BEIGENE

ALPINE & EHA 2021 Summary

June 11, 2021

Agenda and Speakers

• Welcome	Howard Liang, Ph.D.
• ALPINE	Peter Hillmen, MB ChB, Ph.D.
• Perspective	Jennifer Brown, M.D., Ph.D.
• BRUKINSA Program	Jane Huang, M.D.
• Key Takeaways	John Oyler
• Q&A	All

Disclosures

Certain statements contained in this presentation and in the accompanying oral presentation, other than statements of fact that are independently verifiable at the date hereof, may constitute forward-looking statements. Examples of such forward-looking statements include statements regarding BeiGene's research, discovery, and pre-clinical and early-stage clinical programs and plans; recent clinical data for BeiGene's product candidates and approvals of its medicines, such as results from the interim analysis of the Phase 3 ALPINE trial and the potential clinical benefits and advantages of BRUKINSA compared to other BTK inhibitors; the conduct of late-stage clinical trials and expected data readouts, such as the expected timing for the final analysis of the ALPINE trial; additional planned commercial product launches; the advancement of and anticipated clinical development, regulatory milestones and commercialization of BeiGene's medicines and drug candidates. Actual results may differ materially from those indicated in the forward-looking statements as a result of various important factors, including the risk that preliminary data from the interim analysis of the Phase 3 ALPINE trial may differ at the final analysis; the risk that the interim and/or final results of the ALPINE trial will not support filings for regulatory approvals of zanubrutinib for the treatment of patients with CLL, and the timing of any such filings and potential approvals; clinical data continue to support a risk-benefit profile for BRUKINSA; BeiGene's ability to demonstrate the efficacy and safety of its drug candidates; the clinical results for its drug candidates, which may not support further development or marketing approval; actions of regulatory agencies, which may affect the initiation, timing and progress of clinical trials and marketing approval; BeiGene's ability to achieve commercial success for its marketed medicines and drug candidates, if approved; BeiGene's ability to obtain and maintain protection of intellectual property for its medicines and technology; BeiGene's reliance on third parties to conduct drug development, manufacturing and other services; BeiGene's limited experience in obtaining regulatory approvals and commercializing pharmaceutical products and BeiGene's ability to obtain additional funding for operations and to complete the development of its drug candidates or achieve profitability; the impact of the COVID-19 pandemic on BeiGene's clinical development, regulatory, commercial and other operations, as well as those risks more fully discussed in the section entitled "Risk Factors" in BeiGene's most recent quarterly report on Form 10-Q, as well as discussions of potential risks, uncertainties, and other important factors in BeiGene's subsequent filings with the U.S. Securities and Exchange Commission. All information in this presentation is as of the date of this presentation, and BeiGene undertakes no duty to update such information unless required by law.

Some of the clinical data in this presentation relating to BeiGene's investigational drug candidates is from pre-clinical studies or early phase, single-arm clinical trials. When such data or data from later stage trials are presented in relation to other investigational or marketed medicines, the presentation and discussion are not based on head-to-head trials between BeiGene's investigational drug candidates and other medicines unless specified in the trial protocol. BeiGene is still conducting pre-clinical studies and clinical trials and, as additional patients are enrolled and evaluated, data on BeiGene's investigational drug candidates may change.

This presentation and the accompanying oral presentation contain data and information obtained from third-party studies and internal company analysis of such data and information. BeiGene has not independently verified the data and information obtained from these sources. Forward-looking information obtained from these sources is subject to the same qualifications noted above.

Peter Hillmen, MB ChB, Ph.D. Biography

Professor of Experimental Haematology and Honorary Consultant Hematologist
Leeds Teaching Hospitals NHS Trust

Background:

- Received his Degree in Medicine at Leeds Medical School (1985) and completed medical training Leeds (1988)
- Haematology Training at Hammersmith Hospital, London (1989 – 1993) including as a Wellcome Trust Research Fellow at the Royal Postgraduate Medical School completing a PhD in PNH under the supervision of Professor Lucio Luzzatto (1991 – 1993)
- Senior Registrar in Haematology at Leeds Medical School (1994 – 1996)
- Consultant Haematologist Mid-Yorkshire Trust and Leeds General Infirmary (1996 – 2004)
- Chair of the UK NCRI CLL trials sub-committee (2002 – 2018)

Current Roles:

- Consultant Haematologist Leeds Teaching Hospitals NHS Trust (2004)
- Professor of Experimental Haematology, University of Leeds (2013 to date)
- Chair of the UK NCRI Haematological Oncology Research Group (2018 to date)
- Chair of the International Workshop on CLL (2021 to date) and Chair of the International PNH Interest Group (2005 to date)

Research Interests:

- Paroxysmal nocturnal haemoglobinuria (PNH): pathophysiology and treatment
- Chronic lymphocytic leukaemia (CLL): novel therapeutic approaches

Awards:

- IWCLL Binet-Rai Medal in 2017 for outstanding contribution to CLL research

ALPINE Update

Peter Hillmen, MB ChB, Ph.D.

St. James's University Hospital, Leeds

FIRST INTERIM ANALYSIS OF ALPINE STUDY: RESULTS OF A PHASE 3 RANDOMIZED STUDY OF ZANUBRUTINIB VS IBRUTINIB IN PATIENTS WITH RELAPSED/REFRACTORY CHRONIC LYMPHOCYTIC LEUKEMIA/ SMALL LYMPHOCYTIC LYMPHOMA

Peter Hillmen, MBChB, PhD[1]; Barbara Eichhorst, MD[2]; Jennifer R. Brown, MD, PhD[3]; Nicole Lamanna MD[4]; Susan O'Brien, MD[5]; Constantine S. Tam, MBBS, MD[6,7,8,9]; Lugui Qiu, MD, PhD[10]; Maciej Kazmierczak, MD, PhD[11]; Keshu Zhou, MD, PhD[12]; Martin Šimkovič, MD, PhD[13,14]; Jiri Mayer, MD[15]; Amanda Gillespie-Twardy, MD[16], Mazyar Shadman, MD, MPH[17,18]; Alessandra Ferrajoli, MD[19]; Peter S. Ganly, BMBCh, PhD[20,21]; Robert Weinkove, MBBS, PhD[22,23]; Tommi Salmi, MD[24]; Meng Ji, MD[24]; Jessica Yecies, PhD[24]; Kenneth Wu, PhD[24]; William Novotny, MD[24]; Jane Huang, MD[24]; Wojciech Jurczak, MD, PhD[25]

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June 11, 2021 - Presidential Symposium - Clinical (Abstract LB1900)

Background

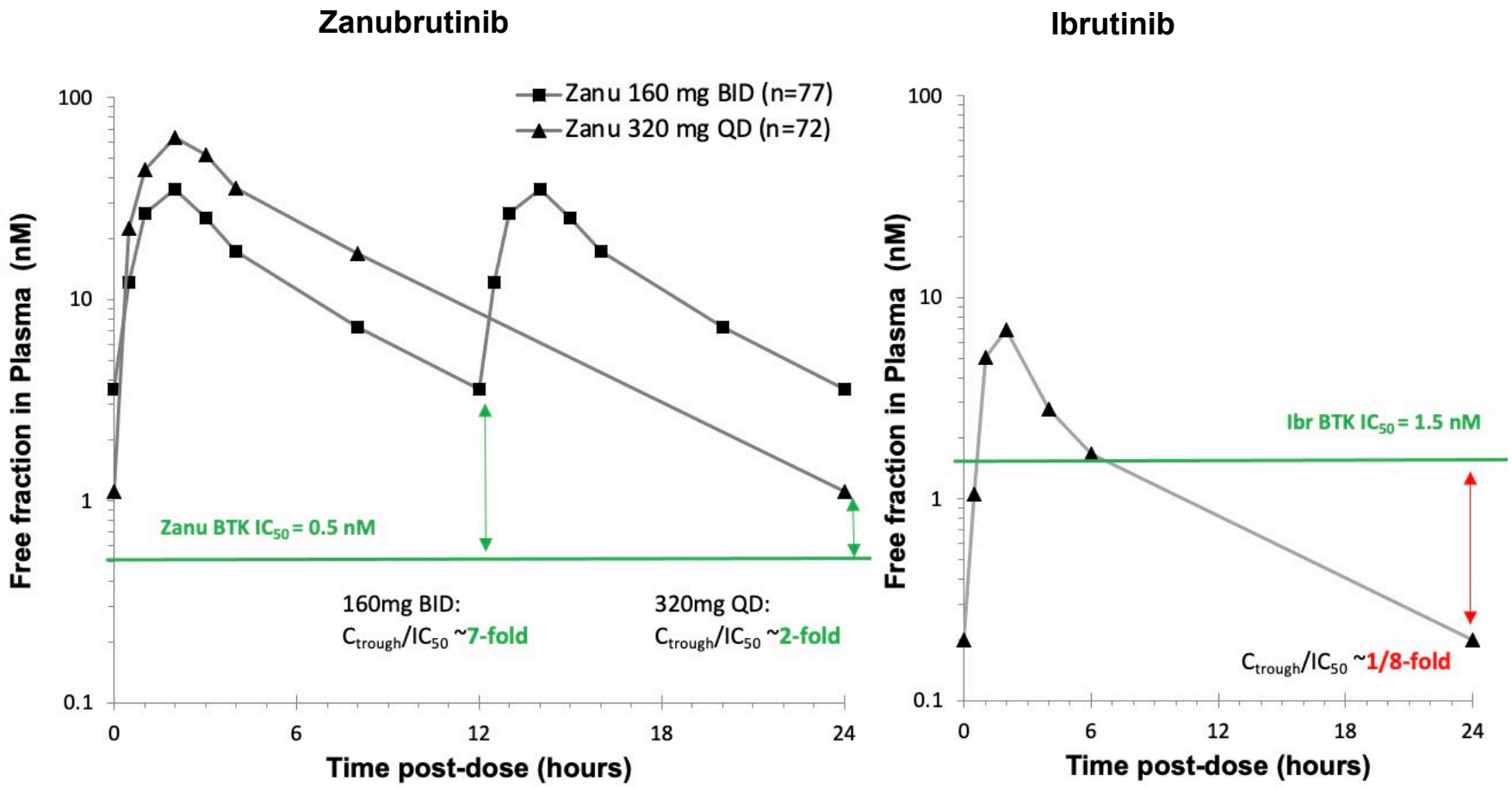
- Treatment of CLL/SLL has been transformed with the advent of effective inhibitors of B-cell receptor signaling[1,2], such as the BTK inhibitor Ibrutinib[3,4]
- Zanubrutinib is an irreversible, potent, next-generation BTK inhibitor designed to maximize BTK occupancy and minimize off-target inhibition of TEC- and EGFR-family kinases[5]
- We hypothesized that Zanubrutinib may minimize toxicities related to Ibrutinib off-target inhibition,[6] and Zanubrutinib[5] may improve efficacy outcomes

BTK, Bruton tyrosine kinase; CLL, chronic lymphocytic leukemia; SLL, small lymphocytic lymphoma.

