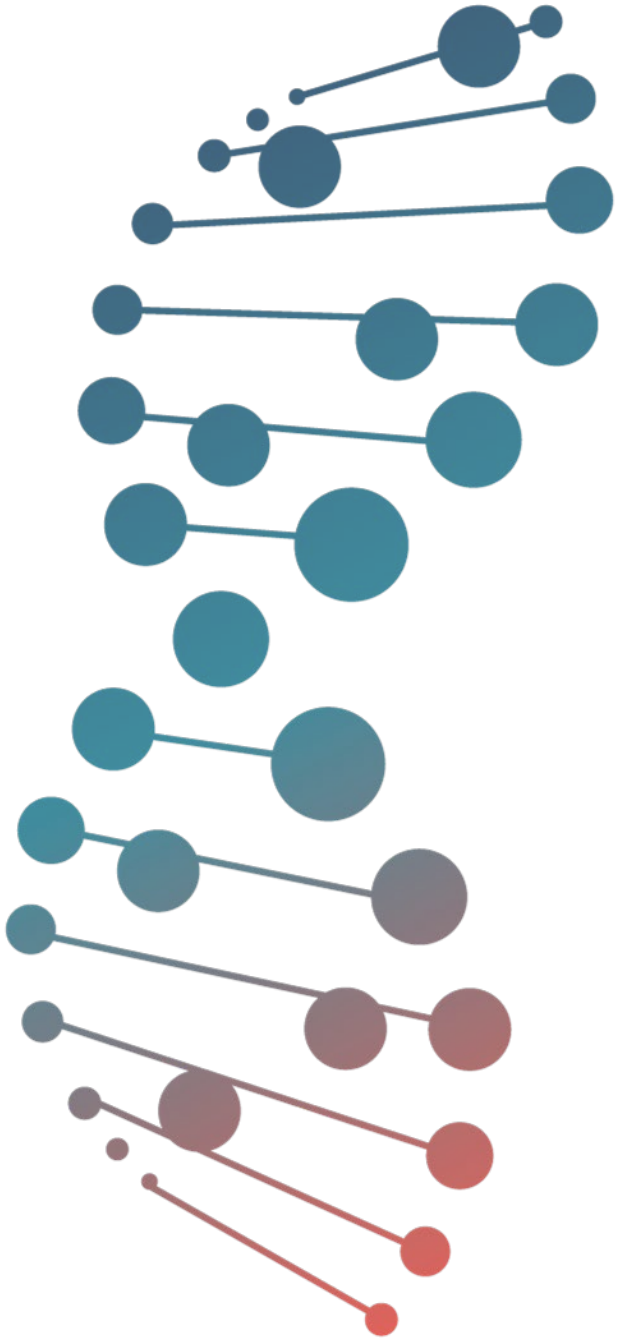
Precision and personalization in CLL and B-cell lymphomas:

Expert perspectives from iwCLL and iwNHL

Tuesday, November 11, 2025 | 17:30–18:30 (CET)

BeGenius

November 2025 | 1125-BGB-3111-MRC-001



Welcome and introductions

Chair: Francesc Bosch

Disclosures

- **Consultant**: Lilly
- **Honoraria**: AbbVie, BeOne Medicines Ltd, Janssen, Kite Pharma, Novartis, Roche, Sanofi, Takeda
- **Scientific advisory boards**: AbbVie, AstraZeneca, Gilead, Janssen, Roche, Sanofi, Takeda

Disclaimers

- The information contained herein is intended for healthcare professionals only and is given for educational purposes only. This document is not intended for professional counseling or advice.
- The views expressed in the presentations are those of the speakers and may not necessarily reflect the opinion of BeOne. BeOne does not guarantee the accuracy or reliability of the information provided herein and expressly disclaims liability for any errors or omissions in this information.
- Zanubrutinib is approved in the EU as monotherapy for adults with chronic lymphocytic leukemia (CLL), for adults with marginal zone lymphoma (MZL) who have received at least one prior anti-CD20–based therapy, for adults with Waldenström's macroglobulinemia (WM) who have received at least one prior therapy or in first-line treatment for patients unsuitable for chemoimmunotherapy, and in combination with obinutuzumab for adults with relapsed or refractory (R/R) follicular lymphoma (FL) who have received at least two prior lines of systemic therapy.[1]
- Prescribing information (PI) may vary depending on local approval in each country. Therefore, before prescribing any product, always refer to local authorities concerning reimbursement status and to local materials such as the PI and/or the summary of product characteristics (SPC) for guidance on prescribing.

CD, cluster of differentiation.

1. BeOne Medicines Ireland Ltd. BRUKINSA – summary of product characteristics; October 2025.

Introducing the panel

Francesc Bosch (chair)
Vall d'Hebron Institute of Oncology, Spain

Renata Walewska
University Hospitals Dorset NHS Foundation Trust, UK

Pier Luigi Zinzani
University of Bologna, Italy

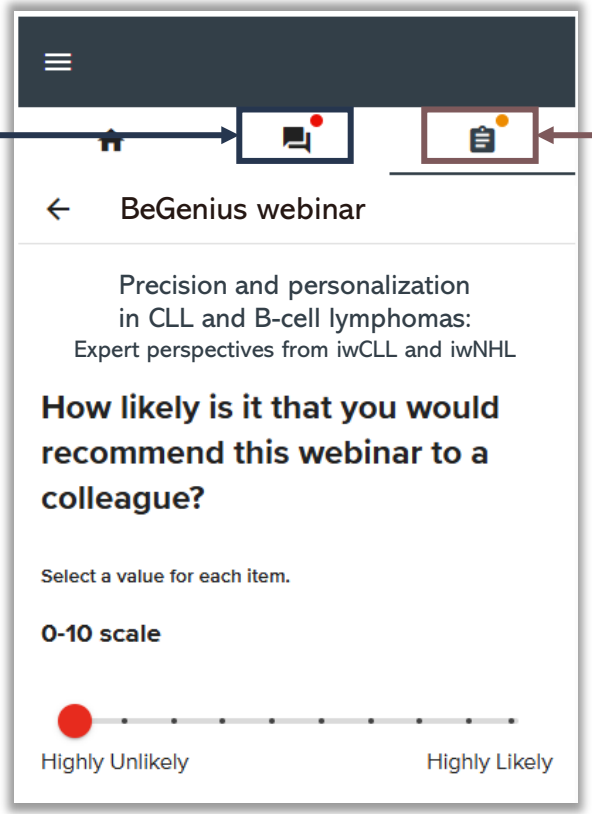
Agenda

Time	Session	Speaker
5 min	Welcome and introductions	Francesc Bosch
15 min	Recent advances in CLL research and management	Renata Walewska
15 min	Emerging trends in MCL and indolent NHL	Pier Luigi Zinzani
20 min	Discussion and audience Q&A	All faculty
5 min	Summary	Francesc Bosch

CLL, chronic lymphocytic leukemia; MCL, mantle cell lymphoma; NHL, non-Hodgkin lymphoma; Q&A, questions and answers.

We want to hear from you!

Exit full-screen view to have your say



Please submit your questions to the faculty here

Please submit your feedback here

Your feedback will help us ensure the content and design of these webinars remain useful to you!

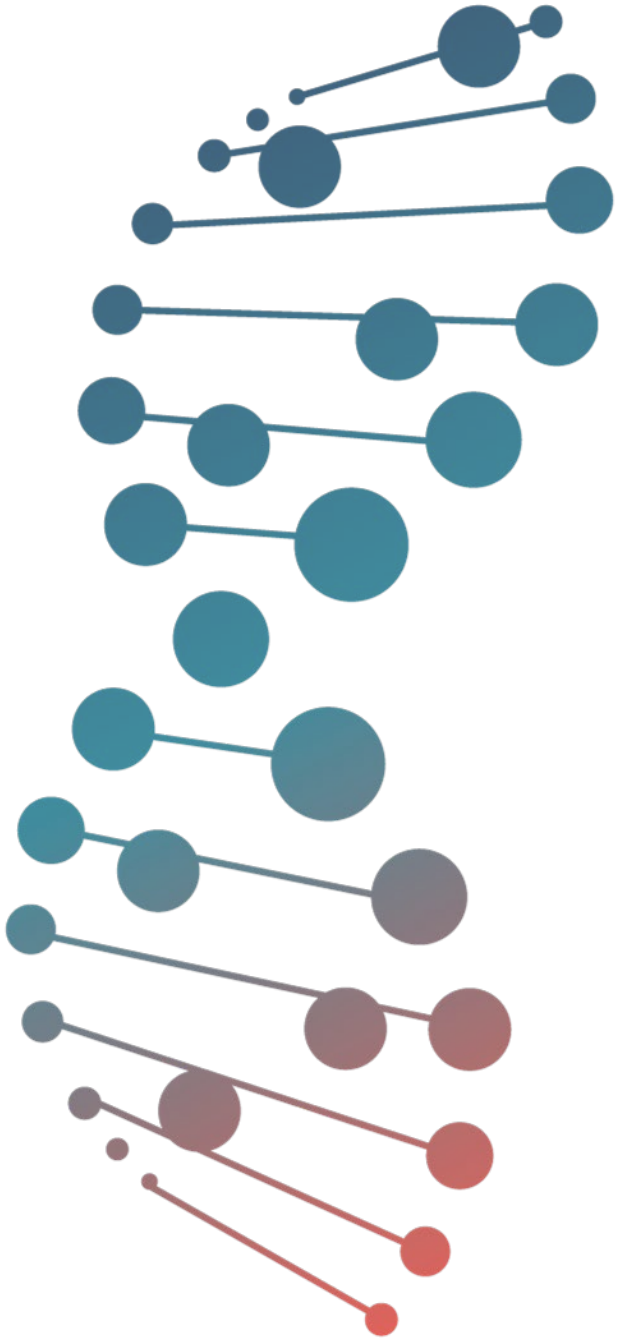
Meeting objective

Provide an expert digest of the key data, themes, and discussions across B-cell malignancies from the international workshops iwCLL and iwNHL

iwCLL, SEPTEMBER 12–15; KRAKÓW, POLAND
Biennial gathering of a global community of physicians and scientists, committed to creating progress in CLL

iwNHL, SEPTEMBER 26–28; CAMBRIDGE, MA, USA
Annual workshop of scientific leaders in NHL and CLL, bringing together top clinical and translational research minds

CLL, chronic lymphocytic leukemia; iwCLL, International Workshop on Chronic Lymphocytic Leukemia; iwNHL, International Workshop on Non-Hodgkin Lymphoma; NHL, non-Hodgkin lymphoma.



Recent advances in CLL research and management

Renata Walewska
University Hospitals Dorset NHS Foundation Trust

Disclosures

- **Speaker engagements:** AbbVie, AstraZeneca, BeOne Medicines Ltd, Eli Lilly, Janssen
- **Advisory boards:** AbbVie, AstraZeneca, BeOne Medicines Ltd, Eli Lilly, Janssen
- **Meeting sponsorship:** AbbVie, AstraZeneca, BeOne Medicines Ltd, Janssen, Takeda
- **Educational material development:** BeOne Medicines Ltd, Limbic, Medscape

What we will discuss

CLL, chronic lymphocytic leukemia.

British Journal of Haematology: 2025 CLL guidelines

PUBLISHED OCTOBER 9, 2025

Received: 5 May 2025 | Accepted: 4 August 2025

DOI: 10.1111/bjh.70100

BJHaem
BRITISH JOURNAL OF HAEMATOLOGY

BSH GUIDELINE

2025 British Society for Haematology Guideline for the treatment of chronic lymphocytic leukaemia

R. Walewska[1] | T. A. Eyre[2] | A. Bloor[3] | G. Follows[4] | S. Iyengar[5] | R. Johnston[6] | H. Marr[7] | N. Martinez-Calle[8] | A. McCaig[9] | H. McCarthy[1] | T. Munir[10] | H. M. Parry[11,12] | N. Parry-Jones[13] | A. Pettitt[14] | J. Riches[15] | I. Ringshausen[16] | A. Schuh[2] | P. E. M. Patten[17,18]

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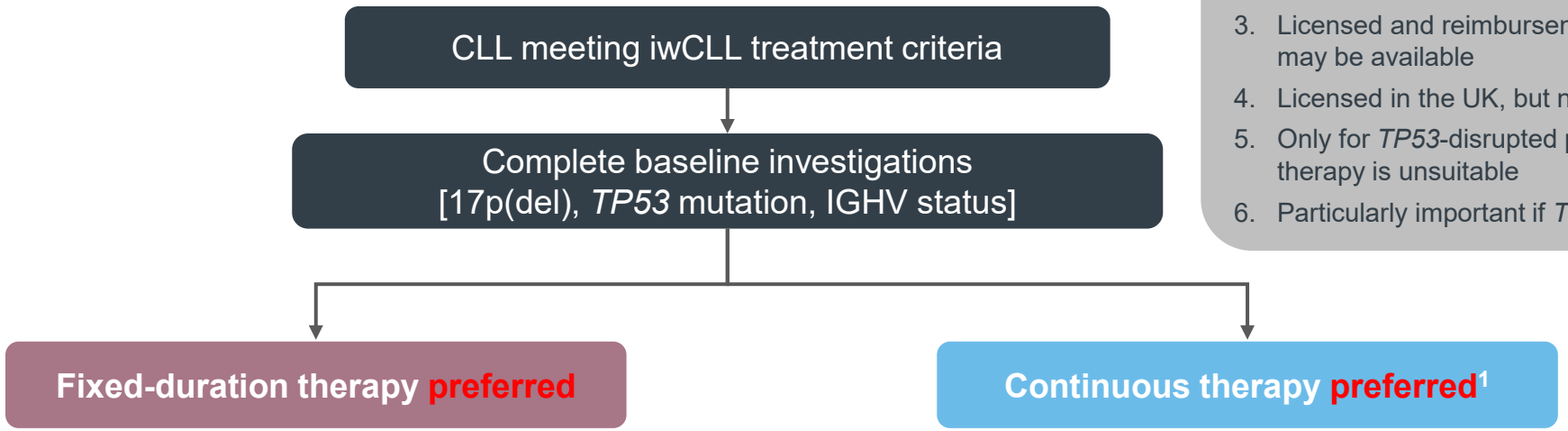
CLL, chronic lymphocytic leukemia.
Walewska R *et al*. *Br J Haematol* 2025; online ahead of print (DOI: 10.1111/bjh.70100).

First-line therapy in CLL

First-line treatment algorithm for CLL: UK



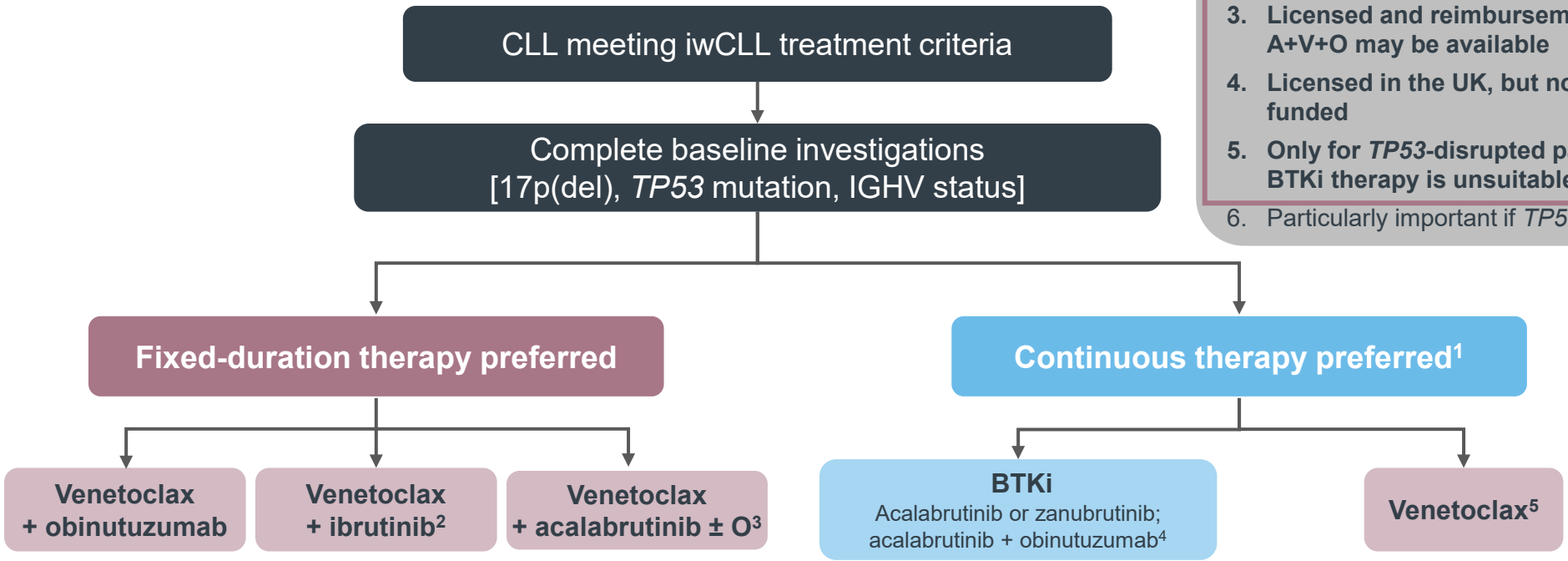
1. **Reimbursed only for patients aged ≥65 years and/or with CIRS >6 and/or CrCl <70 mL/min, or in *TP53*-mutated / 17p-deleted disease (continuous therapy preferred in this setting)**
2. 15 months' duration or MRD-guided (the latter currently not re-imbursed)
3. Licensed and reimbursement pending; A+V+O may be available
4. Licensed in the UK, but not NICE/SMC-funded
5. Only for *TP53*-disrupted patients in whom BTKi therapy is unsuitable
6. Particularly important if *TP53* disrupted

UK-specific elements

A, acalabrutinib; BTKi, Bruton's tyrosine kinase inhibitor; CIRS, Cumulative Illness Rating Scale; CLL, chronic lymphocytic leukemia; CrCl, creatinine clearance; del, deletion; IGHV, immunoglobulin heavy chain variable; MRD, measurable residual disease; NICE, National Institute for Health and Care Excellence; O, obinutuzumab; SMC, Scottish Medicines Consortium; V, venetoclax.

Walewska R *et al*. *Br J Haematol* 2025; online ahead of print (DOI: 10.1111/bjh.70100).

