SEQUOIA: Results of a Phase 3 Randomized Study of Zanubrutinib versus Bendamustine + Rituximab in Patients with Treatment-Naive Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma

Poster number: CLL-137

Brad S. Kahl[1], Krzysztof Giannopoulos[2,3], Wojciech Jurczak[4], Martin Šimkovič[5,6], Mazyar Shadman[7,8], Anders Österborg[9,10], Luca Laurenti[11], Patricia Walker[12], Stephen Opat[13,14], Henry Chan[15], Hanna Ciepluch[16], Richard Greil[17-19], Monica Tani[20], Marek Trněný[21], Danielle M. Brander[22], Ian W. Flinn[23], Sebastian Grosicki[24], Emma Verner[25,26], Jennifer R. Brown[27], **Paolo Ghia[28]**, Jianyong Li[29], Tian Tian[30], Lei Zhou[30], Carol Marimpietri[30], Jason C. Paik[30], Aileen Cohen[30], Tadeusz Robak[31], Peter Hillmen[32], Constantine S. Tam[14,33]

[1]Washington University School of Medicine, St Louis, MO, USA; [2]Experimental Hematooncology Department, Medical University of Lublin, Lublin, Poland; [3]Hematology Department, St. John's Cancer Centre, Lublin, Poland; [4]Maria Sklodowska-Curie National Research Institute of Oncology, Krakow, Poland; [5]Fourth Department of Internal Medicine - Haematology, University Hospital, Hradec Kralove, Czech Republic; [6]Faculty of Medicine, Charles University, Prague, Czech Republic; [7]Fred Hutchinson Cancer Research Center, Seattle, WA, USA; [8]Department of Medicine, University of Washington, Seattle, WA, USA; [9]Department of Oncology-Pathology, Karolinska Institutet, Stockholm, Sweden; [10]Department of Hematology, Karolinska University Hospital, Stockholm, Sweden; [11]Fondazione Policlinico Universitario A Gemelli UCSC, Rome, Italy; [12]Peninsula Private Hospital, Frankston, VIC, Australia; [13]Monash Health, Clayton, VIC, Australia; [14]Monash University, Clayton, VIC, Australia; [15]North Shore Hospital, Auckland, New Zealand; [16]Copernicus Regional Oncology Center, Gdansk, Poland; [17]Third Medical Department with Hematology, Medical Oncology, Rheumatology and Infectiology, Paracelsus Medical University, Salzburg, Austria; [18]Salzburg Cancer Research Institute (SCRI) Center for Clinical Cancer and Immunology Trials (CCCIT), Salzburg, Austria; [19]Cancer Cluster Salzburg (CCS), Salzburg, Austria; [20]Hematology Unit, Santa Maria delle Croci Hospital, Ravenna, Italy; [21]First Department of Medicine, First Faculty of Medicine, Charles University, General Hospital, Prague, Czech Republic; [22]Hematologic Malignancies and Cellular Therapy, Duke University School of Medicine, Durham, NC, USA; [23]Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN, USA; [24]Department of Hematology and Cancer Prevention, Health Sciences Faculty, Medical University of Silesia, Katowice, Poland; [25]Concord Repatriation General Hospital, Concord, NSW, Australia; [26]University of Sydney, Sydney, NSW, Australia; [27]Dana-Farber Cancer Institute, Boston, MA, USA; [28]Università Vita-Salute San Raffaele and IRCCS Ospedale San Raffaele, Milano, Italy; [29]Department of Hematology, The First Affiliated Hospital of Nanjing Medical University, Jiansu Province Hospital, Nanjing, China; [30]BeiGene (Beijing) Co., Ltd., Beijing, China, and BeiGene USA, Inc., San Mateo, CA, USA; [31]Medical University of Lodz, Lodz, Poland; [32]St James's University Hospital, Leeds, UK; [33]The Alfred Hospital, Melbourne, VIC, Australia

INTRODUCTION

- Chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL) are progressive B-cell malignancies that are characterized by progressive accumulation of leukemic cells in the peripheral blood, bone marrow, and lymphoid tissue[1]
- In recent years, treatment of CLL/SLL has been transformed with the advent of effective inhibitors of B-cell receptor signaling, such as the BTK inhibitor, ibrutinib[2]
  - Ibrutinib has well-described off-target effects that may contribute to its toxicity profile, notably an increased risk for cardiovascular disease, including atrial fibrillation, hypertension, and hemorrhage[3]
  - Cardiovascular adverse events (AEs), diarrhea, and rash observed in patients treated with ibrutinib have been associated with off-target inhibition of kinases such as EGFR, HER, and TEC[3]
- Zanubrutinib is an irreversible, potent, next-generation BTK inhibitor designed to maximize BTK occupancy and minimize off-target inhibition of TEC- and EGFR-family kinases[4,5]
  - Efficacy and safety of zanubrutinib have been recently demonstrated in 2 large, randomized studies in Waldenström macroglobulinemia and relapsed/refractory CLL/SLL, with lower rates of atrial fibrillation when compared to ibrutinib[6,7]
  - Preliminary data showing high response rates with zanubrutinib in untreated patients with the high-risk genomic abnormality, del(17p), enrolled in SEQUOIA cohort 2, have been recently published[8,9]
- Here, we present results from the first cohort of SEQUOIA, a phase 3 trial of zanubrutinib versus bendamustine + rituximab (B+R) as first-line treatment for CLL/SLL