1. Aalipour A, Advani RH. *Br J Haematol.* 2013;163:436-443. 2. Ten Hacken E, Burger JA. *Clin Cancer Res*. 2014;20:548-556. 3. Imbruvica (ibrutinib) [package insert]. Sunnyvale, CA, USA: Pharmacyclics LLC and Horsham, PA, USA: Janssen Biotech, Inc; 2019. 4. Imbruvica (ibrutinib) [SPC]. Beerse, Belgium: Janssen-Cilag International NV; 2018. 5. Tam CS, et al. *Blood*. 2019;134:851-859. 6. Coutre S, et al. *Blood Adv*. 2019;3:1799-807.

Pharmacokinetics of Zanubrutinib and Ibrutinib

Free Drug Concentration Time Profiles Relative to IC_{50}



Note: These data are from separate analyses. Limitations of cross-trial comparisons apply.

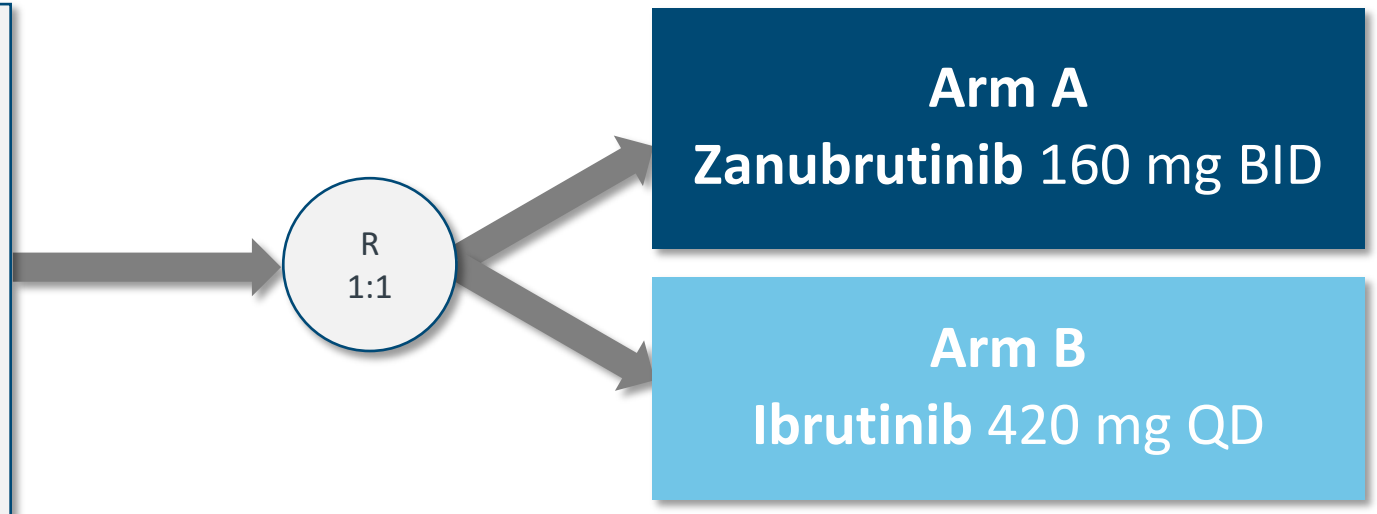
Adapted from: 1. Kaptein, et al. *Blood.* 2018;132:1871. 2. Ou, et al. *Leuk Lymphoma.* In press. 3. Marostica, et al. *Cancer Chemother Pharmacol.* 2015;75:111-121.

ALPINE: Phase 3, Randomized Study of Zanubrutinib vs Ibrutinib in Patients With Relapsed/Refractory CLL or SLL

R/R CLL/SLL with ≥ 1 prior treatment
(Planned N=600, Actual N=652)

Key Inclusion Criteria
- R/R to ≥1 prior systemic therapy for CLL/SLL
- Measurable lymphadenopathy by CT or MRI

Key Exclusion Criteria
- Current or past Richter's transformation
- Prior BTK inhibitor therapy
- Treatment with warfarin or other vitamin K antagonists



Stratification Factors
- Age
- Geographic region
- Refractory status
- Del(17p)/*TP53* mutation status

BID, twice daily; BTK, Bruton tyrosine kinase CLL, chronic lymphocytic leukemia; CT, computed tomography; MRI, magnetic resonance imaging; QD, once daily; R, randomized; R/R, relapsed/refractory; SLL, small lymphocytic lymphoma.

Endpoints and Analysis

Primary endpoint

- **ORR** (PR+CR) as assessed by investigator - noninferiority followed by superiority

Secondary endpoints:

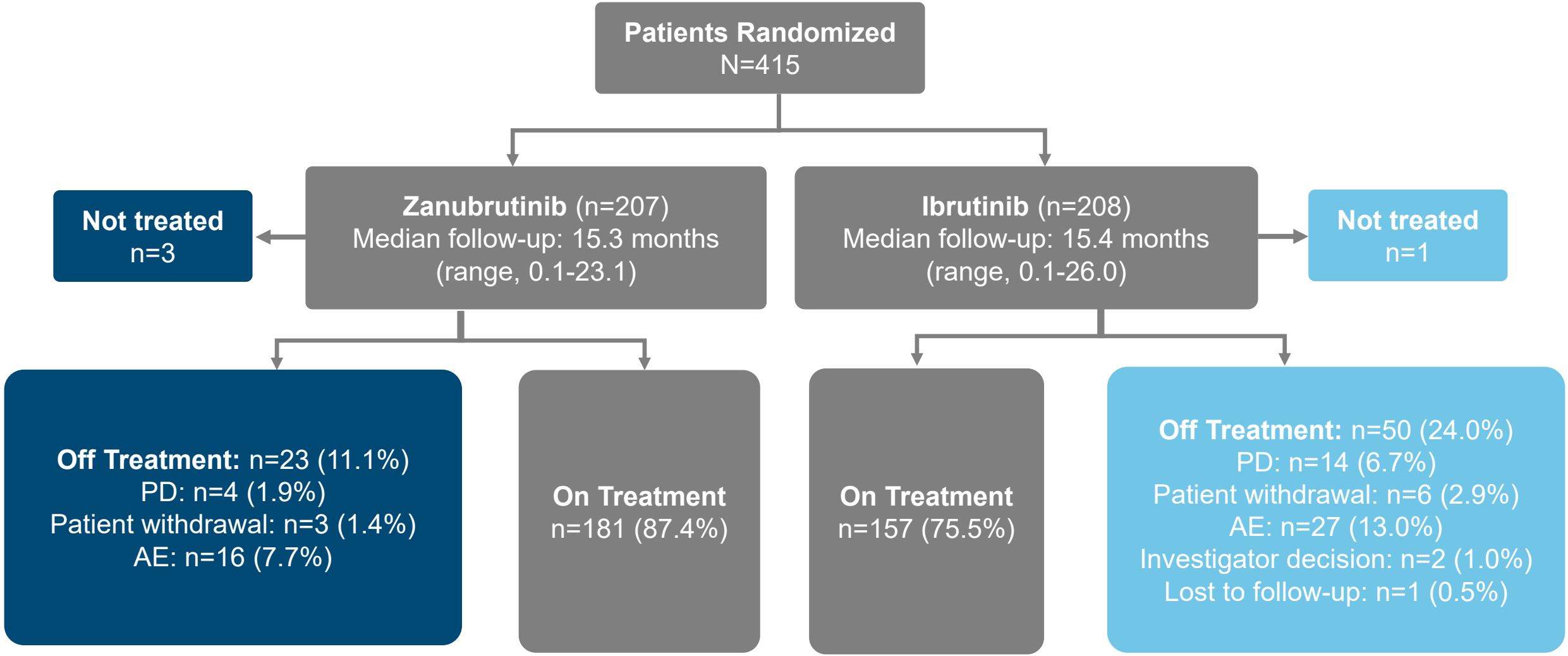
- Atrial fibrillation (any grade)
- ORR (by IRC), DOR, PFS, OS
- Time to treatment failure
- PR-L or higher
- Patient-reported outcomes
- Safety

Preplanned interim analysis

- Data cutoff approximately 12 months after the randomization of 415 patients
- Data presented here are for the first 415 patients, and efficacy results are per investigator assessment

DOR, duration of response; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PR-L, partial response with lymphocytosis.