First-line treatment algorithm for CLL: UK



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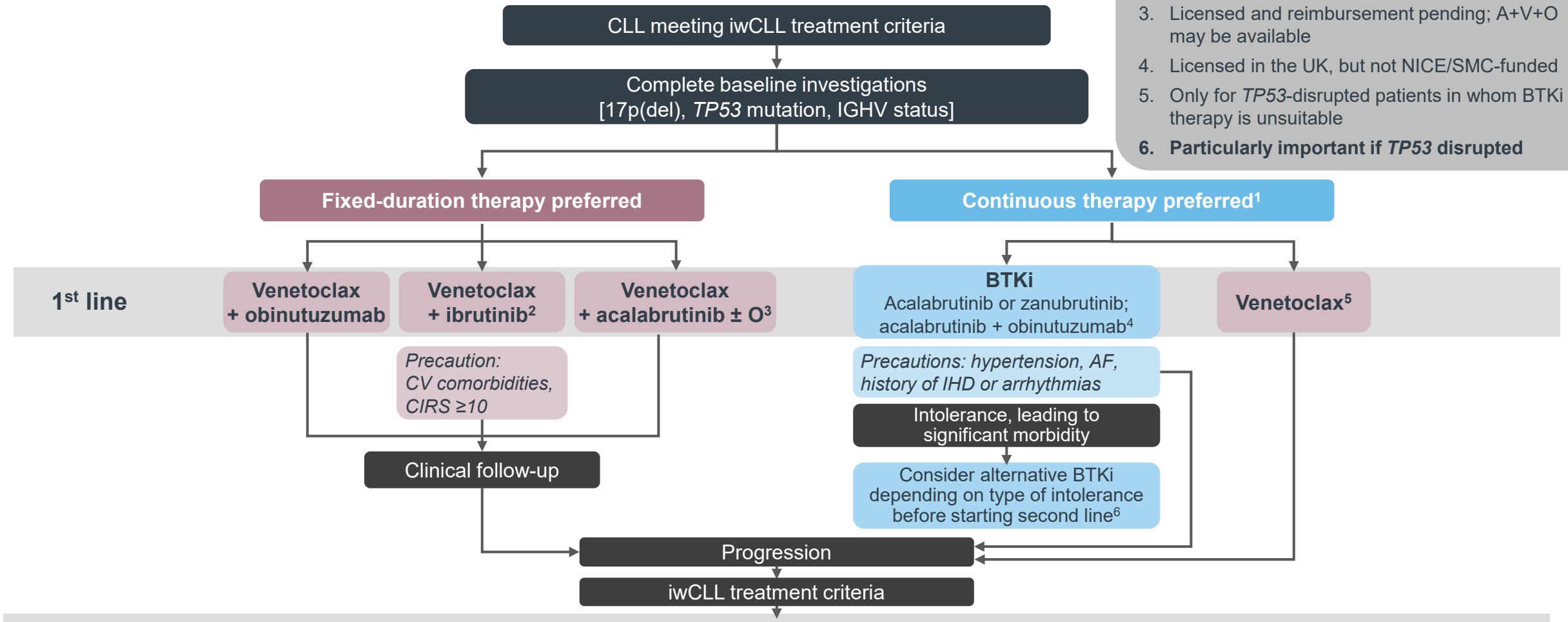


A, acalabrutinib; AF, atrial fibrillation; BTKi, Bruton's tyrosine kinase inhibitor; CIRS, Cumulative Illness Rating Scale; CLL, chronic lymphocytic leukemia; CrCl, creatinine clearance; CV, cardiovascular; del, deletion; IGHV, immunoglobulin heavy chain variable; IHD, ischemic heart disease; iwCLL, International Workshop on Chronic Lymphocytic Leukemia; MRD, measurable residual disease; NICE, National Institute for Health and Care Excellence; O, obinutuzumab; SMC, Scottish Medicines Consortium; V, venetoclax.

Walewska R *et al*. *Br J Haematol* 2025; online ahead of print (DOI: 10.1111/bjh.70100).

Decision tool for first-line treatment of CLL patients

Determining factors		Acala	Zanu	V+O	V+I	A+O	MRD V+I	V+A+/−O
CLL-related factors	IGHV mutated (not subset 2)	+	+	++	++	++	+	Insufficient F/U
	IGHV unmutated or subset 2	++	++	+	+	++	++	Insufficient F/U
	TP53 mutation / 17p deletion	+	+	+/−	+	+	−*	−*
	Bulky disease	++	++	+	++	++	++	Insufficient F/U
Patient vulnerabilities	Infection risk during treatment	+/−	+/−	−	+/−	−	+/−	−†
	Cardiac disease (risk of arrhythmia)	+/−	+/−	++	−	+/−	−	+
	Hypertension	+/−	+/−	+	+/−	+/−	−	+/−
	Bleeding history / anticoagulant use	−	−	+	−	−	−	−
	Renal disease	+	+	+/−	+/−	+	+/−	+/−
Patient priorities and preferences	Minimize initial hospital visits	++	++	−	+/−	−	+/−	−†
	Minimize cumulative toxicities	−	−	+	+	−	+/−	+
	Fixed treatment duration	−	−	++	++	−	+	++
	Continuous treatment	++	++	−	−	++	+/−	−

++ Very good choice
+ Good choice
+/− Neutral / consider with caution
− Not recommended

These grades represent the authors' expert opinion and should not be interpreted as precise rankings.

Importantly, no head-to-head comparisons exist between these regimens; differences in apparent efficacy may reflect trial design, follow-up duration, treatment strategy (fixed-duration vs. MRD-guided vs. continuous), and population differences as much as true differences in treatment effect.

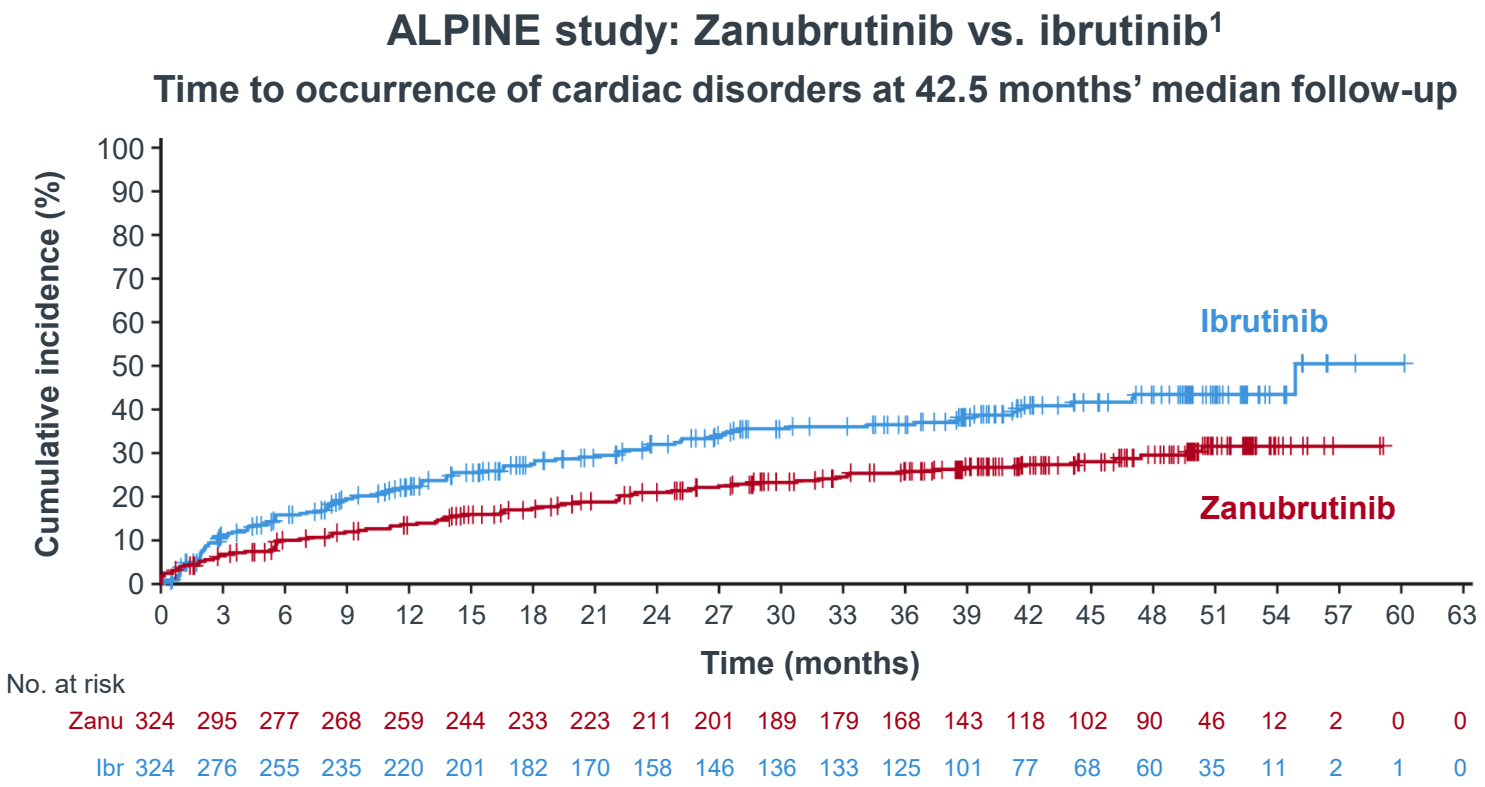
*No data to inform decision; †+/– if treatment used without O.
A/acala, acalabrutinib; CLL, chronic lymphocytic leukemia; F/U, follow-up; I, ibrutinib; IGHV, immunoglobulin heavy chain variable; MRD, measurable residual disease; O, obinutuzumab; V, venetoclax; zanu, zanubrutinib.
Walewska R *et al*. *Br J Haematol* 2025; online ahead of print (DOI: 10.1111/bjh.70100).

Patient vulnerabilities

- Infection risk during treatment
- Cardiac disease (risk of arrhythmia)
- Hypertension
- Bleeding history / anticoagulant use
- Renal disease

Walewska R *et al*. *Br J Haematol* 2025; online ahead of print (DOI: 10.1111/bjh.70100).

Atrial fibrillation rates were lower with zanubrutinib than ibrutinib in ALPINE



Atrial fibrillation/flutter
Ibrutinib: 17% Zanubrutinib: 7%

Fatal cardiac AEs
Ibrutinib: 2% Zanubrutinib: 0%

Based on outcomes from head-to-head trials, zanubrutinib or acalabrutinib are recommended over ibrutinib for patients with CV risk[2]

AE, adverse event; CV, cardiovascular; ibr, ibrutinib; zanu, zanubrutinib.

1. Brown JR *et al*. *Blood* 2024; 144 (26): 2706–2717. 2. Eichhorst B *et al*. *Ann Oncol* 2024; 35 (9): 762–768.

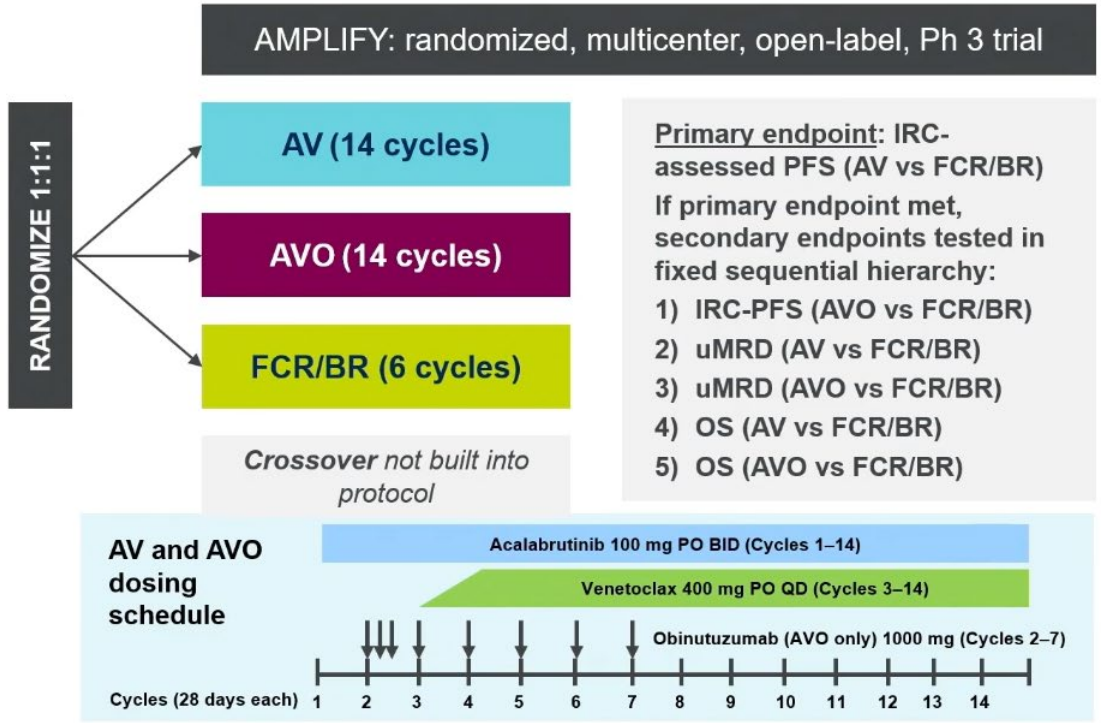
AV and AVO vs. FCR/BR: Interim analysis of the AMPLIFY trial

TN CLL (N=867)

Key inclusion criteria
- Age ≥18 years
- TN CLL requiring treatment per iwCLL 2018 criteria[1]
- Without del(17p) or *TP53*[a]
- ECOG PS ≤2

Key exclusion criteria
- CIRS-Geriatric >6
- Significant cardiovascular disease

Stratification
- Age (>65 vs ≤65 years)
- IGHV mutational status
- Rai stage (≥3 vs <3)
- Geographic region



Cohort
- Median age 61 years; CIRS-Geriatric >5
- No (17p) or *TP53* mutations

Primary endpoint: IRC-assessed PFS (AV vs. FCR/BR)
- Overall PFS significantly improved with fixed-duration AV and AVO vs. FCR/BR at median follow-up of 40.8 months (AV: HR: 0.65; 95% CI: 0.49–0.87; *P*=0.0038; AVO: HR: 0.42; 95% CI: 0.30–0.59; *P*<0.0001)
- Small PFS improvement with AV and AVO vs. FCR/BR in both uIGHV and mIGHV subgroups, although not significant
- CR value unknown
- AV uMRD rates were lower than those with FCR/BR

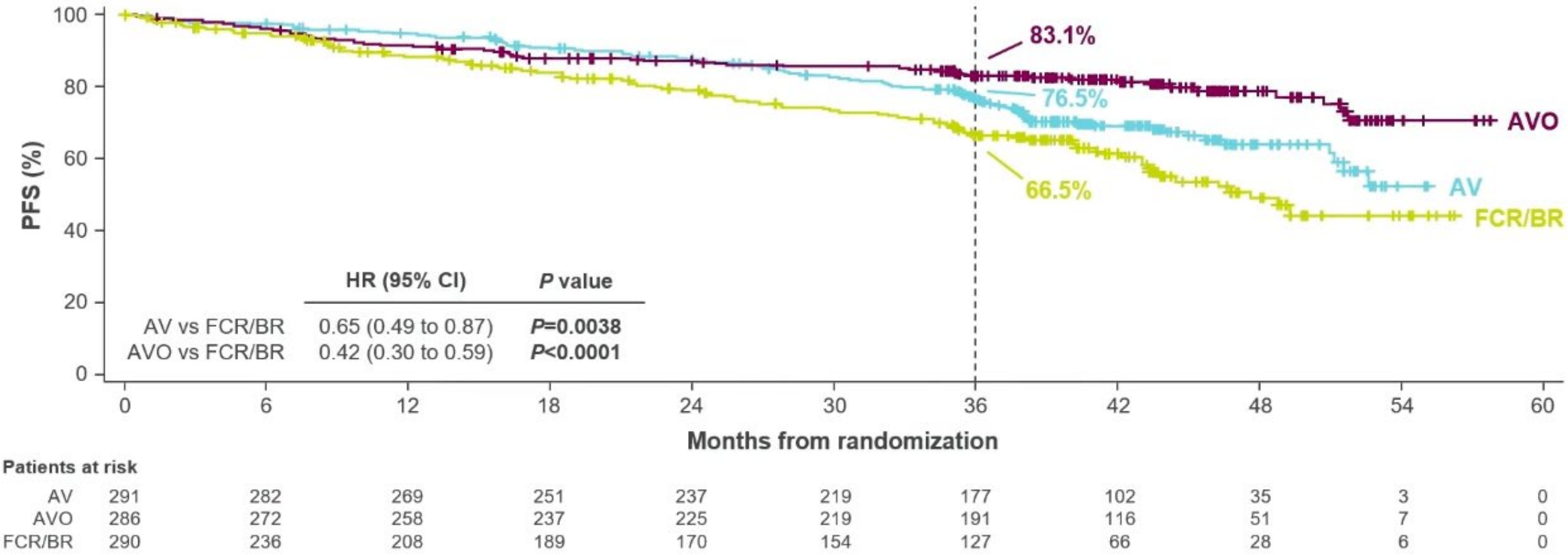
Safety
- Cardiac events occurred in 9.3% (AV), 12% (AVO), and 3.5% (FCR/BR) of patients (Grade ≥3 occurred in 1.7%, 2.5%, and 1.2% respectively)
- Rates of discontinuation, toxicity, and death were relatively high

[a]Assayed by central laboratory.

AV, acalabrutinib-venetoclax; AVO, acalabrutinib-venetoclax-obinutuzumab; BID, twice daily; BR, bendamustine-rituximab; CI, confidence interval; CIRS-Geriatric, Cumulative Illness Rating Scale-Geriatric; CLL, chronic lymphocytic leukemia; del, deletion; ECOG PS, Eastern Cooperative Oncology Group Performance Status; FCR, fludarabine-cyclophosphamide-rituximab; HR, hazard ratio; IGHV, immunoglobulin heavy chain variable; IRC, independent review committee; iwCLL, International Workshop on Chronic Lymphocytic Leukemia; PFS, progression-free survival; Ph, Phase; PO, by mouth; QD, once daily; TN, treatment-naive; uMRD, undetectable minimal residual disease.

Brown JR *et al*. Oral presentation at ASH 2024; San Diego, CA, USA, December 7–10, 2024; Abstract 1009.

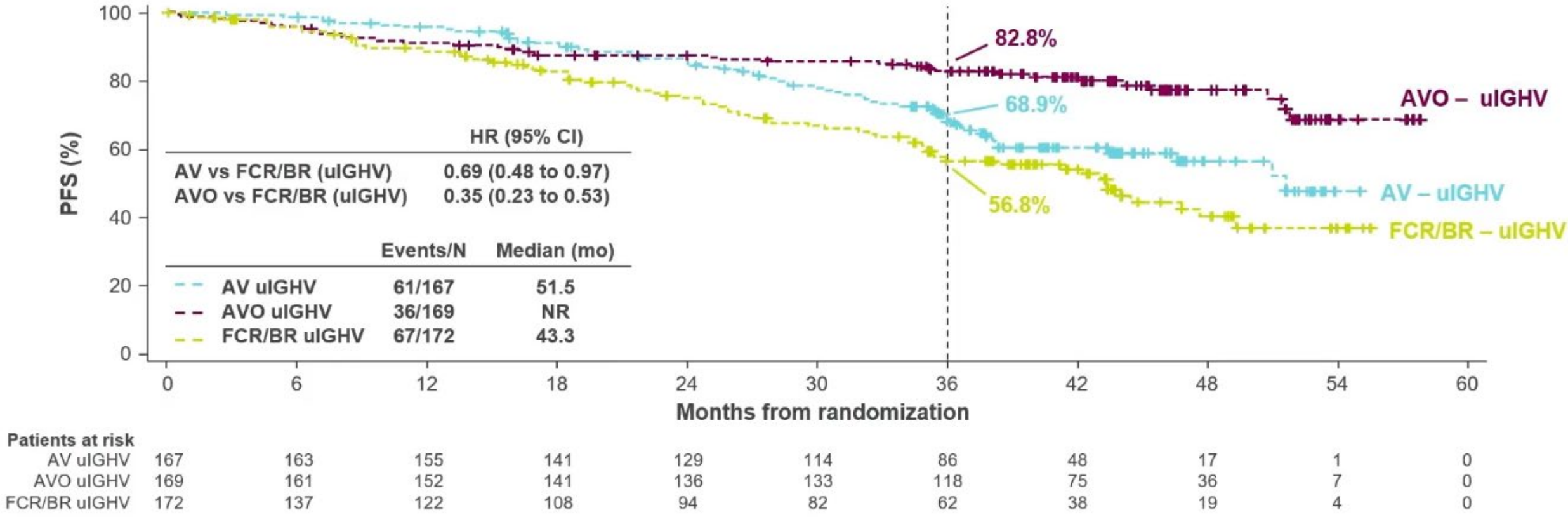
AMPLIFY: IRC-assessed PFS



Median PFS was NR for AV and AVO, and was 47.6 months for FCR/BR

ITT population. Median follow-up from randomization: 40.8 months (range: 0–59 months).
HR (95% CI) computed using a Cox proportional hazards model stratified by the randomization strata. *P*-value based on stratified log-rank test.
AV, acalabrutinib-venetoclax; AVO, acalabrutinib-venetoclax-obinutuzumab; BR, bendamustine-rituximab; CI, confidence interval; FCR, fludarabine-cyclophosphamide-rituximab; HR, hazard ratio; IRC, independent review committee; ITT, intention-to-treat; NR, not reached; PFS, progression-free survival.
Brown JR *et al*. Oral presentation at ASH 2024; San Diego, CA, USA, December 7–10, 2024; Abstract 1009.