METHODS

- SEQUOIA (BGB-3111-304; NCT03336333) is an international, randomized, open-label, phase 3 study of zanubrutinib compared with B+R treatment for patients with previously untreated CLL/SLL
- Eligible patients had received no prior systemic treatment for CLL/SLL, met International Workshop on CLL (iwCLL) criteria for treatment, and were unsuitable for treatment with fludarabine, cyclophosphamide, and rituximab (ie, ≥65 years of age, Cumulative Illness Rating Scale score >6, creatinine clearance < 70 mL/min, and/or history of previous severe infection or multiple infections within the past 2 years)
- Cohort assignment was based on centrally-verified del(17p) status
- In Cohort 1, study patients without del(17p) were randomized to receive either zanubrutinib 160 mg twice daily until progressive disease or unacceptable toxicity or bendamustine 90 mg/m² (days 1 and 2) + rituximab (375 mg/m² for cycle 1, then 500 mg/m² for cycles 2-6) for 6 cycles of 28-days each
  - Randomization stratification factors included age (<65 y vs ≥65 y), Binet Stage (C vs A/B), immunoglobulin heavy chain gene (*IGHV*) mutational status (mutated vs unmutated), and geographic region (North America vs Europe vs Asia-Pacific)
- Patients with del(17p) were assigned to Cohort 2 and received zanubrutinib monotherapy
- The primary endpoint was progression-free survival (PFS) in Cohort 1 as assessed by independent review committee (IRC) per modified iwCLL criteria for CLL and Lugano criteria for SLL
  - The comparison of PFS between the 2 arms in Cohort 1 was based on a log-rank test stratified by the randomization stratification factors of age, Binet stage, and *IGHV* mutational status; hazard ratios (HRs) and 2-sided 95% confidence intervals (CIs) were estimated from a stratified Cox regression model
- Key secondary endpoints included PFS by investigator assessment, overall response rate (ORR) by investigator and IRC assessments, overall survival (OS), and safety
- Adverse events (AEs) were assessed and graded per the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) v4.03 and the Grading Scale for Hematologic Toxicities in CLL Studies

RESULTS

- From October 31, 2017 to July 22, 2019, 479 patients without del(17p) were randomized to receive zanubrutinib (n=241) and B+R (n=238)
- At the data cutoff, 206/240 patients from Cohort 1 were continuing to receive zanubrutinib; in Cohort 2, 188/227 patients completed the B+R regimen and 15 patients crossed over to receive zanubrutinib after centrally-confirmed disease progression
- Treatment groups were well balanced for demographic and disease characteristics; in both arms, the median patient age was 70 years and most patients were men (**Table 1**)
- In the zanubrutinib arm, 53.4% had unmutated *IGHV* and 17.8% had del(11q) compared with 52.4% and 19.3%, respectively, in the B+R arm

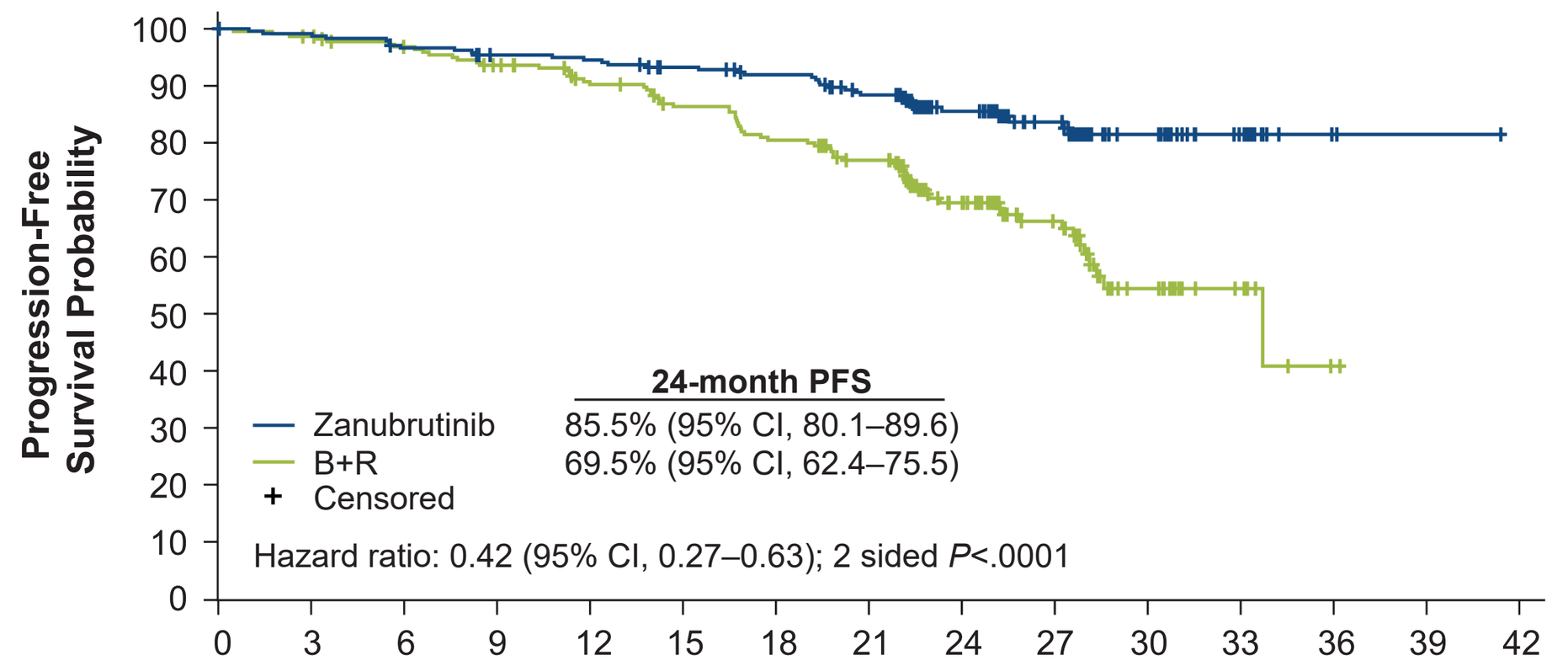
Table 1. Baseline Patient and Disease Characteristics