Patient Disposition



AE, adverse event; PD, progressive disease.

Baseline Patient and Disease Characteristics

Characteristic	Zanubrutinib (n=207)	Ibrutinib (n=208)
Age, median (range)	67 (35, 90)	67 (36, 89)
Age ≥65 years, n (%)	129 (62.3)	128 (61.5)
Male, n (%)	142 (68.6)	156 (75.0)
Disease stage, n (%)		
Binet stage A/B or Ann Arbor stage I/II	122 (58.9)	124 (59.6)
Binet stage C or Ann Arbor stage III/IV	85 (41.1)	84 (40.4)
ECOG performance status ≥1, n (%)	128 (61.8)	132 (63.5)
Prior lines of therapy, median (range)	1 (1-6)	1 (1-8)
>3 prior lines, n (%)	15 (7.3)	21 (10.1)
Prior chemoimmunotherapy, n (%)	166 (80.2)	158 (76.0)
del(17p) and/or mutant *TP53*	41 (19.8)[a]	38 (18.3)
del(17p), n (%)	24 (11.6)	26 (12.5)
TP53 mutated, n (%)	29 (14.0)[a]	24 (11.5)
del11q, n (%)	61 (29.5)	55 (26.4)
Bulky disease (≥ 5 cm), n (%)	106 (51.2)	105 (50.5)

ECOG, Eastern Cooperative Oncology Group.
[a]2 patients with missing values.

Primary Endpoint – ORR

By Investigator Assessment

	Zanubrutinib (n=207), n (%)	Ibrutinib (n=208), n (%)
Primary endpoint: ORR (PR+CR)	162 (**78.3**) 95% CI: 72.0, 83.7	130 (**62.5**) 95% CI: 55.5, 69.1
	Noninferiority was shown by 1-sided p-value <0.0001 Superiority 2-sided *P*=0.0006 compared with statistical boundary of 0.0099	
CR/Cri	4 (1.9)	3 (1.4)
nPR	1 (0.5)	0
PR	157 (75.8)	127 (61.1)
ORR (PR-L+PR+CR)	*183 (88.4)*	*169 (81.3)*
PR-L	21 (10.1)	39 (18.8)
SD	17 (8.2)	28 (13.5)
PD	1 (0.5)	2 (1.0)
Discontinued or new therapy prior to 1st assessment	6 (2.9)	9 (4.3)
	del(17p) (n=24), n (%)	**del(17p) (n=26), n (%)**
ORR (PR+CR)	20 (83.3)	14 (53.8)

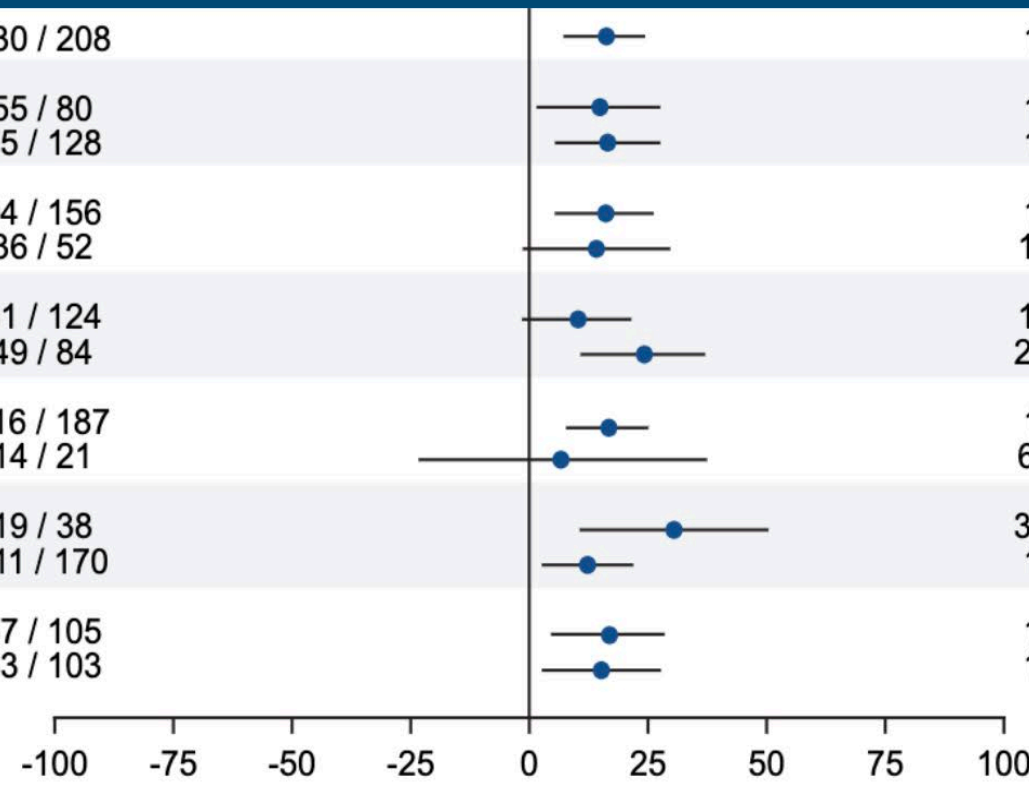
By IRC Assessment

- ORR by IRC was 76.3% (95% CI: 69.9, 81.9) and 64.4% (95% CI: 57.5, 70.9) for Zanubrutinib and Ibrutinib, respectively
- Noninferiority was shown by 1-sided p-value <0.0001
- Superiority 2-sided P=0.0121 compared with statistical boundary of p<0.0099 (non statistically significant)
- Highly concordant with investigator assessment for PR and higher 94.2% and 93.3% for Zanubrutinib and Ibrutinib, respectively

CR, complete response; CRi, complete response with incomplete bone marrow recovery; D/C, discontinuation; DOR, duration of response; NE, not evaluable; nPR, nodular partial response; ORR, overall response rate; PR, partial response; PR-L, partial response with lymphocytosis; SD, stable disease.

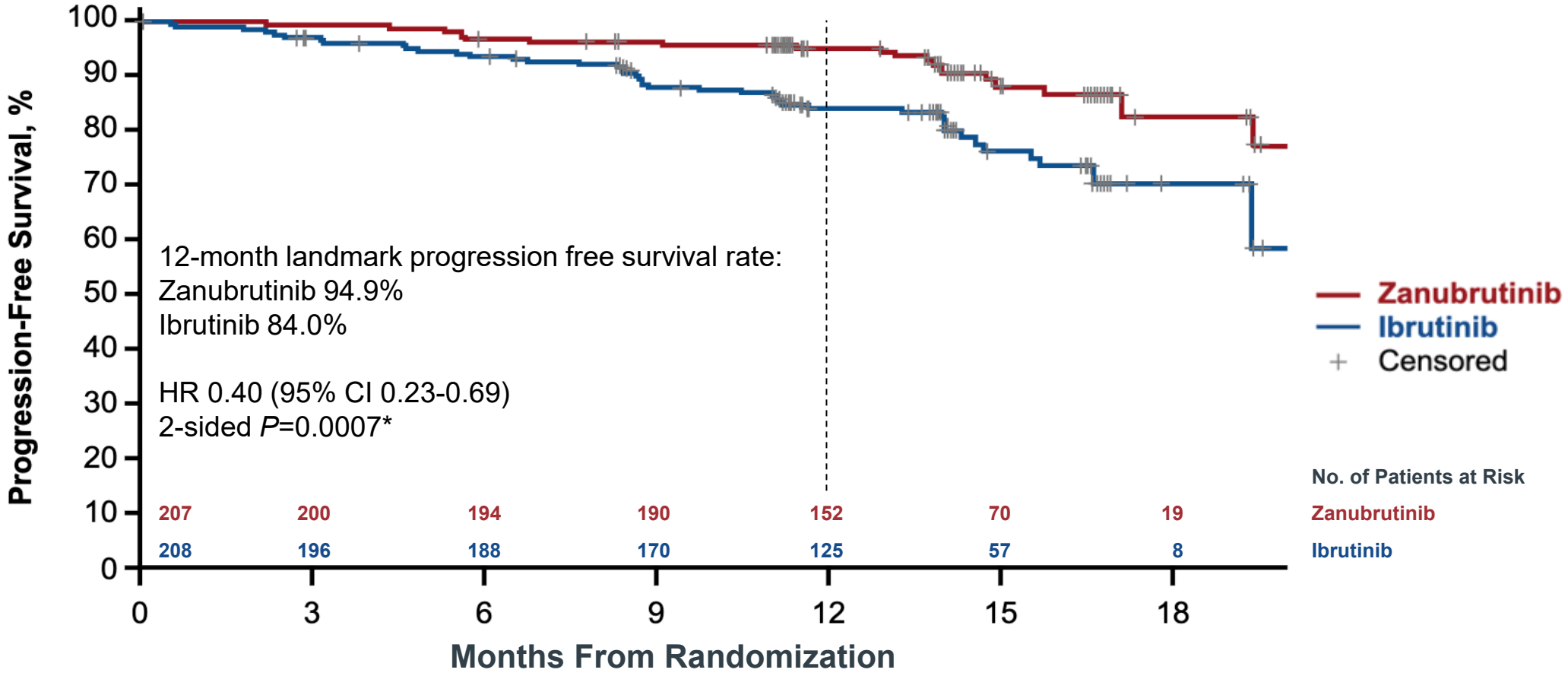
ORR by Investigator Assessment – Key Patient Subgroups