AMPLIFY: PFS in the uIGHV subgroup



PFS assessed by IRC; PFS by IGHV status was a prespecified analysis (ITT population).
HR (95% CI) computed using an unstratified Cox proportional hazards model.
AV, acalabrutinib-venetoclax; AVO, acalabrutinib-venetoclax-obinutuzumab; BR, bendamustine-rituximab; CI, confidence interval; FCR, fludarabine-cyclophosphamide-rituximab; HR, hazard ratio; IRC, independent review committee; ITT, intention-to-treat; mo, months; PFS, progression-free survival; uIGHV, unmutated immunoglobulin heavy chain variable.
Brown JR *et al*. Oral presentation at ASH 2024; San Diego, CA, USA, December 7–10, 2024; Abstract 1009.

AMPLIFY: Events of clinical interest

	AV (n=291)		AVO (n=284)		FCR/BR (n=259)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Any ECI	222 (76.3)	136 (46.7)	242 (85.2)	188 (66.2)	185 (71.4)	141 (54.4)
Cardiac events	27 (9.3)	5 (1.7)	34 (12.0)	7 (2.5)	9 (3.5)	3 (1.2)
Atrial fibrillation	2 (0.7)	1 (0.3)	6 (2.1)	2 (0.7)	2 (0.8)	2 (0.8)
Ventricular tachyarrhythmias[a]	2 (0.7)	0	3 (1.1)	0	0	0
Hypertension	12 (4.1)	8 (2.7)	11 (3.9)	6 (2.1)	7 (2.7)	2 (0.8)
Hemorrhage	94 (32.3)	3 (1.0)	86 (30.3)	6 (2.1)	11 (4.2)	1 (0.4)
Major hemorrhage	3 (1.0)	3 (1.0)	8 (2.8)	6 (2.1)	2 (0.8)	1 (0.4)
Neutropenia (any)[b]	108 (37.1)	94 (32.3)	143 (50.4)	131 (46.1)	132 (51.0)	112 (43.2)
Infections (any)	148 (50.9)	36 (12.4)	153 (53.9)	67 (23.6)	82 (31.7)	26 (10.0)
Second primary malignancies	15 (5.2)	5 (1.7)	12 (4.2)	5 (1.8)	2 (0.8)	0
Excl. non-melanoma skin	8 (2.7)	5 (1.7)	7 (2.5)	4 (1.4)	1 (0.4)	0
Tumor lysis syndrome	1 (0.3)	1 (0.3)	1 (0.4)	1 (0.4)	8 (3.1)	8 (3.1)

Data are n (%). ECIs listed by category and sub-category.
[a]Ventricular tachyarrhythmias consisted of ventricular extrasystoles (n=1 in AV arm; n=2 in AVO arm) and ventricular tachycardia (n=1 each in AV and AVO arms). [b]Includes neutropenia, neutrophil count decreased, and febrile neutropenia.
AEs with an onset date or that worsen on or after the date of first dose and up to and including 30 days following the date of last dose of treatment or up to the day prior to start of subsequent anti-CLL therapy (whichever comes first).
AE, adverse event; AV, acalabrutinib-venetoclax; AVO, acalabrutinib-venetoclax-obinutuzumab; BR, bendamustine-rituximab; CLL, chronic lymphocytic leukemia; ECI, event of clinical interest; FCR, fludarabine-cyclophosphamide-rituximab.
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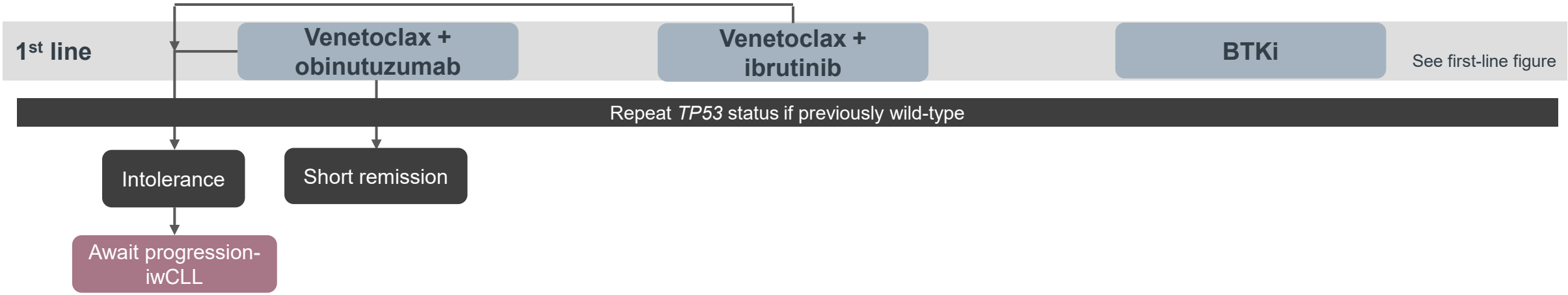
Treating relapsed/refractory CLL

Second and subsequent lines



BTKi, Bruton's tyrosine kinase inhibitor; iwCLL, International Workshop on Chronic Lymphocytic Leukemia.
Walewska R *et al*. *Br J Haematol* 2025; online ahead of print (DOI: 10.1111/bjh.70100).

Prospective studies on retreatment strategies

- BCL2i/CD20 (ReVenG; NCT04895436)[1]
  - Cohort 1: >24 months; Cohort 2: 12–24 months

- BTKi/BCL2i
  - MAVRiC (NCT07024706),[2] minimum of 24 months' remission, AV
  - Zanubrutinib-venetoclax (NCT05168930)[3]

AV, acalabrutinib-venetoclax; BCL2i, B-cell lymphoma 2 inhibitor; BTKi, Bruton's tyrosine kinase inhibitor; CD, cluster of differentiation.

1. Davids MS *et al*. Poster 642 presentated at ASH 2021; Atlanta, GA, USA, December 11–14, 2021. 2. ClinicalTrials.gov NCT07024706. Available at: https://clinicaltrials.gov/study/NCT07024706. Accessed November 2025. 3. ClinicalTrials.gov NCT05168930. Available at: https://clinicaltrials.gov/study/NCT05168930. Accessed November 2025.

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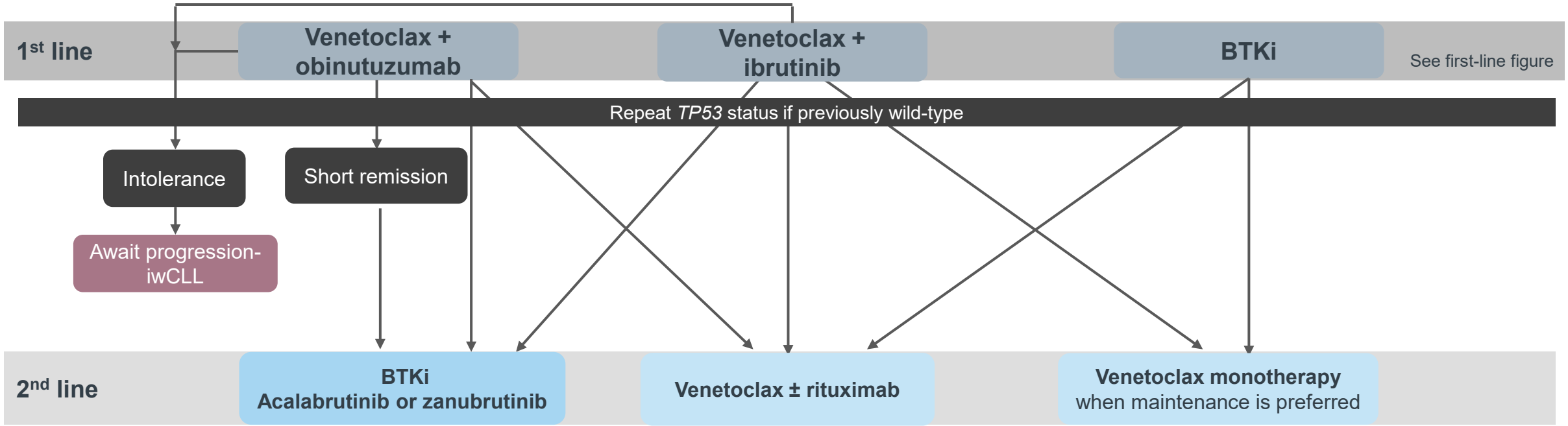

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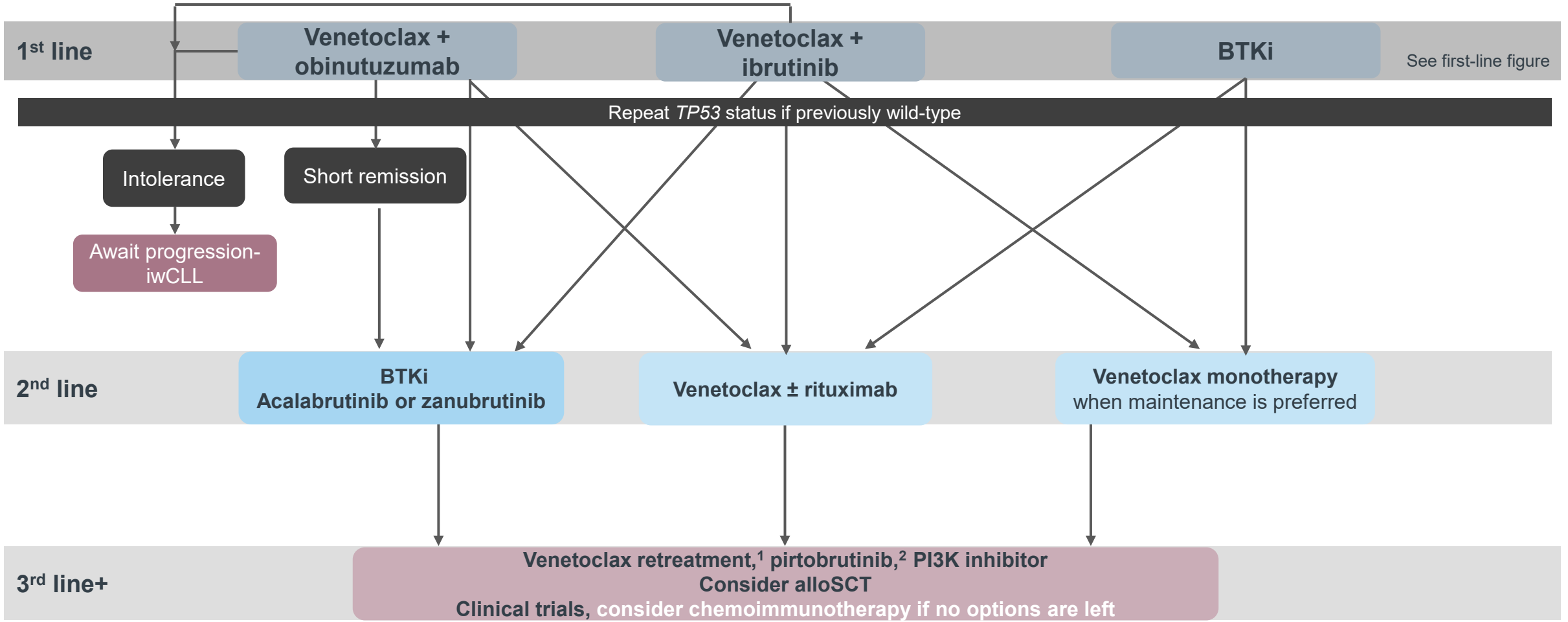
Walewska R *et al*. *Br J Haematol* 2025; online ahead of print (DOI: 10.1111/bjh.70100).

Second and subsequent lines

1. After fixed-duration venetoclax therapy
2. Available only after cBTKi use



alloSCT, allogeneic stem cell transplantation; BTKi, Bruton's tyrosine kinase inhibitor; cBTKi, covalent BTKi; iwCLL, International Workshop on Chronic Lymphocytic Leukemia; PI3K, phosphoinositide 3-kinase.

Walewska R *et al*. *Br J Haematol* 2025; online ahead of print (DOI: 10.1111/bjh.70100).

Decision tool for relapse treatment of CLL patients

Determining factors		I	Acala	Zanu	Ven mono	Ven-R	Idela-R	Pirto
CLL-related factors	Relapse <3 years after FD therapy	++	++	++	+	+	+/–	See legend
	Relapse >3 years after FD therapy	++	++	++	++	++	+/–	See legend
	TP53 mutation / 17p deletion	+	+	+	+/–	+/–	–	See legend
	Intolerance to cBTKi	–	++*	++†	+	++	–	++
	Progression on cBTKi	–	–	–	+	++	+/–	++
Patient vulnerabilities	Infection risk during treatment	+/–	+/–	+/–	+	+	–	+/–
	Cardiac disease (risk of arrhythmia)	–	+/–	+/–	+	+	+	+/–
	Hypertension	–	+/–	+/–	+	+	+	+/–
	Bleeding history / anticoagulant use	–	–	–	+	+	+	–
	Renal disease	+	+	+	–	–	+	+
	Pneumonitis/colitis risk	–	+	+	+	+	–	+
Patient priorities and preferences	Minimize initial hospital visits	++	++	++	–	–	–	++
	Minimize cumulative toxicities	–	+/–	+/–	–	+	–	+/–
	Fixed treatment duration	–	–	–	–	++	–	–
	Continuous treatment	++	++	++	++	–	++	++

++ Very good choice
+ Good choice
+/– Neutral / consider with caution
– Not recommended

These grades represent the authors' expert opinion and should not be interpreted as precise rankings

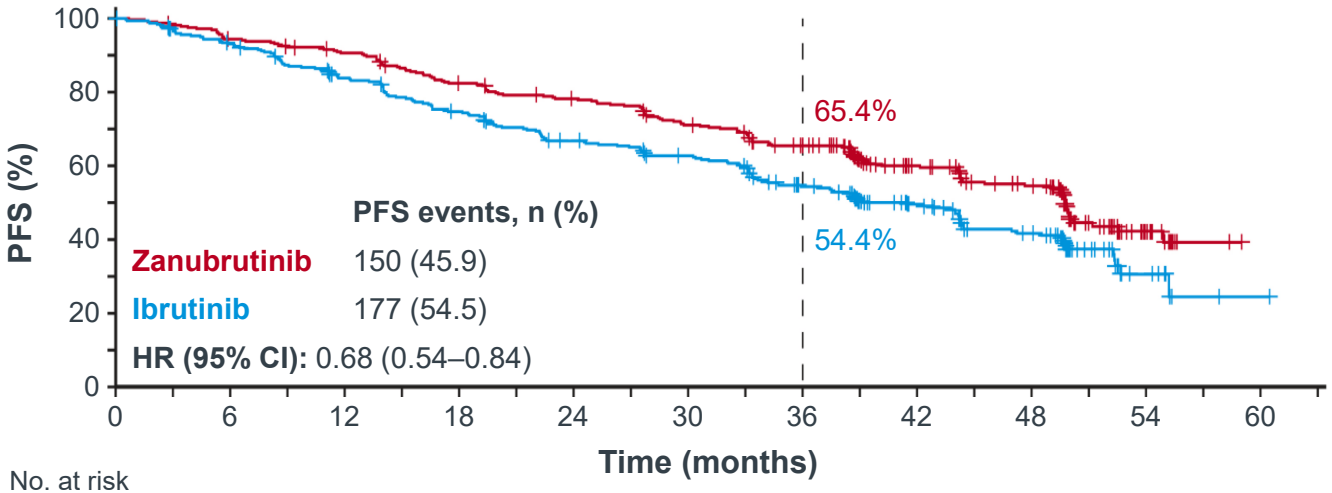
Note: Pirtobrutinib is included, EMA-/MHRA-approved. The table reflects relative efficacy and key clinical considerations for CLL-related factors in relapsed/refractory disease. Importantly, no head-to-head comparisons exist between these regimens; differences in apparent efficacy may reflect trial design, follow-up duration, treatment strategy (fixed-duration vs. continuous) and population differences as much as true differences in treatment effect. For patients relapsing within 3 years of fixed-duration therapy, switching to a BTKi is generally preferred. For later relapse (>3 years), retreatment with venetoclax-based therapy is reasonable, and all options may be considered. For *TP53*-mutated/17p-deleted disease, zanubrutinib may be preferred over other BTKis based on post hoc analyses showing improved outcomes vs. ibrutinib, whereas acalabrutinib has demonstrated non-inferiority vs. ibrutinib in similar settings. For patients discontinuing therapy owing to intolerance, switching within class may be appropriate. Idelalisib is generally less well tolerated owing to higher rates of infection (including cytomegalovirus), colitis, and pneumonitis. Acalabrutinib and zanubrutinib are preferred over ibrutinib owing to improved safety profiles. Overall treatment selection should be guided by shared decision-making, balancing efficacy, toxicity, patient priorities, comorbidities, and treatment burden.
*If ibrutinib/zanubrutinib intolerant. †If ibrutinib/acalabrutinib intolerant.
acala, acalabrutinib; BTKi, Bruton's tyrosine kinase inhibitor; cBTKi, covalent BTKi; CLL, chronic lymphocytic leukemia; EMA, European Medicines Agency; FD, fixed-duration; I, ibrutinib; idela, idelalisib; MHRA, Medicines and Healthcare products Regulatory Agency; mono, monotherapy; pirto, pirtobrutinib; R, rituximab; ven, venetoclax; zanu, zanubrutinib.
Walewska R *et al. Br J Haematol* 2025; online ahead of print (DOI: 10.1111/bjh.70100).

