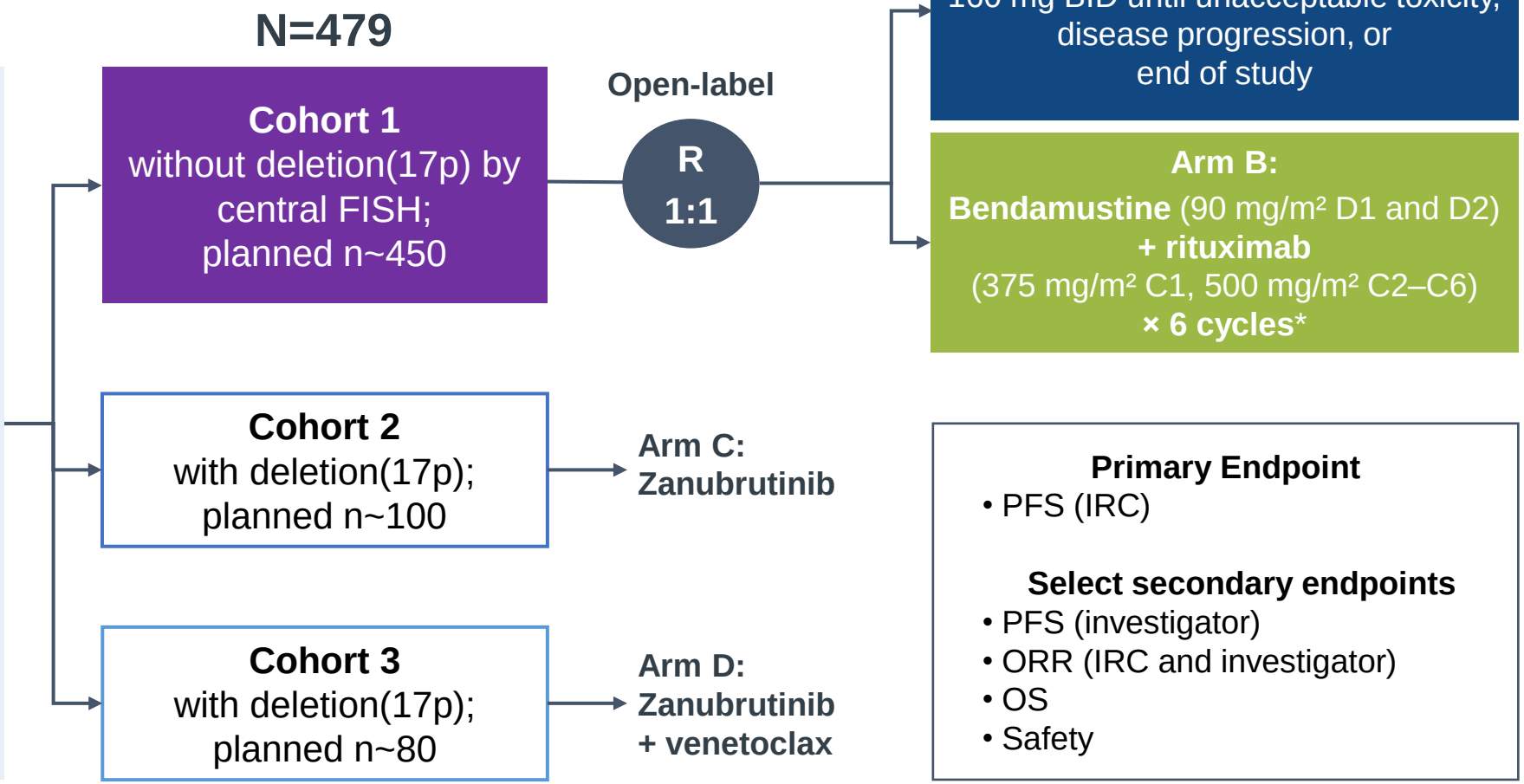
Phase III SEQUOIA study

Key eligibility criteria

- Untreated CLL/SLL
- Met iwCLL criteria for treatment
- ≥65 years of age *or* unsuitable for treatment with FCR
- ECOG PS ≤2
- Anticoagulation and CYP3A inhibitors allowed

Stratification factors:

- Age
- Binet stage
- IGHV status
- Geographic region



Primary Endpoint

- PFS (IRC)

Select secondary endpoints

- PFS (investigator)
- ORR (IRC and investigator)
- OS
- Safety

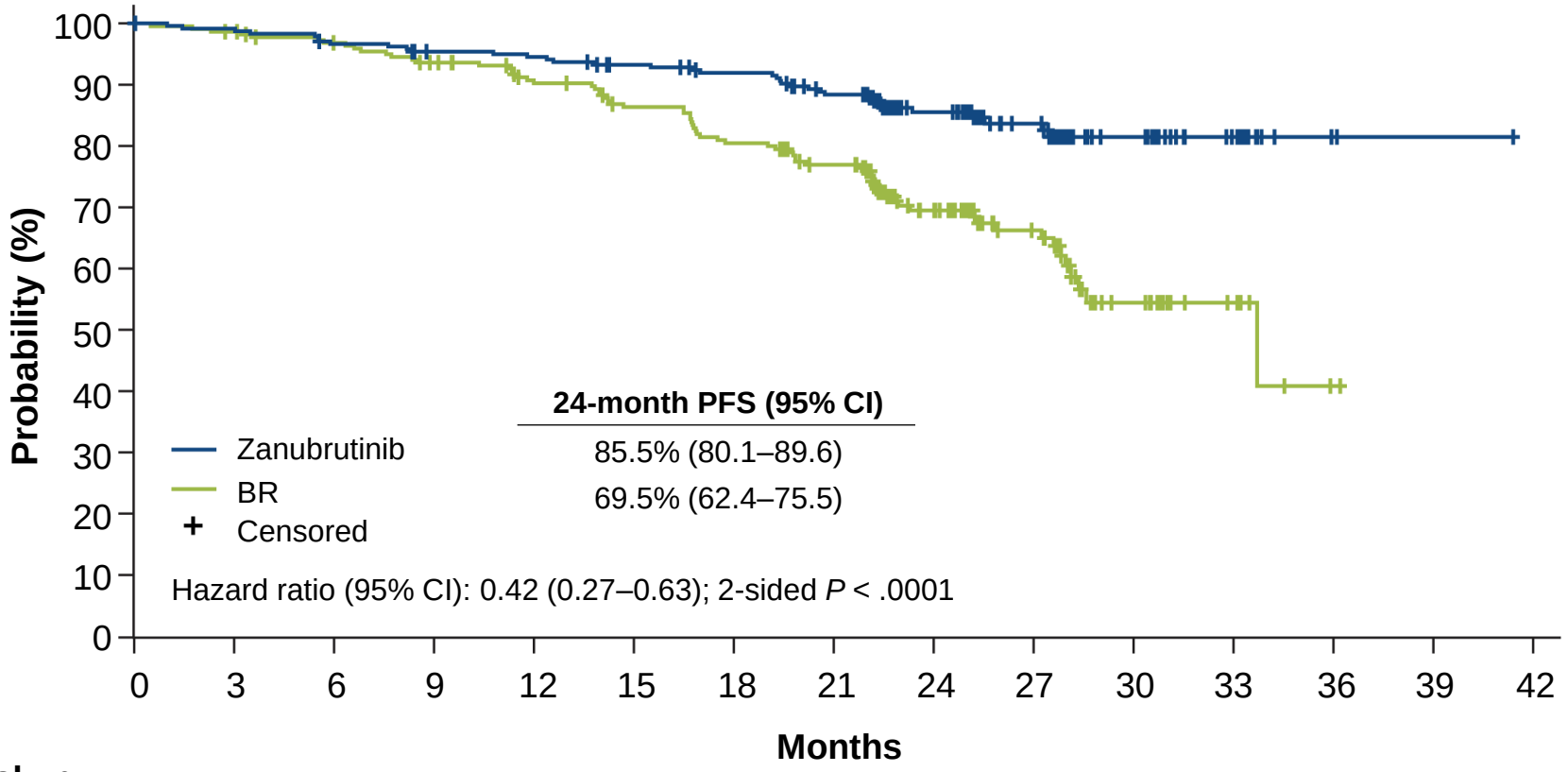
*1 cycle = 28 days.

BID, twice a day; C, Cycle; CLL, chronic lymphocytic leukemia; CYP3A, cytochrome P450 3A; D, Day; ECOG PS, Eastern Cooperative Oncology Group Performance Status; FCR, fludarabine, cyclophosphamide, and rituximab; FISH, fluorescence *in situ* hybridization; IRC, independent review committee; IGHV, immunoglobulin heavy chain variable region; iwCLL, International Workshop on Chronic Lymphocytic Leukemia; R, randomization; SLL, small lymphocytic lymphoma.

Tam CS *et al*. Abstract 396 from the 63rd ASH Annual Meeting & Exposition; Atlanta, Georgia, USA, December 11–14, 2021. Beigene Medical. SEQUOIA: Results. Available at: https://www.beigenemedical.com/CongressDocuments/Tam_BGB-3111-304_ArmsAB_ASH_Presentation_2021_2.pdf. Accessed February 2022.

