

SEQUOIA 5-year Follow-up in Arm C: Frontline Zanubrutinib Monotherapy in Patients with del(17p) and Treatment-naïve CLL/SLL

Constantine S. Tam,¹ Paolo Ghia,^{2,3} Mazyar Shadman,^{4,5} Talha Munir,⁶ Stephen S. Opat,⁷ Patricia A. Walker,⁸ Masa Lasica,⁹ Ian W. Flinn,¹⁰ Tian Tian,¹¹ Stephanie Agresti,¹¹ Jamie Hirata,¹¹ Jennifer R. Brown¹²

¹Alfred Hospital and Monash University, Melbourne, VIC, Australia; ²Università Vita-Salute San Raffaele, Milano, Italy; ³IRCCS Ospedale San Raffaele, Milano, Italy; ⁴Fred Hutchinson Cancer Center, Seattle, WA, USA; ⁵University of Washington, Seattle, WA, USA; ⁶Leeds Teaching Hospitals NHS Trust, Leeds, UK; ⁷Lymphoma Research Group, School of Clinical Sciences at Monash Health, Monash University, Clayton, VIC, Australia; ⁸Peninsula Health and Peninsula Private Hospital, Frankston, Melbourne, VIC, Australia; ⁹St Vincent's Hospital Melbourne, Fitzroy, VIC, Australia; ¹⁰Tennessee Oncology/OneOncology, Nashville, TN, USA; ¹¹BeOne Medicines Ltd, San Carlos, CA, USA; ¹²Dana-Farber Cancer Institute, Boston, MA, USA

Key Takeaways

- Arm C from the pivotal SEQUOIA study is the largest prospective cohort (N=110) of uniformly treated patients with **del(17p)** TN CLL/SLL
- With a median follow-up of 5 years, zanubrutinib demonstrates durable efficacy in patients with del(17p)
 - The estimated 60-month PFS with zanubrutinib was 72.2%, similar to that observed in patients without del(17p) treated with zanubrutinib, highlighting robust efficacy across all types of patients with TN CLL/SLL
- Zanubrutinib was well tolerated with no unexpected safety signals

CLL, chronic lymphocytic leukemia; SLL, small lymphocytic lymphoma; TN, treatment-naïve; PFS, progression-free survival.

Introduction

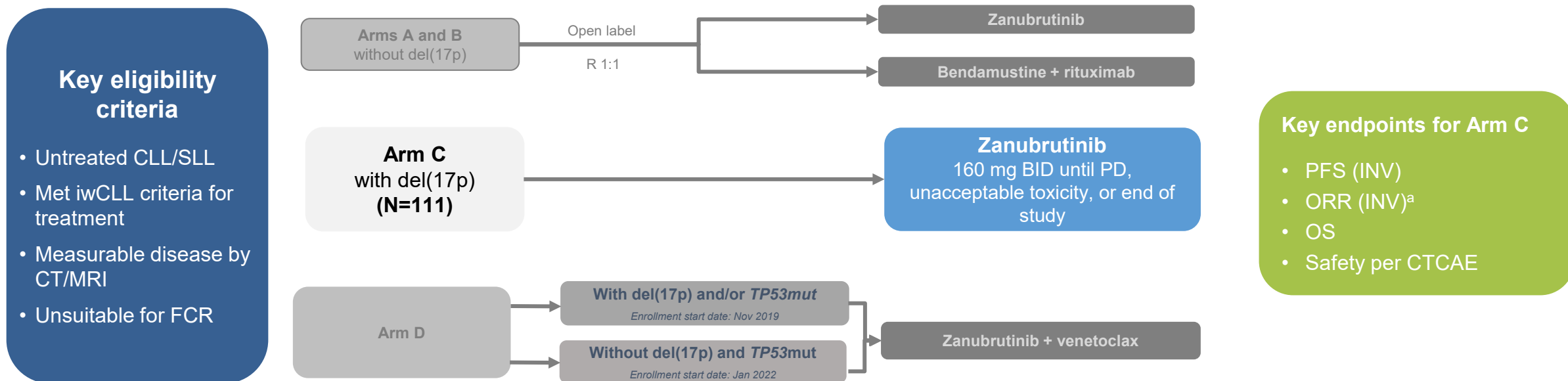
- Zanubrutinib is a highly potent and selective next-generation BTK inhibitor that was designed to provide complete and sustained target inhibition and is the only BTKi to demonstrate superiority over ibrutinib in a head-to-head phase 3 trial¹⁻⁴
- SEQUOIA (NCT03336333) is a registrational phase 3, open-label, randomized study that evaluated zanubrutinib in broad range of treatment naïve (TN) CLL patients, including those with high-risk features⁵⁻⁷
 - In Arms A and B, zanubrutinib monotherapy (Arm A) demonstrated superior PFS compared with bendamustine + rituximab (Arm B) in patients **without del(17p)** at 26.2-month follow-up and sustained PFS benefit at 5-year follow-up (Arm A: 75.8%)^{5,6}
 - In Arm C, patients **with del(17p)** treated with zanubrutinib monotherapy have achieved high overall response rates and PFS, despite being at high risk for disease progression and death⁷
- Here, we present updated results from SEQUOIA Arm C after approximately 5 years of follow-up in a **historically difficult to treat del(17p) patient population**