Selection of BTKi in the relapsed setting

ALPINE[1]

Zanubrutinib vs. ibrutinib

Median follow-up: 42.5 months



No. at risk

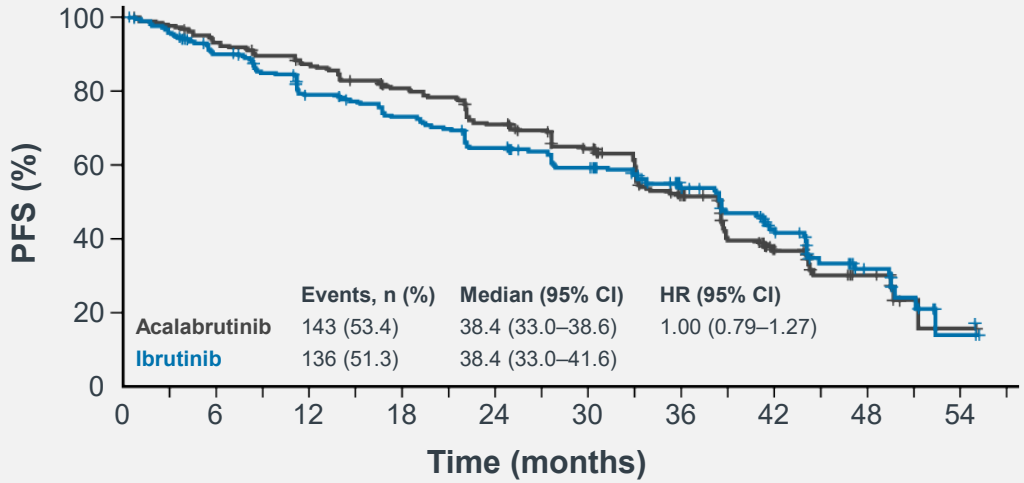
Zanu	327	315	302	295	287	272	258	247	242	236	218	210	189	151	128	109	104	43	19	2	0	0
Ibr	325	305	293	273	258	242	229	212	200	194	183	173	148	116	101	77	74	30	10	2	1	0

Sustained PFS benefit with zanubrutinib over ibrutinib, consistent in high-risk patients and across multiple sensitivity analyses[1]

ELEVATE-RR[2]

Acalabrutinib vs. ibrutinib

Median follow-up: 40.9 months



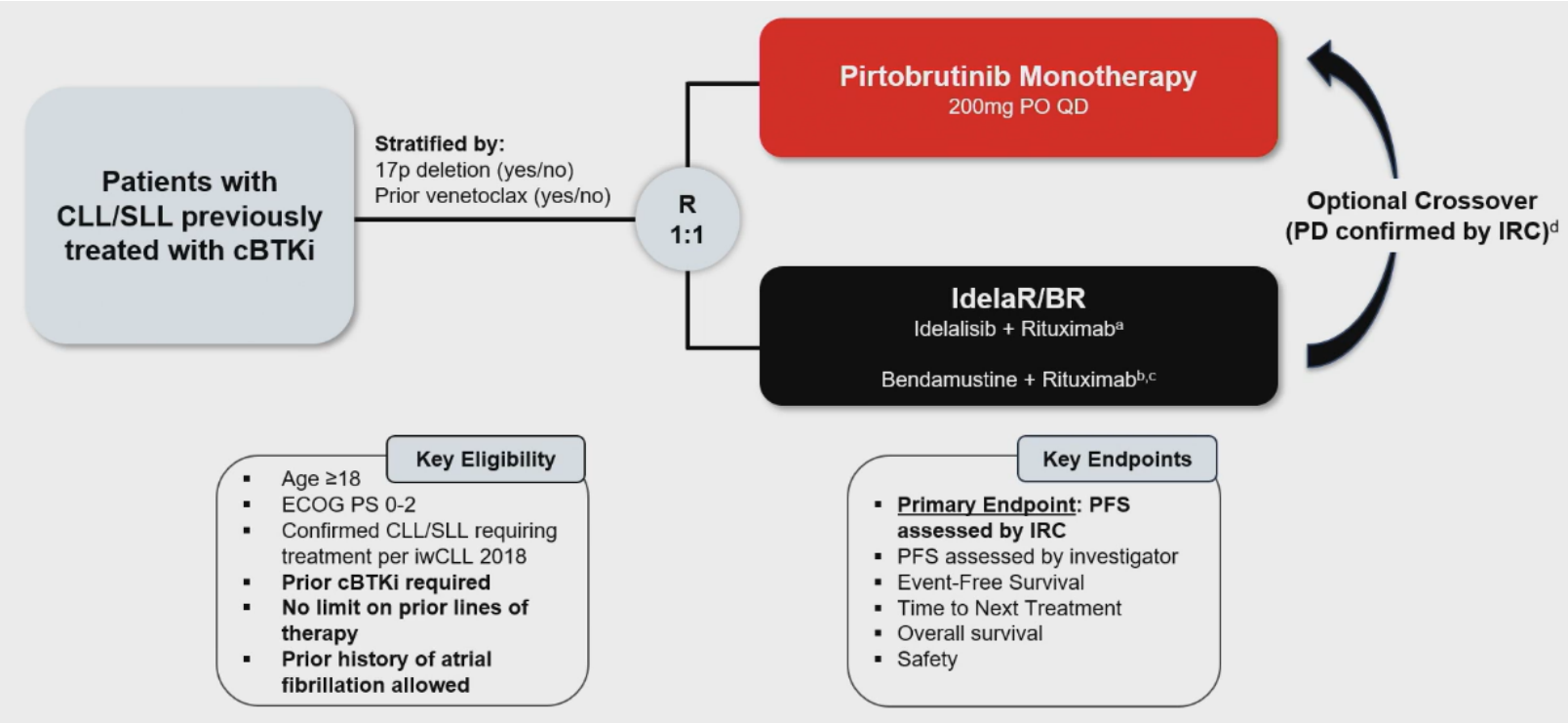
Median PFS with both acalabrutinib and ibrutinib with del(11q) or del(17p): 38.4 months[2]

This slide includes data from different clinical trials. These data are meant for demonstration purposes only and are not meant for cross-trial comparison.

BTKi, Bruton's tyrosine kinase inhibitor; CI, confidence interval; del, deletion; HR, hazard ratio; ibr, ibrutinib; PFS, progression-free survival; zanu, zanubrutinib.

1. Brown JR *et al*. *Blood* 2024; 144 (26): 2706–2717. 2. Byrd JC *et al*. *J Clin Oncol* 2021; 39 (31): 3441–3452.

Pirtobrutinib vs. IdelaR/BR: Phase 3 BRUIN CLL-321 study[1,2]



Primary endpoint: PFS assessed by IRC[2]

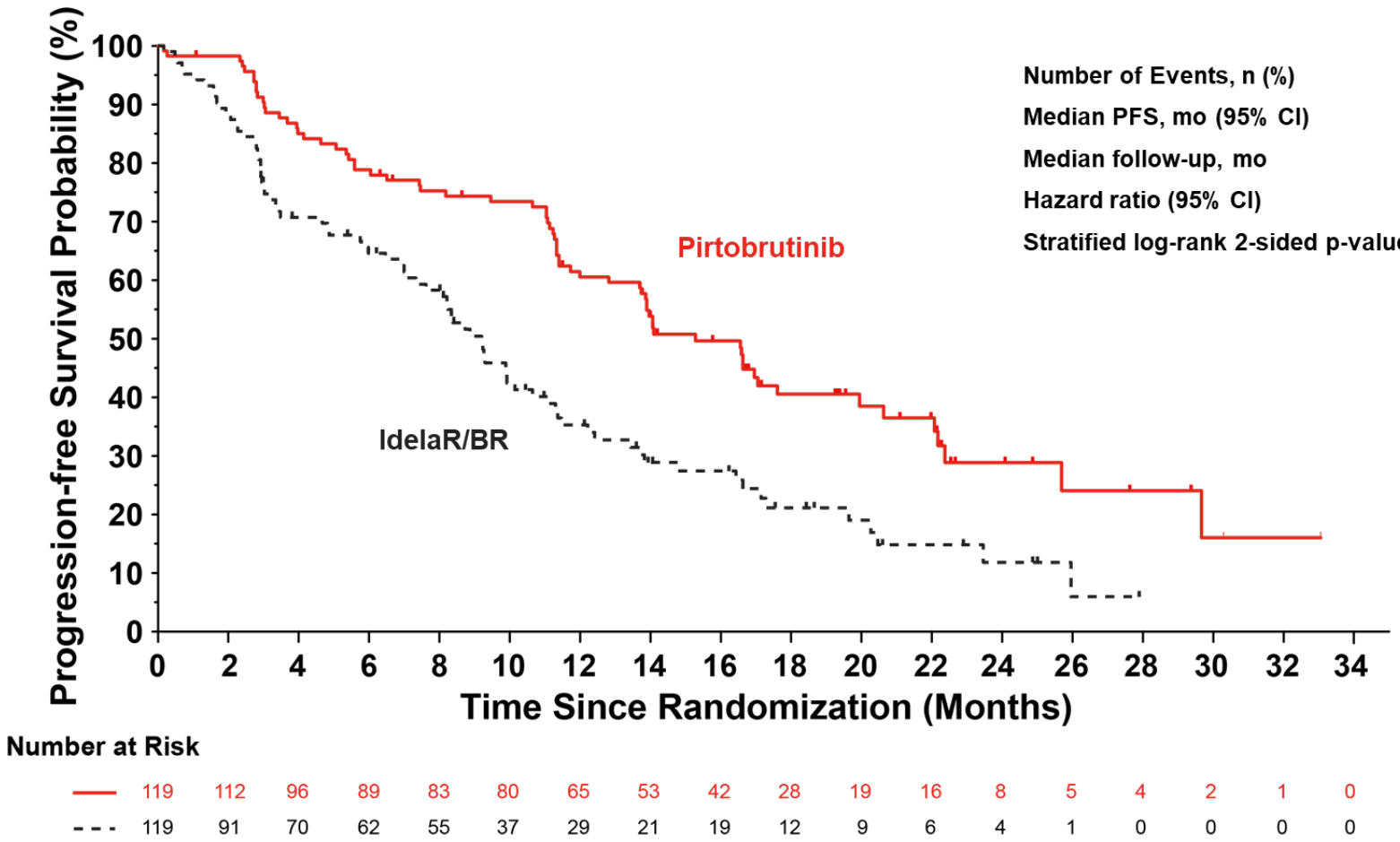
- PFS was significantly improved with pirtobrutinib vs. IdelaR/BR (HR: 0.54; 95% CI: 0.39–0.75; *P*=0.0002[e])
  - Primary endpoint was met at the Aug-23 data cut-off (HR: 0.58; 95% CI: 0.38–0.89; *P*=0.01)[1]
- This benefit was consistent among clinically relevant subgroups (key risk factors)

Safety[2]

Pirtobrutinib was well tolerated, with low rates of treatment-related discontinuation

Treatment was given in 28-day cycles. PFS was assessed based on iwCLL 2018.
[a]Idelalisib dosed at 150 mg PO BID. Day 1 of Cycle 1, first dose of rituximab at 375 mg/m², next 4 infusions at 500 mg/m² every 2 weeks, next 3 infusions at 500 mg/m² every 4 weeks. [b]Bendamustine (70 mg/m²) administered IV Day 1, Day 2 of Cycles 1–6. [c]Day 1 of Cycle 1, first dose of rituximab at 375 mg/m², next 5 infusions Day 1 of Cycle 2 through Cycle 6 at 500 mg/m². [d]Eligible patients receiving investigator's choice of IdelaR/BR could cross over to receive pirtobrutinib monotherapy upon confirmation of PD by IRC per protocol. [e]Nominal *P*-value.
BID, twice daily; BR, bendamustine-rituximab; cBTKi, covalent BTKi; CI, confidence interval; CLL, chronic lymphocytic leukemia; ECOG PS, Eastern Cooperative Oncology Group Performance Status; HR, hazard ratio; IdelaR, idelalisib-rituximab; IRC, independent review committee; IV, intravenous; iwCLL, International Workshop on Chronic Lymphocytic Leukemia; PD, progressive disease; PFS, progression-free survival; PO, by mouth; QD, once daily; R, randomized; SLL, small lymphocytic lymphoma.
1. Sharman P *et al*. Oral presentation at ASH 2024; San Diego, CA, USA, December 7–10, 2024; Abstract 886. 2. Sharman JP *et al*. *J Clin Oncol* 2025; 43 (22): 2538–2549.

INV-assessed progression-free survival



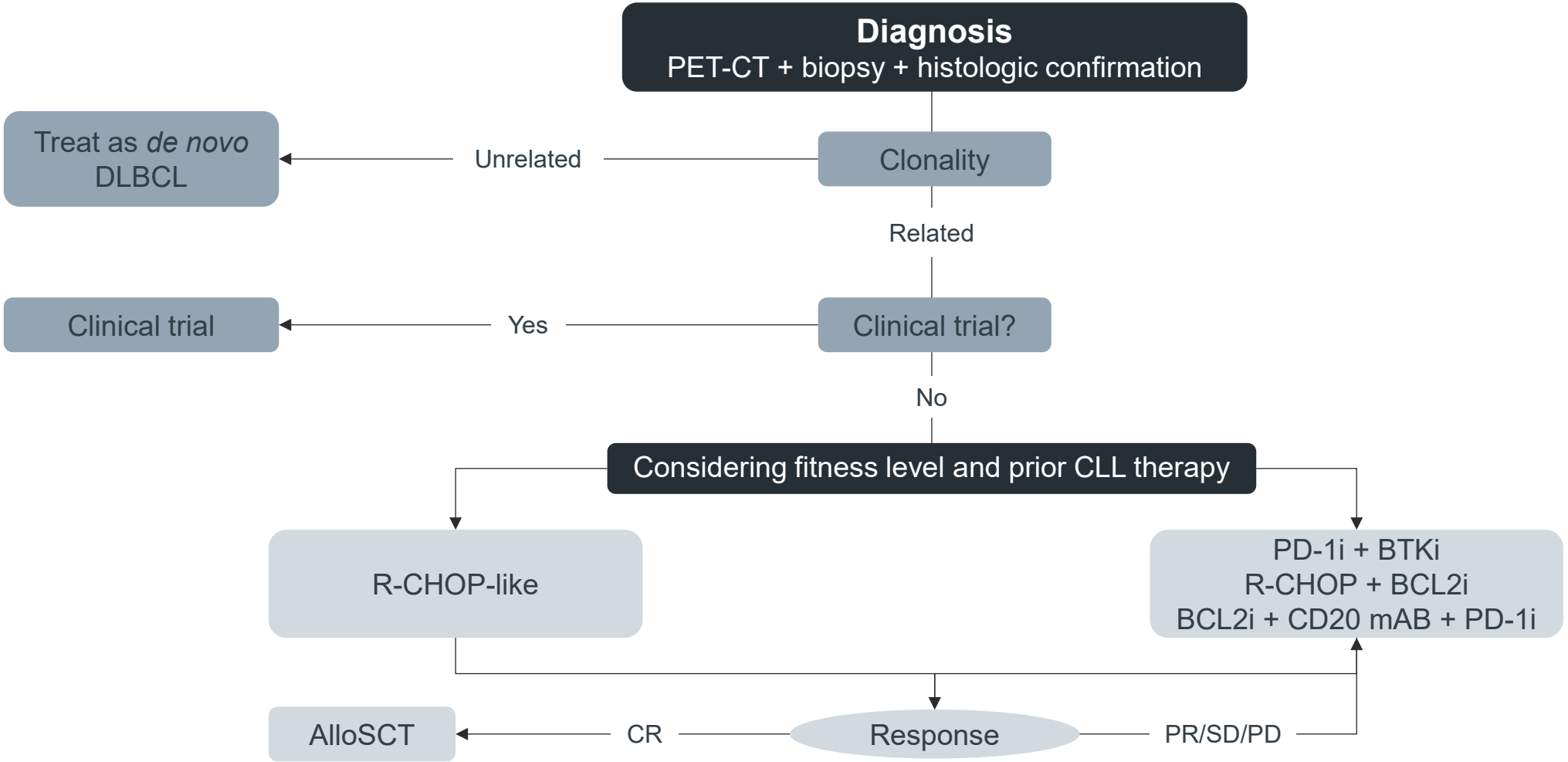
	Pirtobrutinib n=119	IdelaR/BR n=119
Number of Events, n (%)	69 (58)	77 (65)
Median PFS, mo (95% CI)	**15.3** (12.8-19.9)	**9.2** (7.3-10.6)
Median follow-up, mo	19.4	17.5
Hazard ratio (95% CI)	**0.48 (0.34-0.67)**	
Stratified log-rank 2-sided p-value	<0.0001*	

Pirtobrutinib reduced risk of progression or death by 52% according to investigator assessment

*Nominal *P*-value.
BR, bendamustine-rituximab; CI, confidence interval; IdelaR, idelalisib-rituximab; INV, investigator; mo, months; PFS, progression-free survival.
Sharman JP *et al*. *J Clin Oncol* 2025; 43 (22): 2538–2549.

Richter transformation

RT treatment algorithm



alloSCT, allogeneic stem cell transplantation; BCL2i, B-cell lymphoma 2 inhibitor; BTKi, Bruton's tyrosine kinase inhibitor; CD, cluster of differentiation; CLL, chronic lymphocytic leukemia; CR, complete response; DLBCL, diffuse large B-cell lymphoma; mAB, monoclonal antibody; PD, progressive disease; PD-1i, programmed death-1 inhibitor; PET-CT, positron emission tomography–computed tomography; PR, partial response; R-CHOP, rituximab-cyclophosphamide-doxorubicin-vincristine-prednisone; RT, Richter transformation; SD, stable disease.

Al-Sawaf O. Oral presentation at iwCLL 2025; Kraków, Poland, September 12–15, 2025.

Did the incidence of RT change with more effective RT therapy?

Trial	Patient population	Arm	RT incidence	Median follow-up
RESONATE-2	Untreated, age ≥65, no del(17p)	Ibr	4.4% (6/136)	9.6 years
	Untreated, age ≥65, no del(17p)	Clb	3.0% (4/133)	9.6 years
ELEVATE-TN	Untreated	Acala-Obi	0.6% (2/179)	4 years
	Untreated	Acala	0.6% (2/179)	4 years
	Untreated	Clb-Obi	0.6% (2/179)	4 years
SEQUOIA	Untreated, no del(17p)	Zanu	1.0% (6/590)	2 years
		BR	1.0% (6/590)	2 years
GLOW	Untreated, age ≥65 / comorbid	Ibr-Ven	2.8% (3/106)	46 months
		Clb-Obi	1.9% (2/105)	46 months
CLL14	Untreated, comorbid	Ven-Obi	0.9% (2/216)	76.4 months
		Clb-Obi	1.9% (4/216)	76.4 months
CLL13	Untreated, fit	Ven-Obi	0.6% (1/179)	~3 years
		Ven-R	0.6% (1/179)	~3 years
		Ibr-Ven	0.6% (1/179)	~3 years
		FCR/BR	0.6% (1/179)	~3 years
FLAIR	Previously untreated CLL, no del(17p)	Ibr-Ven	0.8% (2/263)	54 months
		Ibr	0.4% (1/263)	54 months
		FCR	1.5% (4/263)	54 months

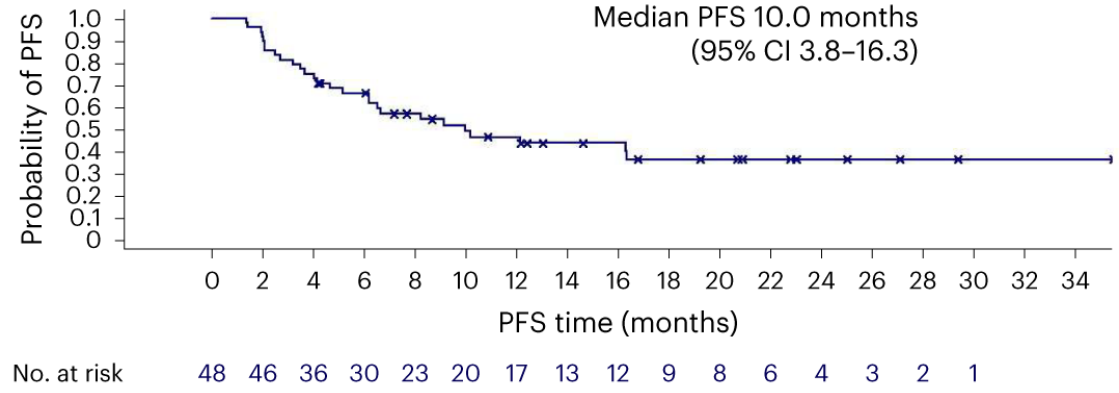
No consistent downward trend in the rates of RT in first-line trials

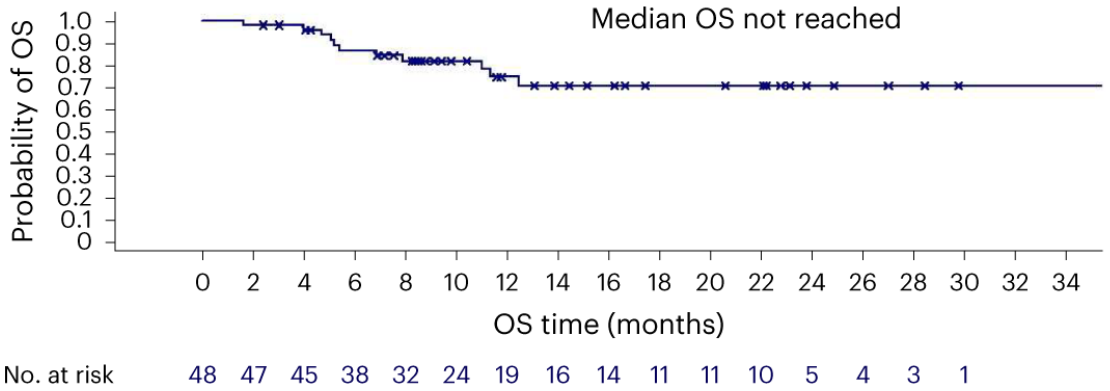
This slide includes data from different clinical trials. These data are meant for demonstration purposes only and are not meant for cross-trial comparison.

acala, acalabrutinib; BR, bendamustine-rituximab; Clb, chlorambucil; CLL, chronic lymphocytic leukemia; del, deletion; FCR, fludarabine-cyclophosphamide-rituximab; ibr, ibrutinib; obi, obinutuzumab; R, rituximab; RT, Richter transformation; ven, venetoclax; zanu, zanubrutinib.

