

SEQUOIA



SEQUOIA Trial Design



Phase 3

Study Identifier:
BGB-3111-304, NCT03336333

Primary Endpoints: PFS by IRC in Cohort 1

Key Secondary Endpoints: Cohort 1: ORR, OS, DoR, safety; Cohort 2: ORR, OS, PFS, DoR; Cohort 3: ORR (INV), PFS (INV), uMRD4 rate (10^{-4} sensitivity), safety per CTCAE

Key eligibility criteria

- TN CLL/SLL requiring treatment
- ≥ 65 years of age or < 65 years of age and unsuitable for FCR treatment
- Measurable disease by CT/MRI
- No current or past history of Richter's transformation

Stratification factors

- Age (< 65 vs ≥ 65 years)
- Binet Stage (C vs. A or B)
- IGHV mutational status (mutated vs. unmutated)
- Geographic region (NA vs EU vs. APAC)

Treatment

del(17p) FISH test

Cohort 1:
without del(17p)

R 1:1

Arm A
Zanubrutinib 160 mg PO BID until PD
(n=241)

Arm B
Bendamustine + rituximab $\times 6$
(n=238)

Cohort 2:
with del(17p)

Arm C
Zanubrutinib 160 mg PO BID until PD
(n=111)

Cohort 3:
With del(17p) and/or TP53 mut OR without del(17p)

Arm D
Zanubrutinib 160 mg PO BID + venetoclax
(n=114)

Follow-up

Safety and survival

APAC=Asia/Pacific, BID=twice daily, CLL=chronic lymphocytic leukemia, CT=computed tomography, DoR=duration of response, EU=European Union, FCR=fludarabine, cyclophosphamide, and rituximab (chemotherapy regimen), FISH=fluorescence in situ hybridization, IGHV=immunoglobulin heavy chain variable region, INV=investigator, IRC=independent review committee, MRI=magnetic resonance imaging, NA=North America, ORR=objective response rate, OS=overall survival, PD=progressive disease, PFS=progression-free survival, PO=per oral, R=randomized, SLL=small lymphocytic lymphoma, TN=treatment-naïve.

1. ClinicalTrials.gov. <https://clinicaltrials.gov/ct2/show/NCT03336333>. Accessed October 9, 2025. 2. Brown JR et al. ASCO 2018. Abstract TPS7581; 3. Shadman M, et al. Oral Presentation at ASCO 2025;abstract 7009.

Baseline Demographics and Disease Characteristics

	Cohort 1: Patients Without del(17p)		Cohort 2: Patients With del(17p)	Cohort 3: With del(17p) and/or TP53 mut OR without del(17p)
	Arm A: Zanubrutinib (n=241)	Arm B: BR (n=238)	Arm C: Zanubrutinib (n=111) ^a	Arm D: Zanubrutinib + Venetoclax (n=114)
Age, median (range), years	70 (40-86)	70 (35-87)	71 (42-87)	67 (26-87)
Age ≥65 years, n (%)^b	198 (82)	195 (82)	95 (86)	68 (60)
Male, n (%)	154 (64)	144 (61)	79 (71)	64 (56)
ECOG PS 2, n (%)	15 (6)	20 (8)	14 (13)	-
Geographic region, n (%)				
North America	34 (14)	28 (12)	12 (11)	NR
Europe	174 (72)	172 (72)	52 (47)	NR
Asia-Pacific	33 (14)	38 (16)	47 (42)	NR
Binet stage C, n (%)^c	70 (29)	70 (29)	39 (35)	46 (43)
Bulky disease ≥5 cm, n (%)	69 (29)	73 (31)	44 (40)	49 (43)
Cytopenia at baseline, n (%)^d	102 (42)	110 (46)	61 (55)	NR
Unmutated IGHV, n/N (%)^e	125/234 (53)	121/231 (52)	67/103 (65)	86/110 (78)
del(11q), n (%)	43 (18)	46 (19)	37 (33)	18 (16)
TP53 mutation, n/N (%)	15/232 (6)	13/223 (6)	47/109 (43)	49 (43)
Complex karyotype with ≥3 abnormalities, n/N (%)^f	23/164 (14)	22/161 (14)	33/88 (38)	47 (41)

^aOne patient without del(17p) was misassigned to the nonrandomly assigned cohort of patients with del(17p). The patient is excluded from the efficacy analysis in this cohort; ^bPatients aged ≥75 years included 63 patients in group A (26%), 53 patients in group B (22%), and 27 patients in group C (24%); ^cPatients with SLL had Binet stage calculated as if they had CLL; ^dDefined as having anemia (hemoglobin ≤110 g/L), thrombocytopenia (platelets ≤100×10⁹/L), or neutropenia (absolute neutrophil count ≤1.5×10⁹/L);

^eTwenty-two patients had insufficient RNA quantity/quality for polymerase chain reaction amplification of immunoglobulin heavy chain variable region for sequencing or had missing data; ^fPatients with missing/insufficient metaphase activity were omitted from the complex karyotype analysis.

BR=bendamustine plus rituximab, CLL=chronic lymphocytic leukemia, ECOG=Eastern Cooperative Oncology Group, IGHV=immunoglobulin heavy chain variable, NR=not reported, PS=performance status, SLL=small lymphocytic lymphoma,

1. Shadman M et al. *J Clin Oncol.* 2025;43:780-787; 2. Tam CS, et al. Oral Presentation at ASCO 2025;abstract 7011; 3. Shadman M, et al. *J Clin Oncol.* 2025 Jul 20;43(21):2409-2417.