BTK, Bruton tyrosine kinase; CLL, chronic lymphocytic leukemia; PFS, progression-free survival; R/R, relapsed/refractory; SLL, small lymphocytic lymphoma; TN, treatment-naïve.

1. Guo Y, et al. *J Med Chem*. 2019;62(17):7923-7940; 2. Brukinsa (zanubrutinib). Prescribing information. BeiGene USA; 2024; 3. Brukinsa (zanubrutinib). Summary of product characteristics. BeiGene Ireland Limited; 2024;

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SEQUOIA Study Design



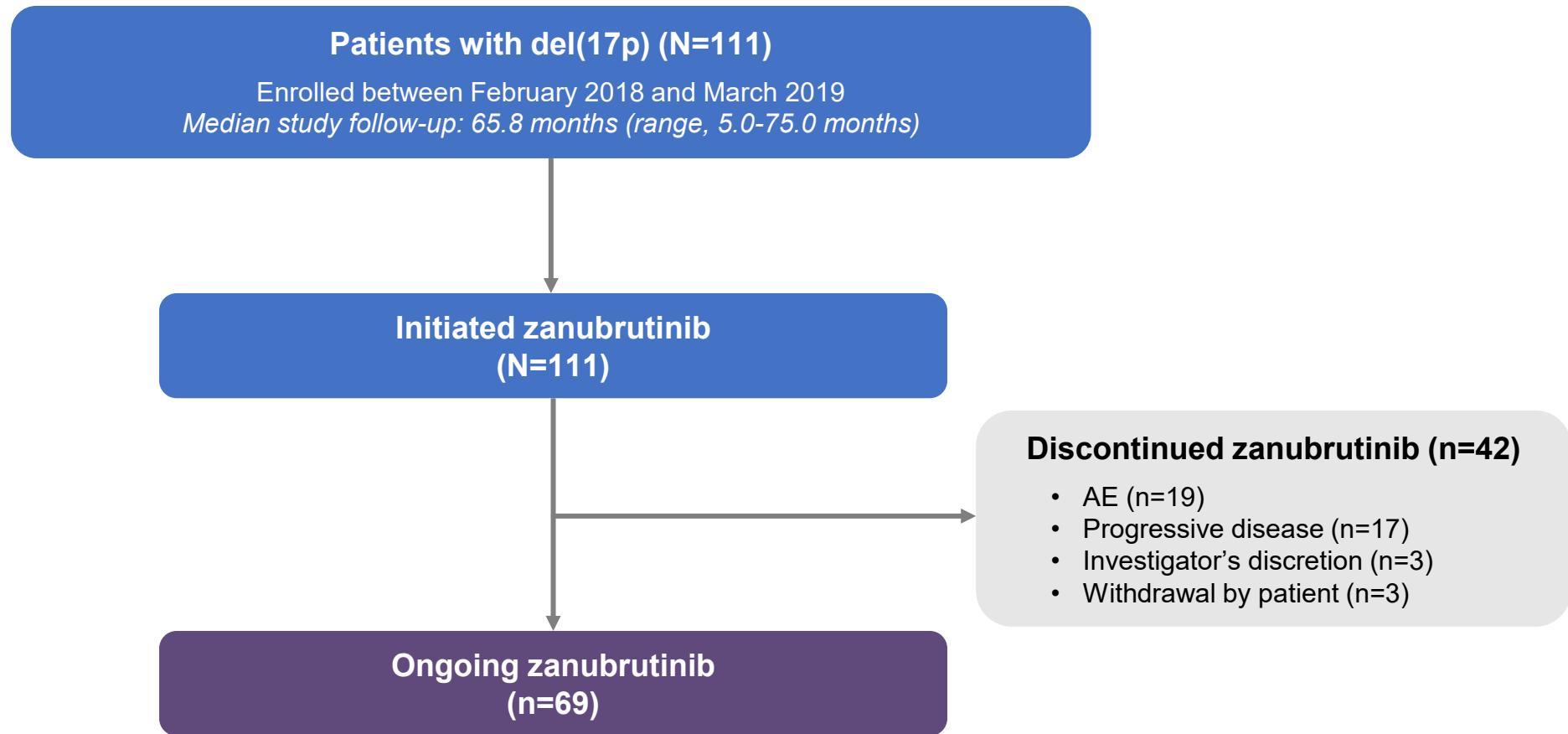
Assessments for Arm C:

- Sensitivity analyses were performed for PFS and OS with deaths due to COVID infection, censored at the time of death if no prior progression was observed
- Response assessments were performed every 12 weeks after the first dose of study drug for 96 weeks, then every 24 weeks until PD
- Adverse events were graded by CTCAE version 4.03 and documented from the time of first dose of study drug, until 30 days after the last dose of study drug, or until PD (whichever occurred later), or until the first day of a new CLL/SLL treatment

^aResponses were assessed by investigator per the 2008 iwCLL guidelines¹ with modification for treatment-related lymphocytosis² for patients with CLL and per Lugano criteria³ in patients with SLL. ORR was defined as achievement of PR-L or better. BID, twice daily; CT, computed tomography; Events; CLL, chronic lymphocytic leukemia; CTCAE, Common Terminology Criteria for Adverse Events; FCR, fludarabine, cyclophosphamide, and rituximab; INV, investigator-assessed; iwCLL, International Workshop on Chronic Lymphocytic Leukemia; MRD, minimal residual disease; MRI, magnetic resonance imaging; Mut, mutation; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR-L, partial response with lymphocytosis; R, randomized; SLL, small lymphocytic lymphoma.

1. Hallek M, et al. *Blood*. 2008;111(12):5446–56. 2. Cheson BD, et al. *J Clin Oncol*. 2012;30(23):2820–2822. 3. Cheson BD, et al. *J Clin Oncol*. 2014;32(27):3059–3967.

Patient Disposition



Data cutoff: April 30, 2024.
AE, adverse event.

Baseline Demographics and Clinical Characteristics

Baseline characteristics	All patients (N=111)
Age, median (range), years	71 (42-87)
≥65 years, n (%)	95 (85.6)
Male, n (%)	79 (71.2)
ECOG PS 0/1, n (%)	97 (87.3)
CLL, n (%)	100 (90.1)
SLL, n (%)	11 (9.9)
Binet stage C, n (%)^a	37 (37.0)
Bulky disease, n (%)	
LDi ≥5 cm	44 (39.6)
LDi ≥10 cm	12 (10.8)
Median time from initial diagnosis, months	21.39
TP53 mutated, n (%)	47 (42.3)
del(17p), n (%)	110 (99.1)
del(17p) and TP53 mutated, n (%)	47 (42.3)
IGHV mutated, n (%)	36 (32.4)
IGHV unmutated, n (%)	67 (60.4)
Complex karyotype, n (%)	
≥3 abnormalities	31 (27.9)
≥5 abnormalities	21 (18.9)