Al-Sawaf O. Oral presentation at iwCLL 2025; Kraków, Poland, September 12–15, 2025.

RT1 trial: Tislelizumab plus zanubrutinib





Trial summary

- 48 patients with RT
- Median prior lines for CLL/RT: 3 (range: 1–6)
- Clonal relationship
  - Related: 26 (54.2%)
  - Unknown: 22 (45.8%)

Efficacy data:

- ORR: 58.3% (95% CI: 43.2–72.4)
- CRR: 18.8%
- PR: 39.6%
- 12-month OS: 74.7% (95% CI: 58.4–91.0)

Safety data:

- 56/57 patients experienced at least one Grade ≥1 AE*
- Cardiac toxicities were uncommon, and no AF was reported

RT1 extension cohort

- Triple combination:
  - Tislelizumab-zanubrutinib-sonrotoclax
- Enrollment commenced in September 2024

*For the safety analysis, all 57 included patients who had received at least one dose of any study medication were considered.
AE, adverse event; AF, atrial fibrillation; CI, confidence interval; CLL, chronic lymphocytic leukemia; CRR, complete response rate; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PR, partial response; RT, Richter transformation.
Al-Sawaf O *et al. Nat Med* 2024; 30 (1): 240–248.

What's in development?

BTK degraders	BCR pathway inhibitors	BiTEs / surface Ag-targeting agents	Pro-apoptotic therapies

• Bexobrutideg (NX-5948)
• BGB-16673
• ABBV-101
• AC676
• NX-2127
• UBX-303061
	• PKC-beta inhibitor
	  ○ MS-553
	• MALT-1 inhibitor
	  ○ ABBV-525
	  ○ JNJ-67856633
	  ○ SGR-1505
		• CD20 × CD3 BiTE
		  ○ Epcoritamab
		  ○ Mosunetuzumab
		• CD19 × CD3 BiTE
		  ○ AZD0486
		• ROR1 × CD3 BiTE
		  ○ NVG-111
		• Anti-CCR7
		  ○ CAP-100
			• BCL2/BCLXL inhibitor
			  ○ ABBV-453
			  ○ BP1002
			  ○ Lisaftoclax
			  ○ LP-118
			  ○ Sonrotoclax
			• CDK9 inhibitor
			  ○ PRT2527
			  ○ SLS009
			  ○ Voruciclib

Ag, antigen; BCL2, B-cell lymphoma 2; BCLXL, B-cell lymphoma extra large; BCR, B-cell receptor; BiTE, bispecific T-cell engager; CCR, CC chemokine receptor; CD, cluster of differentiation; CDK, cyclin-dependent kinase; MALT, mucosa-associated lymphoid tissue; PKC, protein kinase C.
Slide courtesy of speaker.

BTK degraders: Clinical data in CLL

	NX-5948 (bexobrutideg)[1]	BGB-16673[2]
Patient characteristics	R/R CLL (n=48)	R/R CLL (n=66)
	Four prior lines of Tx (range: 2–12)	Four prior lines of Tx (range: 2–10)
	98% prior BTKi, 83% prior BCL2i	94% prior BTKi, 82% prior BCL2i
	45% *TP53* mutated	65% *TP53* mutated and/or del(17p)
Dose range	50–600 mg	50–500 mg
Safety	Contusion (46%) > Fatigue (31%) > Neutropenia (29%)	Fatigue (37%) > Contusion (30%) > Neutropenia (29%)
	Grade ≥3 neutropenia 23% Grade ≥3 pneumonia 4%	Grade ≥3 neutropenia 24% Grade ≥3 pneumonia 11%
	Other Grade 3 toxicity rare	Other Grade 3 toxicity rare
ORR/CR	ORR: 80.9% CR: 2.1%	ORR: 84.8% CR: 4.5%

This slide includes data from different clinical trials. These data are meant for demonstration purposes only and are not meant for cross-trial comparison.

BCL2i, B-cell lymphoma 2 inhibitor; BTKi, Bruton's tyrosine kinase inhibitor; CLL, chronic lymphocytic leukemia; CR, complete response; del, deletion; ORR, overall response rate; R/R, relapsed/refractory; Tx, treatment.

Danilov AV. The emerging promise of targeted protein degraders. Oral presentation at iwCLL 2025; Kraków, Poland, September 12–15, 2025.

1. Danilov A *et al*. Oral presentation at ICML 2025; Lugano, Switzerland, June 17–21, 2025; Abstract 093. 2. Scarfò L *et al*. Oral presentation at EHA 2025; Milan, Italy, June 12–15, 2025; Abstract S158.

Bispecifics in RT: EPCORE CLL-1 (NCT04623541): RT cohort with epcoritamab monotherapy

Key RT inclusion criteria
- Prior clinical history of CLL or SLL
- Biopsy-proven transformation to CD20⁺ DLBCL
- Ineligible for or declined chemotherapy
- Measurable disease by PET and/or CT/MRI
- ≤2 prior LOTs for RT
- ECOG PS 0–2

Hospitalization was required for 24 hours after the first full dose of epcoritamab (C1D15)

Median follow-up: overall RT 22.9 months (range: 0.5+ to 39.9)
1L RT 23.9 months (range: 0.5+ to 39.9)

Overall RT (N=42)
1L RT (n=21)

2 step-up dosing[a]

Epcoritamab 48 mg 28-day cycles
QW C1–3
Q2W C4–9
Q4W C10+

→ Efficacy assessment by PET-CT obtained Q6W until C6, and then Q24W thereafter

→ Treatment until disease progression or unacceptable toxicity

Primary endpoint: ORR by IRC
Key secondary endpoints: CR rate; DoR; DoCR; time to response and to CR, PFS, OS; and safety/tolerability

Data cut-off: March 21, 2025.
[a]Patients received subcutaneous epcoritamab with 2 step-up doses (i.e. 0.16 mg priming and 0.8 mg intermediate doses before first full dose) and corticosteroid prophylaxis to mitigate CRS.
1L, first-line; 1L RT, first-line rituximab-containing therapy; C, Cycle; CD, cluster of differentiation; CLL, chronic lymphocytic leukemia; CR, complete response; CRS, cytokine release syndrome; CT, computed tomography; 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; IRC, independent review committee; LOT, line of treatment; MRI, magnetic resonance imaging; ORR, overall response rate; OS, overall survival; PET, positron emission tomography; PFS, progression-free survival; Q2W, every 2 weeks; Q4W, every 4 weeks; Q6W, every 6 weeks; Q24W, every 24 weeks; QW, every week; RT, Richter transformation; SLL, small lymphocytic lymphoma.
Kater A. Epcoritamab monotherapy in patients with first-line Richter transformation: 2-year follow-up results from the Phase 1b/2 EPCORE CLL-1 clinical trial. Oral presentation at iwCLL 2025; Kraków, Poland, September 12–15, 2025.
1. Genmab US, Inc. EPKINLY (epcoritamab-bysp). Package insert. Genmab; Plainsboro, NJ, USA, 2024. 2. Kater AP et al. HemaSphere 2024; 8 (Suppl 1); Abstract S163.

EPCORE CLL-1: Initial results

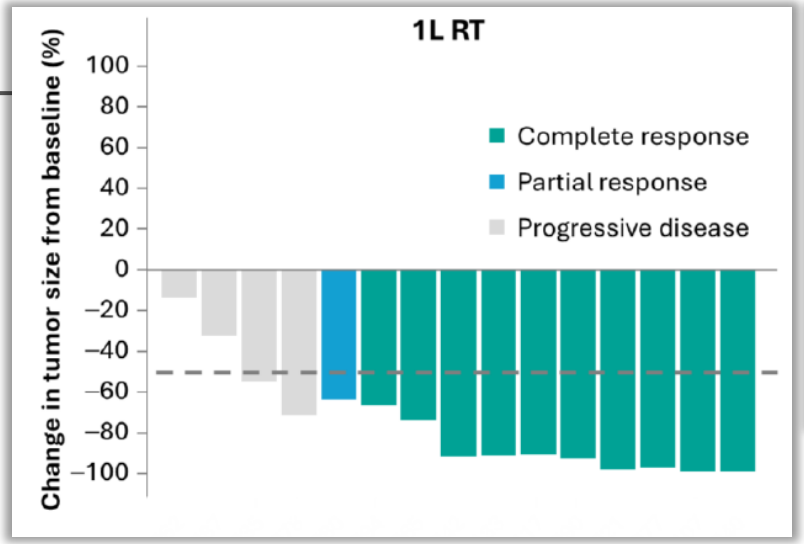
95% of patients had prior CLL-directed therapy

Median follow-up of 23.9 months

- **ORR**: 57%
  - **CR rate**: 52%
- Median time to response: 1.4 months

Median PFS: 8.5 months

Median OS: 27.5 months



Response, n (%)	1L RT (n=21)
Overall response rate [95% CI]	12 (57) [34.0–78.2]
Complete response	11 (52)
Partial response	1 (5)
Stable disease	0
Progressive disease	5 (24)

Evaluable patients had a baseline and ≥1 post-baseline tumor assessment; 1 patient with CR had data entered after the data cut-off: change in tumor size from baseline was 95%. Median follow-up: 23.9 months (range: 0.5+ to 39.9) in the 1L RT cohort. Only patients with post-baseline evaluable sum of product perpendicular diameter are included in the waterfall plot.

Safety was consistent and manageable, with no new safety signals

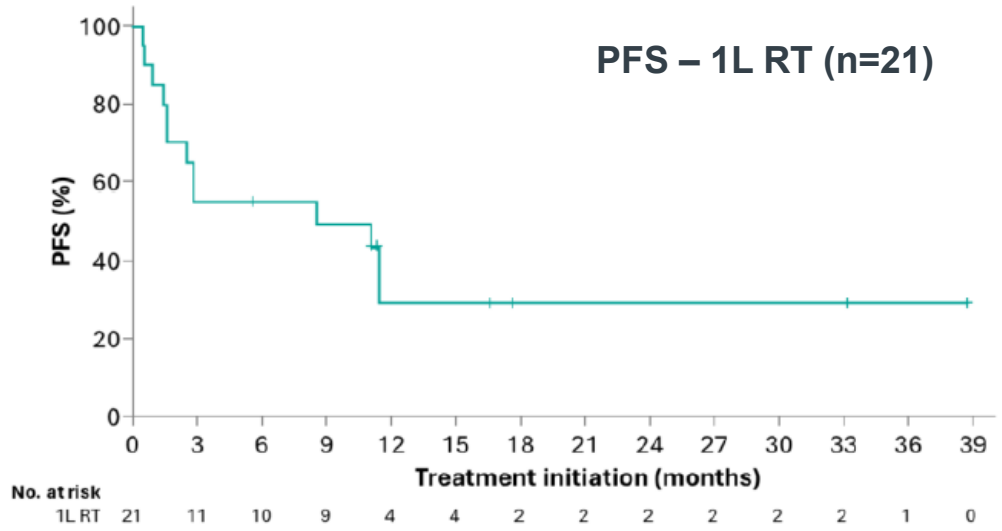
Baseline B-cell levels and on-treatment **IL-6 levels** were linked with **CRS severity**

1L, first-line; CI, confidence interval; CLL, chronic lymphocytic leukemia; CR, complete response; CRS, cytokine release syndrome; IL, interleukin; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; RT, Richter transformation.

Kater A. Oral presentation at iwCLL 2025; Kraków, Poland, September 12–15, 2025.

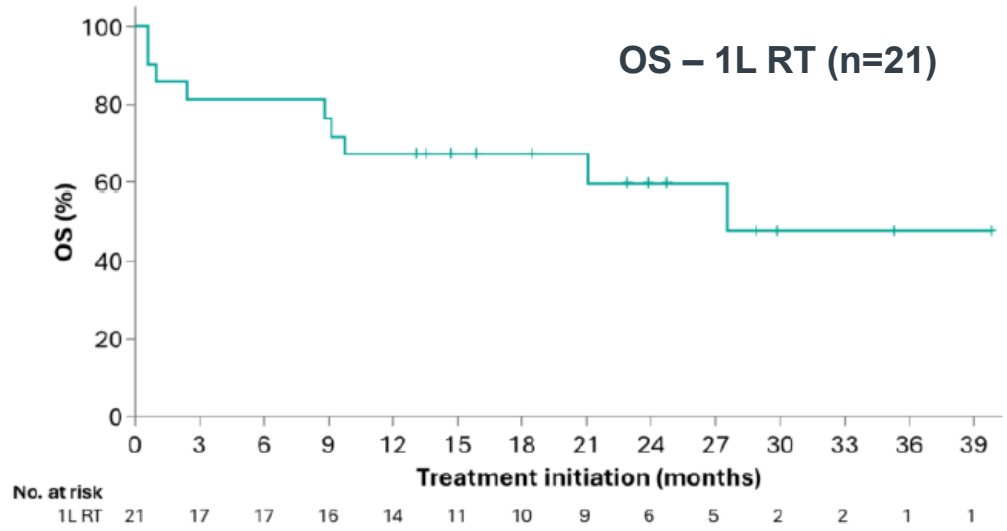
EPCORE CLL-1: PFS and OS

PFS – 1L RT (n=21)



	1L RT (n=21)
PFS events, n	13
Median PFS, (95% CI)	8.5 (1.5–NR)
Estimated patients remaining progression-free at 6 months, %	55

OS – 1L RT (n=21)



	1L RT (n=21)
OS events, n	9
Median OS, (95% CI)	27.5 (9.1–NR)
Estimated patients remaining alive at 24 months, %	59

1L RT, first-line rituximab-containing therapy; CI, confidence interval; CLL, chronic lymphocytic leukemia; NR, not reached; OS, overall survival; PFS, progression-free survival.

Kater A. Oral presentation at iwCLL 2025; Kraków, Poland, September 12–15, 2025.

Summary

First-line CLL[1]

- It is important to consider factors such as patient vulnerabilities and preferences
- Where continuous therapy is preferred, recent UK CLL guidelines recommend BTKi (zanubrutinib or acalabrutinib / acalabrutinib + obinutuzumab) or venetoclax

Relapsed / refractory CLL

- Choice of treatment for relapsed or refractory disease depends on prior therapy
  - UK CLL guidelines recommend as standard second-line options: continuous cBTKi therapy (with zanubrutinib or acalabrutinib), venetoclax + rituximab, or venetoclax monotherapy[1]
- Current efficacy and safety data with pirtobrutinib are promising[2]

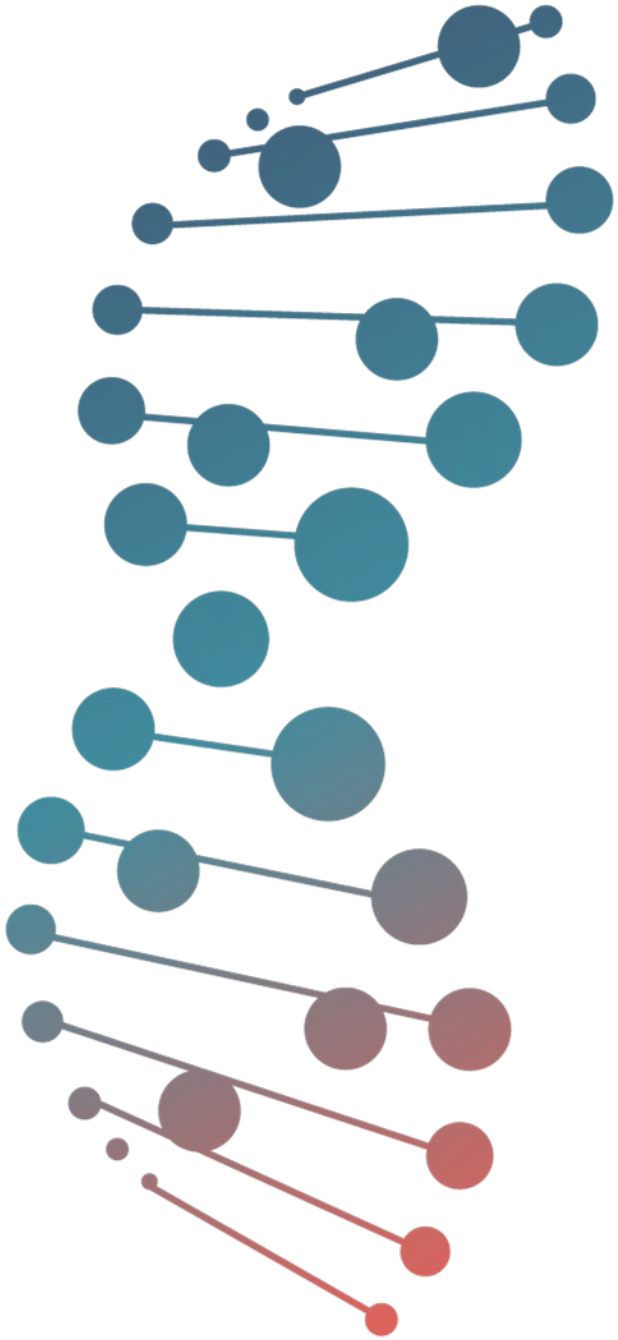
Richter transformation

- Encouraging results have been released from the RT1 trial in this difficult-to-treat population[3]
  - The triple combination trial extension (tislelizumab-zanubrutinib-sonrotoclax) is underway
- Emerging approaches for RT include BTK degraders and bispecific antibodies

BTKi, Bruton's tyrosine kinase inhibitor; cBTKi, covalent Bruton's tyrosine kinase inhibitor; CLL, chronic lymphocytic leukemia; RT, Richter transformation.