Subgroup	Response/Patients		Risk Difference (95% CI),%[a]
	Zanubrutinib	Ibrutinib	
All patients	162 / 207	130 / 208	15.8 (7.1, 24.4)
Age Group			
<65 years	65 / 78	55 / 80	14.6 (1.5, 27.7)
≥65 years	97 / 129	75 / 128	16.6 (5.3, 27.9)
Sex			
Male	108 / 142	94 / 156	15.8 (5.4, 26.2)
Female	54 / 65	36 / 52	13.8 (-1.7, 29.4)
Disease stage			
Binet stage of A/B or Ann Arbor stage I/II bulky	92 / 122	81 / 124	10.1 (-1.3, 21.4)
Binet stage C or Ann Arbor stage III/IV	70 / 85	49 / 84	24.0 (10.7, 37.3)
Prior lines of therapy			
1-3	151 / 192	116 / 187	16.6 (7.6, 25.7)
> 3	11 / 15	14 / 21	6.7 (-23.5, 36.8)
Baseline del17p/*TP53* mutation status			
Present	33 / 41	19 / 38	30.5 (10.5, 50.5)
Absent	127 / 164	111 / 170	12.1 (2.5, 21.7)
Bulky disease			
Yes	85 / 106	67 / 105	16.4 (4.5, 28.3)
No	77 / 101	63 / 103	15.1 (2.5, 27.6)



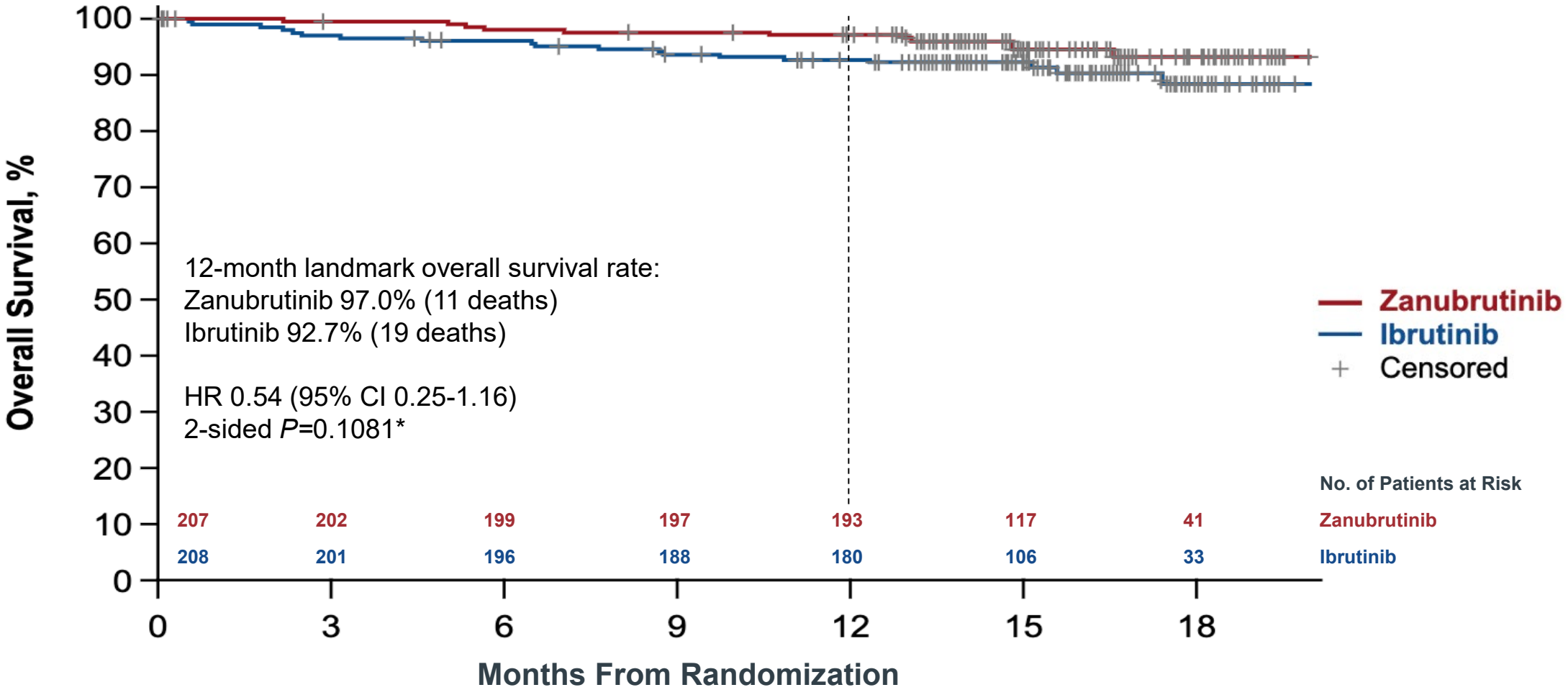
[a]Unstratified rate difference and 95% CI.

PFS by Investigator Assessment



*Not a prespecified analysis. PFS data were early at the time of interim analysis and formal analysis will be performed when the target number of events is reached.
Median PFS follow-up was 14.0 months for both Zanubrutinib and Ibrutinib arms by reverse KM method. PFS, progression-free survival.

Overall Survival



*Not a prespecified analysis.

Safety Summary

Safety Analysis Population	Zanubrutinib (n=204), n (%)	Ibrutinib (n=207), n (%)
Any AE	195 (95.6)	205 (99.0)
Any grade ≥3 AE	114 (55.9)	106 (51.2)
Serious AEs	56 (27.5)	67 (32.4)
Fatal AEs	8 (3.9)	12 (5.8)
AEs leading to dose reduction	23 (11.3)	25 (12.1)
AEs leading to dose interruption	81 (39.7)	84 (40.6)
AEs leading to treatment discontinuation	16 (**7.8**)	27 (**13.0**)

AE, adverse event.

Most Frequent AEs (>10% All Grade in Either Arm)

Safety Analysis Population	Zanubrutinib (n=204), n (%)	Ibrutinib (n=207), n (%)
Patients with any AE	195 (95.6)	205 (99.0)
Diarrhea	34 (16.7)	40 (19.3)
Neutropenia	40 (19.6)	32 (15.5)
Anemia	27 (13.2)	31 (15.0)
Upper respiratory tract infection	44 (21.6)	29 (14.0)
Arthralgia	19 (9.3)	29 (14.0)
Hypertension	32 (15.7)	27 (13.0)
Muscle spasms	6 (2.9)	23 (11.1)
Contusion	21 (10.3)	18 (8.7)
Urinary tract infection	22 (10.8)	17 (8.2)
Cough	26 (12.7)	13 (6.3)

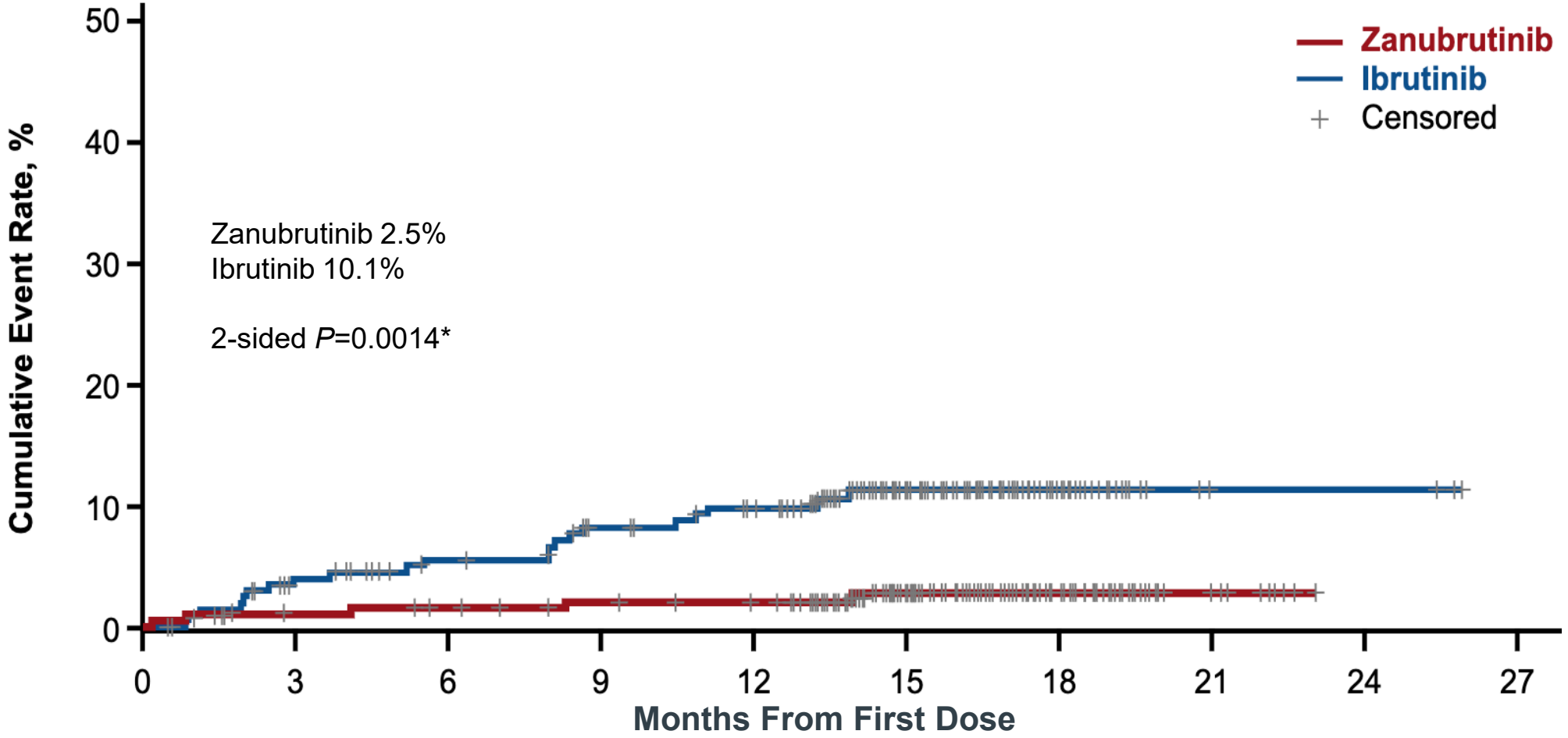
AE, adverse event.