Primary Endpoint: PFS-IRC in Cohort 1 (Without del[17p])

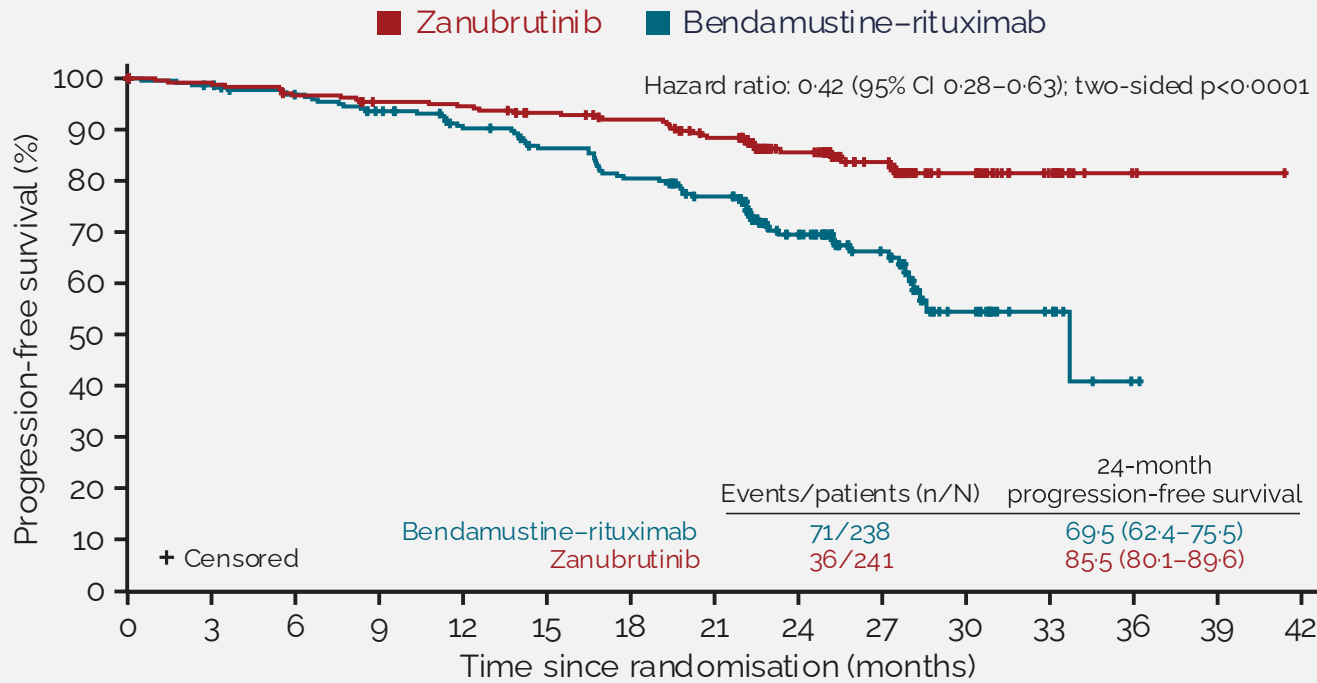
At the prespecified interim analysis, after a median follow-up of 26.2 months, the primary endpoint was met; the difference in PFS between Arms A and B met prespecified criteria for superiority¹



Median follow-up:
26.2 months

Median PFS was not reached in either arm

After a median follow-up of 43.7 months, median PFS was not reached in patients who received zanubrutinib; in patients who received BR, median PFS was 42.2 months²



Number at risk
(number censored)

Bendamustine-rituximab 238 (0) 218 (17) 210 (21) 200 (24) 187 (30) 176 (33) 164 (33) 150 (40) 89 (89) 54 (121) 20 (148) 8 (160) 1 (166) 0 (167)

Zanubrutinib 241 (0) 237 (2) 230 (3) 224 (6) 222 (6) 214 (11) 208 (14) 195 (19) 123 (86) 79 (128) 31 (174) 17 (188) 2 (203) 1 (205) 0 (205)

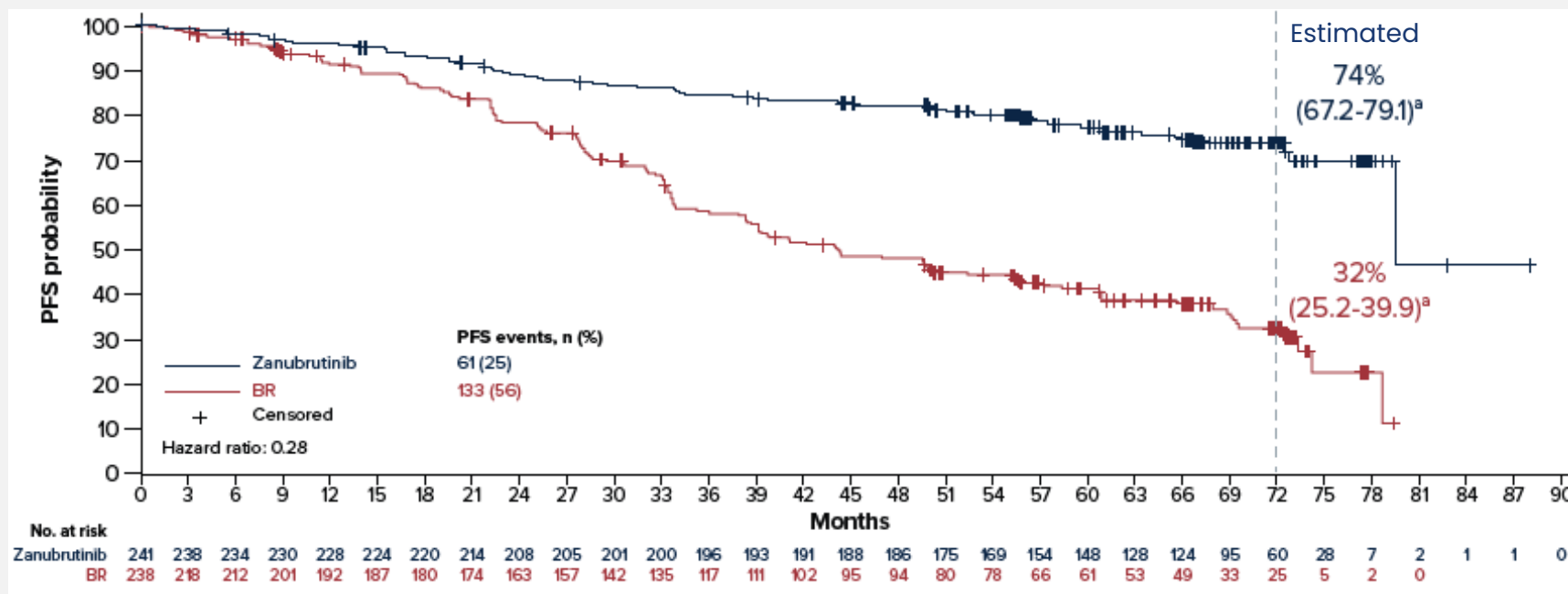
Data cutoff: May 7, 2021.