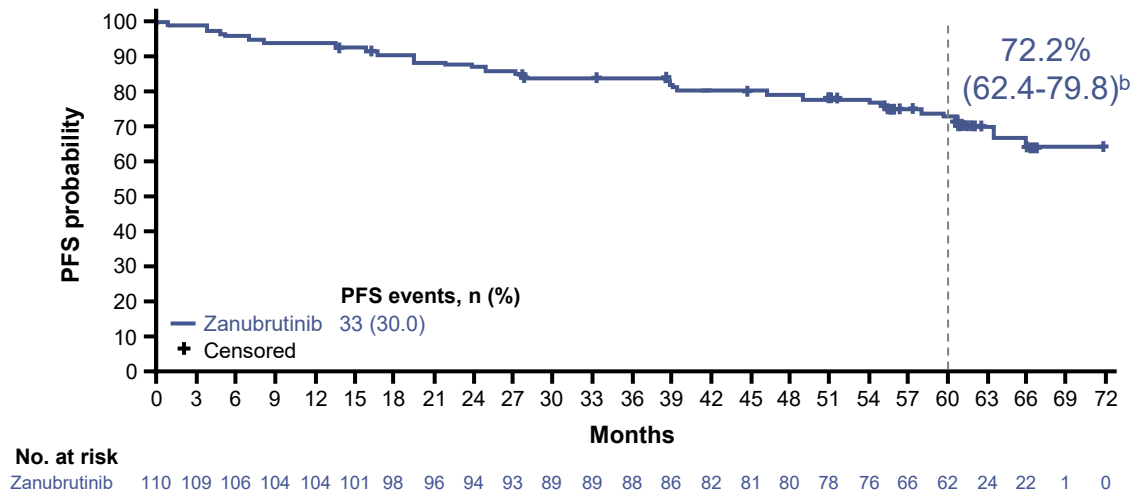
^aBinet stage was assessed at study entry for patients with CLL.

CLL, chronic lymphocytic leukemia; ECOG PS, Eastern Cooperative Oncology Group performance status; IGHV, immunoglobulin heavy-chain variable region; LDi, longest diameter; SLL, small lymphocytic lymphoma.