AEs of Special Interest

	Any Grade		Grade ≥3	
Safety Analysis Population	**Zanubrutinib (n=204), n (%)**	**Ibrutinib (n=207), n (%)**	**Zanubrutinib (n=204), n (%)**	**Ibrutinib (n=207), n (%)**
Cardiac disorders[a]	28 (13.7)	52 (25.1)	5 (2.5)	14 (6.8)
Atrial fibrillation and flutter (key secondary endpoint)	**5 (2.5)**	**21 (10.1)**	**2 (1.0)**	**4 (1.9)**
Hemorrhage Major hemorrhage[b]	73 (35.8) 6 (2.9)	75 (36.2) 8 (3.9)	6 (2.9) 6 (2.9)	6 (2.9) 6 (2.9)
Hypertension	34 (16.7)	34 (16.4)	22 (10.8)	22 (10.6)
Infections	122 (59.8)	131 (63.3)	26 (12.7)	37 (17.9)
Neutropenia[c]	58 (28.4)	45 (21.7)	38 (18.6)	31 (15.0)
Thrombocytopenia[c]	19 (9.3)	26 (12.6)	7 (3.4)	7 (3.4)
Secondary primary malignancies Skin cancers	17 (8.3) 7 (3.4)	13 (6.3) 10 (4.8)	10 (4.9) 3 (1.5)	4 (1.9) 2 (1.0)

AE, adverse events. All events are of any grade unless otherwise specified.
[a] Cardiac disorders leading to treatment discontinuation: Zanubrutinib 0 patients and Ibrutinib 7 (3.4%) patients.
[b] Includes hemorrhages that were serious or grade ≥3 or CNS hemorrhages of all grades.
[c] Pooled terms including neutropenia, neutrophil count decreased, and febrile neutropenia; thrombocytopenia and platelet count decreased.

Atrial Fibrillation/Flutter



Patients at Risk										
Zanubrutinib	204	197	194	190	187	114	40	9	0	0
Ibrutinib	207	190	179	168	160	91	26	3	3	0

* Compared with statistical boundary of 0.0099 for interim analysis.

Conclusions

- In this interim analysis of the randomized, Phase 3 ALPINE study in patients with relapsed/refractory CLL/SLL, Zanubrutinib, compared with Ibrutinib, was shown to have:
  - A superior overall response rate by investigator assessment
  - An improved PFS*
  - A lower rate of atrial fibrillation/flutter
- These data support that more selective BTK inhibition, with more complete and sustained BTK occupancy, results in improved efficacy and safety outcomes

*Not a prespecified analysis. PFS data were early at the time of interim analysis and formal analysis will be performed when the target number of events is reached.

Jennifer Brown, M.D., Ph.D Biography

Director of the CLL Center of the Division of Hematologic Malignancies, *Dana-Farber Cancer Institute*
Professor of Medicine, *Harvard Medical School*

Background:

- B.S. and M.S. simultaneously at Yale University, graduating summa cum laude with distinction in molecular biophysics and biochemistry (MB&B)
- MD and PhD in molecular genetics at Harvard Medical School (1998); awarded the James Tolbert Shipley Prize for research
- Internship and Residency in Internal Medicine at Massachusetts General Hospital
- Fellowship in Hematology and Medical Oncology at the Dana-Farber Cancer Institute
- Faculty of DFCI and Harvard Medical School (2004), with an active clinical-translational research program in CLL
- Published 250+ scientific literature papers, predominantly in CLL
- Prior CLL Research Consortium Active Member
- Alliance Leukemia and Leukemia Correlative Science Committees Member
- International Workshop on CLL (iwCLL) member
- Research Interests:
  - CLL, novel targeted therapeutics development and genomics (focus on the inherited predisposition to CLL)
- Awards:
  - The Clinical Innovation Award, Dana-Farber Cancer Institute (2014)
  - George Canellos Award for Excellence in Clinical Investigation and Patient Care, Dana-Farber Cancer Institute (2014)

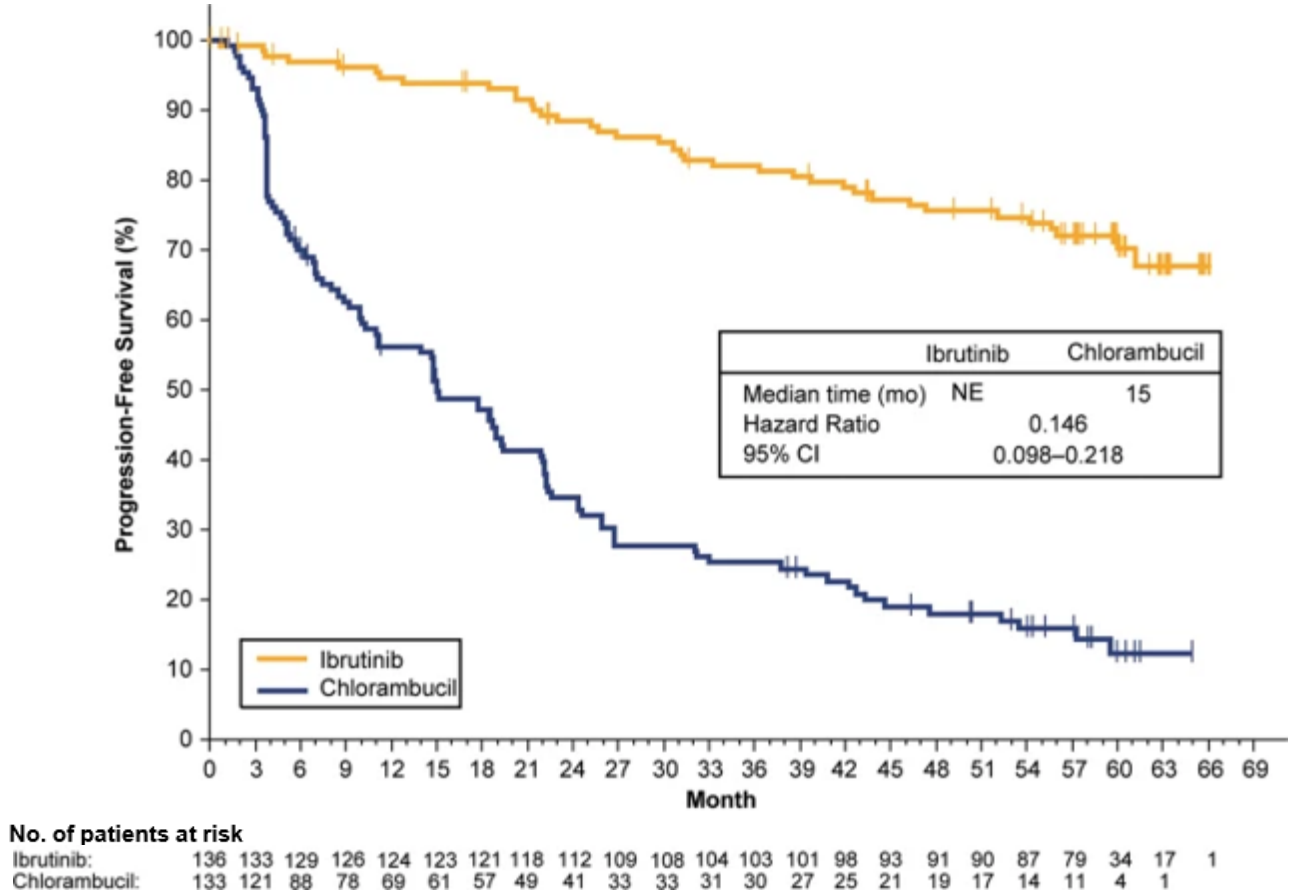
Perspective

Jennifer Brown, M.D., Ph.D

Dana Farber Cancer Institute,
Harvard Medical School

Ibrutinib: First-in-Class BTKi Effective, But Not Tolerable

Median follow-up 60 months



PFS 70%
41% discontinuation

Burger JA et al. *Leukemia* 2020;34:787-798.