SEQUOIA: zanubrutinib versus BR in untreated CLL

PFS per IRC assessment



Patients at risk, n

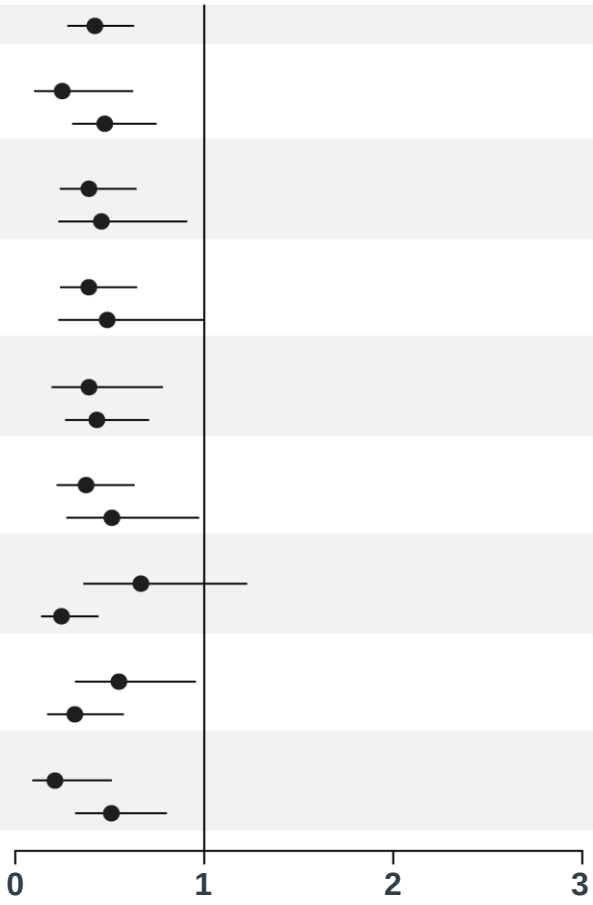
Zanubrutinib	241	237	230	224	222	214	208	195	123	79	31	17	2	1	0
BR	238	218	210	200	187	176	164	150	89	54	20	8	1	0	

BR, bendamustine and rituximab; CI, confidence interval; IRC, independent review committee; PFS, progression-free survival.
Ghia P *et al*. Poster P662 presented at EHA 2022; Vienna, Austria, June 9–17, 2022.

SEQUOIA: zanubrutinib versus BR in untreated CLL

PFS per IRC assessment by key patient subgroups

Subgroup	Event/Patient Zanu	Event/Patient BR	Hazard ratio (95% CI), %
All Patients	36/241	71/238	0.42 (0.28–0.63)
Age (years)			
< 65	6/45	19/46	0.25 (0.10–0.62)
≥ 65	30/196	52/192	0.47 (0.30–0.74)
Sex			
Male	24/154	47/144	0.39 (0.24–0.64)
Female	12/87	24/94	0.45 (0.23–0.91)
Binet stage			
A or B	24/171	52/168	0.39 (0.24–0.64)
C	12/70	19/70	0.48 (0.23–1.00)
ECOG PS			
0	12/110	24/101	0.39 (0.19–0.78)
≥ 1	24/131	47/137	0.43 (0.26–0.71)
Bulky disease, LDi			
< 5 cm	21/172	44/165	0.37 (0.22–0.63)
≥ 5 cm	15/69	27/73	0.52 (0.27–0.97)
***IGHV* mutational status**			
Mutated	18/109	25/110	0.67 (0.36–1.22)
Unmutated	15/125	45/121	0.24 (0.13–0.43)
Cytopenias at baseline			
Yes	21/102	34/109	0.55 (0.32–0.95)
No	15/139	37/129	0.31 (0.17–0.57)
Chromosome 11q deletion			
Yes	7/43	22/46	0.21 (0.09–0.50)
No	29/198	49/192	0.50 (0.32–0.80)



BR, bendamustine and rituximab; CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group Performance Status; IGHV, gene encoding the immunoglobulin heavy chain variable region; IRC, independent review committee; LDi, longest diameter; Zanu, zanubrutinib.

Ghia P *et al*. Poster P662 presented at EHA 2022; Vienna, Austria, June 9–17, 2022.

SEQUOIA: zanubrutinib versus BR in untreated CLL

Adverse event summary

	Zanubrutinib (n = 240)	BR (n = 227)
Any AE, n (%)	224 (93.3)	218 (96.0)
Grade ≥3 AE, n (%)	126 (52.5)	181 (79.7)
Serious AE, n (%)	88 (36.7)	113 (49.8)
Fatal AE, n (%)	11 (4.6)	11 (4.8)
AE leading to dose reduction, n (%)	18 (7.5)	84 (37.4)
AE leading to dose interruption/delay, n (%)	111 (46.3)	154 (67.8)
AE leading to discontinuation, n (%)	20 (8.3)	31 (13.7)

AE, adverse event; BR, bendamustine and rituximab.

Ghia P *et al*. Poster P662 presented at EHA 2022; Vienna, Austria, June 9–17, 2022.

SEQUOIA: zanubrutinib versus BR in untreated CLL

Patient-reported outcomes

	Week 12 LS mean difference* (95% CI)	*P*-value	Week 24 LS mean difference* (95% CI)	*P*-value
Global health status	0.7 (–3.3 to 4.7)	0.73	4.9 (0.9 to 9.0)	**0.017**
Functional domains				
Physical functioning	1.0 (–1.9 to 3.9)	0.51	3.8 (0.8 to 6.7)	**0.012**
Role functioning	4.4 (–0.5 to 9.4)	0.080	4.8 (–0.2 to 9.7)	**0.061**
Symptoms				
Diarrhea	–1.7 (–5.4 to 2.0)	0.36	–6.2 (–10 to –2.5)	**0.0012**
Fatigue	–3.7 (–8.1 to 0.7)	0.97	–4.5 (–8.9 to –0.1)	**0.047**
Nausea/vomiting	–3.9 (–6.5 to –1.3)	**0.0035**	–4.2 (–6.8 to –1.6)	**0.0015**
Pain	4.7 (0.1 to 9.3)	**0.047**	0.4 (–4.3 to 5.1)	**0.87**

*LS mean difference between zanubrutinib and BR arms.
BR, bendamustine and rituximab; CLL, chronic lymphocytic leukemia; LS, least squares
Ghia P *et al*. Poster P662 presented at EHA 2022; Vienna, Austria, June 9–17, 2022.

Elevate-TN Phase 3 study in untreated CLL

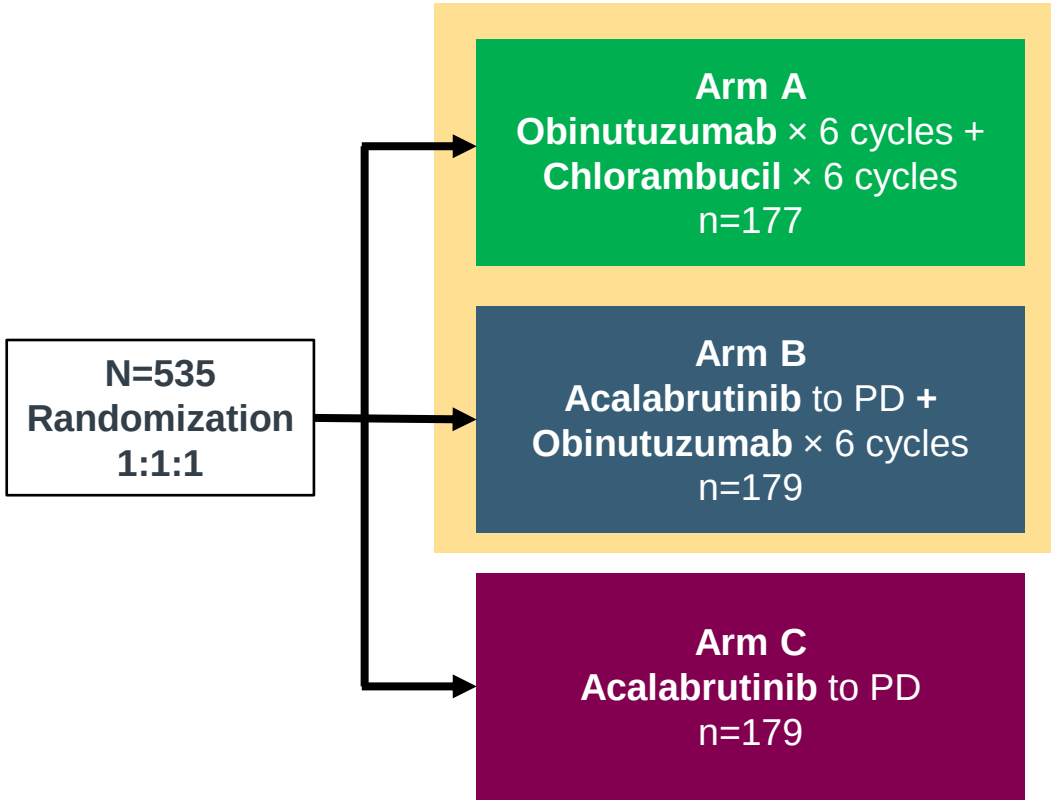
Study design

Key inclusion criteria

- Age ≥65 years **or** 18-65 years **and** ≥1 of the following criteria:
  - CrCl = 30–69 mL/min
  - CIRS-G score >6