BR=bendamustine plus rituximab, CI=confidence interval, HR=hazard ratio, NE=not evaluable, IQR=interquartile range, IRC=independent review committee, PFS=progression-free survival.

1. Tam et al. *Lancet Oncol.* 2022. 22;S1460-2045; 2. Shadman M et al. *J Clin Oncol.* 2025;43:780-787.

Extended Follow-Up: PFS-IRC in Cohort 1 (Without del[17p])

In an extended follow-up analysis, median PFS zanubrutinib demonstrated sustained PFS superiority vs BR (HR, 0.28; 95% CI, 0.20-0.38; P<.0001).



Median follow-up:
72.8 months

Estimated 72-month PFS rates were 74% and 32% in zanubrutinib- and BR-treated patients, respectively

Data cut-off: April 30, 2025.

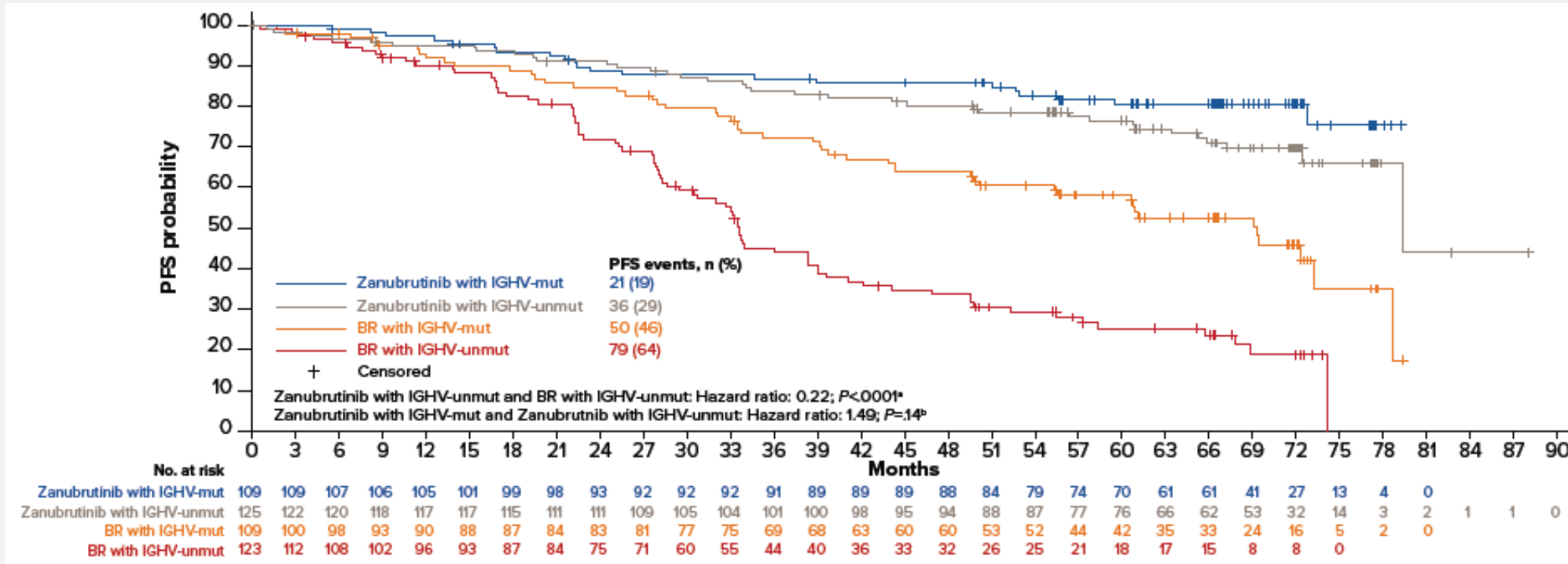
^a95% CI values.

BR=bendamustine and rituximab, CI=confidence interval, HR=hazard ratio, PFS=progression-free survival.

Tam S, et al. Poster Presentation at ASH 2025;Poster 2129.