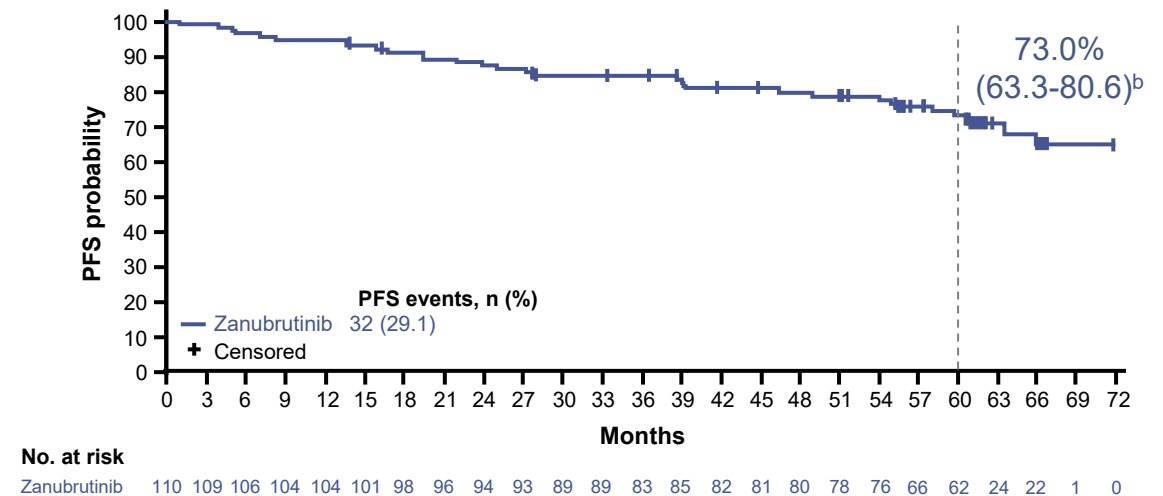
Progression-free Survival

- Median PFS was not reached with zanubrutinib

PFS^a



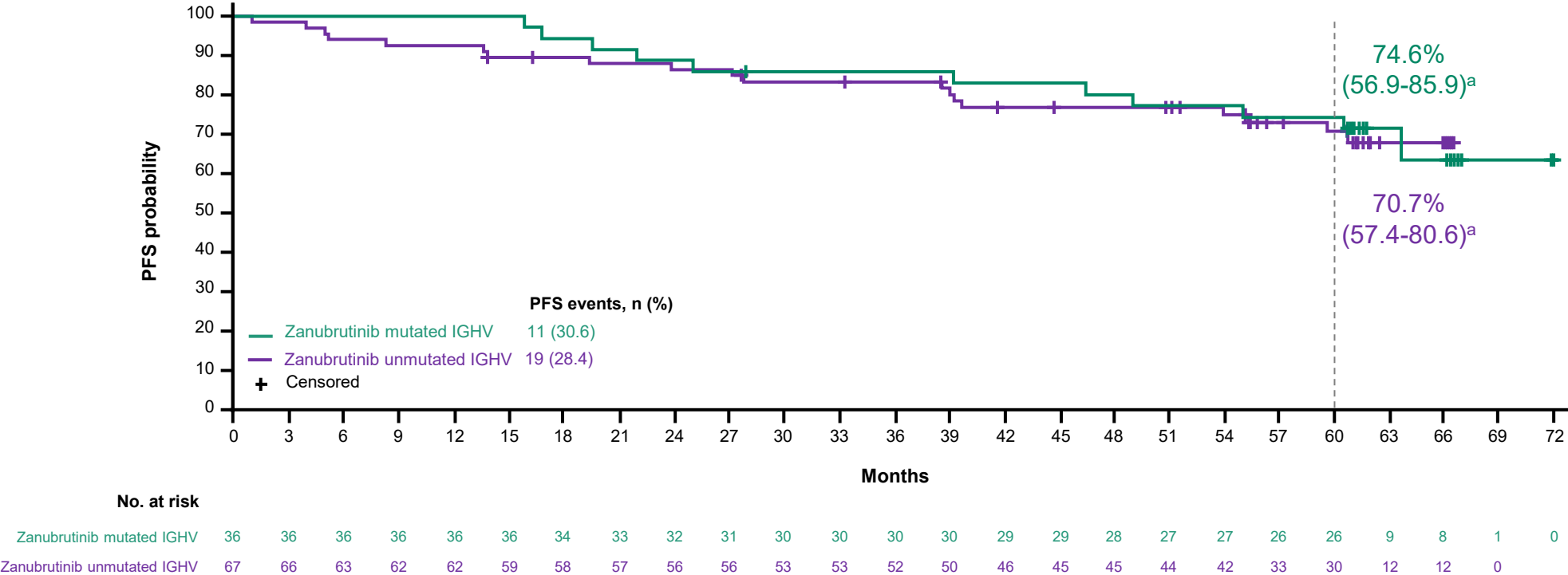
PFS with COVID-19 adjustment^a



^aData are presented in patients with del(17p), confirmed by central laboratory (N=110). ^b95% CI values.
PFS, progression-free survival.