Characteristics	Zanubrutinib (n=241)	B+R (n=238)
Age, median (IQR), years	70 (66–75)	70 (66–74)
Age ≥65, n (%)	196 (81.3)	192 (80.7)
Male, n (%)	154 (63.9)	144 (60.5)
ECOG PS 2, n (%)	15 (6.2)	20 (8.4)
Geographic region, n (%)		
North America	34 (14.1)	28 (11.8)
Europe	174 (72.2)	172 (72.3)
Asia/Pacific	33 (13.7)	38 (16.0)
Binet stage C,[a] n (%)	70 (29.0)	70 (29.4)
Bulky disease ≥5 cm, n (%)	69 (28.6)	73 (30.7)
Cytopenia at baseline,[b] n (%)	102 (42.3)	109 (45.8)
Unmutated *IGHV* gene, n/N (%)	125/234 (53.4)	121/231 (52.4)
del(11q), n (%)	43 (17.8)	46 (19.3)
***TP53* mutation, n/N (%)**	15/232 (6.5)	13/223 (5.8)

[a]Patients with SLL had Binet stage calculated as if they had CLL. [b]Defined as having anemia (hemoglobin ≤110 g/L) or thrombocytopenia (platelets ≤100×10⁹/L) or neutropenia (absolute neutrophil count ≤1.5×10⁹/L).
B+R, bendamustine + rituximab; CLL, chronic lymphocytic leukemia; del(11q), chromosome 11q deletion; ECOG PS, Eastern Cooperative Oncology Group performance status; IQR, interquartile range; *IGHV*, gene encoding the immunoglobulin heavy chain variable region; SLL, small lymphocytic lymphoma; *TP53*, gene encoding tumor protein p53.

- At median follow-up (26.2 months), PFS was significantly prolonged with zanubrutinib treatment vs B+R by IRC assessment (HR, 0.42; 95% CI, 0.28–0.63; 2-sided *P*<.0001; **Figure 1A**)
  - Similar PFS was observed by investigator assessment (HR, 0.42; 95% CI, 0.27–0.66; 2-sided *P*=.0001)
  - Estimated 24-month PFS by IRC assessment for zanubrutinib vs B+R was 85.5% vs 69.5%, respectively
- Zanubrutinib treatment benefit was observed across patient subgroups defined by age, Binet stage, bulky disease, and del(11q) status (**Figure 1B**) and for patients with unmutated *IGHV* (HR, 0.24; 2-sided *P*<.0001), but not for mutated *IGHV* (HR, 0.67; 2-sided *P*=.1858; **Figure 1C**)

Figure 1A. PFS per IRC Assessment

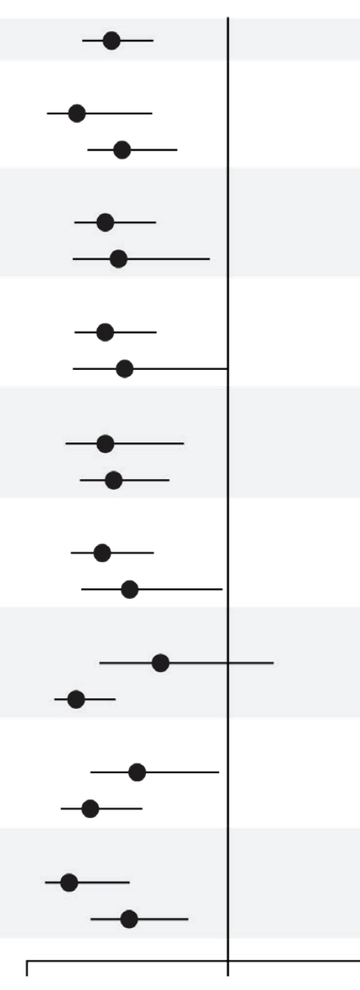


No. of patients at risk															
Months	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42
Zanubrutinib	241	237	230	224	222	214	208	195	123	79	31	17	2	1	0
B+R	238	218	210	200	187	176	164	150	89	54	20	8	1	0	

B+R, bendamustine + rituximab; IRC, independent review committee; PFS, progression-free survival.