PFS by IGHV Mutation Status in Cohort 1 (Without del[17p])

PFS remained prolonged with zanubrutinib versus BR in both patients with mutated and unmutated IGHV genes



Median follow-up:
72.8 months

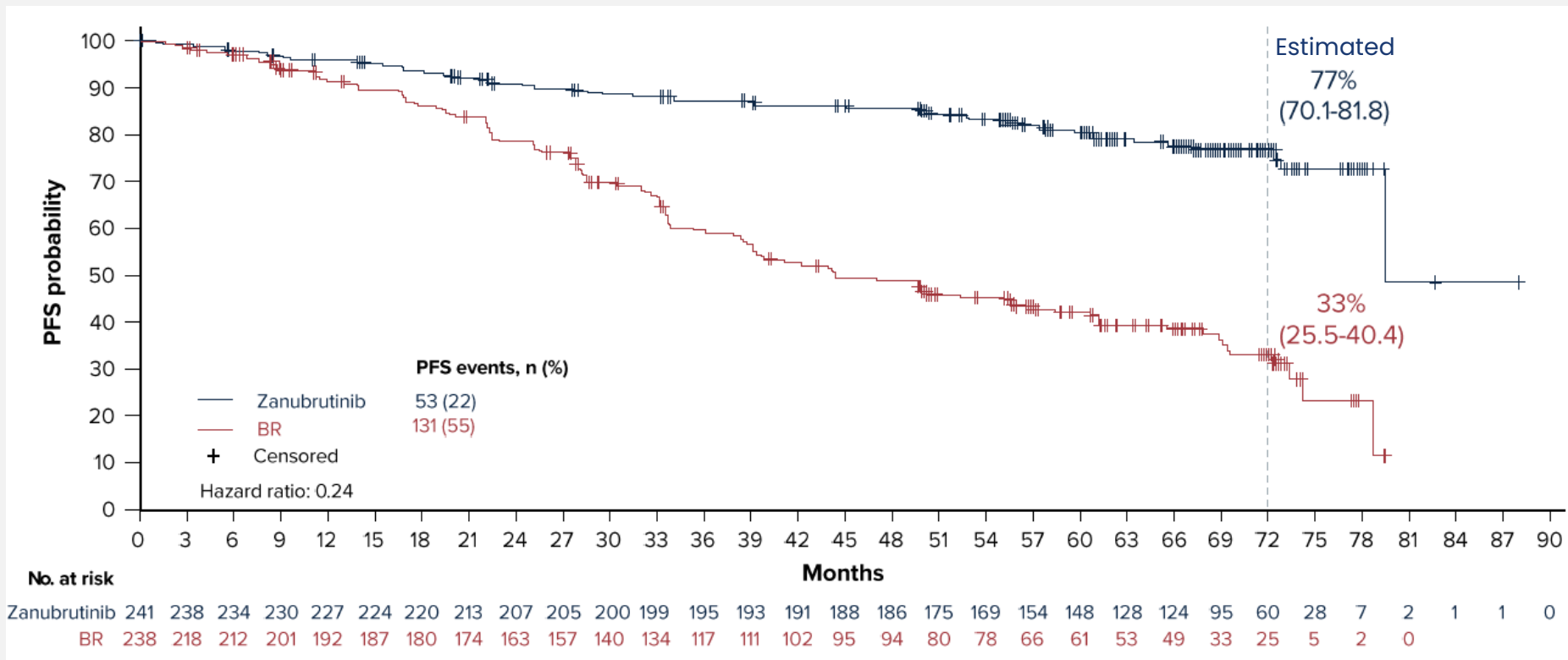
Data cut-off: April 30, 2025.

^aOne sided p-value. ^bTwo-sided p-value. ^c95% CI values.

BR=bendamustine and rituximab, HR=hazard ratio, IGHV-mut=immunoglobulin heavy-chain variable region-mutated, IGHV-unmut=immunoglobulin heavy-chain variable region-unmutated, PFS=progression-free survival.

Tam S, et al. Poster Presentation at ASH 2025;Poster 2129.

PFS in Cohort 1 Adjusted for COVID-19



Median follow-up:
72.8 months

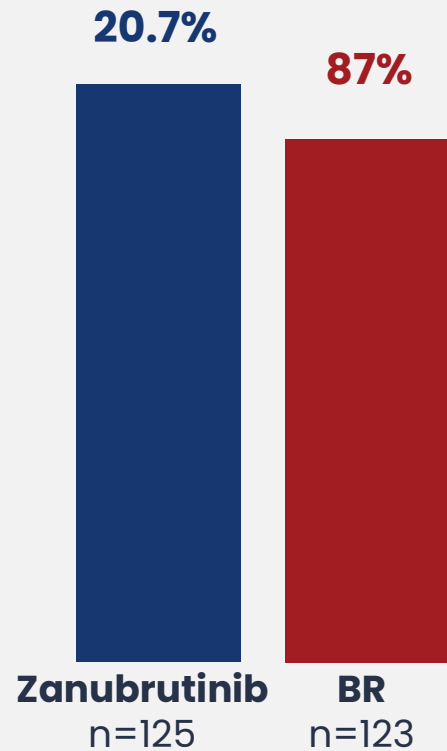
When adjusted for COVID-19, respective 72-month PFS rates were 77% and 33%

Data cut-off: April 30, 2025.
BR=bendamustine and rituximab, HR=hazard ratio, PFS=progression-free survival.
Tam S, et al. Poster Presentation at ASH 2025;Poster 2129.