Stratification

- Del(17p) status (~9%)
- Geographic region
- ECOG PS (0–1 vs. 2)



Crossover was allowed upon IRC-confirmed PD from Arm A to Arm C

Primary end point

- PFS by IRC: Arm A vs B

Secondary end points

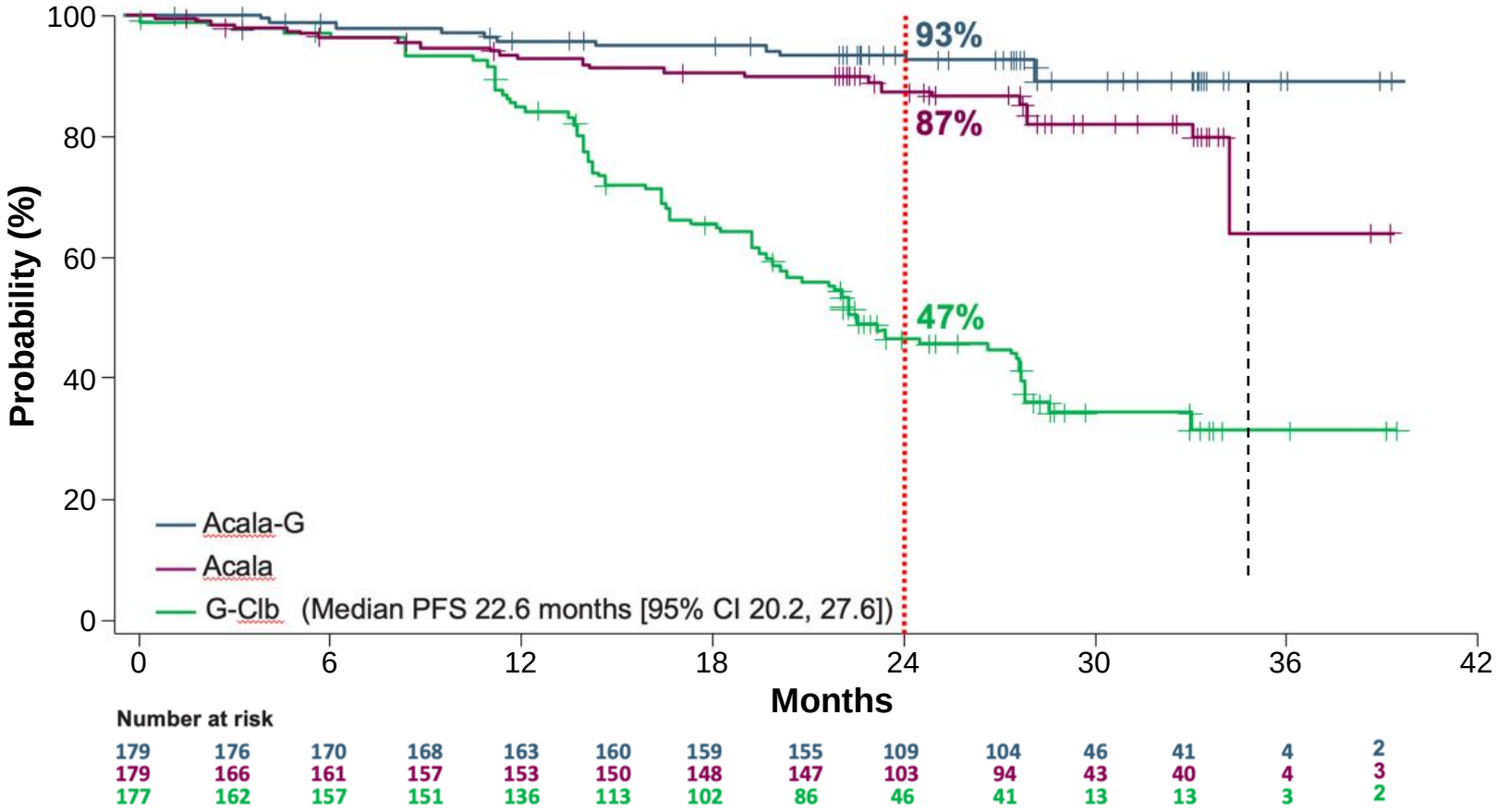
- PFS by IRC: Arm A vs C
- ORR by IRC, OS, TTNT (Arm A vs B and A vs C)
- Safety

CLL, chronic lymphocytic leukemia; CIRS-G, Cumulative Illness Rating Scale-Geriatric; CrCl, creatinine clearance; ECOG PS, Eastern Cooperative Oncology Group Performance Status; IRC, independent review committee; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; TTNT, time to next treatment.

Sharman J *et al*. Poster P666 presented at EHA 2022; Vienna, Austria, June 9–17, 2022.

ELEVATE-TN

PFS per IRC assessment



	Hazard ratio (95% CI), *P*
Acala-G vs. G-Clb	**0.10** (0.06–0.17), <0.0001
Acalabrutinib vs. G-Clb	**0.20** (0.13–0.30), <0.0001
Acala-G vs. acalabrutinib[a]	**0.49** (0.26–0.95)

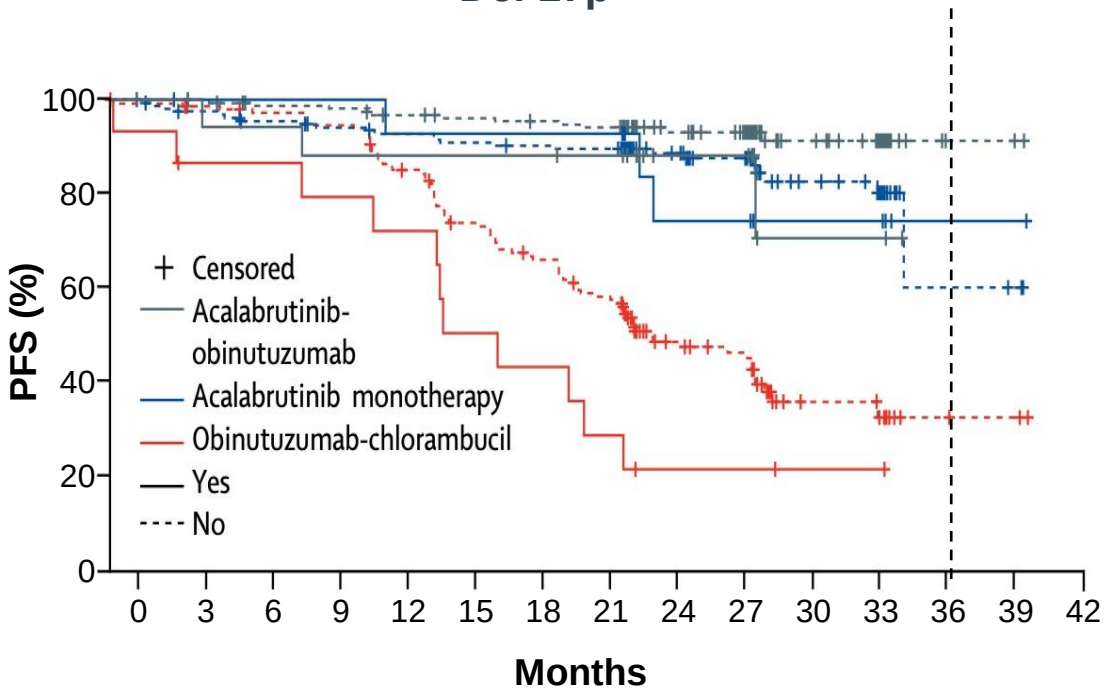
iLLUMINATE (Ibr+G) 30-mo PFS: 79%[2]
RESONATE-2 (Ibr) 24-mo PFS: 89%[3]

Acala, acalabrutinib; CI, confidence interval; G-Clb, obinutuzumab and chlorambucil; IRC, independent review commitee; PFS, progression-free survival.
Sharman J *et al*. Poster P666 presented at EHA 2022; Vienna, Austria, June 9–17, 2022.