Progression-free Survival by IGHV Mutation Status

PFS with mutated and unmutated IGHV

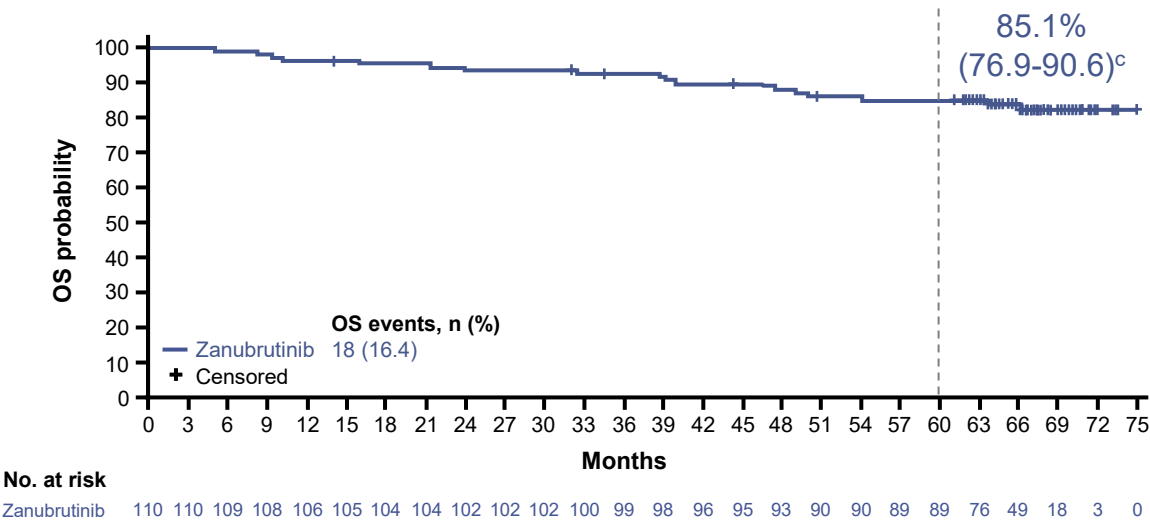


^a95% CI values.
IGHV, immunoglobulin heavy-chain variable region; PFS, progression-free survival

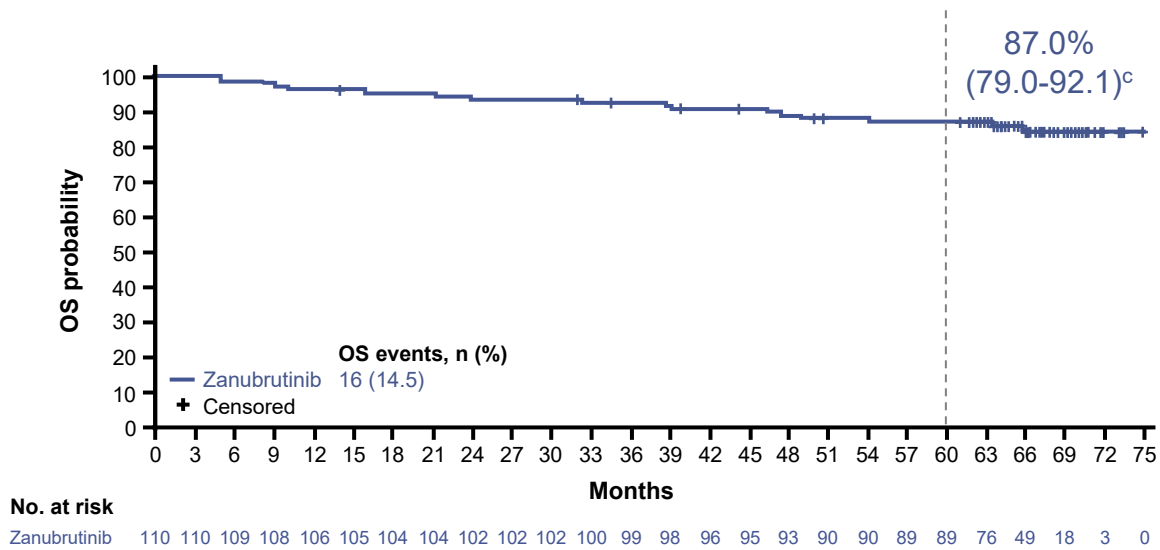
Overall Survival

- Median OS was not reached with zanubrutinib and 18 deaths occurred during the study^a

OS^b



OS with COVID-19 adjustment^b



^aDue to adverse event (n=6), progressive disease (n=5), other (n=3), or unknown (n=4). Reasons for death due to 'Other' included events of infections occurring outside of the adverse event report period. ^bData is presented in patients with del(17p), confirmed by central laboratory (N=110). ^c95% CI values. OS, overall survival.