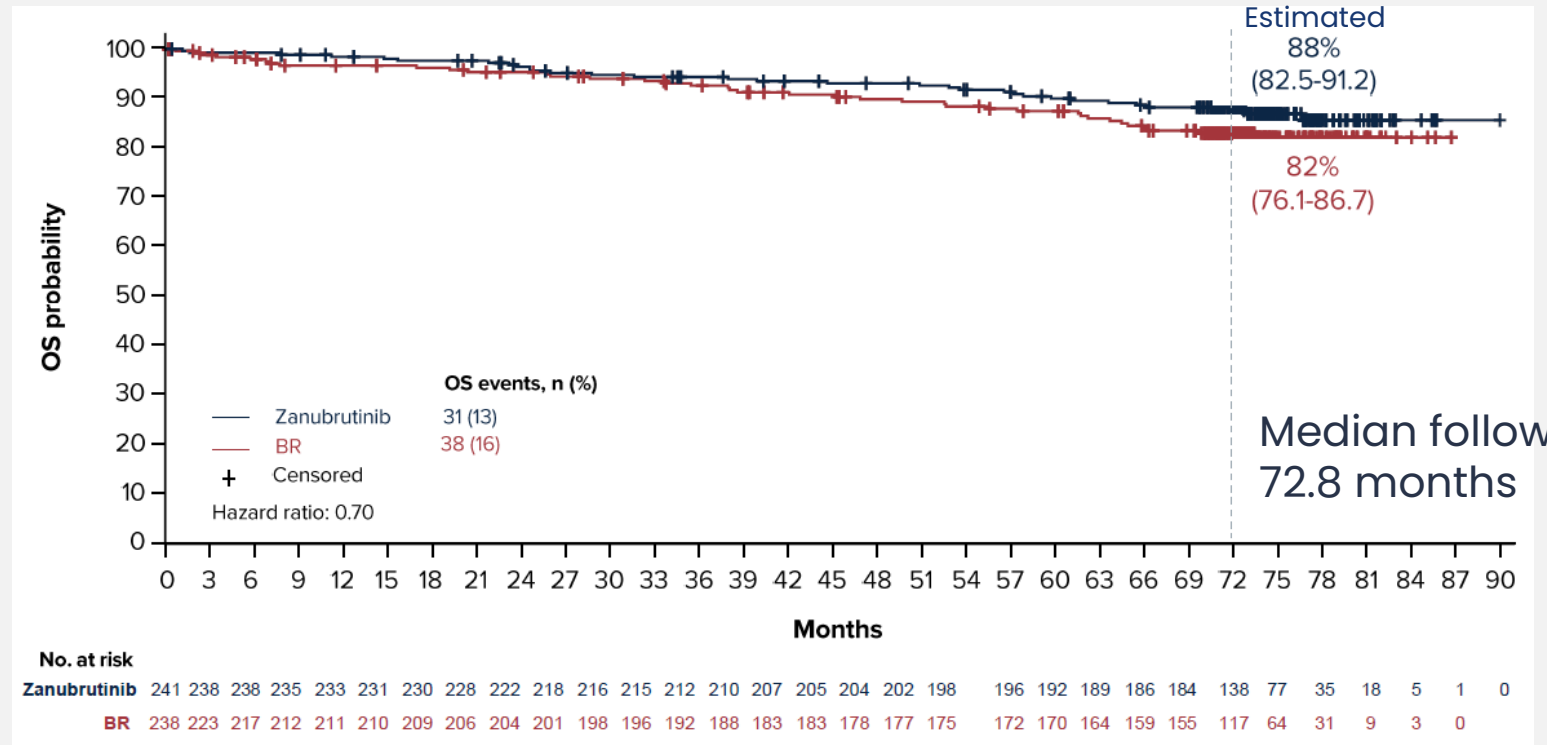
ORR Rates and Overall Survival in Cohort 1



ORR in patients with IGHV-unmutated disease

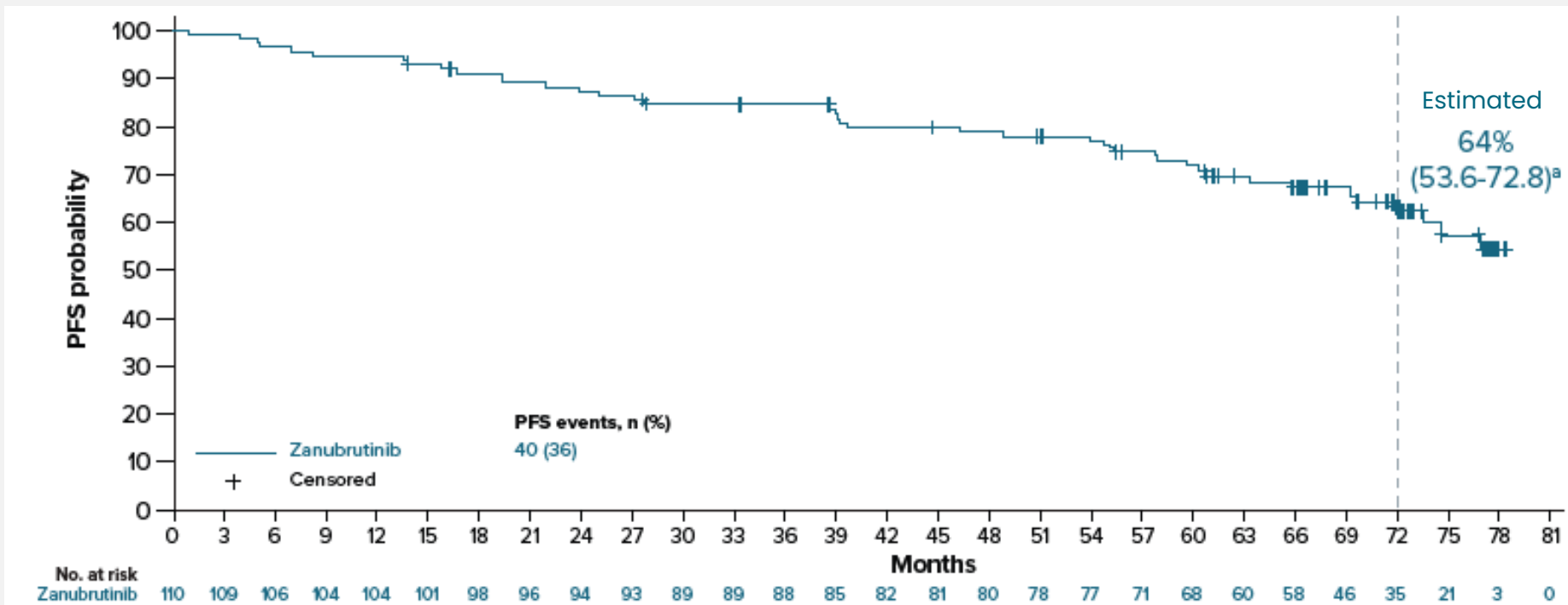


COVID-adjusted Overall Survival



The estimated OS at 72 months was 84% with zanubrutinib and 80% with BR; after adjusting for COVID-19, OS was 88% and 82%, respectively.