Retrospective Analysis of Toxicities and Outcomes for Ibrutinib-Treated Patients: Discontinuations due to Toxicity

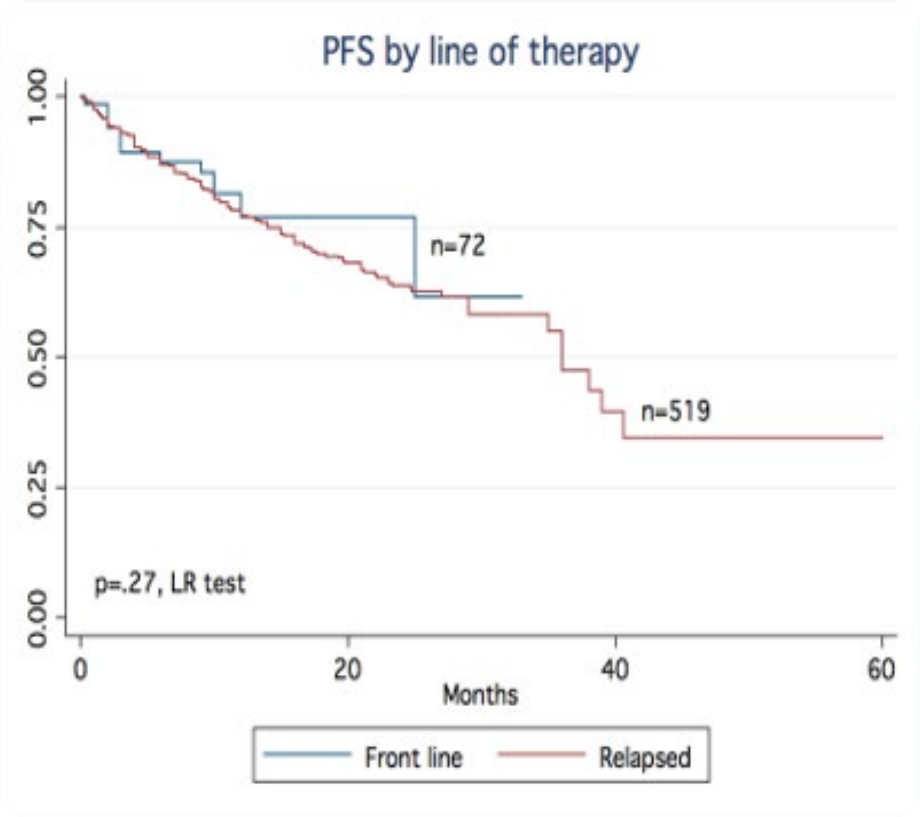
- Ibrutinib toxicity was the most common reason for discontinuation in all settings
  - In front line CLL, most commonly due to: arthralgia (42%), atrial fibrillation (25%), and rash (17%)
  - In R/R CLL, most commonly due to: atrial fibrillation (12%), infection (11%), pneumonitis (10%), bleeding (9%), and diarrhea (7%)
- Ibrutinib starting dose (420 mg/day vs. <420 mg/day) did not impact the proportion of patients who discontinued due to toxicity (51% vs 50%)

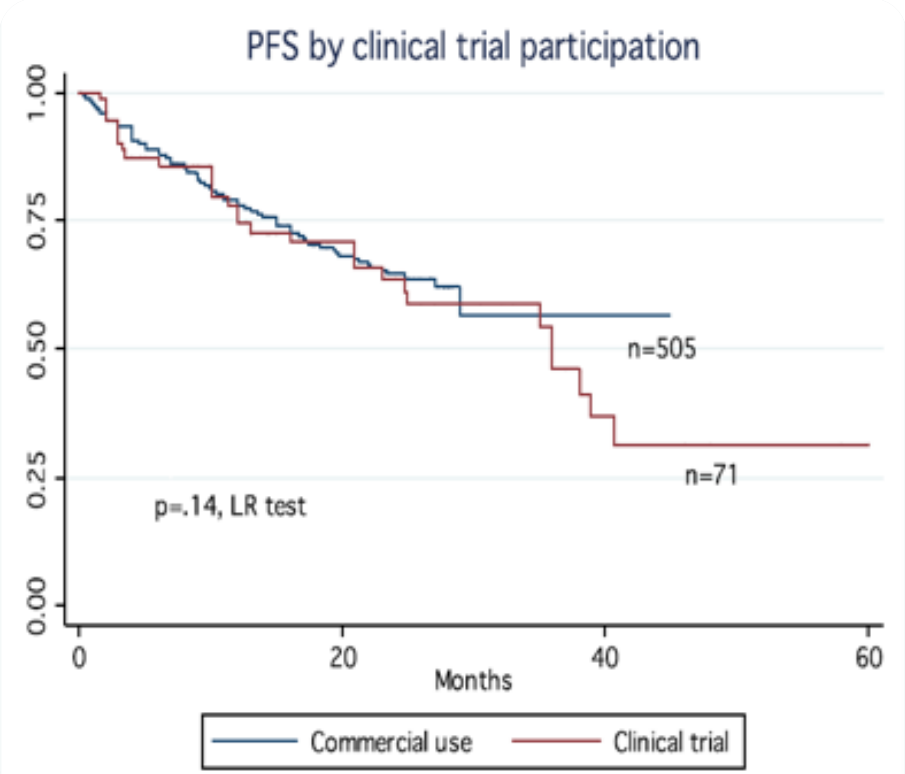
Months to discontinuation, median	Toxicity
Bleeding	8
Diarrhea	7.5
Atrial fibrillation	7
Infection	6
Arthralgia	5
Pneumonitis	4.5
Rash	3.5

Mato et al. ASH 2016. Abstract #3222.

Retrospective Analysis of Toxicities and Outcomes for Ibrutinib-Treated Patients

Median PFS and OS for entire cohort were 36 months and NR, respectively (median follow-up 17 months)





Mato et al. ASH 2016. Abstract #3222.

Severe CV Toxicities and Ibrutinib

- Case reports of Ventricular Arrhythmias and Deaths in the setting of Ibrutinib
- CV Adverse Drug Reactions with Overreporting in the WHO VigiBase

TABLE 1 Disproportionality Analysis in VigiBase

	Ibrutinib	Entire Database (Since Inception)	IC/IC_{025}	Entire Database (Since 2013)	ROR ($_{95}$CI)
Total number of ICSRs available	13,572	16,343,451		8,318,890	
Number of ICSRs and statistics by CV-ADR subgroups					
Cardiac supraventricular arrhythmias	959 (7.07)	68,597 (0.42)	4.06/3.97	28,242 (0.34)	23.1 (21.6-24.7)
CNS hemorrhagic events	505 (3.72)	179,621 (1.10)	1.76/1.63	85,402 (1.03)	3.7 (3.4-4.1)
Heart failure	363 (2.67)	142,502 (0.87)	1.61/1.46	65,680 (0.79)	3.5 (3.1-3.8)
Cardiac ventricular arrhythmias	70 (0.52)	33,504 (0.20)	1.32/0.96	9,220 (0.11)	4.7 (3.7-5.9)
Cardiac conduction disorders	50 (0.37)	26,008 (0.16)	1.19/0.76	8,834 (0.11)	3.5 (2.7-4.6)
CNS ischemic events	254 (1.87)	161,618 (0.99)	0.92/0.73	70,529 (0.85)	2.2 (2.0-2.5)
Hypertension and related end-organ damages	295 (2.17)	239,232 (1.46)	0.57/0.40	109,148 (1.31)	1.7 (1.5-1.9)

Salem JE et al. JACC 2019, 74 (13)1667

Zanubrutinib (BGB-3111): Kinase Selectivity Relative to Ibrutinib

Selectivity in Assays — IC_{50} (nM)

Targets	Assays	Ibrutinib IC_{50} (nM)	BGB-3111 IC_{50} (nM)	Ratio (BGB-3111:Ibrutinib)
BTK	BTK-pY223 Cellular Assay	3.5	1.8	0.5
	Rec-1 Proliferation	0.34	0.36	1.1
	BTK Occupation Cellular Assay	2.3	2.2	1.0
	BTK Biochemical Assay	0.20	0.22	1.1
EGFR	p-EGFR HTRF Cellular Assay	101	606	6.0
	A431 Proliferation	323	3,210	9.9
ITK	ITK Occupancy Cellular Assay	189	3,265	17
	p-$PLC_{\gamma 1}$ Cellular Assay	77	3,433	45
	IL-2 Production Cellular Assay	260	2,536	9.8
	ITK Biochemical Assay	0.9	30	33
JAK3	JAK3 Biochemical Assay	3.9	200	51
HER2	HER2 Biochemical Assay	9.4	661	70
TEC	TEC Biochemical Assay	0.8	1.9	2.4

Abstract 832: Phase I BGB-3111 in B-Cell Malignancies

ASPEN: Ibrutinib vs Zanubrutinib in WM
Any Grade AEs

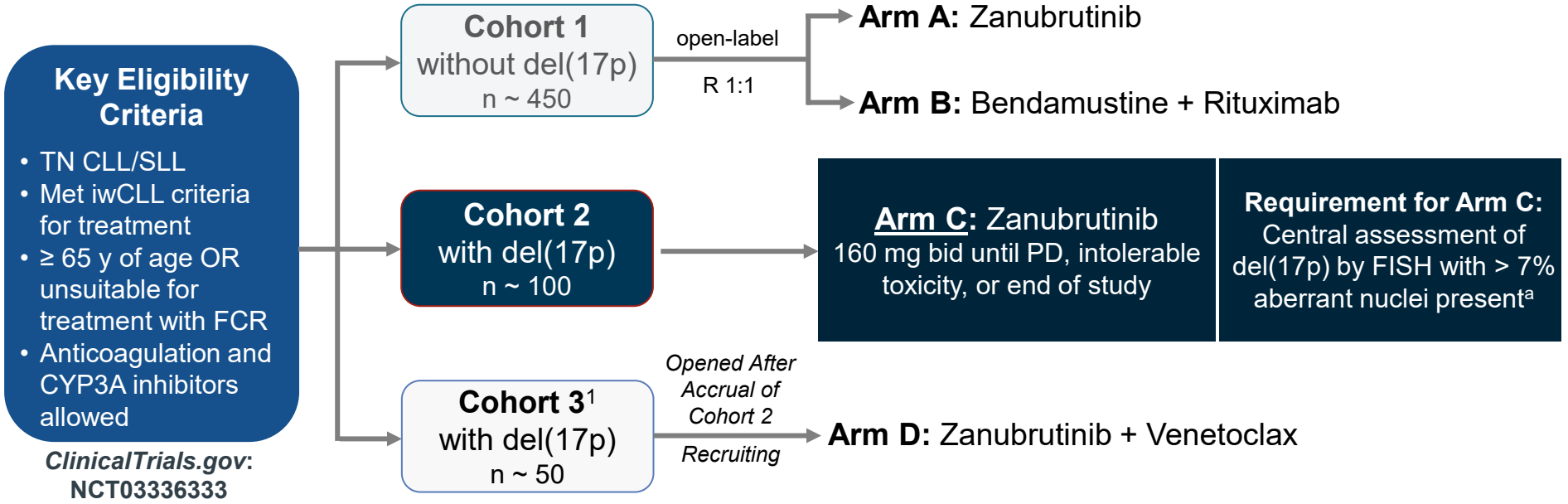
	Ibrutinib	Zanubrutinib
Atrial fibrillation	15%	2%
Hypertension	16%	11%
Edema	19%	9%
Contusion	24%	13%
Pneumonia	12%	2%
Neutropenia	13% (8% grade 3)	29% (20% grade 3)
D/c due to AEs	9%	4%