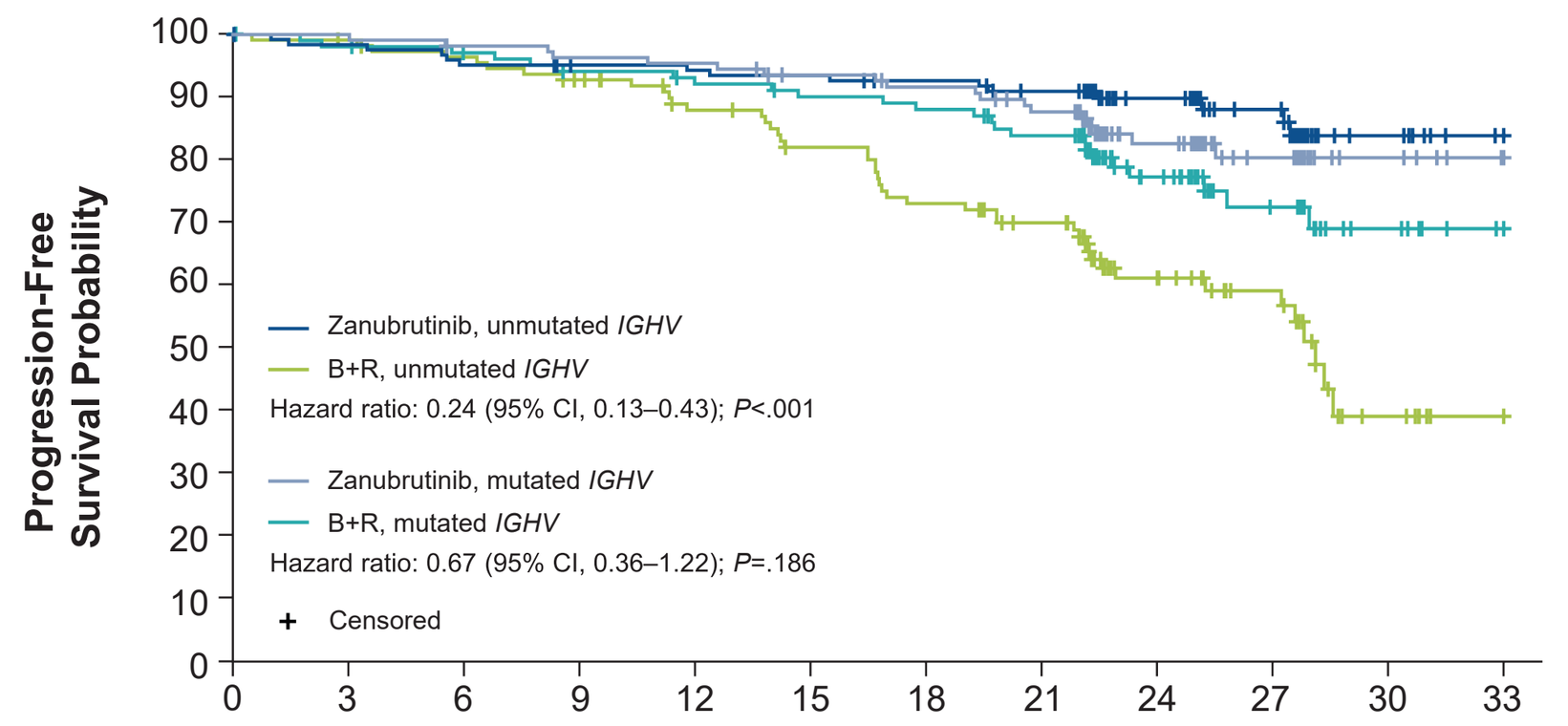
Figure 1B. PFS by Patient Subgroup

Subgroup	Event/Patient Zanubrutinib	Event/Patient B+R	Hazard Ratio (95% CI), %[a]
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 vs ≥5 cm)			
<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[b]			
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)



[a]Hazard ratios were calculated using a stratified Cox regression model. [b]Defined as having anemia (hemoglobin ≤110 g/L) or thrombocytopenia (platelets ≤100×10⁹/L) or neutropenia (absolute neutrophil count ≤1.5×10⁹/L).
B+R, bendamustine + rituximab; ECOG PS, Eastern Cooperative Oncology Group performance status; *IGHV*, gene encoding the immunoglobulin heavy chain variable region; IRC, independent review committee; LDi, longest diameter; PFS, progression-free survival.