1. Walewska R *et al*. *Br J Haematol* 2025; online ahead of print (DOI: 10.1111/bjh.70100). 2. Sharman JP *et al*. *J Clin Oncol* 2025; 43 (22): 2538–2549. 3. Al-Sawaf O *et al*. *Nat Med* 2024; 30 (1): 240–248.

Thank you for your attention



Emerging trends in MCL and indolent NHL

Pier Luigi Zinzani
University of Bologna, Italy

Disclosures

- **Consultant:** EUSA Pharma, MSD, Novartis, Secura Bio
- **Speaker bureau:** ADC Therapeutics, BeOne Medicines Ltd, Bristol Myers Squibb, Celltrion, Gilead, Incyte, Janssen-Cilag, Kyowa Kirin, MSD, Roche, Sandoz, Secura Bio, Servier, TG Therapeutics, Takeda
- **Advisory board:** ADC Therapeutics, Bristol Myers Squibb, Celltrion, Gilead, Incyte, Janssen-Cilag, Kyowa Kirin, MSD, Roche, Sandoz, Secura Bio, Servier, TG Therapeutics, Takeda

What I will cover…

Emerging trends in

- Mantle cell lymphoma
- Marginal zone lymphoma
- Follicular lymphoma

Selections from my presentation at iwNHL

10:50am - 12:30pm

Session 7: Novel Therapies II

Chairs: Laurie Sehn & Alexey Danilov

BTK Inhibitors combinations:

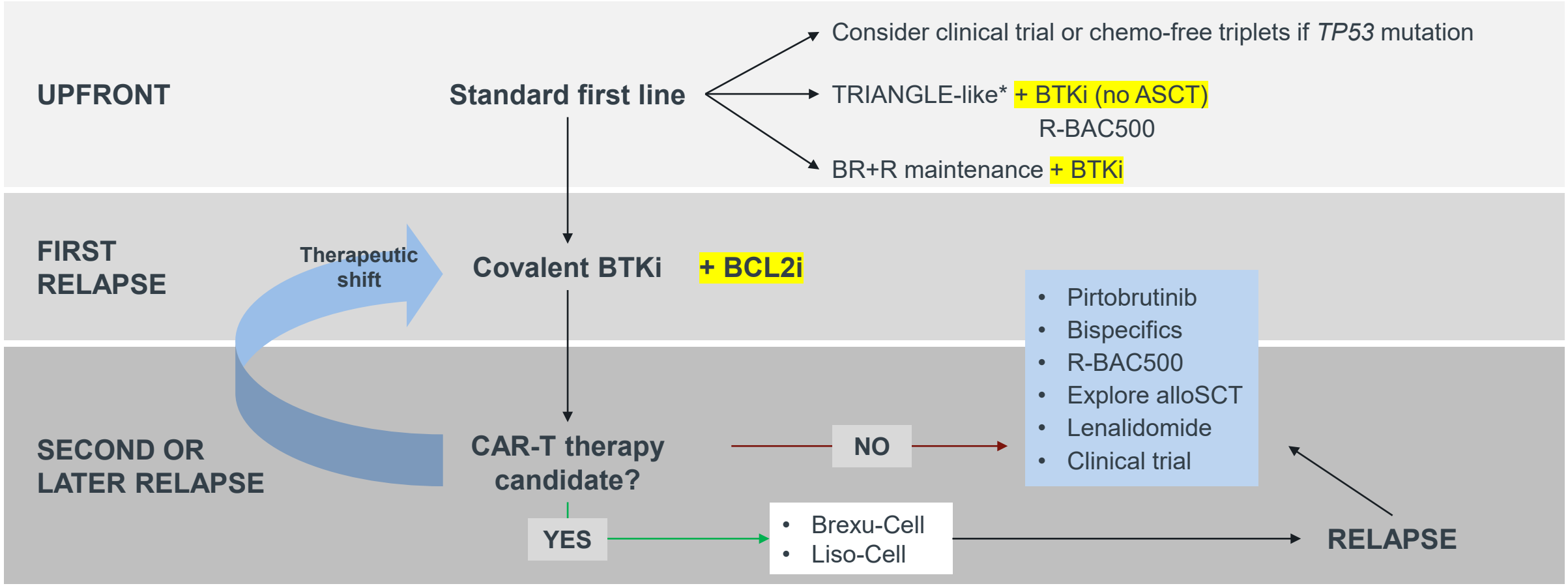
- Ibrutinib; Loretta Nastoupil
- Zanubrutinib; *Pier Luigi Zinzani*
- Acalabrutinib; *Krish Patel*
- *Pirtobrutinib; Michael Wang*

Developments with BTK inhibitors, including zanubrutinib, are shaping the direction of management strategies for these three lymphomas

BTK, Bruton's tyrosine kinase; iwNHL, International Workshop on Non-Hodgkin Lymphoma.

Mantle cell lymphoma

BTK inhibitors are at the heart of the evolution in mantle cell lymphoma management across treatment lines

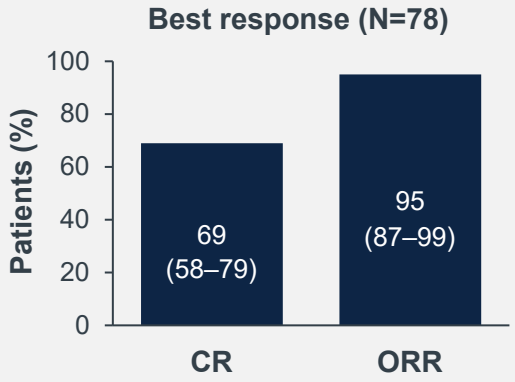


*The treatment regimens in TRIANGLE are: R-CHOP/R-DHAP + ASCT vs. R-CHOP/R-DHAP + ASCT + ibrutinib vs. R-CHOP/R-DHAP + ibrutinib.
alloSCT, allogeneic stem cell transplant; ASCT, autologous stem cell transplant; BCL2i, B-cell lymphoma 2 inhibitor; BR+R, bendamustine-rituximab + rituximab; BTK, Bruton's tyrosine kinase; BTKi, BTK inhibitor; CAR-T, chimeric antigen receptor T-cell; R-BAC500, rituximab, bendamustine, cytarabine (500 mg/m²); R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone; R-DHAP, rituximab, dexamethasone, high-dose cytarabine, cisplatin.
Moioli A and Visco C. *Br J Haematol* 2025; 207 (2): 687–689.

BTK inhibitor combinations across lines of therapy

SYMPATICO (NCT03112174)[1]

Ibr-Ven in cohort aged ≥65 years or with *TP53* mutations



mDOR (n=74): 37.1 months

Safety outcomes were consistent with known safety profiles of the individual agents, with higher AE rates in patients aged ≥65 years

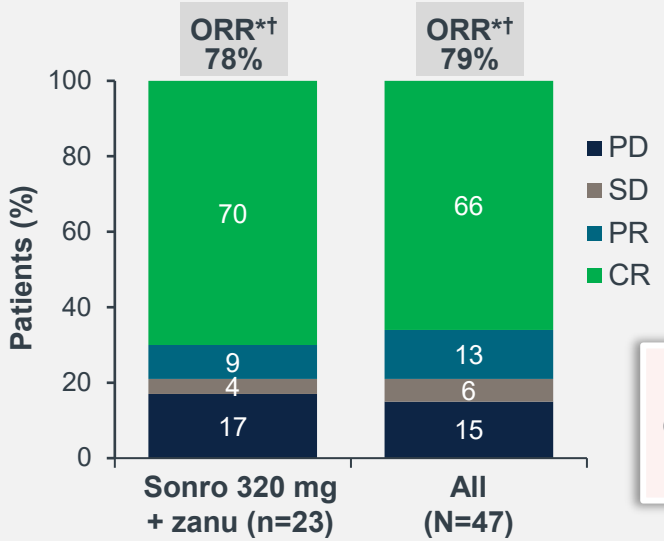
ECHO (NCT02972840)[2]

BR with or without acalabrutinib – analysis of patients with Ki-67 index ≥30%, high-risk MIPI, blastoid/pleomorphic histology, or *TP53* mutation

	High-risk (n=370)		Overall (N=598)	
	ABR	**PBR**	**ABR**	**PBR**
ORR	89.8%	84.7%	91.0%	88.0%
CR	67.9%	47.5%	66.6%	53.5%
mPFS, months	49.5	36.0	66.4	49.6

BGB-11417-101 (NCT04277637)[3]

Sonrotoclax + zanubrutinib



Estimated 24-month event-free DoR rate: 84% (95% CI: 65.3%–93.1%)

FU, months (range)	**13.2** (0.7–31.6)	**16.4** (0.7–42.2)

- No laboratory or clinical TLS
- Majority of TEAEs were low-grade
- No new safety signals across dose levels
- No atrial fibrillation/flutter

This slide includes data from different clinical trials. These data are meant for demonstration purposes only and are not meant for cross-trial comparison purposes.

*Responses were assessed per Lugano 2014 criteria and are shown as the percentages of responding patients who had ≥1 post-baseline tumor assessment after dosing with sonrotoclax unless treatment was discontinued due to clinical progression or death prior to tumor assessment. †ORR was defined as PR or better.

AE, adverse event; ABR, acalabrutinib + bendamustine-rituximab; BR, bendamustine-rituximab; BTK, Bruton's tyrosine kinase; CI, confidence interval; CR, complete response; DoR, duration of response; FU, follow-up; Ibr-Ven, ibrutinib-venetoclax; Ki-67 index, Ki-67 proliferation index; MIPI, Mantle Cell Lymphoma International Prognostic Index; , median DoR; mPFS, median PFS; ORR, overall response rate; PBR, placebo + bendamustine-rituximab; PFS, progression-free survival; PR, partial response; SD, stable disease; PD, progressive disease; sonro, sonrotoclax; TEAE, treatment-emergent AE; TLS, tumor lysis syndrome; zanu, zanubrutinib.1. Wang M *et al*. Oral presentation at ASCO 2025; Chicago, IL, USA, May 29–June 2, 2025; Abstract 7017. 2. Dreyling M *et al*. Oral presentation at EHA 2025, Milan, Italy, June 12–15, 2025; Abstract S233. 3. Tam CS *et al*. Oral presentation at EHA 2025, Milan, Italy, June 12–15, 2025; Abstract S234.

Mature studies with zanubrutinib in MCL across lines of therapy

	BGB-3111-206 N=86	BOVen (IIT) N=25
Therapeutic line	**Patients with ≥1 and <5 prior lines of therapy[1]**	**Previously untreated patients[3]**
Key inclusion criteria	Relapse or failure to achieve at least PR to last regimen Age 18–75 years ECOG PS: ≤2[1]	Presence of *TP53* mutations Age ≥65 years **or** patients <65 years ineligible for HDT/ASCT ECOG PS: ≤2[3]
Treatment (n)	Zanubrutinib[1]	Zanubrutinib, obinutuzumab, and venetoclax (n=25)[3]
Median follow-up	35.3 months[1]	28.2 months[3]
ORR	83.7%[1]	96.0%[3]
CR	77.9%[1]	88.0%[3]
PFS	Median: 33.0 months[1]	Estimated 2-year: 72%[3]
OS	Estimated 3-year: 74.8%[1]	Estimated 2-year: 76%[3]
≥1 AE	88.4%[1]	Not stated
Grade ≥3 AE	50.0%[1]	48.0%[4]
Most common Grade ≥3 AE	Neutrophil count decreased (18.6%)[1]	Neutrophil count decreased (16.0%)[3]
Serious AE	29.1%[2]	48.0%[3]
Most common serious AE	Not stated	COVID-19 infection (20%)[4]

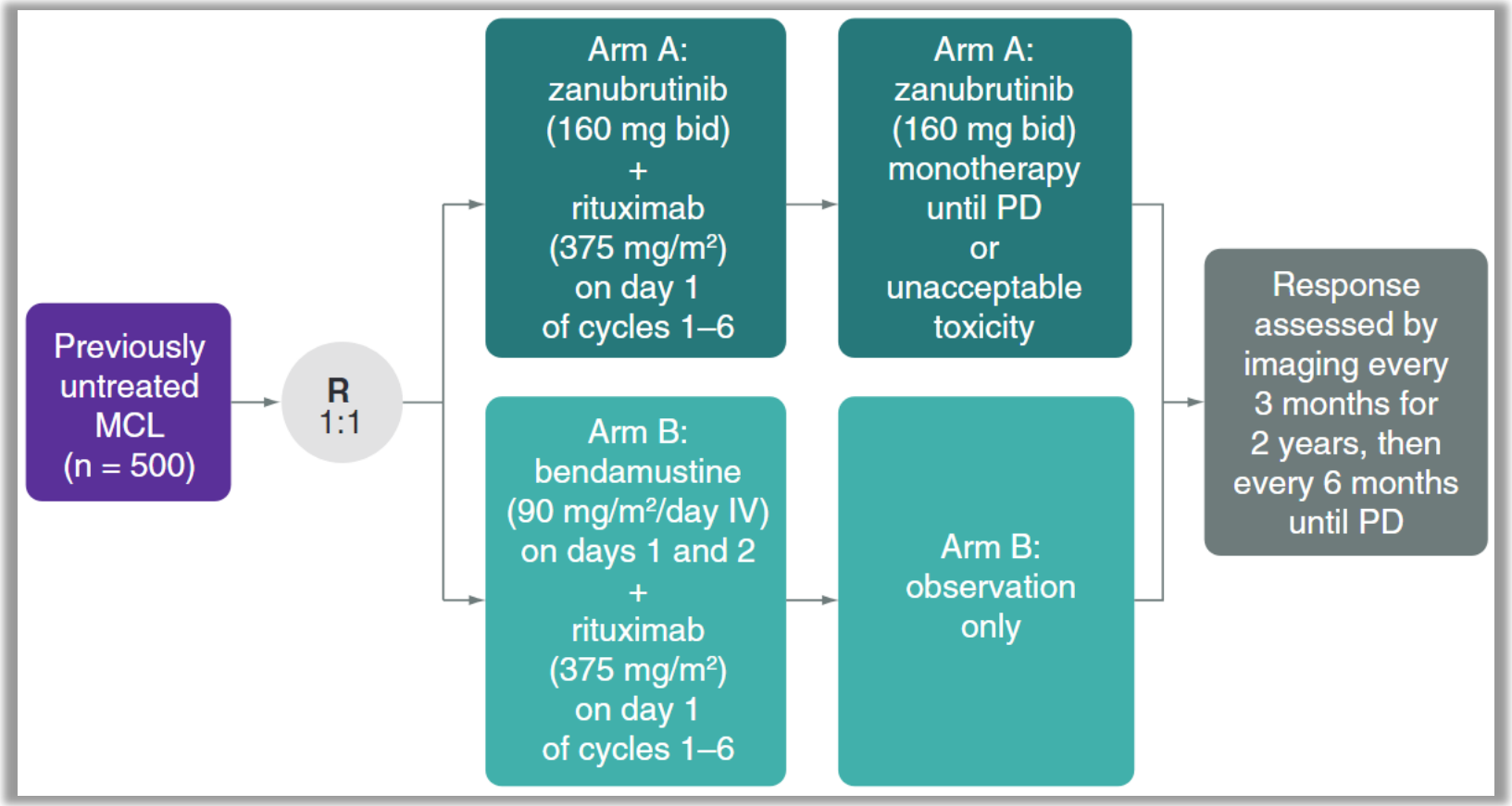
This slide includes data from different clinical trials. These data are meant for demonstration purposes only and are not meant for cross-trial comparison purposes.

AE, adverse event; ASCT, autologous stem cell transplant; COVID-19, coronavirus disease 2019; CR, complete response, ECOG PS, Eastern Cooperative Oncology Group Performance Status; HDT, high-dose therapy; IIT, investigator-initiated trial; MCL, mantle cell lymphoma; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PR, partial response; zanu, zanubrutinib.

1. Song Y *et al*. *Blood* 2022; 139 (21): 3148–3158 – manuscript and supplementary appendix. 2. Song Y *et al*. Poster presentation at EHA 2021; Poster EP789. 3. Kumar A *et al*. *Blood* 2025; 145 (5): 497–507.
4. Kumar A *et al*. Oral presentation at ASH 2023; Abstract 739.

Early-stage trial with zanubrutinib in untreated MCL

MANGROVE: A Phase 3 study of zanubrutinib plus rituximab versus bendamustine plus rituximab in transplant-ineligible, untreated mantle cell lymphoma



bid, twice daily; IV, intravenous; MCL, mantle cell lymphoma; PD, progressive disease; R, randomization.

Dreyling M *et al*. *Future Oncol* 2021; 17 (3): 255–262.

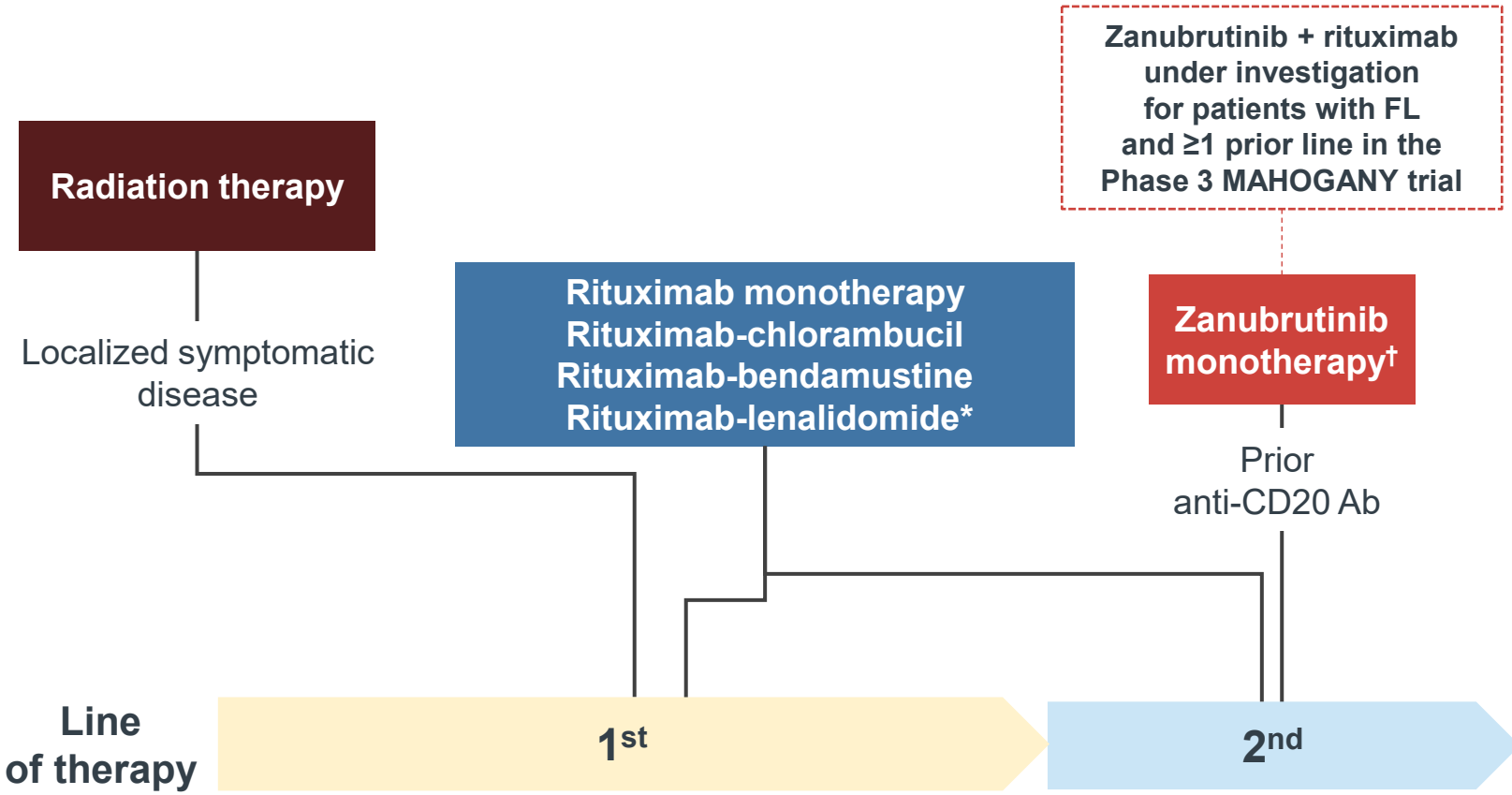
Selected ongoing or upcoming clinical trials in MCL

NCT *	Title	1L / 2L+	Phase	Multisite	Location	Open
NCT05833763	A Phase 2 trial of glofitamab and pirtobrutinib in previously treated with a BTK inhibitor **(GOIDiLOX)**	2L+	2	Y	AUS	Y
NCT06054776	Acalabrutinib, obinutuzumab, and glofitamab for the treatment of R/R MCL	2L+	1/2	N	USA	Y
NCT06192888	Pilot study of glofitamab and lenalidomide in patients with R/R MCL previously treated with a BTK inhibitor	2L+	2	Y	USA	Y
NCT05861050	Glofitamab with obinutuzumab, venetoclax, and lenalidomide for the treatment of patients with newly diagnosed high-risk MCL **(GLOVe)**	1L	1/2	Y	USA	Y
NCT06656221	A prospective, single-center study evaluating the efficacy and safety of glofitamab combined with orelabrutinib and bortezomib in patients with high-risk MCL	N/A	N/A	N/A	China	N
NCT06558604	A Phase 2 study of glofitamab in combination with venetoclax plus zanubrutinib or venetoclax alone in subjects with untreated or R/R high-risk MCL	1L+	2	Y	France	Y
NCT06357676	Glofitamab plus ibrutinib with obinutuzumab for the treatment of patients with MCL	1L	2	Y	USA	N

*All study information was collected from the relevant NCT study page and accessed in November 2025.
1L, first-line; 2L, second-line; BTK, Bruton's tyrosine kinase; MCL, mantle cell lymphoma; N, no; N/A, not applicable; R/R, relapsed/refractory; Y, yes.
Slide courtesy of speaker.