19.4 months median follow-up

Tam et al. Blood 2020

SEQUOIA (BGB-3111-304)

Study Design



- **Endpoints for Arm C: ORR (IRC and investigator assessments), PFS, DOR, safety**
- **Response assessment: per modified iwCLL criteria for CLL[2,3] and Lugano criteria for SLL[4] (IRC and investigator assessments)**

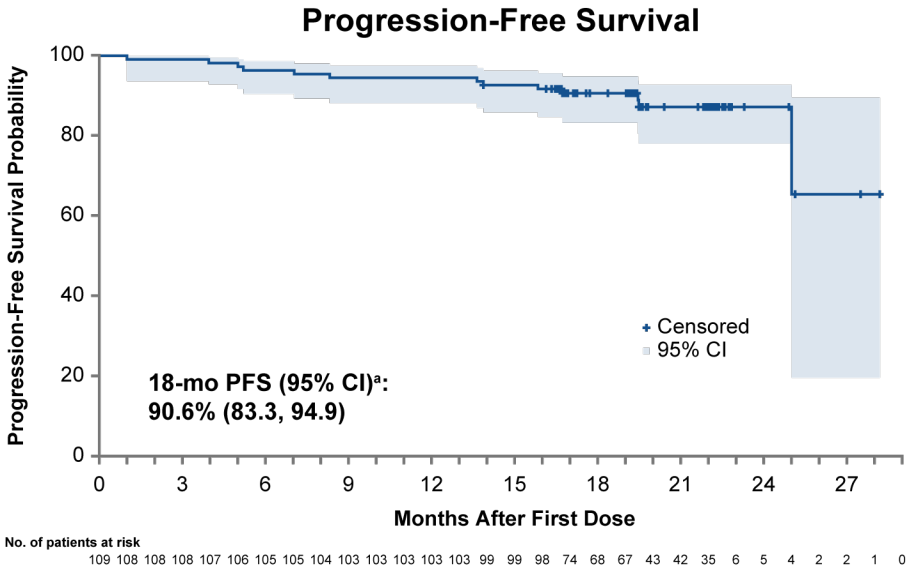
bid, twice daily; CLL/SLL, chronic lymphocytic leukemia/small lymphocytic lymphoma; DOR, duration of response; FCR, fludarabine, cyclophosphamide, and rituximab; FISH, fluorescence in situ hybridization; IRC, independent review committee; iwCLL, international workshop on CLL; ORR, overall response rate; PD, progressive disease; PFS, progression-free survival; R, randomized; TN, treatment-naïve.

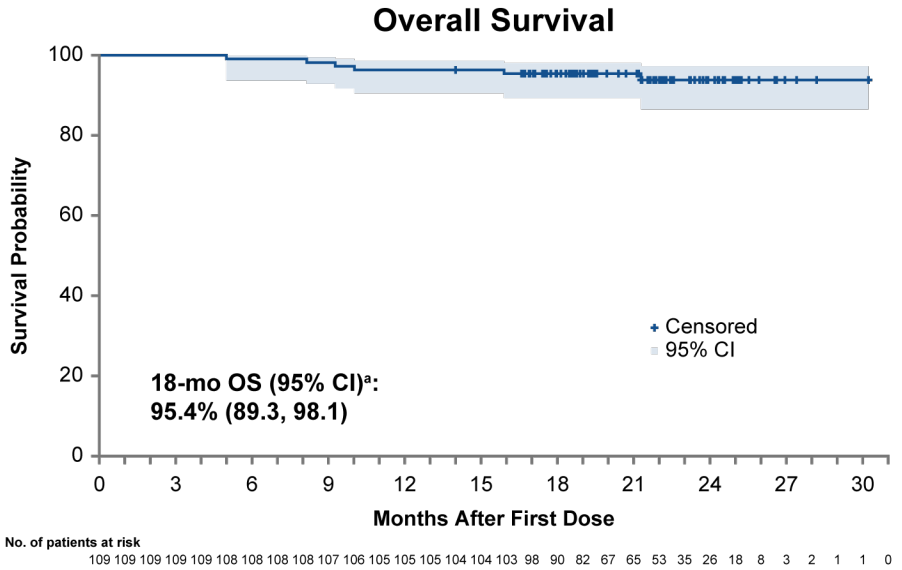
[a] *TP53* mutational status was not centrally assessed prior to enrollment.

1. Tam CS, et al. *ASH.* 2020; Abstract: 1318. 2. Hallek M, et al. *Blood*. 2008;111:5446-5456. 3. Cheson BD, et al. *J Clin Oncol.* 2012;30:2820-2822. 4. Cheson BD, et al. *J Clin Oncol*. 2014;32:3059-3067.

SEQUOIA Arm C (del-17p): PFS and OS

Investigator Assessment





- 12 patients had investigator-reported PD
  - 5 patients had investigator-assessed RT
  - Median time to transformation was 13.6 mo (range, 3.9 - 15.7)
- 1 patient had PD after discontinuing study drug treatment due to AE

- Reasons for death
  - 2 AE (pneumonia, renal failure (in the context of PD))
  - 3 PD (2 RT)
  - 1 sepsis after PD due to RT
- No reported sudden deaths

Data cutoff: August 10, 2020. Median follow-up (range): 21.9 months (5.0 – 30.2)
AE, adverse events; CI, confidence interval; mo, month(s); OS, overall survival; PD, progressive disease; PFS, progression-free survival; RT, Richter transformation.
[a] 2-sided Clopper-Pearson 95% confidence intervals.

Key Results of ALPINE

- Off therapy: 11% Zanubrutinib vs 24% Ibrutinib
- D/c for AEs: 7.8% Zanubrutinib vs 13% Ibrutinib
  - Afib: 2.5% Zanubrutinib vs 10.1% Ibrutinib
- Del17p ORR: 83% Zanubrutinib vs 54% Ibrutinib
- 12 mos PFS: Zanubrutinib 95% vs Ibrutinib 84%
- Favorable OS trend

Conclusions

- ALPINE (and prior data) demonstrate:
  - Improved tolerability of Zanubrutinib compared to ibrutinib
  - Encouraging activity in deletion 17p
  - Improved 12-month PFS with favorable OS trend, compared to Ibrutinib

BRUKINSA Program Update

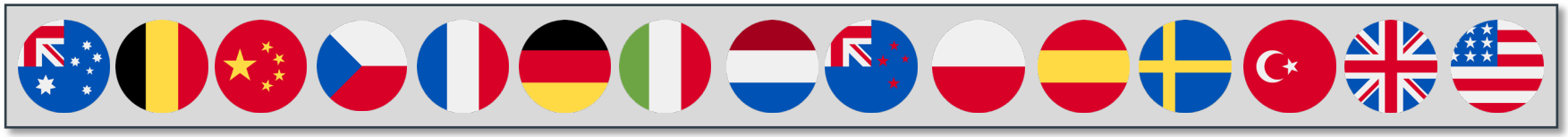
Jane Huang, M.D.