Figure 1C. PFS by *IGHV* Status

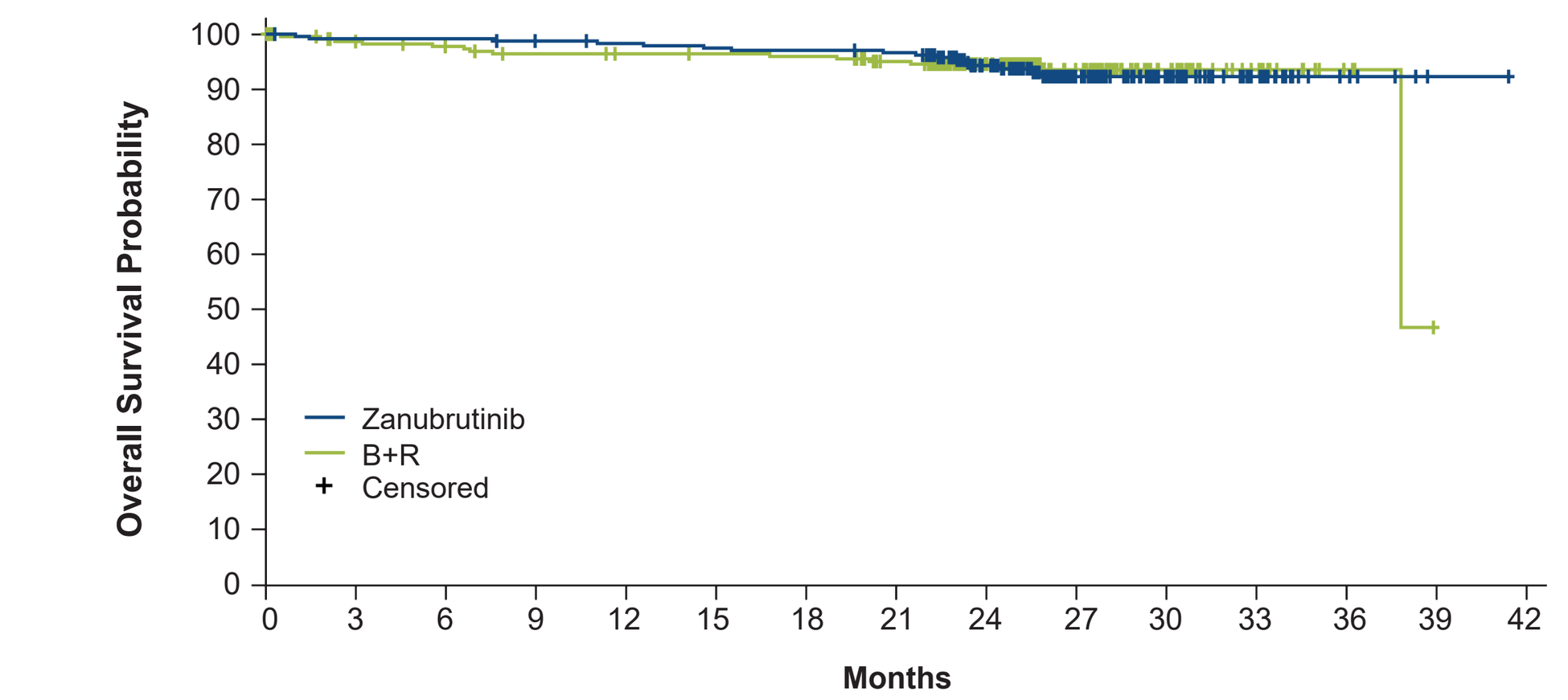


No. of patients at risk												
Months	0	3	6	9	12	15	18	21	24	27	30	33
Zanubrutinib - Unmutated	125	121	117	114	113	112	109	104	68	44	14	6
B+R - Unmutated	121	110	106	100	90	82	73	65	39	25	6	1
Zanubrutinib - Mutated	109	109	106	104	103	97	94	88	53	33	15	10
B+R - Mutated	110	101	98	94	91	88	86	80	47	27	14	7

B+R, bendamustine + rituximab; *IGHV*, gene encoding the immunoglobulin heavy chain variable region; IRC, independent review committee; PFS, progression-free survival.

- For zanubrutinib vs B+R:
  - ORR by IRC was 94.6% vs 85.3% and the complete response rate was 6.6% vs 15.1%
  - ORR by investigator assessment was 97.5% vs 88.7%
  - Estimated 24-month OS was 94.3% vs 94.6% (**Figure 2**)

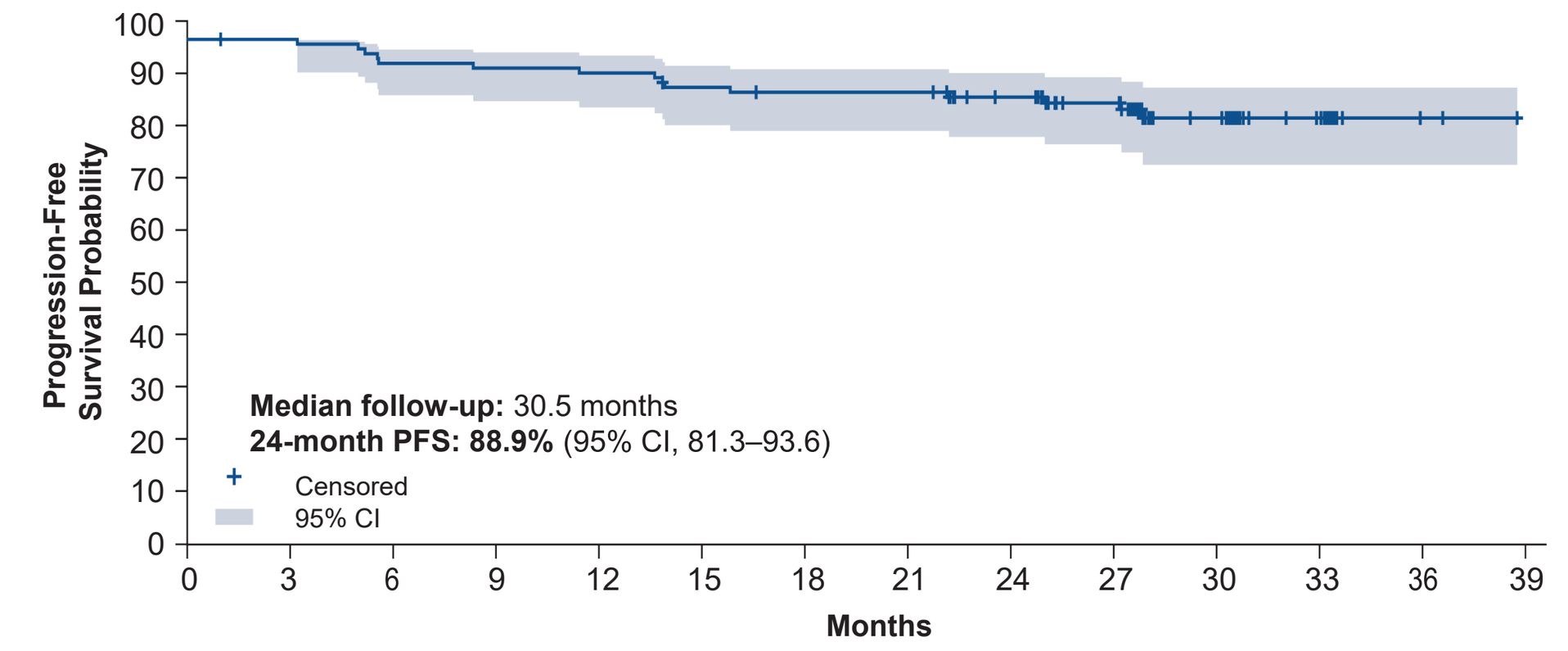
Figure 2. Overall Survival



No. of patients at risk															
Months	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42
Zanubrutinib	241	238	238	235	233	231	230	228	179	97	48	22	6	1	0
B+R	238	222	217	212	210	209	208	198	141	84	41	16	4	0	

Median follow-up: 26.2 months. B+R, bendamustine + rituximab.