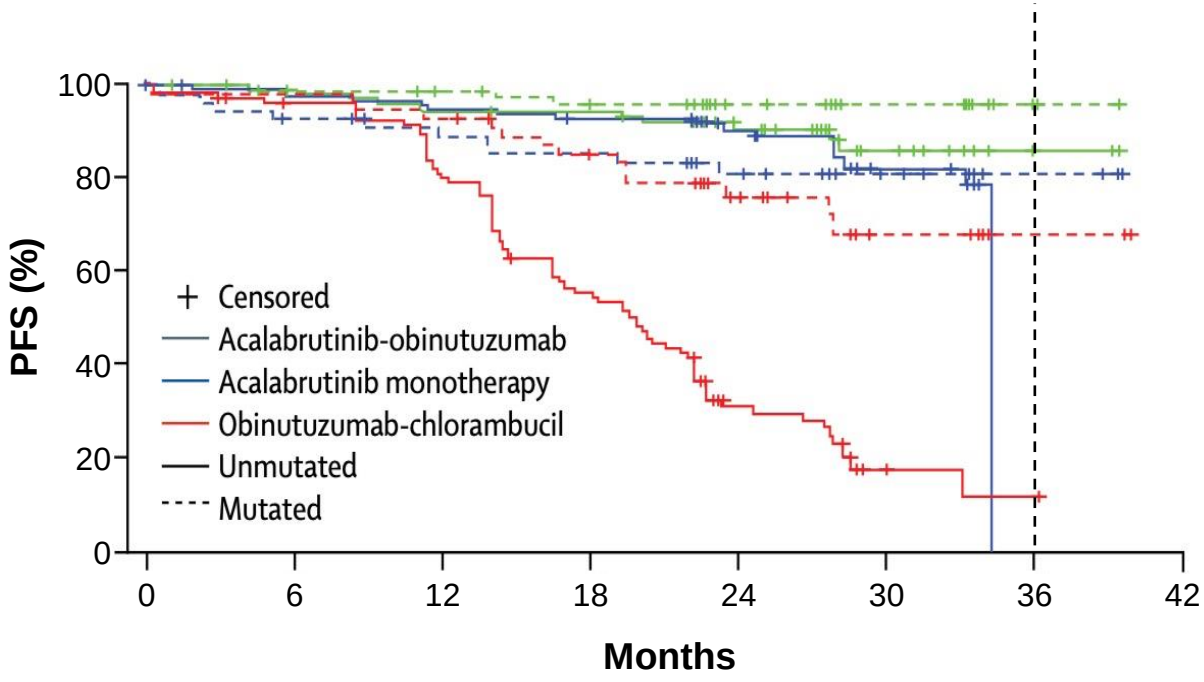
ELEVATE-TN

PFS in high-risk populations

Del 17p



IGHV mutation status

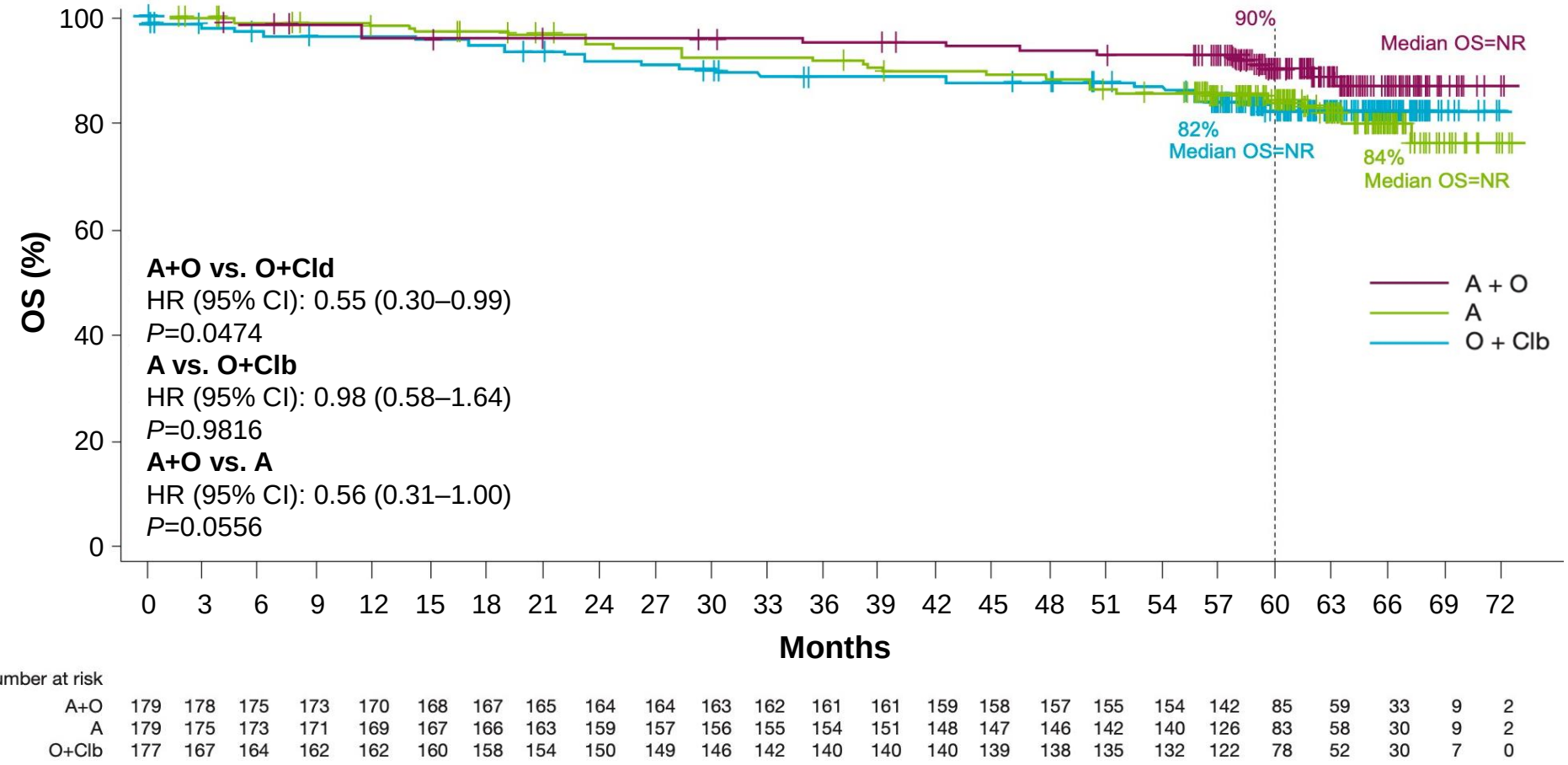


PFS, progression-free survival.

Sharman J *et al*. Poster P666 presented at EHA 2022; Vienna, Austria, June 9–17, 2022.

ELEVATE-TN

Overall survival



A, acalabrutinib; Clb, chlorambucil; OD, overall survival; NR, not reached; O, obinutuzumab.
Sharman J *et al*. Poster P666 presented at EHA 2022; Vienna, Austria, June 9–17, 2022.

Ibrutinib plus venetoclax in untreated CLL

Phase III NCRI FLAIR trial interim analysis

- Interim analysis in the first 274 patients reaching 2 years post-randomization
  - Ibrutinib n=138
  - Ibrutinib plus venetoclax n=136
- Ibrutinib plus venetoclax is an effective and well tolerated combination resulting in a high rate of MRD negativity in blood (71.3%) and marrow (65.4%) in the first 2 years of treatment

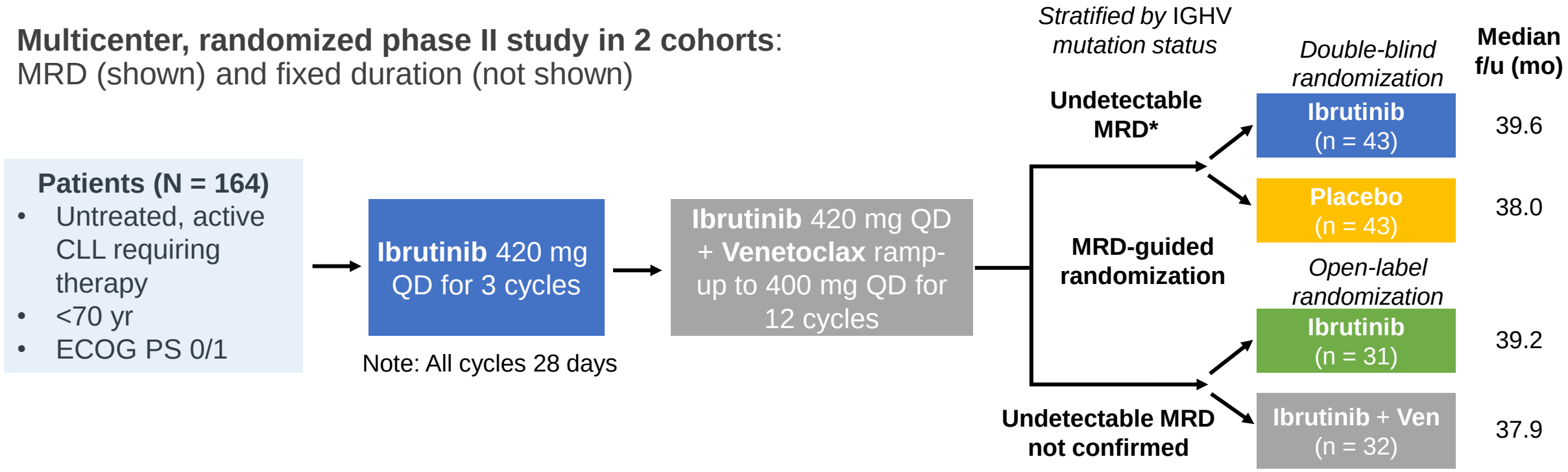
	I (n=138)	I+V (n=136)
9-months post-randomization, % (95% CI)		
MRD negative in the bone marrow	0.0 (0.00–2.64)	36.0 (27.98–44.70)
MRD negative in the peripheral blood	0.0 (0.00–2.64)	41.2 (32.81–49.93)
24 months post-randomization, % (95% CI)		
MRD negative in the bone marrow	0.0 (0.00–2.64)	65.4 (56.81–73.38)
MRD negative in the peripheral blood	0.0 (0.00–2.64)	71.3 (62.95–78.75)

CI, confidence interval; CLL, chronic lymphocytic leukemia; I, ibrutinib; MRD, minimal residual disease; V, venetoclax.