Marginal zone lymphoma

Overview of the MZL treatment landscape



Compared with FL, **there are relatively few therapies specifically approved for MZL**

MZL is a heterogeneous disease, with different subtypes requiring different therapeutic approaches

Please consult local guidance for details on licensed indications and reimbursement criteria.

*Rituximab-based therapies are commonly used in clinical settings for MZL, but none has specific EMA-approved indications in MZL. †Zanubrutinib monotherapy is approved by the EMA for the treatment of adult patients with MZL who have received at least one prior anti-CD20–based therapy.

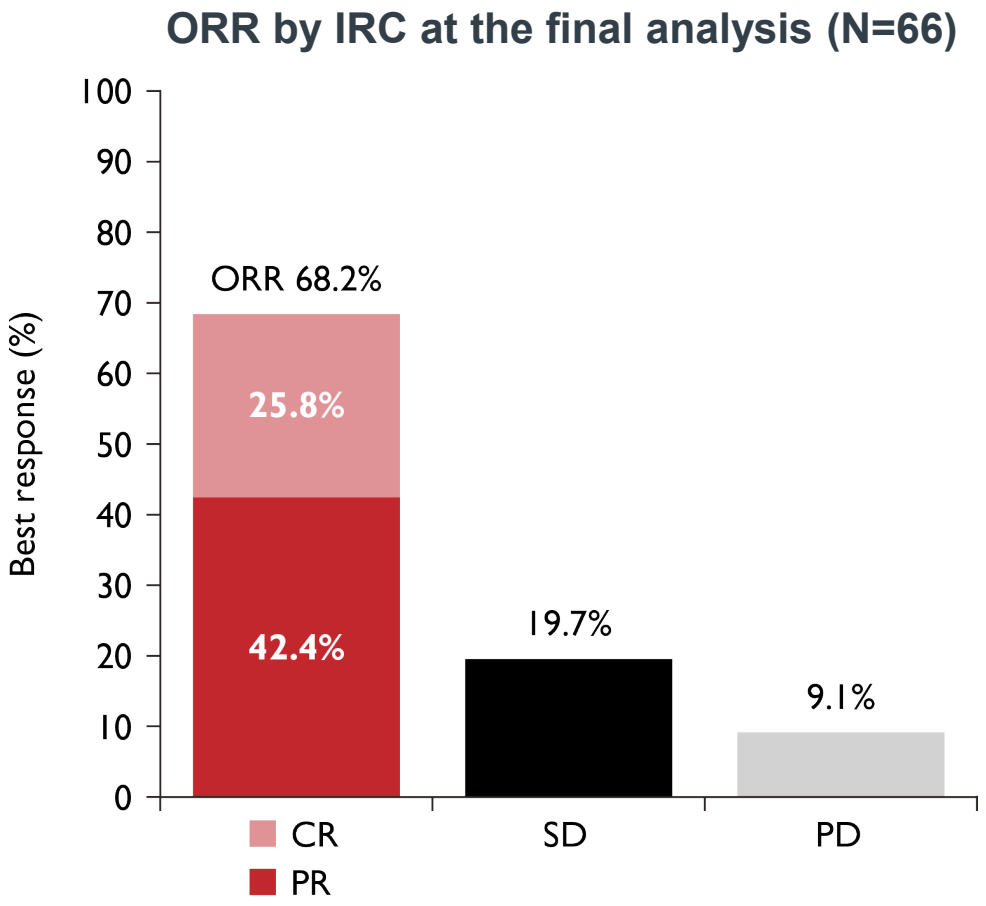
Ab, antibody; CD20, cluster of differentiation 20; EMA, European Medicines Agency; FL, follicular lymphoma; MZL, marginal zone lymphoma.

Walewska R *et al*. *Br J Haematol* 2024; 204 (1): 86–107.

Slide courtesy of speaker.

Zanubrutinib monotherapy was approved for R/R MZL based on the MAGNOLIA study

BTKi monotherapy
≥1 prior Tx



Primary endpoint of ORR by IRC was met in the primary analysis

In the final analysis (median follow-up: 28 months), **ORR was 68% by PET and/or CT and 67% by CT only**

24-month PFS (95% CI): 70.9% (57.2–81.0)
24-month DoR (95% CI): 72.9% (54.4–84.9)

Efficacy was observed across all MZL subtypes, including nodal MZL, splenic MZL, and extranodal mucosa-associated lymphoid tissue

No unexpected safety signals were observed; atrial fibrillation/flutter and hypertension were uncommon

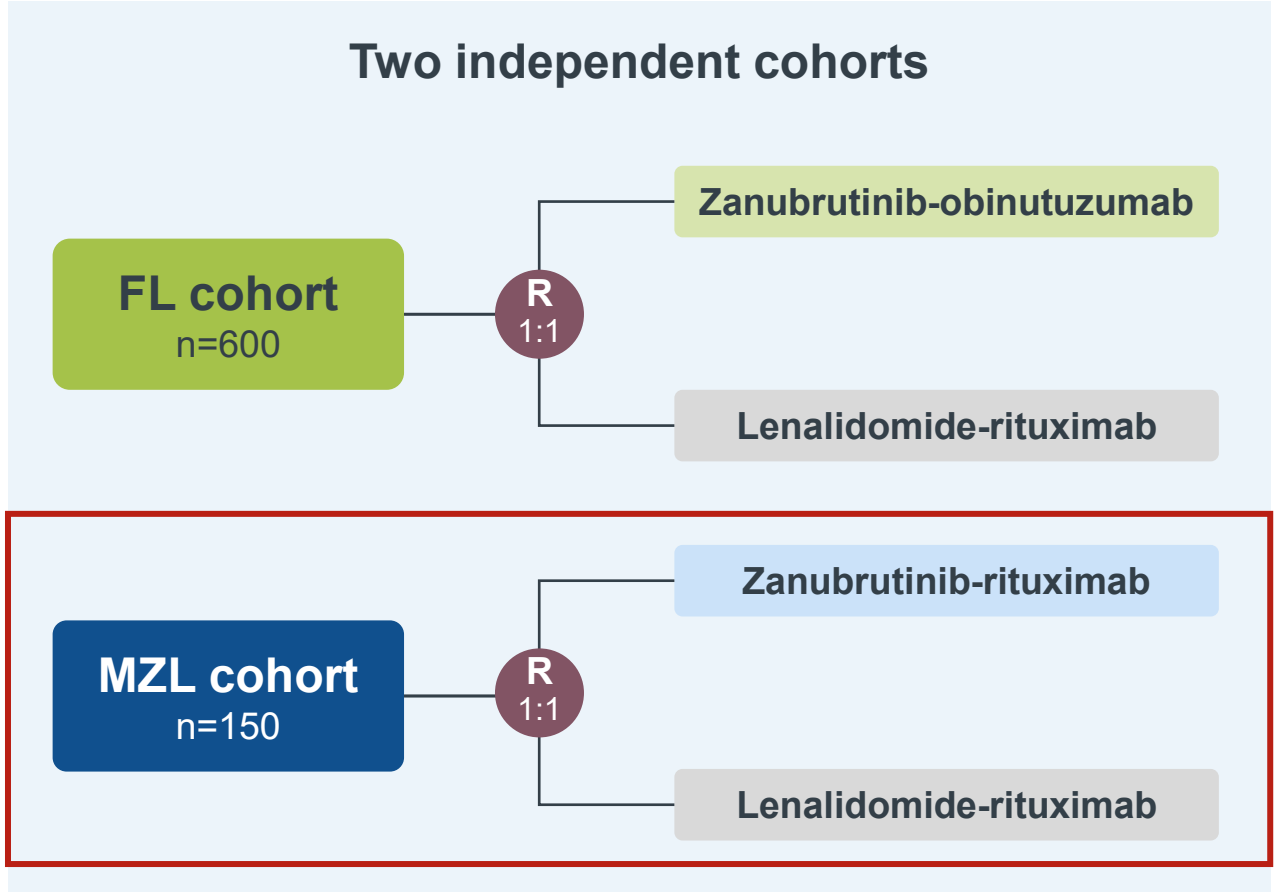
BTKi, Bruton's tyrosine kinase inhibitor; CI, confidence interval; CR, complete response; CT, computed tomography; DoR, duration of response; IRC, independent review committee; MZL, marginal zone lymphoma; ORR, overall response rate; PD, progressive disease; PET, positron emission tomography; PFS, progression-free survival; PR, partial response; R/R, relapsed/refractory; SD, stable disease; Tx, treatment.

Opat S *et al. Blood Adv* 2023; 7 (22): 6801–6811.

MAHOGANY: Randomized, open-label, Phase 3 trial of zanubrutinib + anti-CD20 in patients with FL or MZL with one prior systemic therapy[1]

Key eligibility criteria

- Age ≥18 years
- Histologically confirmed R/R FL (Grade 1–3A) or MZL (eMZL, nMZL, or sMZL)
- Previous treatment with ≥1 prior line of systemic therapy, including an anti-CD20–based regimen
- In need of treatment according to modified GELF criteria[2]
- Adequate bone marrow and organ functions
- No prior treatment with BTKi
- Prior lenalidomide treatment allowed unless no response or short remission (DoR <24 months)
- No clinically significant cardiovascular disease, severe or debilitating pulmonary disease, or history of a severe bleeding disorder

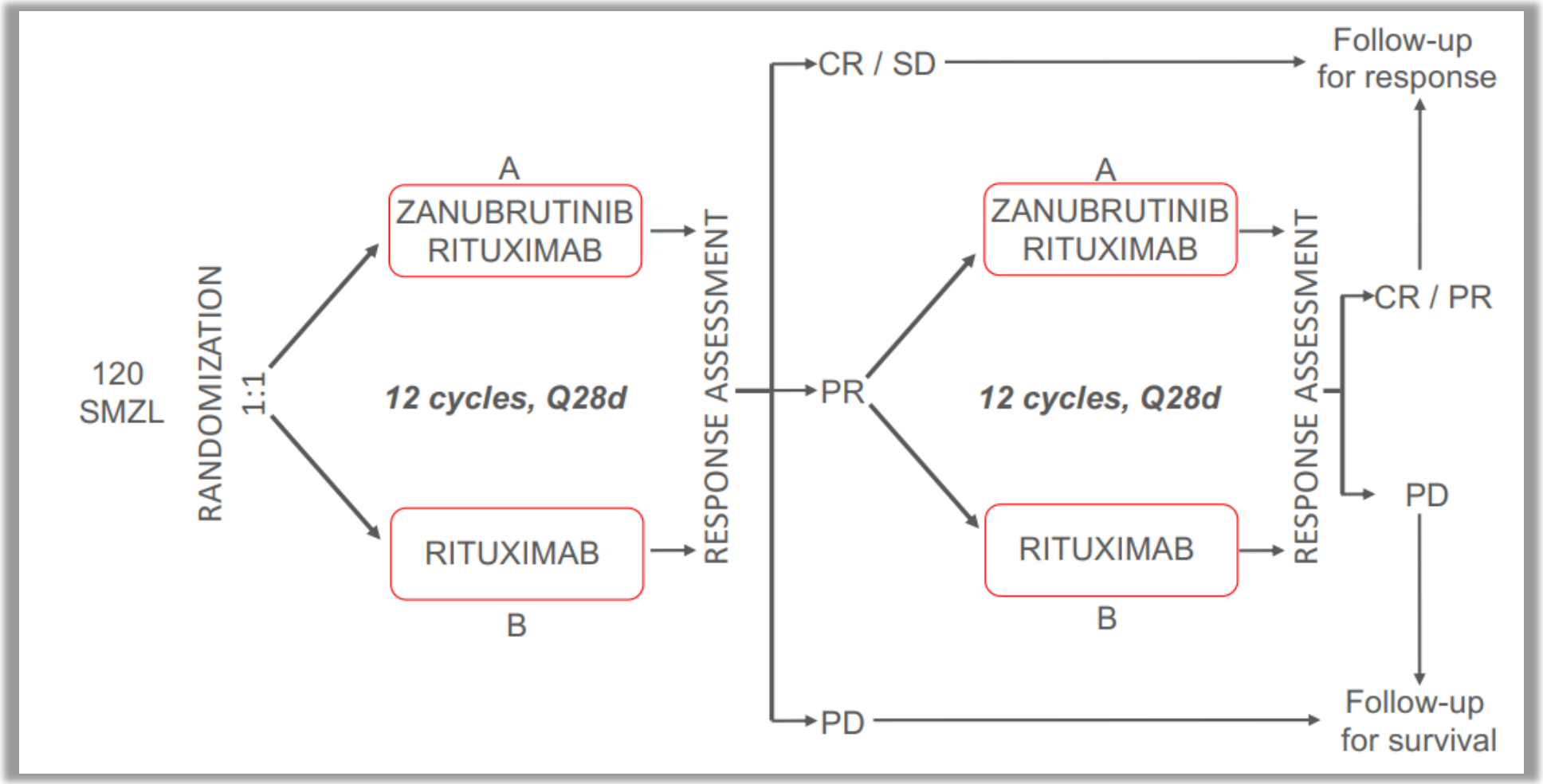


BTKi, Bruton's tyrosine kinase inhibitor; CD20, cluster of differentiation 20; DoR, duration of response; eMZL, extranodal MZL; FL, follicular lymphoma; GELF, Groupe d'Etude des Lymphomes Folliculaires; MZL, marginal zone lymphoma; nMZL, nodal MZL; R, randomization; R/R, relapsed/refractory; sMZL, splenic MZL.

1. Sehn LH *et al.* Oral presentation at ICML 2023; Lugano, Switzerland, June 13–17, 2023; Abstract 994. 2. Brice P *et al. J Clin Oncol* 1997; 15 (3): 1110–1117.

Zanubrutinib + rituximab in previously untreated splenic MZL

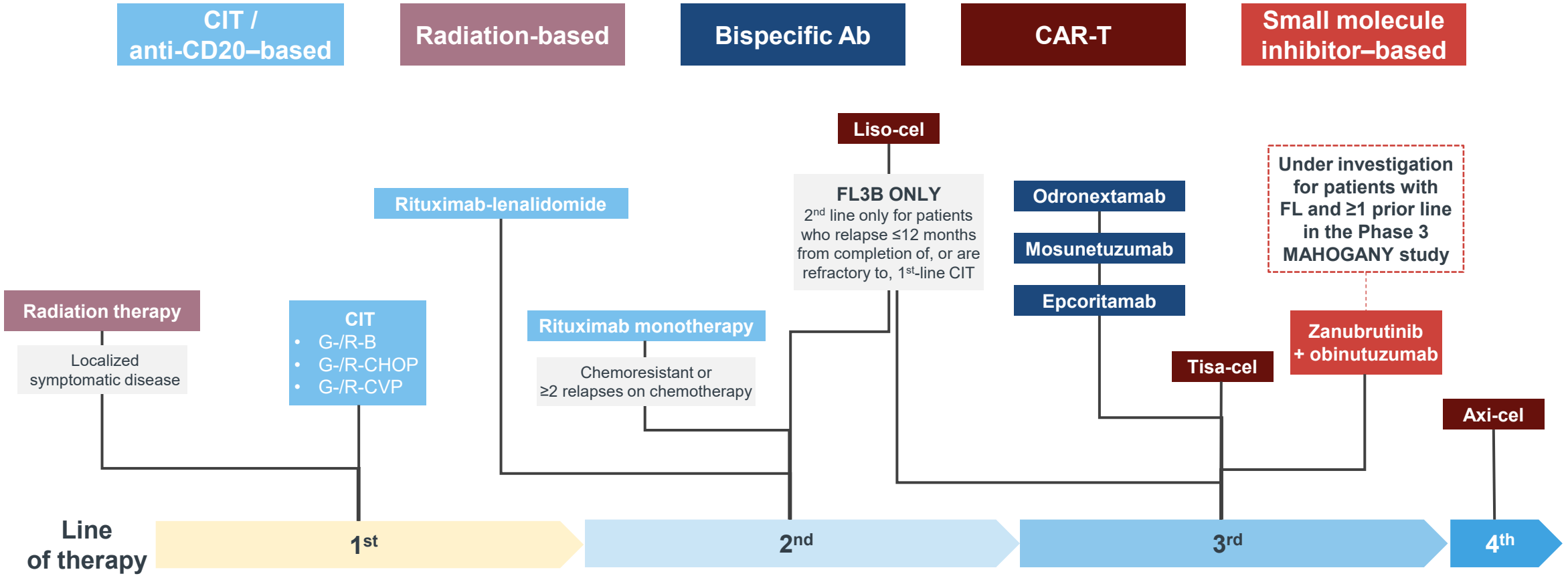
Phase 3 IELSG48 (RITZ) study



Trial registered as NCT05735834.
CR, complete response; MZL, marginal zone lymphoma; PD, progressive disease; PR, partial response; Q28d, every 28 days; SD, stable disease; SMZL, splenic MZL.
Slide courtesy of speaker.

Follicular lymphoma

Overview of the FL treatment landscape*



Please consult local guidance for details on licensed indications and reimbursement criteria.

*Information collated from the relevant Summary of Product Characteristics hosted on the European Medicines Agency website (available at: https://www.ema.europa.eu; accessed May 2025).