Figure 3. Cohort 2: PFS in Patients with del(17p)



No. of patients at risk														
Months	0	3	6	9	12	15	18	21	24	27	30	33	36	39
Zanubrutinib	110	109	104	103	102	98	96	96	86	74	37	19	2	0

del(17p), chromosome 17p deletion; PFS, progression-free survival.

- The proportion of patients that experienced any AE was similar in the zanubrutinib (93.3%) and B+R (96.0%) arms (**Table 2**); Grade 3 AEs occurred in a higher percentage of patients in the B+R arm (79.7%) vs the zanubrutinib arm (52.5%)
- For the zanubrutinib vs B+R arm, treatment discontinuation due to AEs occurred in 8.3% vs 13.7% of patients, respectively; AEs leading to death occurred in 4.6% vs 4.8%, respectively
- AEs of special interest were observed at the following frequencies in the zanubrutinib vs B+R arm, respectively (**Table 4**):
  - Atrial fibrillation (any grade): 3.3% vs 2.6%
  - Bleeding (any grade) 45.0% vs 11.0%; bleeding (Grade ≥3): 3.8% vs 1.8%
  - Hypertension (any grade): 14.2% vs 10.6%
  - Infections (any grade): 62.1% vs 55.9%; infections (Grade ≥3): 16.3% vs 18.9%
  - Neutropenia (any grade): 15.8% vs 56.8%; neutropenia (Grade ≥3): 11.7% vs 51.1%

Table 2. Adverse Event Summary

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

[a]Safety was assessed in patients who received ≥1 dose of treatment; 1 patient in the zanubrutinib arm and 11 patients in the B+R arm did not receive treatment.
AE, adverse event; B+R, bendamustine + rituximab.

Table 3. Common Adverse Events (≥12% of Patients in Any Arm)

	Zanubrutinib (n=240[a])		B+R (n=227[a])	
AE, n (%)	**Any Grade**	**Grade ≥3**	**Any Grade**	**Grade ≥3**
Contusion	46 (19.2)	0 (0.0)	8 (3.5)	0 (0.0)
Upper respiratory tract infection	41 (17.1)	2 (0.8)	27 (11.9)	2 (0.9)
Neutropenia[b]	37 (15.4)	27 (11.3)	129 (56.8)	116 (51.1)
Diarrhea	33 (13.8)	0 (0.0)	30 (13.2)	4 (1.8)
Arthralgia	32 (13.3)	2 (0.8)	20 (8.8)	1 (0.4)
Fatigue	28 (11.7)	3 (1.3)	36 (15.9)	2 (0.9)
Rash	26 (10.8)	0 (0.0)	44 (19.4)	6 (2.6)
Constipation	24 (10.0)	1 (0.4)	43 (18.9)	0 (0.0)
Nausea	24 (10.0)	0 (0.0)	74 (32.6)	3 (1.3)
Pyrexia	17 (7.1)	0 (0.0)	60 (26.4)	8 (3.5)
Vomiting	17 (7.1)	0 (0.0)	33 (14.5)	3 (1.3)
Anemia	11 (4.6)	1 (0.4)	43 (18.9)	4 (1.8)
Thrombocytopenia	9 (3.8)	4 (1.7)	31 (13.7)	16 (7.0)
Infusion-related reaction	1 (0.4)[c]	0 (0.0)	43 (18.9)	6 (2.6)

[a]Safety was assessed in patients who received ≥1 dose of treatment; 1 patient in the zanubrutinib arm and 11 patients in the B+R arm did not receive treatment.
[b]Pooled term with neutrophil count decreased. [c]Due to amphotericin B infusion.
AE, adverse event; B+R, bendamustine + rituximab.

Table 4. Adverse Events of Interest

	Zanubrutinib (n=240[a])		B+R (n=227[a])	
AE, n (%)	**Any Grade**	**Grade ≥3**	**Any Grade**	**Grade ≥3**
Anemia	11 (4.6)	1 (0.4)	44 (19.4)	4 (1.8)
Neutropenia[b]	38 (15.8)	28 (11.7)	129 (56.8)	116 (51.1)
Thrombocytopenia[c]	11 (4.6)	5 (2.1)	40 (17.6)	18 (7.9)
Arthralgia	32 (13.3)	2 (0.8)	20 (8.8)	1 (0.4)
Atrial fibrillation	8 (3.3)	1 (0.4)	6 (2.6)	3 (1.3)
Bleeding[d]	108 (45.0)	9 (3.8)	25 (11.0)	4 (1.8)
Major bleeding[e]	12 (5.0)	9 (3.8)	4 (1.8)	4 (1.8)
Diarrhea	33 (13.8)	2 (0.8)	31 (13.7)	5 (2.2)
Hypertension[f]	34 (14.2)	15 (6.3)	24 (10.6)	11 (4.8)
Infections[g]	149 (62.1)	39 (16.3)	127 (55.9)	43 (18.9)
Myalgia	9 (3.8)	0 (0.0)	3 (1.3)	0 (0.0)
Other cancers	31 (12.9)	17 (7.1)	20 (8.8)	7 (3.1)
Dermatologic other cancers	16 (6.7)	2 (0.8)	10 (4.4)	2 (0.9)