Hillmen P *et al*. Oral presentation at EHA 2022; Vienna, Austria, June 9–17, 2022 (Abstract S145).

CAPTIVATE (MRD cohort)
Study design

Multicenter, randomized phase II study in 2 cohorts:
MRD (shown) and fixed duration (not shown)



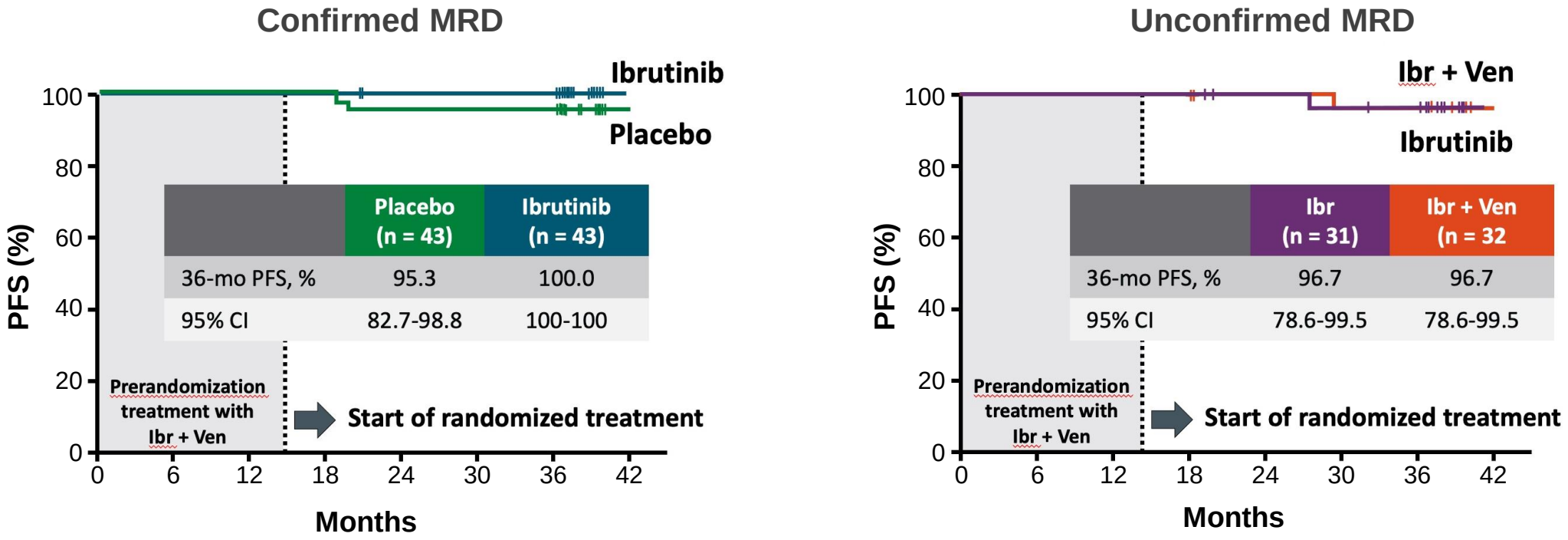
- Primary endpoint analysis: 95% to 100% 1-yr DFS rate in patients with confirmed undetectable MRD[1]
- Secondary endpoints: undetectable MRD, response, PFS, safety[2]

*Defined as undetectable MRD (<10-4 by flow cytometry) serially over at least 3 cycles in both PB and BM.
CLL, chronic lymphocytic leukemia; ECOG PS, Eastern Cooperative Oncology Group Performance Status; f/u, follow-up; MRD, minimal residual disease; QD, once a day; ven, venetoclax.
Moreno C *et al*. Poster P669 presented at EHA 2022; Vienna, Austria, June 9–17, 2022.

CAPTIVATE (MRD cohort)

3-year PFS

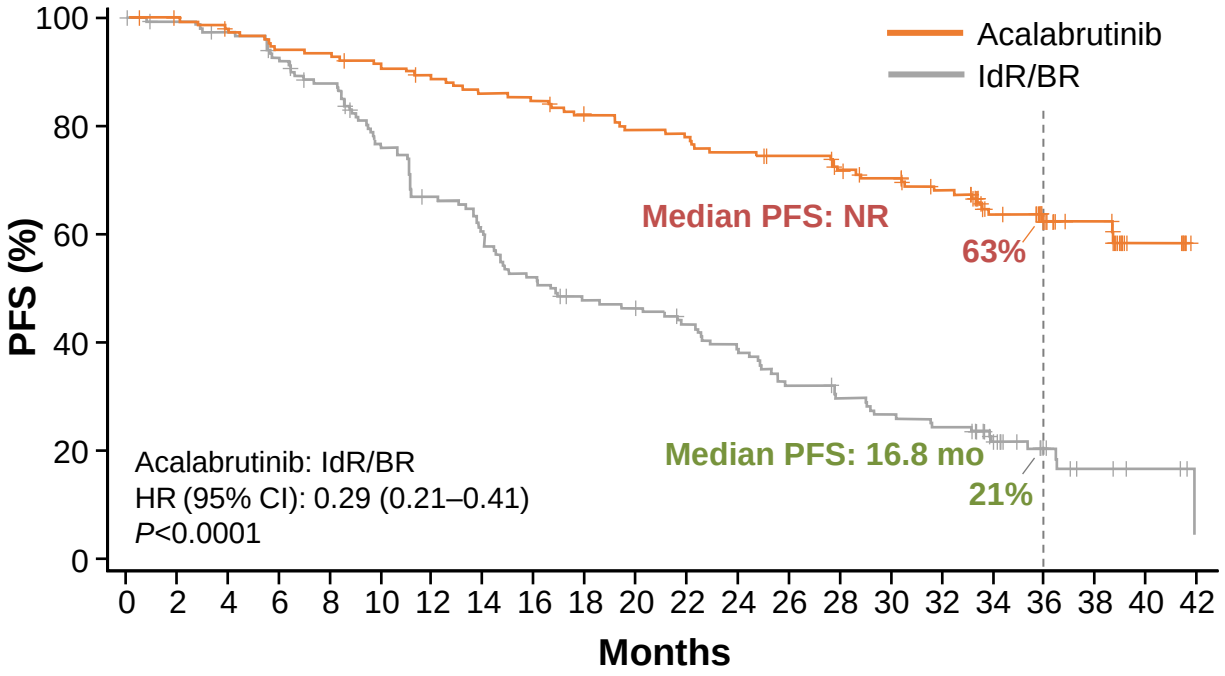
- 1 new PFS event (PD in uMRD arm) in 1-year since primary analysis
- 3-year OS: 99% overall (97%–100% across randomized arms)



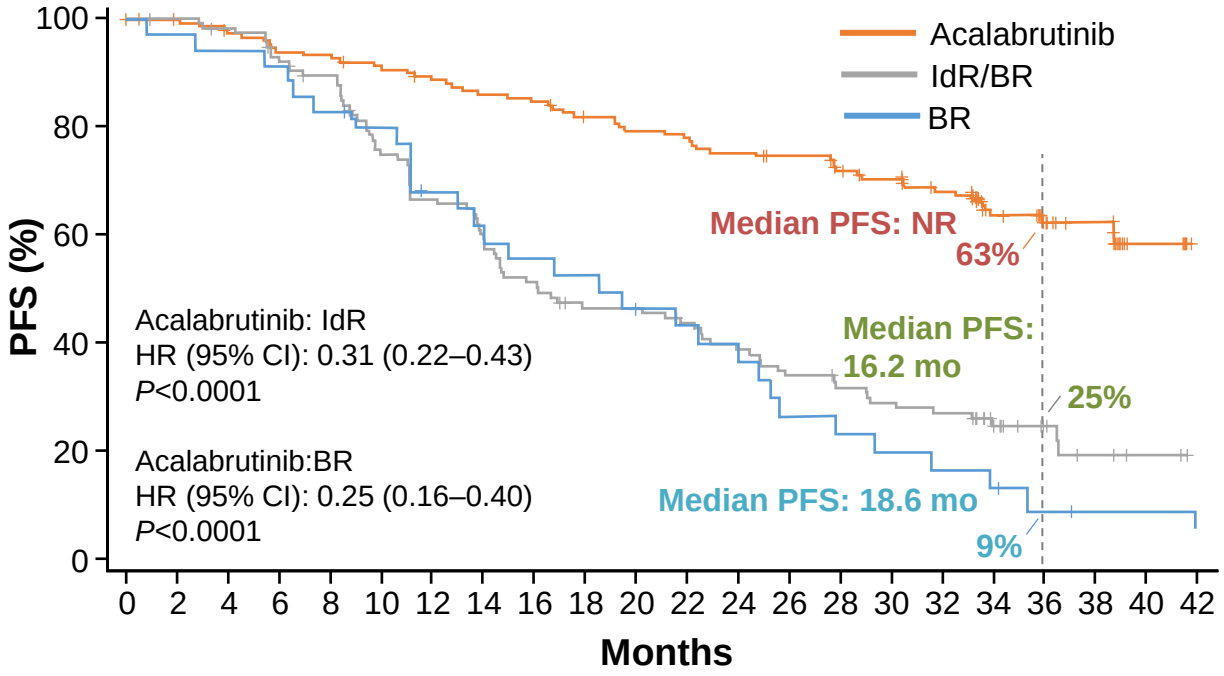
CI, confidence interval; ibr, ibrutinib; MRD, minimal residual disease; PD, progressive disease; PFS, progression-free survival; uMRD, undetectable MRD; ven, venetoclax.
Moreno C *et al*. Poster P669 presented at EHA 2022; Vienna, Austria, June 9–17, 2022.