ORR and CR+CRi Rates

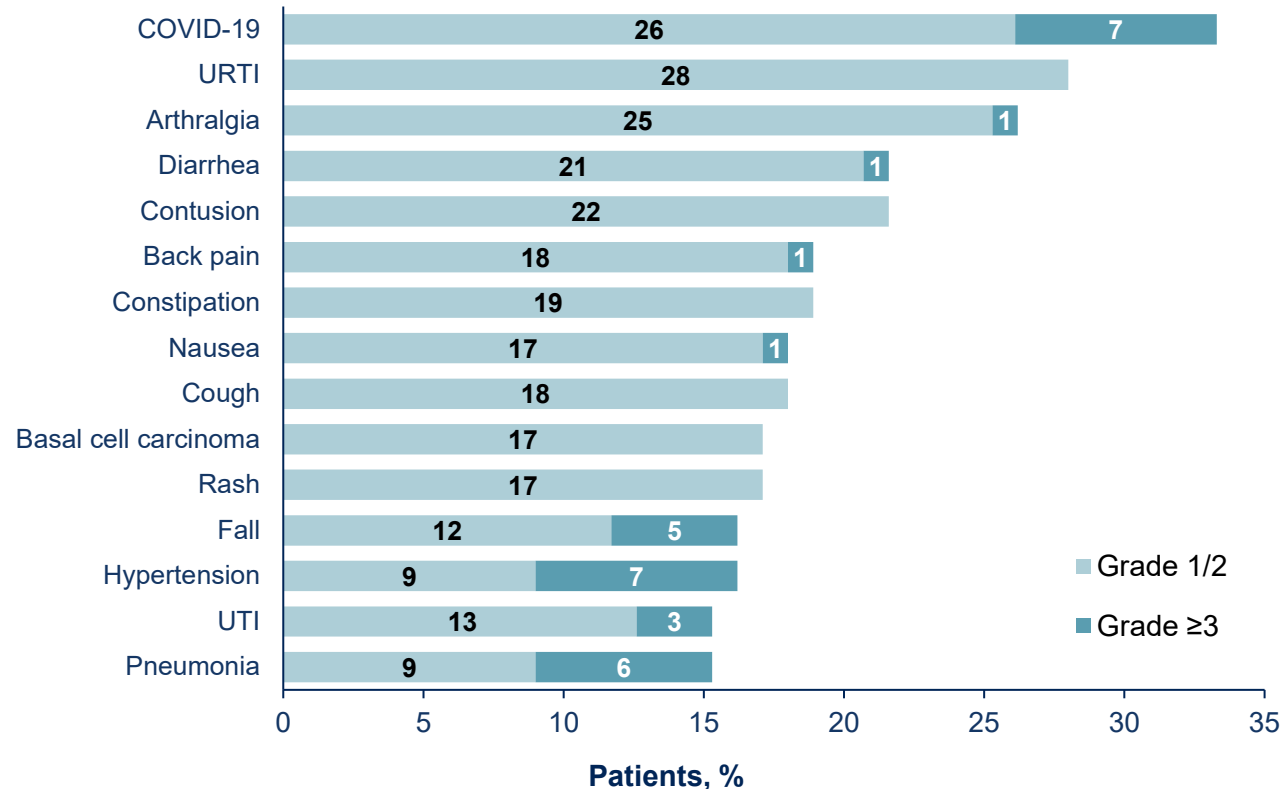
	Zanubrutinib (N=110) ^a
ORR, n (%)	107 (97.3)
Best overall response, n (%)	
CR/CRi rate	20 (18.2)
nPR	3 (2.7)
PR	84 (76.4)
PR-L	0
SD	2 (1.8)
PD	1 (0.9)

^aPatients with del(17p), confirmed by central laboratory.