[a]Safety was assessed in patients who received ≥1 dose of treatment; 1 patient in the zanubrutinib arm and 11 patients in the B+R arm did not receive treatment. [b]Neutropenia, neutrophil count decreased, or febrile neutropenia. [c]Thrombocytopenia or platelet count decreased. [d]Pooled term of all-cause bleeding including bruising, petechiae, purpura, and contusion. [e]Major bleeding included all Grade ≥3, serious, and any-grade central nervous system hemorrhage. [f]Hypertension, blood pressure increased, or hypertensive crisis. [g]All infection terms pooled.
AE, adverse event; B+R, bendamustine + rituximab.

CONCLUSIONS

- In this global registrational trial, zanubrutinib demonstrated statistically significant improvement in PFS compared with B+R as assessed by IRC
- Superiority was also observed in PFS by investigator assessment and in ORR by both IRC and investigator assessments
- Zanubrutinib was well tolerated, with low rates of atrial fibrillation
- These data support the potential utility of zanubrutinib in the frontline management of patients with previously untreated CLL/SLL

REFERENCES

1. Zelenetz AD, et al. *J Natl Compr Canc Netw*. 2015;13:326-362.
2. Scheffold A and Stilgenbauer S. *Curr Oncol Rep*. 2020;22:16.
3. Estupiñán HY, et al. *Front Cell Dev Biol*. 2021;9:630942.
4. Guo Y, et al. *J Med Chem*. 2019;62:7923-7940.
5. Tam CS, et al. *Blood*. 2019;134:851-859.
6. Tam CS, et al. *Blood*. 2020;146:2038-2050.
7. Hillmen P, et al. EHA 2021. Abstract LB1900.
8. Tam CS, et al. *Haematologica*. 2020;106:2354-2363.
9. Brown JR, et al. *Blood*. 2020;136(suppl 1):11-12.

CORRESPONDENCE

ghia.paolo@hsr.it

ACKNOWLEDGMENTS

We would like to thank the SEQUOIA investigators, site support staff, and especially the patients for participating in this study. We also would like to thank Vanitha Ramakrishnan, Maria Salaverri, Sowmya Kuwahara, Fangfang Yin, Andy Szeto, and Axel Gayko for their contributions to biomarker analysis, operational support, and data analysis. This study was sponsored by BeiGene. Editorial support was provided by Medical Expressions and was funded by BeiGene.

DISCLOSURES

BSK: consultant for Genentech, ADCT, AbbVie, AstraZeneca, BeiGene, Pharmacyclics, BMS, TG Therapeutics, Teva, Janssen, MEI; research funding from Genentech, ADCT, AbbVie, Acerta, AstraZeneca, BeiGene.

KG: consultant for AbbVie, Amgen, AstraZeneca, BeiGene, Janssen, Sanofi-Genzyme, Novartis, Takeda, Roche, Karyopharm, GSK, Sandoz; research funding from AbbVie, Amgen, AstraZeneca, BeiGene, Janssen, Sanofi-Genzyme, Novartis, Takeda, Roche, Gilead, TG Therapeutics; honoraria from AbbVie, Amgen, AstraZeneca, BeiGene, Janssen, Sanofi-Genzyme, Novartis, Takeda, Roche, Karyopharm, GSK, Gilead, Sandoz, Pfizer, Teva; member of the board of directors or of the advisory committee for Polish Myeloma Consortium, Next Generation Hematology Association.

WJ: research funding from AbbVie, AstraZeneca, BeiGene, Celgene, Debbiopharm, Epizyme, Incyte, Janssen, Merck, Roche, Takeda, TG Therapeutics.

MŠimkovič: consultant for AbbVie, AstraZeneca, Janssen-Cilag; shareholder for AbbVie, Merck, Eli Lilly, J&J; honoraria from AbbVie, Janssen-Cilag; member of the board of directors or of the advisory committee for AbbVie, AstraZeneca; travel fees from Gilead, Janssen-Cilag, AbbVie.

MShadman: consultant for AbbVie, Genentech, AstraZeneca, Sound Biologics, Pharmacyclics, BeiGene, Bristol Myers Squibb, Morphosys, TG Therapeutics, Innate Pharma, Kite Pharma, Adaptive Biotechnologies, Epizyme, Eli Lilly, and Atara Biotherapeutics, Adaptimmune; research funding for Mustang Bio, Celgene, Bristol Myers Squibb, Pharmacyclics, Gilead, Genentech, AbbVie, TG Therapeutics, BeiGene, AstraZeneca, Sunesis, Atara Biotherapeutics, GenMab; member of the board of directors or of the advisory committee for AbbVie, Genentech, AstraZeneca, Sound Biologics, Pharmacyclics, BeiGene, Bristol Myers Squibb, Morphosys, TG Therapeutics, Innate Pharma, Kite Pharma, Adaptive Biotechnologies, Epizyme, Eli Lilly, and Atara Biotherapeutics, Adaptimmune.

AÖ: research funding from BeiGene, Gilead.

LL: research funding from Roche, AbbVie; honoraria from AbbVie, Roche, BeiGene, Janssen, AstraZeneca.

PW: consultant for BeiGene, Acerta.