PFS-IRC in Cohort 2 (With del[17p])



Median follow-up:
76.7 months



Estimated 72-month PFS rates by IGHV mutation status:

- Mutated IGHV: 65%
- Unmutated IGHV: 64%

Estimated 72-month OS was 83%; 85% after COVID-19 adjustment.

Data cut-off: April 30, 2025.

^a95% CI values.

BR=bendamustine and rituximab, CI=confidence interval, HR=hazard ratio, PFS=progression-free survival.

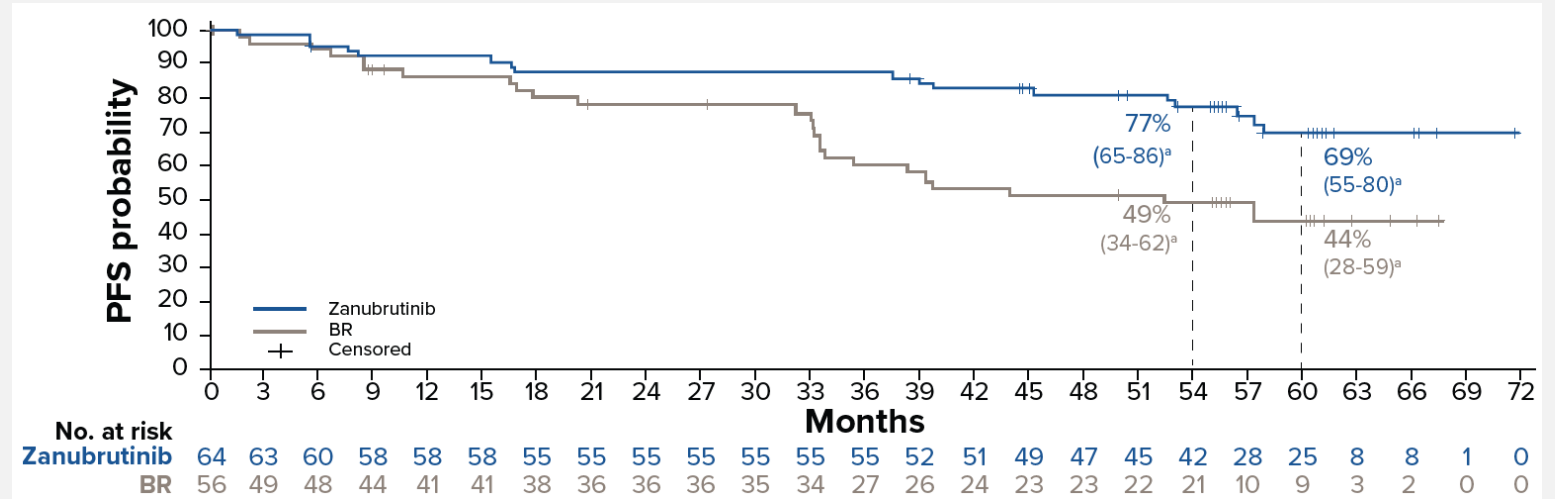
Tam S, et al. Poster Presentation at ASH 2025;Poster 2129.

PFS in Older Adult Patients: Cohort 1 and 2

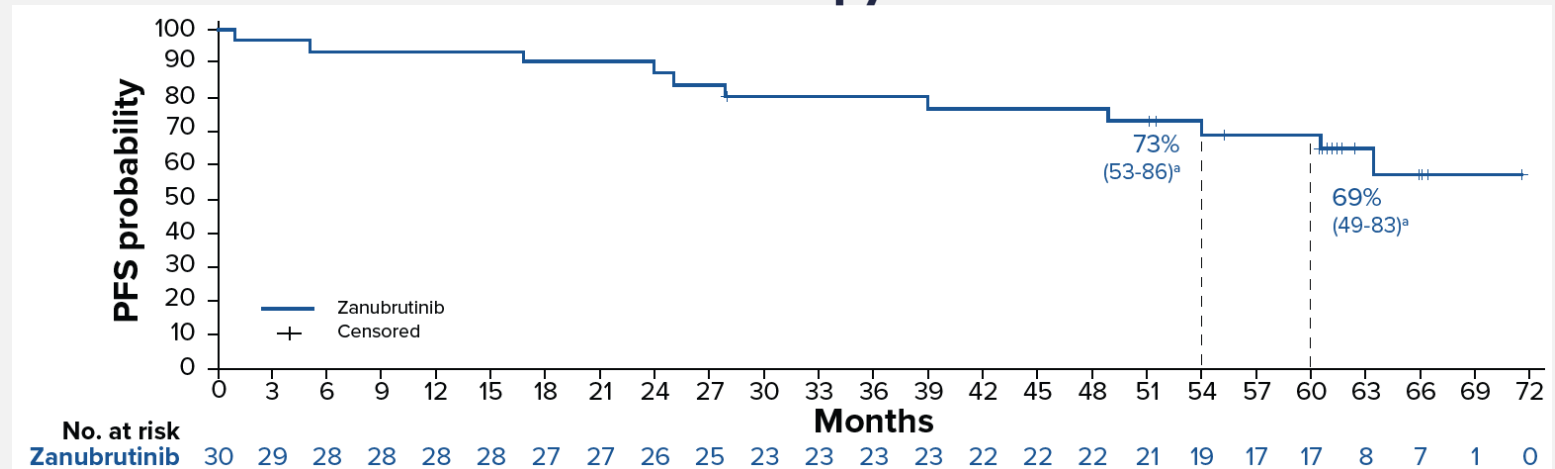


- In arms A and B, estimated PFS rates at 54 and 60 months were higher for zanubrutinib (77% and 69%) vs with BR (49% and 44%)
 - When adjusted for COVID-19, respective PFS rates were 79% and 71% with zanubrutinib and 49% and 44% with BR
- In arm C, patients with del(17p), the 54- and 60-month PFS rates with zanubrutinib were 73% and 69% respectively
 - When adjusted for COVID-19, the 54- and 60-month PFS rates were 73% and 69%

Arms A and B: Zanubrutinib and BR



Arm C: Zanubrutinib monotherapy



Data cut-off: April 30, 2024.