Ab, antibody; axi-cel, axicabtagene ciloleucel; CAR-T, chimeric antigen receptor T-cell; CD20, cluster of differentiation 20; CIT, chemoimmunotherapy; FL, follicular lymphoma; FL3B, FL Grade 3B; G-/R-B, obinutuzumab/rituximab, bendamustine; G-/R-CHOP, obinutuzumab/rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone; G-/R-CVP, obinutuzumab/rituximab, cyclophosphamide, vincristine, prednisone; liso-cel, lisocabtagene maraleucel; tisa-cel, tisagenlecleucel.

Slide courtesy of speaker.

ROSEWOOD: Randomized, Phase 2 study of zanubrutinib + obinutuzumab vs. obinutuzumab in R/R FL[1]

BTKi
+ anti-CD20
≥2 prior Tx

Response by ICR	Zanubrutinib + obinutuzumab (n=145)	Obinutuzumab (n=72)
ORR, % (95% CI)	**68.3 (60.0–75.7)**	**45.8 (34.0–58.0)**
Risk difference, % (95% CI)	**22.0 (8.3–35.8)**	
2-sided *P*-value	**0.0017**	
BOR, n (%)		
CR	54 (37.2)	14 (19.4)
PR	45 (31.0)	19 (26.4)
SD	25 (17.2)	14 (19.4)
Non-progressive disease	3 (2.1)	4 (5.6)
PD	13 (9.0)	15 (20.8)
Discontinued prior to first tumor assessment	4 (2.8)	6 (8.3)
NE	1 (0.7)	0

Median follow-up: 12.5 months

Primary endpoint
ORR per ICR was significantly higher with zanubrutinib + obinutuzumab, with a risk difference of 22%

PFS[2]
- Zanubrutinib + obinutuzumab: 28 months
- Obinutuzumab: 10.4 months

HR (95% CI): 0.50 (0.33–0.75); *P*<0.001

The **safety profile of zanubrutinib + obinutuzumab was consistent with the safety profile of each drug**[2]

Incidences of atrial fibrillation and hypertension were low and similar between both treatment arms

BOR, best overall response; BTKi, Bruton's tyrosine kinase inhibitor; CD20, cluster of differentiation 20; CI, confidence interval; CR, complete response; FL, follicular lymphoma; HR, hazard ratio; ICR, independent central review; NE, not evaluable; ORR, overall response rate; PD, progressive disease; PFS, progression-free survival; PR, partial response; R/R, relapsed/refractory; SD, stable disease; Tx, treatment.

1. Zinzani PL *et al*. Oral presentation at ASCO 2022; Chicago, IL, USA, June 3–7, 2022; Abstract 7510. 2. Zinzani PL *et al*. *J Clin Oncol* 2023; 41 (33): 5107–5117.

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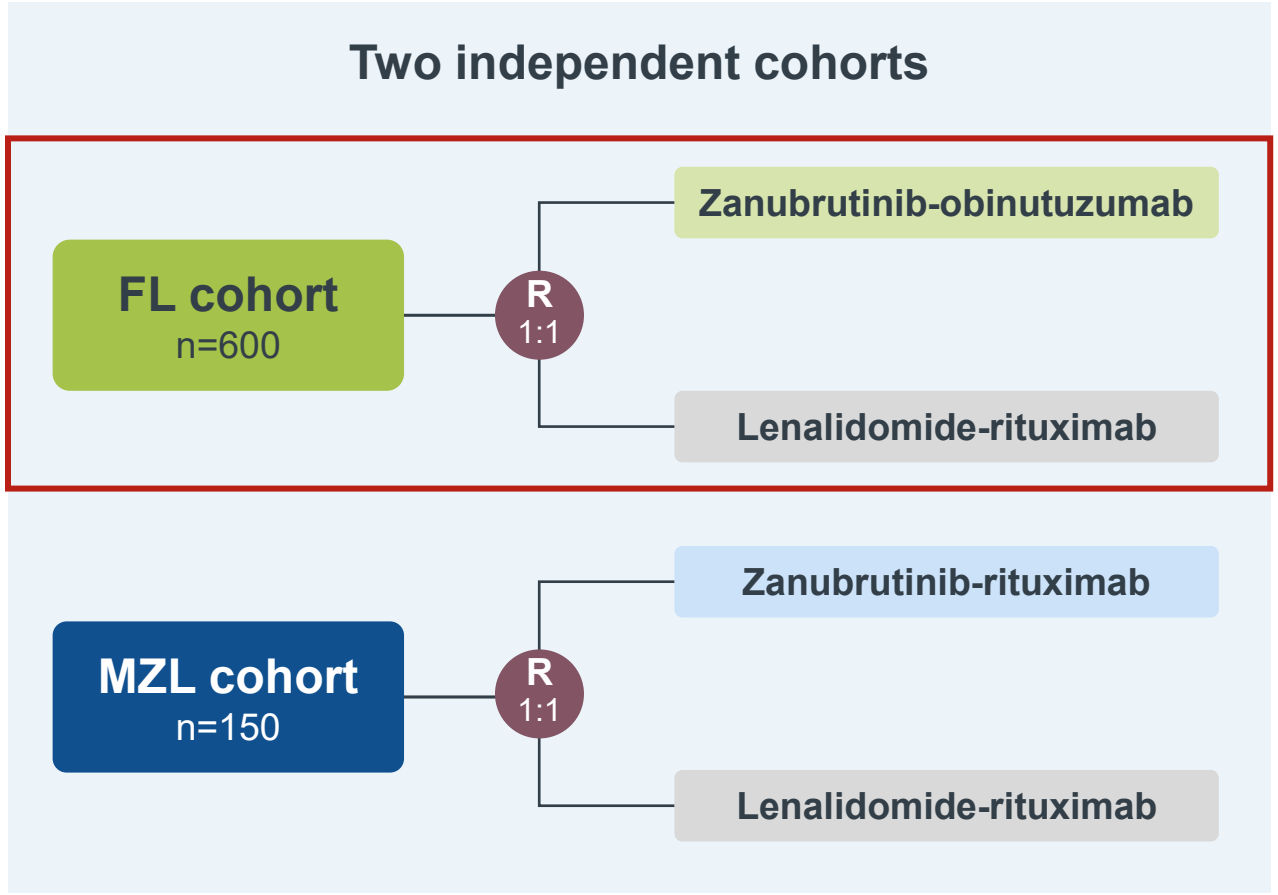
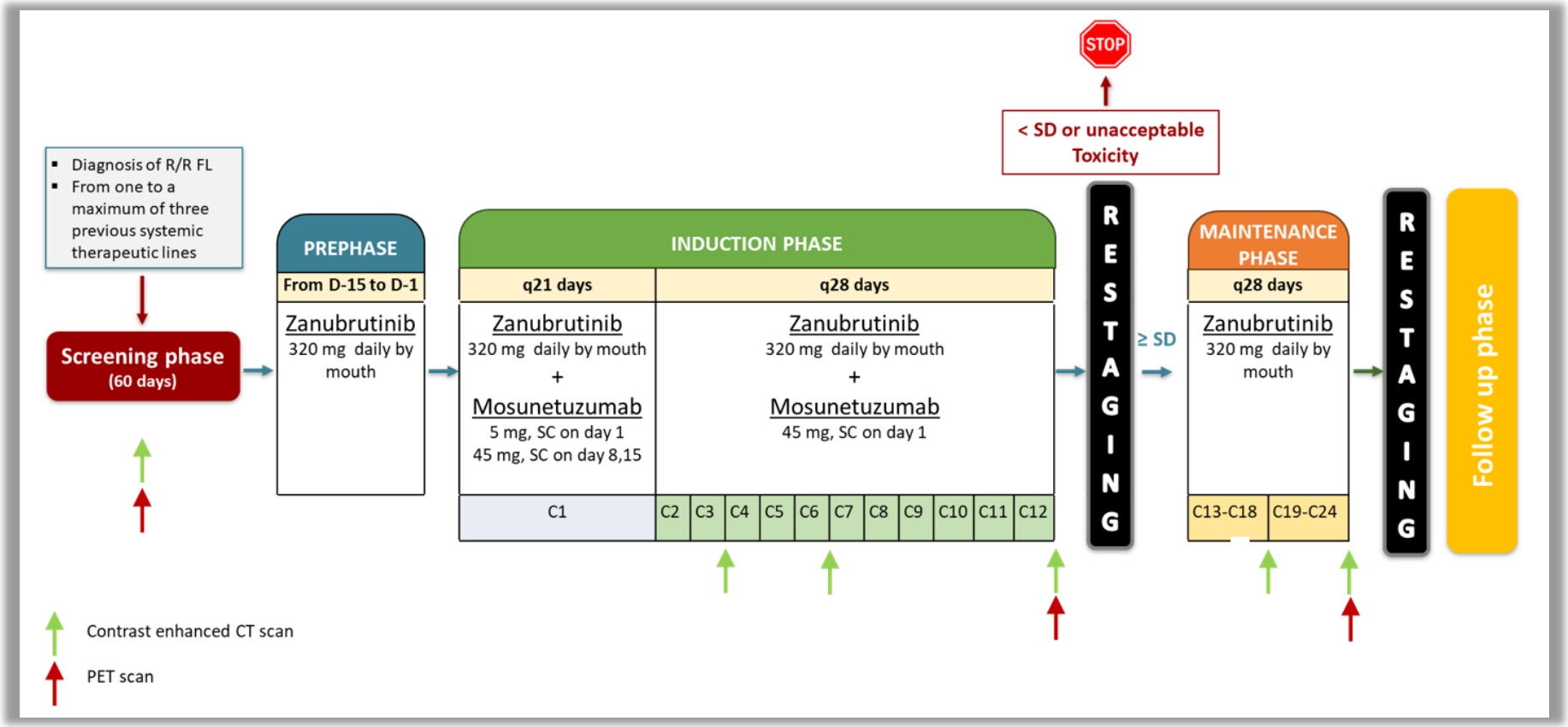


BTKi, Bruton's tyrosine kinase inhibitor; CD20, cluster of differentiation 20; DoR, duration of response; eMZL, extranodal MZL; FL, follicular lymphoma; GELF, Groupe d'Etude des Lymphomes Folliculaires; MZL, marginal zone lymphoma; nMZL, nodal MZL; R, randomization; R/R, relapsed/refractory; sMZL, splenic MZL.

1. Sehn LH *et al.* Oral presentation at ICML 2023; Lugano, Switzerland, June 13–17, 2023; Abstract 994. 2. Brice P *et al. J Clin Oncol* 1997; 15 (3): 1110–1117.

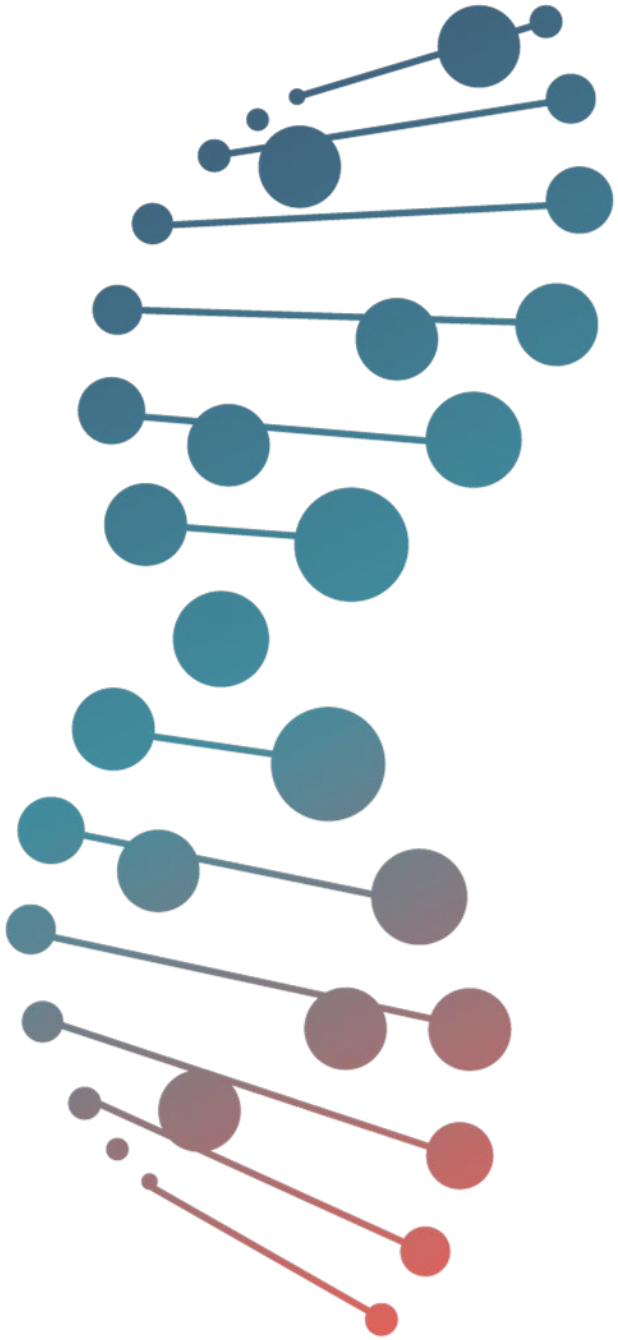
Mosunetuzumab and zanubrutinib in R/R FL (MOZART)

A chemotherapy-free, Phase 2 trial from Fondazione Italiana Linfomi (FIL)



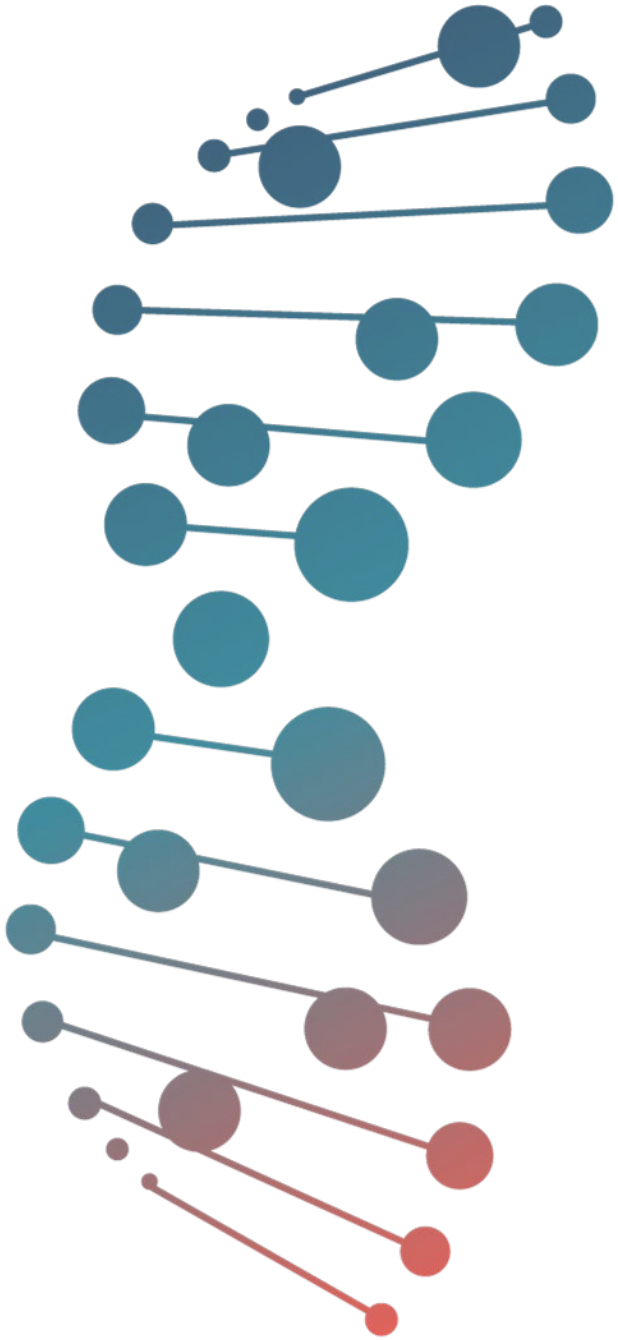
Study registered with EU CT number: 2023-506049-52-00.
C, cycle; CT, computed tomography; D, day; FL, follicular lymphoma; PET, positron emission tomography; q[21/28] days, every [21/28] days; R/R, relapsed/refractory; SC, subcutaneous; SD, stable disease.
Slide courtesy of speaker.

Thank you for your attention



Discussion and audience Q&A

All faculty



Summary

Chair: Francesc Bosch

Summary

iwCLL

The **program reflected the dynamic and rapidly evolving landscape of CLL**

- Against the backdrop of an ever-expanding range of treatment options, expert **speakers shared the latest recommendations on treatment selection and sequencing**
- A major **focus was on investigational and novel therapeutic regimens**, including:
  - The combination of the next-generation BTKi zanubrutinib and investigational next-generation BCL2i sonrotoclax
  - Agents with new MOAs in early-phase clinical trials, such as BTK degraders
  - Emerging targets that hold promise for future therapeutic strategies

iwNHL

The **agenda for iwNHL spanned the full spectrum of NHL**

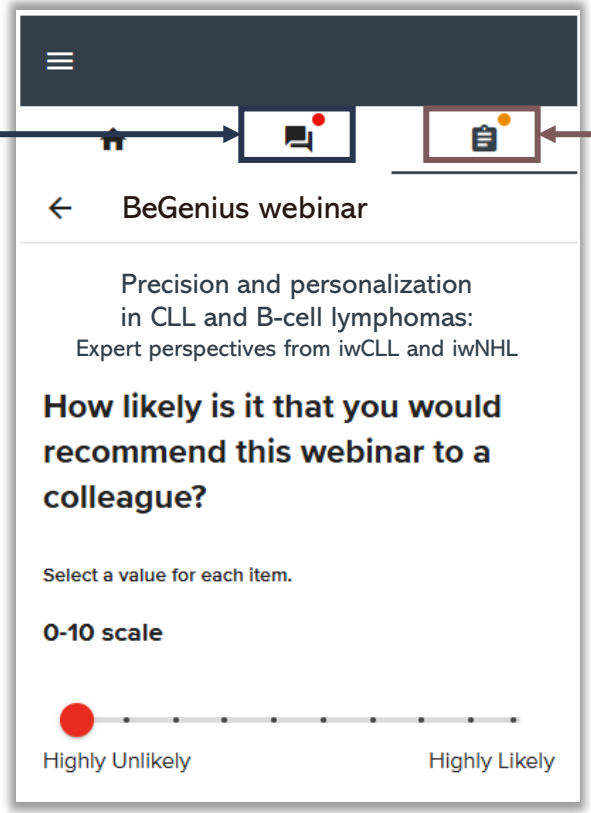
- The **workshop opened with a session on mantle cell lymphoma**, highlighting a treatment landscape in transition to a targeted therapy era, with BTK inhibitors central to treatment strategies
- As the BTK inhibitor with the broadest label in B-cell malignancies, **zanubrutinib featured prominently** – with discussion of its current roles, as well as recent developments and ongoing investigations in mantle cell lymphoma, follicular lymphoma, and marginal zone lymphoma

BCL2i, BCL2 inhibitor; BTKi, BTK inhibitor; CLL, chronic lymphocytic leukemia; iwCLL, International Workshop on Chronic Lymphocytic Leukemia; iwNHL, International Workshop on Non-Hodgkin Lymphoma; MOA, mode of action; NHL, non-Hodgkin lymphoma.

We want to hear from you!

Exit full-screen view to have your say

Please submit your questions to the faculty here



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Your feedback will help us ensure the content and design of these webinars remain useful to you!

Thank you for your attention