Investigator-assessed PFS with acalabrutinib, IdR, and BR

Acalabrutinib vs. IdR/BR



Acalabrutinib vs. IdR vs. BR



Median time on study was 36.0 (acalabrutinib) and 35.2 (IdR/BR) months.

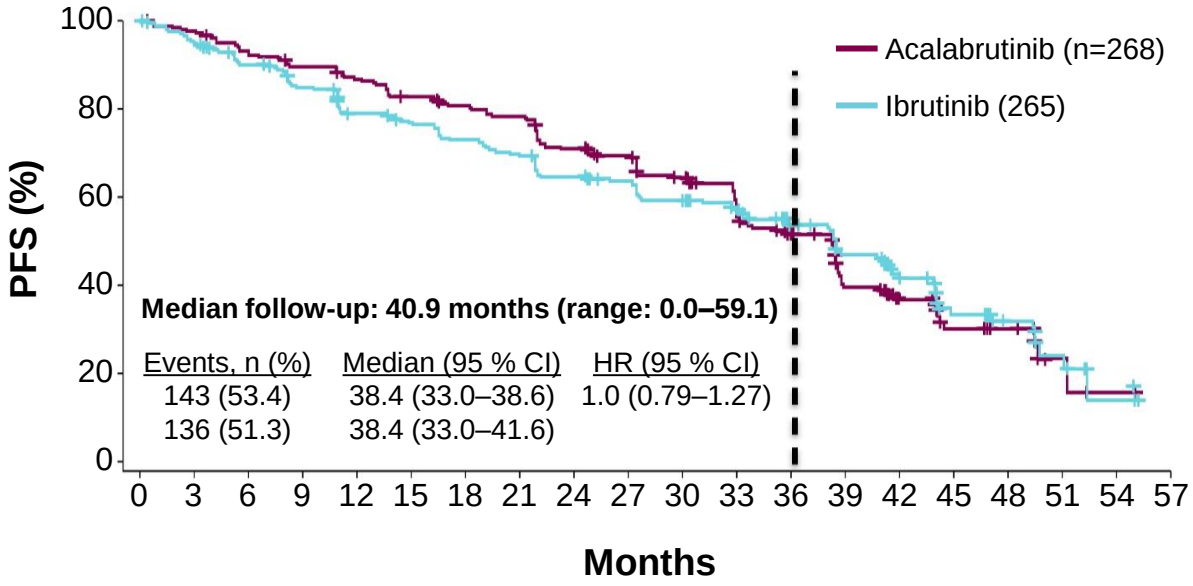
BR, bendamustine and rituximab; HR, hazard ratio; IdR, idelalisib and rituximab; NR, not reached; PFS, progression-free survival

Jurczak W. *et al*. Blood 2021; 138 (Suppl 1): 393. Ghia P. *et al*. *J Clin Oncol*. 2020; 38 (25): 2849–2861. Ghia P. *et al*. Poster P668 presented at EHA 2022; Vienna, Austria, June 9–17, 2022.

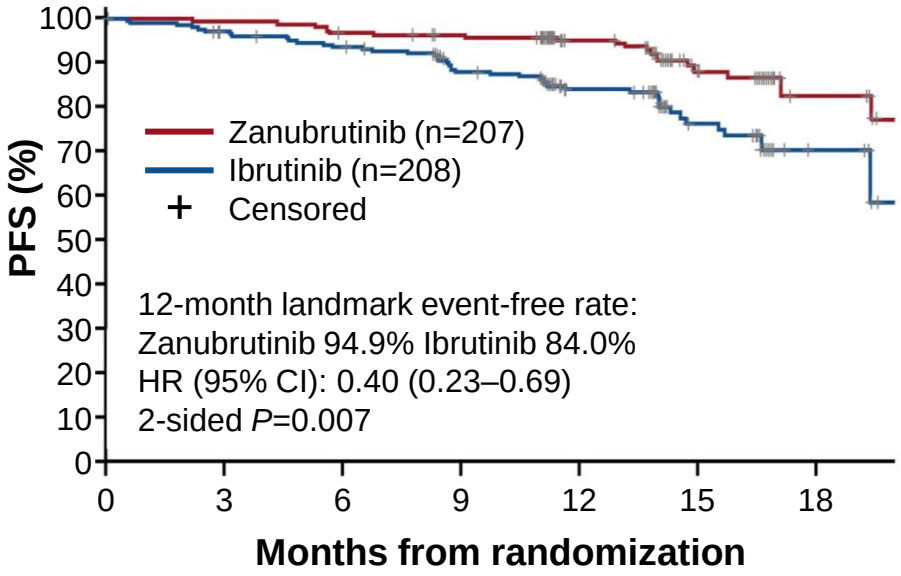
ELEVATE R/R and ALPINE

Next-generation BTKis vs. ibrutinib

ELEVATE R/R
Acalabrutinib vs. ibrutinib (N=533)[1]



ALPINE
Zanubrutinib vs. ibrutinib (N=652)[2]



This slide shows data from two separate trials and the limitations of cross-trial comparisons apply.

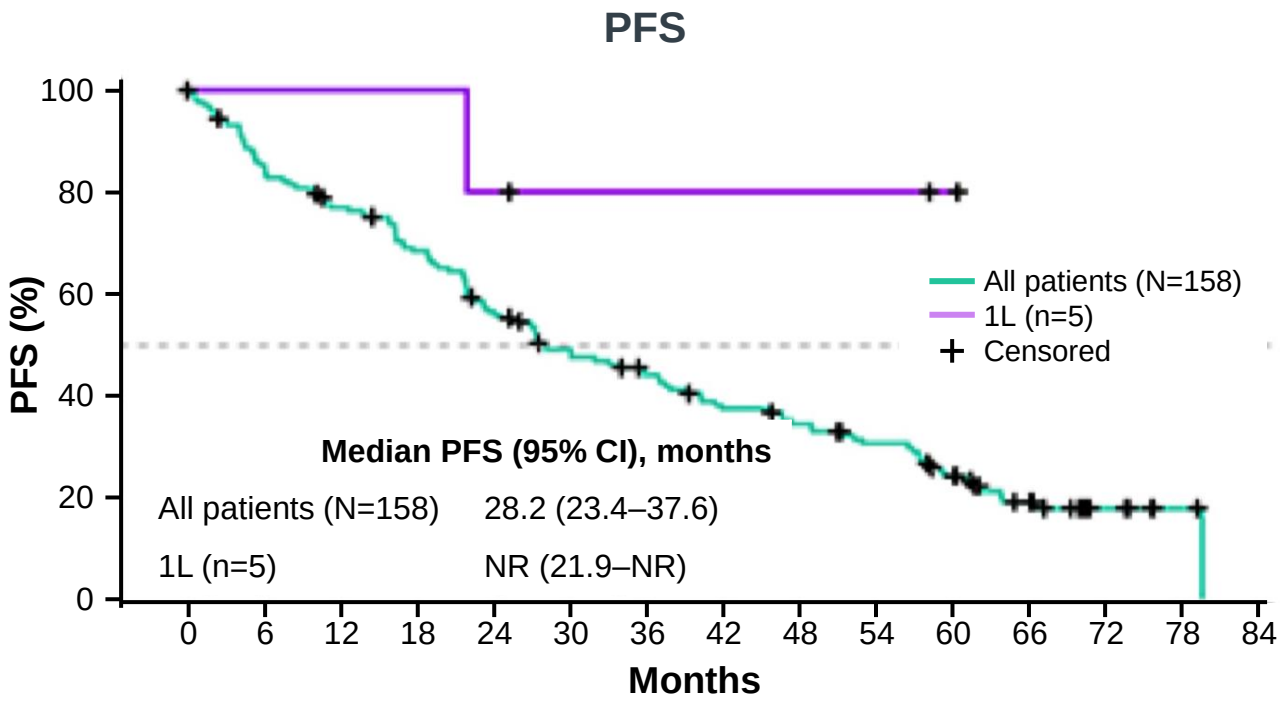
HR, hazard ratio; R/R, relapsed/refractory.

1. Byrd JC *et al*. Oral presentation at ASCO 2021; Virtual, June 4–8, 2021 (Abstract 7500). 2. Hillmen P *et al*. Oral presentation at EHA 2021; Virtual, June 14–16, 2021 (Abstract LB1900).