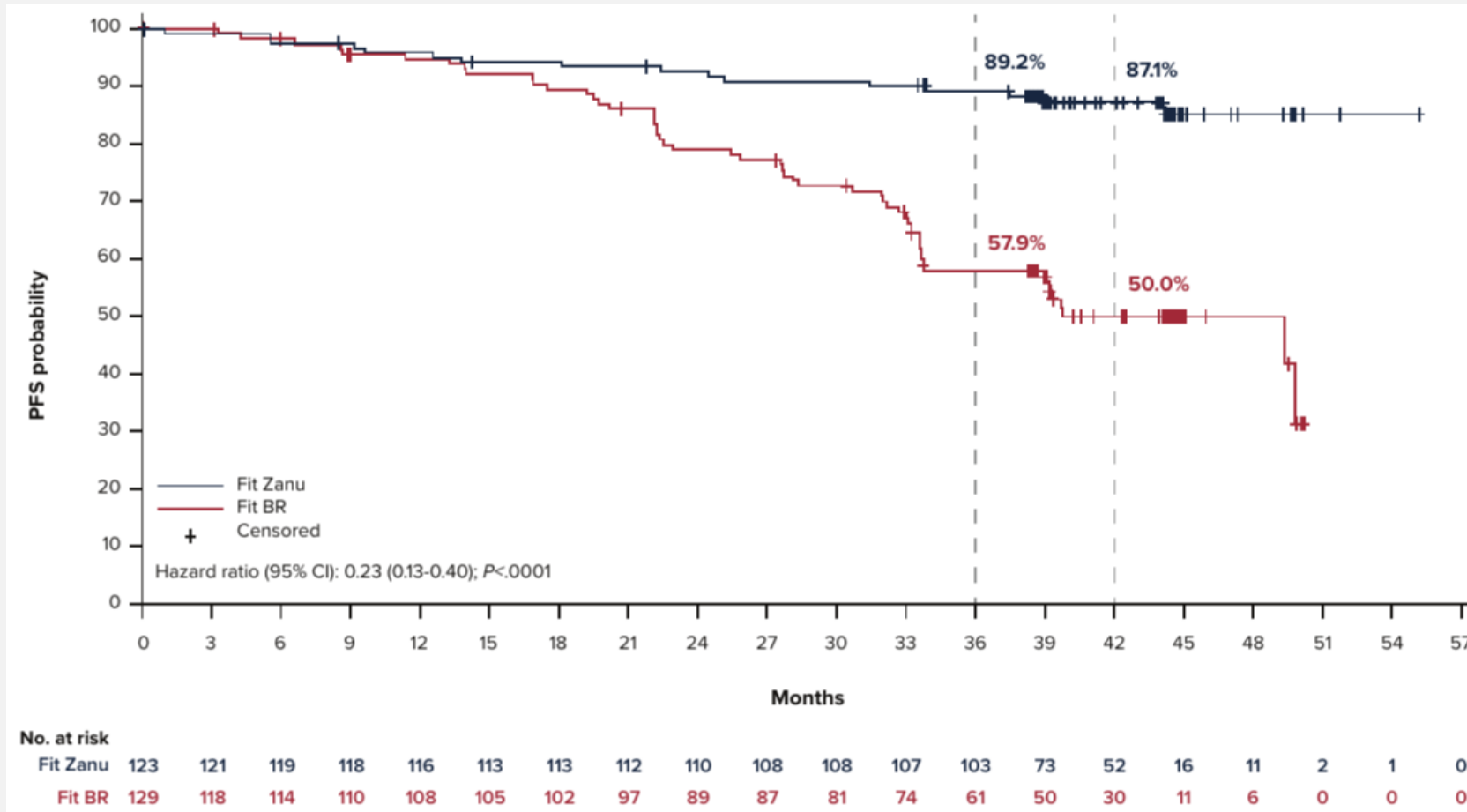
^a95% CI values.

BR=bendamustine + rituximab, CI=confidence interval, PFS=progression-free survival.

Tedeschi A, et al. Poster Presentation at iwCLL 2025;Poster 1421.