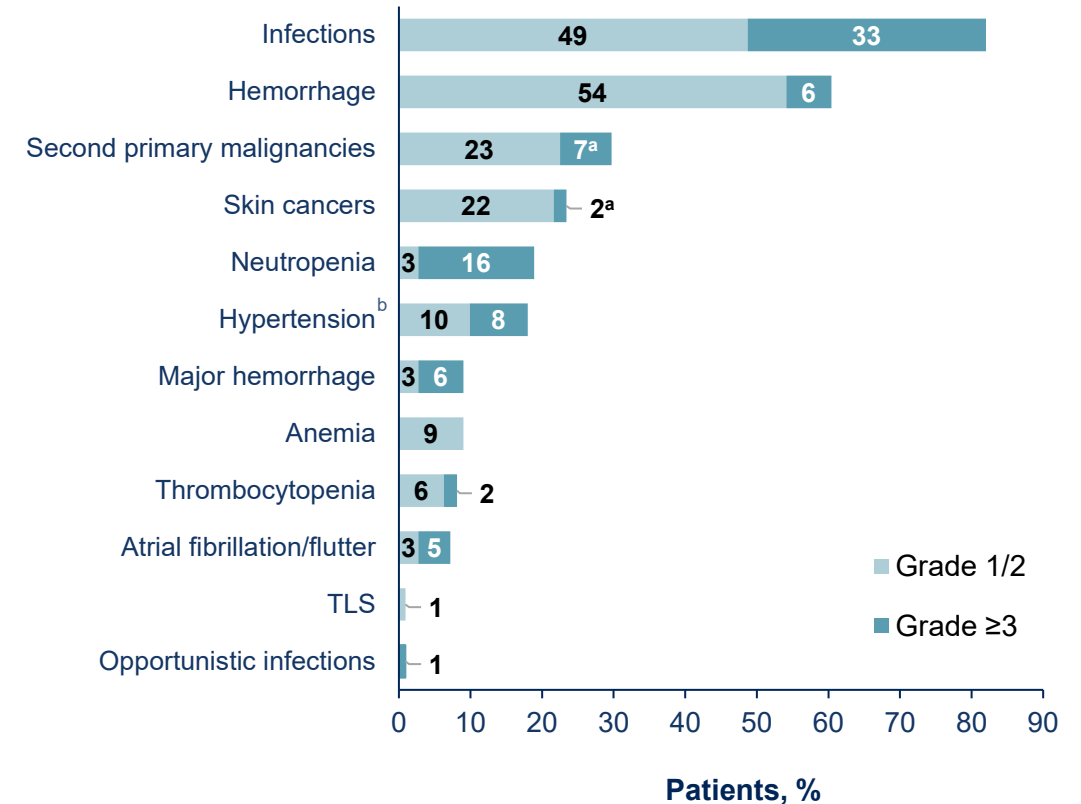
CR, complete response; CRi, complete response with incomplete hematopoietic recovery; ORR, overall response rate; nPR, nodular partial response; PD, progressive disease; PR, partial response; PR-L, partial response with lymphocytosis; SD, stable disease.

No New Safety Signals were Identified with Zanubrutinib

TEAEs by preferred term in ≥15% of patients



TEAEs of special interest



- AEs led to death in 6 patients (5.4%)

^aIncludes two patients with malignant melanoma. ^bIncludes hypertension, increased blood pressure, hypertensive crisis and hypertensive heart disease.
 AE, adverse event; TEAE, treatment-emergent adverse event; TLS, tumor lysis syndrome; URTI, upper respiratory tract infection; UTI, urinary tract infection.

Conclusions

- SEQUOIA Arm C reports on the largest prospective cohort of uniformly treated patients with del(17p) TN CLL/SLL
- With a median follow-up of 5-years, zanubrutinib demonstrates durable efficacy in patients with del(17p)
 - The estimated 60-month PFS with zanubrutinib was 72.2%, similar to that observed in patients without del(17p)¹, highlighting that zanubrutinib overcomes the negative prognostic impact of del(17p)
- The benefit of zanubrutinib in patients with del(17p) was also demonstrated in the phase 3 ALPINE study, which demonstrated PFS superiority of zanubrutinib over ibrutinib²
- Zanubrutinib remains a valuable frontline treatment option for patients with CLL/SLL with or without del(17p)



CLL, chronic lymphocytic leukemia; PFS, progression-free survival; SLL, small lymphocytic lymphoma; TN, treatment-naïve.

1. Shadman M, et al. *J Clin Oncol*. 2025;43(7):780-787. 2. Brown J. et al. *Blood*. 2024;144(26):2706-2717. 3. szeke. Sequoia Tree. Retrieved from <https://www.flickr.com/photos/43355249@N00/41563931240> on May 28, 2025. Creative Commons Attribution 2.0 International License.

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Corresponding Author: *Constantine.tam@alfred.org.au*