Venetoclax monotherapy in del(17p) CLL

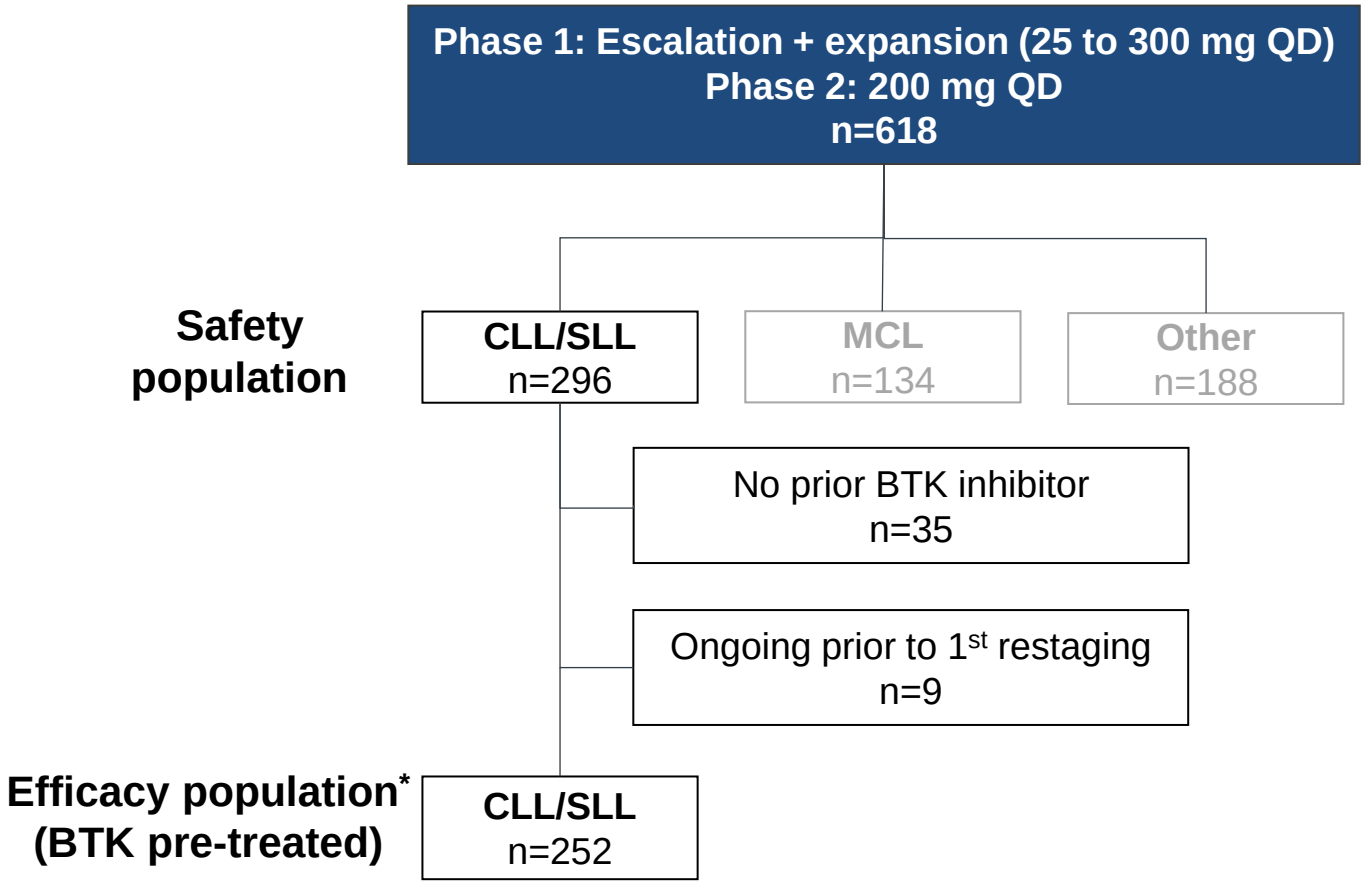
Phase II trial: 6-year follow-up and genomic analyses

- ORR: 77% (N=158)
  - Median time on study, 26.6 months
- At a median follow-up of 70 months:
  - 48% of patients were alive
  - 24% were progression-free
  - 16% remained on venetoclax



CLL, chronic lymphocytic leukemia; del, deletion; NR, not reached; ORR, overall response rate; PFS, progression-free survival.
Stilgenbauer S *et al*. Oral presentation at EHA 2022; Vienna, Austria, June 9–17, 2022 (Abstract S146).

Phase 1/2 BRUIN study of pirtobrutinib



Phase 1 3+3 design

- 28-day cycles
- Intra-patient dose escalation allowed
- Cohort expansion permitted at doses deemed safe

Eligibility

- Age ≥18 years
- ECOG PS 0–2
- CLL or other B-cell NHL
- Active disease and in need of treatment
- Previously treated

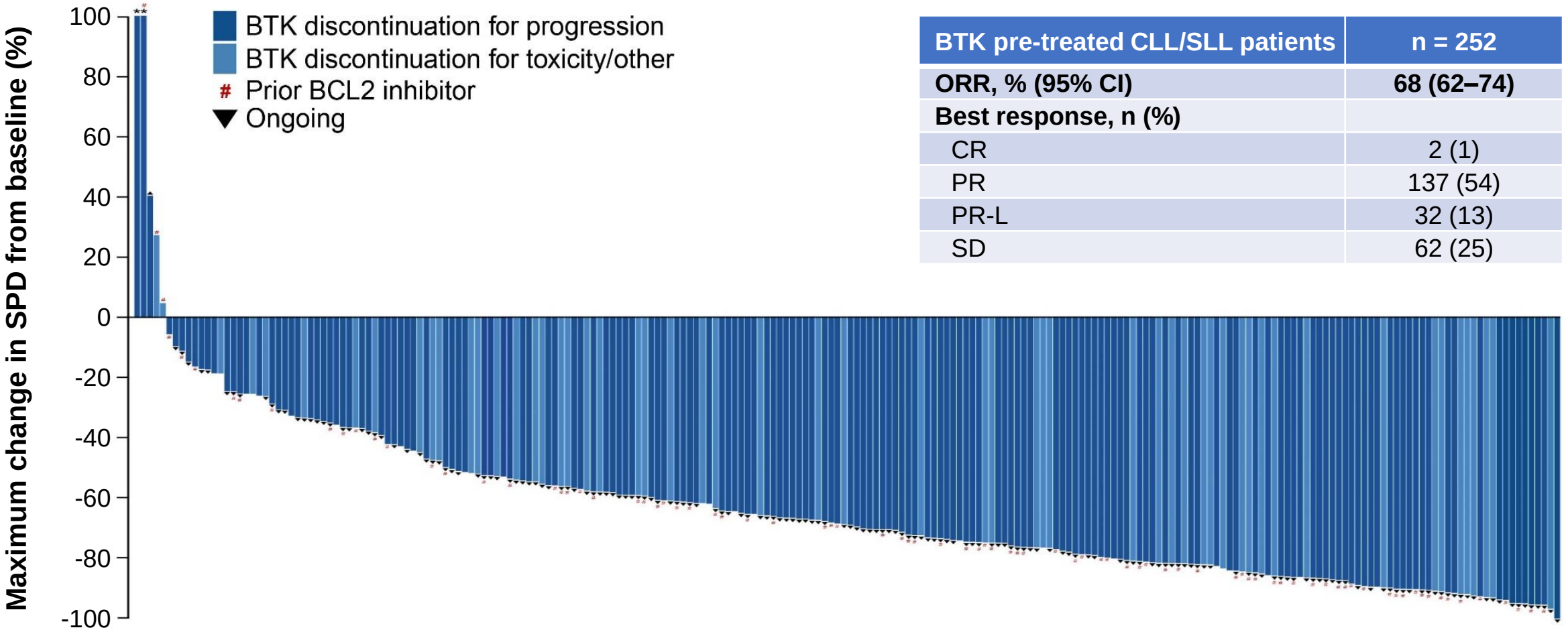
Key endpoints

- Safety/tolerability
- Determine MTD and recommended phase 2 dose
- Pharmacokinetics
- Efficacy according to ORR & DoR based on disease criteria (iwCLL, IWWM, Lugano)

Data cutoff: 16 July 2021. *Efficacy evaluable patients are those who had at least one post-baseline response assessment or had discontinued treatment prior to first post-baseline response assessment.
CLL, chronic lymphocytic leukemia; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group Performance Status; iwCLL, International Workshop on Chronic Lymphocytic Leukemia; MTD, maximum tolerated dose; NHL, non-Hodgkin's lymphoma; ORR, overall response rate; SLL, small lymphocytic lymphoma.
Mato AR *et al*. Oral presentation at EHA 2022; Vienna, Austria, June 9–17, 2022 (Abstract S147).