PFS in Fit Subgroup Treated With Zanubrutinib or BR: Cohort 1

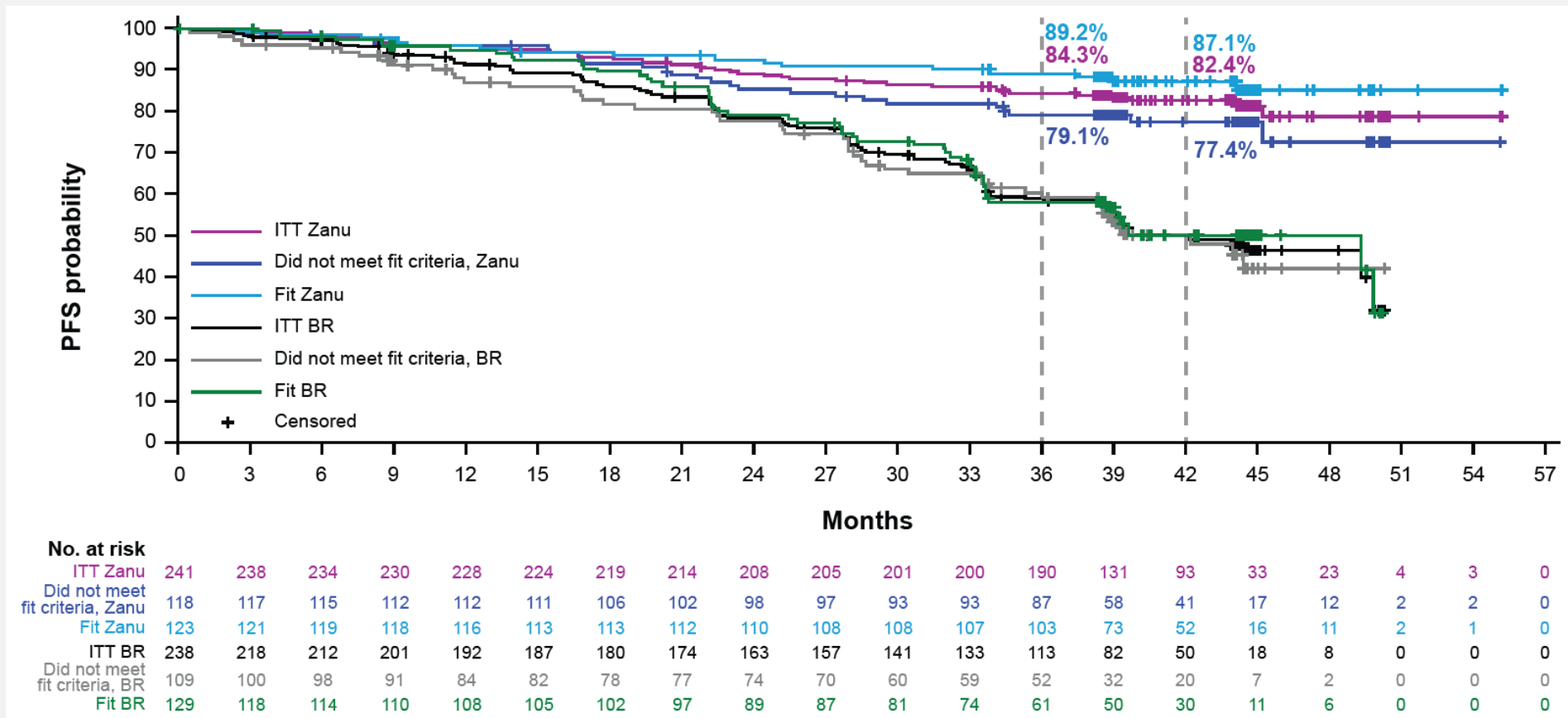
- With a median follow-up of 40.3 months, PFS estimates were higher with zanubrutinib vs BR at 36 months (89.2% vs 57.9%, respectively) and 42 months (87.1% vs 50.0%, respectively)



BR=bendamustine-rituximab, CI=confidence interval, PFS=progression-free survival.
 Shadman M, et al. Poster Presentation at iwCLL 2025;Poster 1426.

PFS in Fit Patients, ITT Group, and Patients Who Did Not Meet the Fit Criteria Who Were Treated With Zanubrutinib

- In patients treated with zanubrutinib, higher PFS estimates were observed in the fit subgroup compared with the intention-to-treat patients and those who did not meet the fit criteria at 36 months (89.2% and 84.3%, respectively) and 42 months (87.1% and 82.4%, respectively) and 48 months (87.1% and 77.4%, respectively)



BR=bendamustine-rituximab, ITT=intention to treat, PFS=progression-free survival, Zanu=zanubrutinib. Shadman M, et al. Poster Presentation at iwCLL 2025;Poster 1426.

Most Common Treatment-Emergent/Post-Treatment AESIs: Cohort 1 (Patients Without del(17p))

With this long-term follow-up (median 72.8 months), the safety profile of zanubrutinib remains consistent with prior reports; no new safety signals were observed.

n (%)	Arm A: Zanubrutinib (n=240) ^a		Arm B: BR (n=227) ^a	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Any AESI	224 (93)	142 (59)	210 (93)	163 (72)
Common (≥15% in either group)				
Anemia	24 (10)	2 (1)	48 (21)	6 (3)
Neutropenia	34 (14)	26 (11)	104 (46)	94 (41)
Contusion	57 (24)	0	9 (4)	0
Hypertension	49 (20)	31 (13)	29 (13)	15 (7)
COVID-19	100 (42)	23 (10)	21 (14)	4 (2)
Upper respiratory tract infection	51 (21)	2 (1)	34 (15)	2 (1)
Pneumonia	38 (16)	18 (8)	27 (12)	12 (5)
Urinary tract infection	38 (16)	4 (2)	23 (10)	6 (3)
Basal cell carcinoma	23 (10)	2 (1)	10 (4)	1 (0)

Data cut-off: April 30, 2025.

^aThe safety-evaluable population.

AESI=adverse event of special interest, BR=bendamustine and rituximab.

Tam S, et al. Poster Presentation at ASH 2025;Poster 2129.

Most Common Treatment-Emergent/Post-Treatment AEsIs: Cohort 2 (With del[17p])

With this long-term follow-up (median 72.8 months), the safety profile of zanubrutinib remains consistent with prior reports; no new safety signals were observed.

n (%)	Arm C: Zanubrutinib (n=111)	
	Any Grade	Grade ≥3
Any AEsI	103 (93)	65 (59)
Common (≥15% in either group)		
Anemia	11 (10)	0
Neutropenia	13 (12)	12 (11)
Contusion	24 (22)	0
Hypertension	21 (19)	11 (10)
COVID-19	43 (39)	8 (7)
Upper respiratory tract infection	32 (29)	0
Pneumonia	18 (16)	7 (6)
Urinary tract infection	18 (16)	3 (3)
Basal cell carcinoma	19 (17)	0