SO: consultant for AbbVie, AstraZeneca, Janssen, Roche; research funding from AbbVie, AstraZeneca, BeiGene, Gilead, Janssen, Pharmacyclics, Roche, Sandoz, Takeda; honoraria from AbbVie, AstraZeneca, Celgene, CSL Behring, Gilead. Janssen, Merck, Roche, Takeda

HChan: speaker's bureau for Janssen, Roche; member of the board of directors or of the advisory committee for Janssen, AbbVie, Eusa, GSK; travel fees from Amgen, Celgene.

RG: consultant for Celgene, Novartis, Roche, BMS, Takeda, AbbVie, AstraZeneca, Janssen, MSD Merck, Gilead, Daiichi Sankyo, Sanofi; research funding for Celgene, Roche, Merck, Takeda, AstraZeneca Novartis, Amgen, BMS, MSD, Sandoz, AbbVie Gilead, Daiichi Sankyo; honoraria for Celgene, Roche, Merck, Takeda, AstraZeneca Novartis, Amgen, BMS, MSD, Sandoz, AbbVie, Gilead, Daiichi Sankyo, Sanofi; member of the board of directors or of the advisory committee for Celgene, Novartis, Roche, BMS, Takeda, AbbVie, AstraZeneca, Janssen, MSD Merck, Gilead, Daiichi Sankyo, Sanofi; travel fees from Roche, Amgen, Janssen, AstraZeneca, Novartis, MSD, Celgene, Gilead, BMS, AbbVie, Daiichi Sankyo.

MTrněný: consultant for Janssen, Gilead Sciences, Takeda, Bristol Myers Squibb, Amgen, AbbVie, Roche, MorphoSys, Incyte, Novartis; honoraria from Janssen, Gilead Sciences, Bristol-Myers Squibb, Amgen, AbbVie, Roche, AstraZeneca, MorphoSys, Incyte, Portolla, Takeda, Novartis; member of the board of directors or of the advisory committee for Janssen, Takeda, Roche, Bristol Myers Squibb, AbbVie, Portolla, MorphoSys, Incyte, Novartis; travel fees from Gilead, Takeda, Bristol Myers Squibb, Roche, Janssen, AbbVie.

DMB: consultant for AbbVie, Genentech, Pharmacyclics, Pfizer, TG Therapeutics, Verastem; research funding from AbbVie, ArQule, Ascentage, AstraZeneca, BeiGene, DTRM, Genetech, Juno/Celgene/BMS, LOXO, MEI Pharma, Novartis, Pharmacyclics, TG Therapeutics; panel member for NCCN

IWF: consultant for AbbVie, AstraZeneca, BeiGene, Century Therapeutics, Genentech, Gilead Sciences, Great Point Partners, Hutchison MediPharma, Iksuda Therapeutics, Janssen, Juno Therapeutics, Kite Pharma, MorphoSys, Novartis, Nurix Therapeutics, Pharmacyclics, Roche, Seattle Genetics, Servier Pharmaceuticals, Takeda, TG Therapeutics, Unum Therapeutics, Verastem, Vincerx Pharma, Yingli Pharmaceuticals; all payments made to Sarah Cannon Research Institute; research funding from AbbVie, Acerta Pharma, Agios, ArQule, AstraZeneca, BeiGene, Calithera Biosciences, Celgene, Constellation Pharmaceuticals, Curis, Forma Therapeutics, Forty Seven, Genentech, Gilead Sciences, IGM Biosciences, Incyte, Infinity Pharmaceuticals, Janssen, Juno Therapeutics, Karyopharm Therapeutics, Kite Pharma, Loxo, Merck, MorphoSys, Novartis, Pfizer, Pharmacyclics, Portola Pharmaceuticals, Rhizen Pharmaceuticals, Roche, Seattle Genetics, Takeda, Teva, TG Therapeutics, Trillium Therapeutics, Triphase Research & Development Corp., Unum Therapeutics, Verastem; all payments made to Sarah Cannon Research Institute.

EV: research funding from Janssen Cilag Pty Ltd.

JRB: consultant for AbbVie, Acerta/AstraZeneca, BeiGene, Bristol Myers Squibb/Juno/Celgene, Catapult, Eli Lilly, Genentech/Roche, Janssen, MEI Pharma, Morphosys AG, Nextcea, Novartis, Pfizer, Rigel; research funding from Gilead, Loxo/Lilly, SecuraBio, Sun, TG Therapeutics.

PG: consultant for AbbVie, AstraZeneca, ArQule/MDS, BeiGene, Celgene/Juno/BMS, Janssen, Roche; research funding from AbbVie, AstraZeneca, Janssen, Gilead, Sunesis; honoraria from AbbVie, AstraZeneca, ArQule/MDS, BeiGene, Celgene/Juno/BMS, Janssen, Roche.

TT, **LZ**, **CM**, **JCP**, **AC:** employees and shareholders of BeiGene (Beijing) Co., Ltd., Beijing, China and BeiGene USA, Inc.,

TR: research funding from AstraZeneca, AbbVie, Janssen, Octapharma, Gilead, Pharmacyclics, Pfizer, GlaxoSmithKline, Biogen.

PH: research funding from Janssen, AbbVie, Pharmacyclics, Roche, Gilead; honoraria from Janssen, AbbVie, Pharmacyclics, AstraZeneca, SOBI, BeiGene.

CST: research funding from Janssen and AbbVie; honoraria from Janssen, AbbVie, BeiGene, Roche, Novartis.

HCiepluch, **MTani**, **SG**, **JL:** no conflicts of interest.

Poster:

Plain Language Summary:

Presented at 10th Annual Meeting of the Society of Hematologic Oncology (SOHO), September 28-October 1, 2022; Houston, Texas