BRUIN study

Responses in patients with CLL/SLL



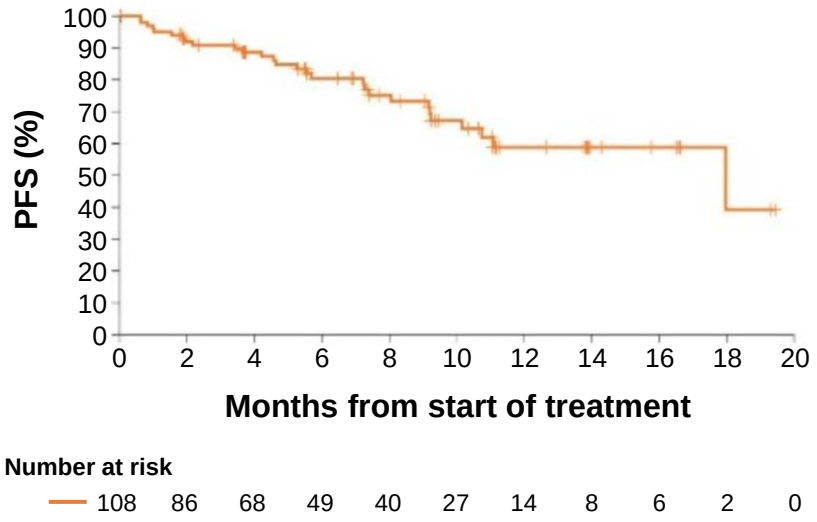
BTK pre-treated CLL/SLL patients	n = 252
ORR, % (95% CI)	**68 (62–74)**
Best response, n (%)	
CR	2 (1)
PR	137 (54)
PR-L	32 (13)
SD	62 (25)

CLL, chronic lymphocytic leukemia; CR, complete response; ORR, overall response rate; PR, partial response; PR-L, partial response with lymphocytosis; SD, stable disease; SLL, small lymphocytic lymphoma; SPD, sum of the products of diameters.

Mato AR *et al*. Oral presentation at EHA 2022; Vienna, Austria, June 9–17, 2022 (Abstract S147).

BRUIN study
Updated results

PFS in patients pre-treated with at least a BTKi and BLC2i (median prior lines of therapy=5)



		ORR, % (95% CI) (0 25 50 75 100)	Median lines of prior therapy, median (range)	Treated, n	Efficacy-evaluable, n
Patient subgroups	All BTKi pre-treated		3 (1–11)	261	252
	≥12 months follow-up		3 (1–11)	119	119
	Del(17p) and/or *TP53*^{mut}		3 (1–10)	77	76
	BTK C481 and *PLCG2* mutations		3 (1–6)	26	26
Prior therapy	BTKi + BCL2i		5 (1–11)	108	102
	BTKi + PI3Ki		5 (2–11)	51	45
	BTKi+chemotherapy+ anti-CD20		4 (2–11)	200	192
	BTKi+chemotherapy+ anti-CD20+BCL2i		5 (3–11)	92	86
	BTKi+chemotherapy +anti-CD20+BCL2i+PI3Ki		6 (3–11)	33	27
Reason to discontinue prior BTKi	Progression		4 (1–11)	196	190
	Toxicity/other		3 (1–11)	65	62

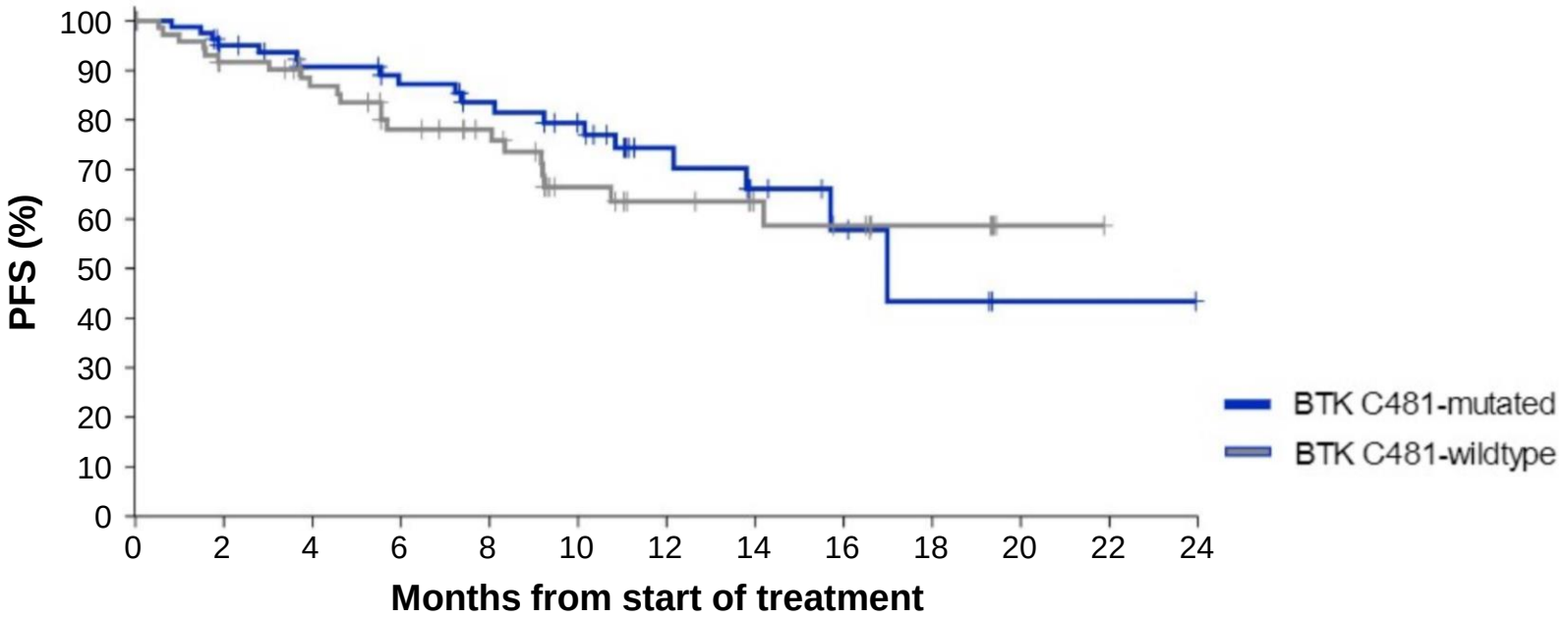
ORR, overall response rate; PFS, progression-free survival.

Mato AR *et al*. Oral presentation at EHA 2022; Vienna, Austria, June 9–17, 2022 (Abstract S147).

BRUIN study

Impact of BTK C481 mutation status

PFS according to BTK C481 mutation status in patients who progressed during treatment with a prior BTK inhibitor



PFS, progression-free survival.

Mato AR *et al*. Oral presentation at EHA 2022; Vienna, Austria, June 9–17, 2022 (Abstract S147).

BRUIN study
Safety outcomes

AEs, %	All doses and patients (n=618)						
	TEAEs in ≥15% of patients, %					TRAEs, %	
	Grade 1	Grade 2	Grade 3	Grade 4	Any grade	Grades 3/4	Any grade
Fatigue	13	8	1	-	23	1	9
Diarrhea	15	4	<1	<1	19	<1	8
Neutropenia	1	2	8	6	18	8	10
Contusion	15	2	-	-	17	-	12
AEs of interest, %							
Bruising	20	2	-	-	22	-	15
Rash	9	2	<1	-	11	<1	5
Arthralgia	8	3	<1	-	11	-	3
Hemorrhage	5	2	1	-	8	<1	2
Hypertension	1	4	2	-	7	<1	2
Atrial fibrillation/flutter	-	1	<1	<1	2	-	<1

- No DLTs reported and MTD not reached
- 96% of patients received ≥1 dose of pirtobrutinib at or above the recommended phase II dose (200 mg once a day)
- 6 patients (1%) permanently discontinued treatment due to TRAEs

AE, adverse event; DLT, dose-limiting toxicities; MTD, maximum tolerated dose; TEAE, treatment emergent AE; TRAE, treatment-related AE.
Mato AR *et al*. Oral presentation at EHA 2022; Vienna, Austria, June 9–17, 2022 (Abstract S147).

Take-home messages

- Targeted therapy is the undebatable standard of care in R/R CLL
- Targeted therapy is moving to the first line CLL
  - An approved standard of care in 17del/*TP53*^{mut} patients
  - An emerging standard of care for all untreated CLL patients

- Next generation BTK inhibitors may prove to be better to ibrutinib due to better efficacy and safety
- Regimens with BCL-2 inhibitors may allow for time-limited therapy

- Inhibition of BTK and BCL-2 are alternative solutions
  - Neither may be regarded as superior, however long-lasting therapy seems to be more efficient in high-risk patients
- Time-limited protocols may be based on MRD

CLL, chronic lymphocytic leukemia; del, deletion; MRD, minimal residual disease; mut, mutated; R/R, relapsed/refractory.

Panel discussion

Audience Q&A

Summary

Chair: Professor Christian Buske

Summary

Recent reports demonstrate the increasing importance of targeted agents at all stages of treatment for lymphomas and CLL

Maturing clinical data reported for anti-CD20×CD3 bispecific antibodies demonstrated the potential for this class in the treatment of aggressive and indolent lymphomas

CAR T-cell therapy is progressing rapidly with 3-year follow-up of KTE-X19 in patients with R/R MCL showing durable long-term responses with a manageable safety profile

Targeted therapy with BTKi or BCL2i is the basis for standard of care regimens in R/R CLL and is moving into the first-line setting, with a key clinical decision being whether to use continuous or time-limited therapy

BCL-2i, B-cell lymphoma 2 inhibitor; BTKi, Bruton's tyrosine kinase inhibitor; CAR-T, chimeric antigen receptor T-cell; CD, cluster of differentiation; CLL, chronic lymphocytic leukemia; MCL, mantle cell lymphoma; R/R, relapsed/refractory.

We would appreciate your feedback!
Please complete the post-meeting survey.

Thank you for your attention

BeiGeneius