Chief Medical Officer, Hematology

Broad BRUKINSA Development

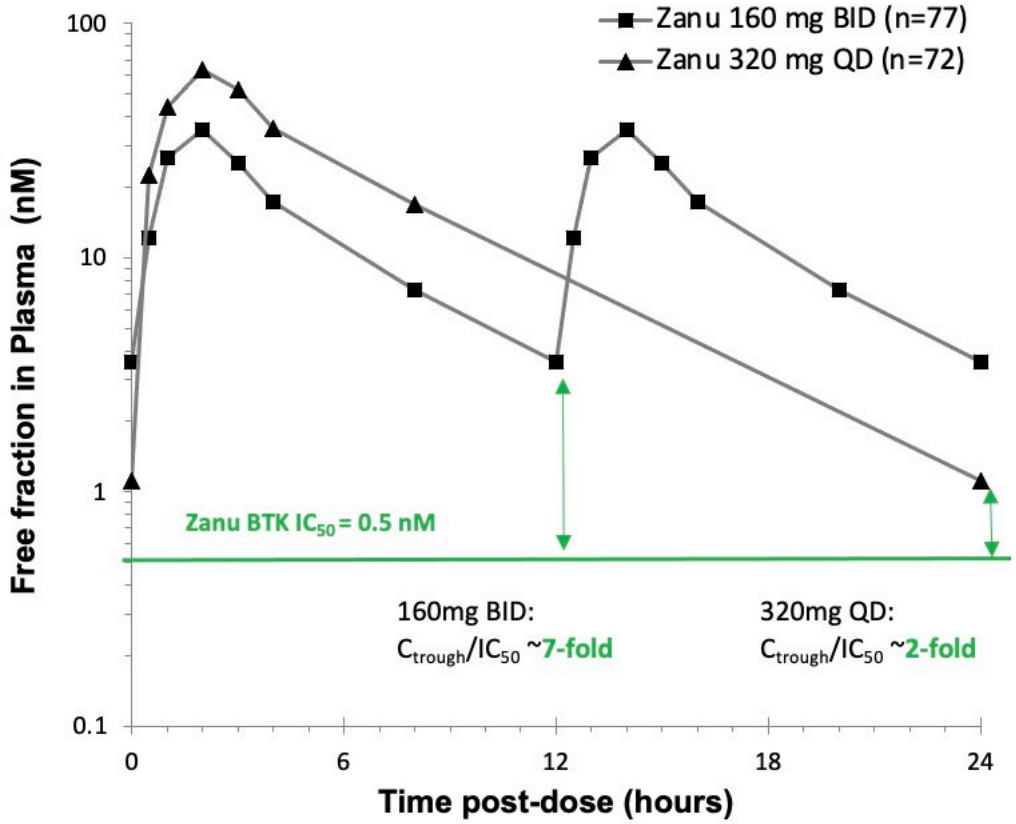
PHASE 1 PHASE 2 PHASE 3 Vs. Ibrutinib

	CLL/SLL	WM	MCL	MZL	DLBCL	FL	Mixed heme malignancies	Non-oncology
BRUKINSA Patients	> 1,100	> 300	>175	>100	>125	>250		
Company Sponsored	P3 P3 P2 P2	P3 P2 P2	P3 P2	P3 P2	P2 P2 P1	P2 P1	P2 P2 P1 P1 P1	P2
Investigator	P2 P2 P2 P2 P2 P2			P2	P2		P2 P2 P2 P2 P2	P2 P2 P2 P2 P1 P1

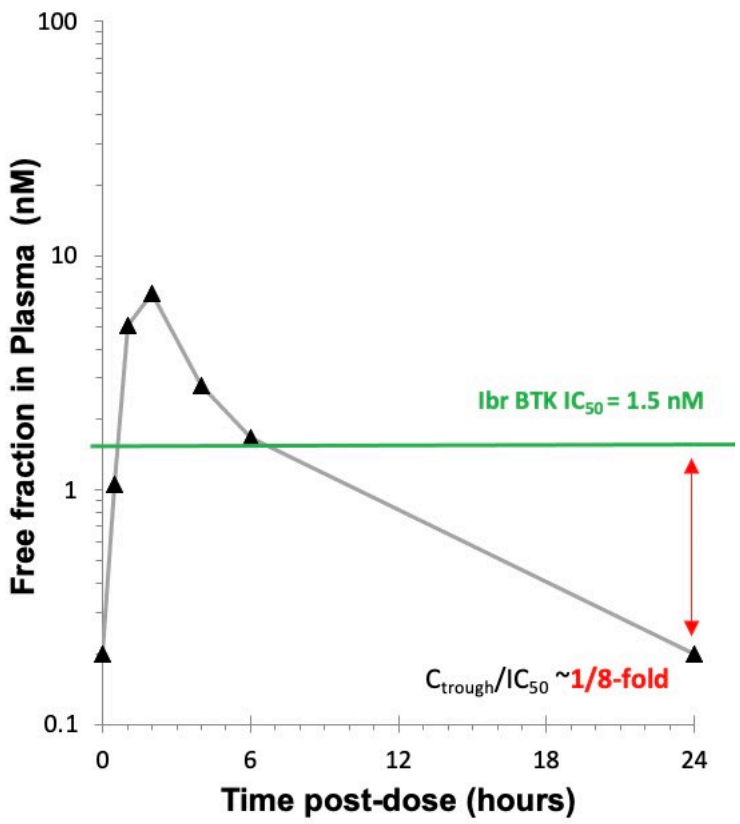


BTKi PK: Relative Time Spent Above IC_{50}

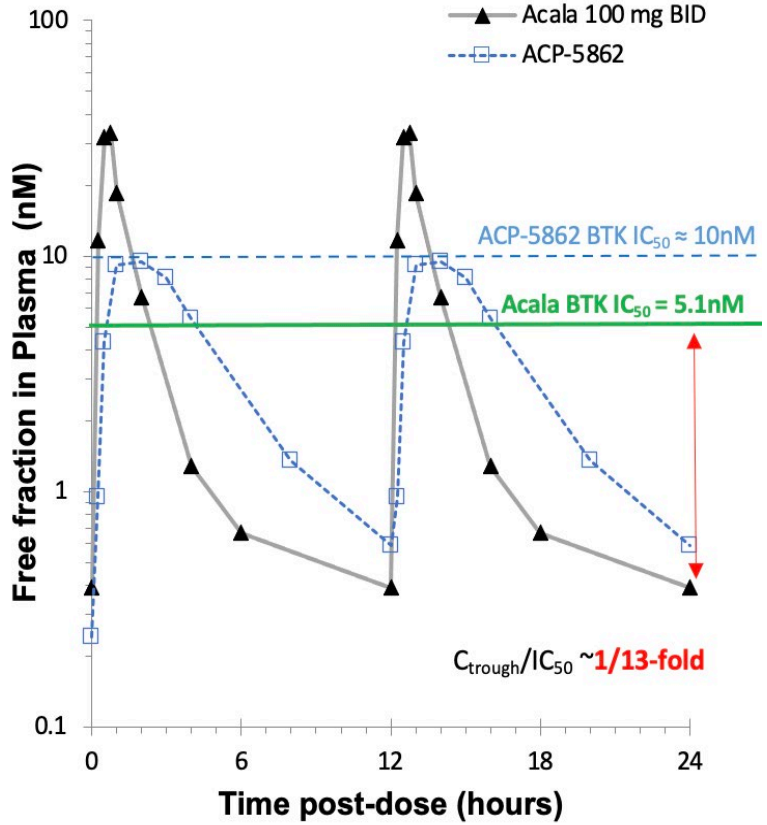
Zanubrutinib



Ibrutinib 560 mg QD



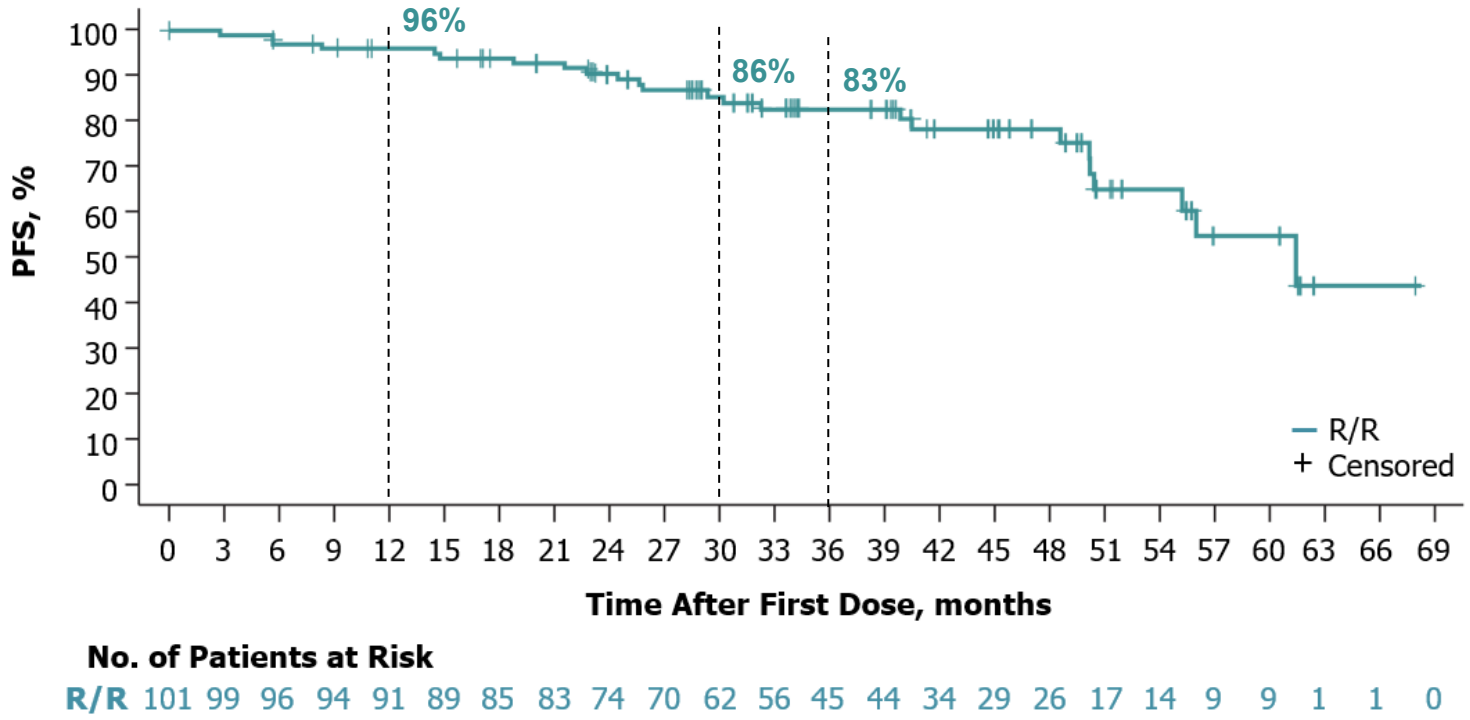
Acalabrutinib



Note: These data are from 3 separate analyses. Limitations of cross-trial comparisons apply.

BTK potencies of zanubrutinib, ibrutinib and acalabrutinib (IC_{50}) were based on biochemical assays from Kaptein et al *Blood* 2018;132:1871. PK and plasma protein binding data were obtained from published work (Byrd et al. *NEJM* 2016;374:323-32. Advani et al *JCO* 2013;31:88-94. Zhou et al. *CPT: PSP* 2019;8:489-99. Edlund et al. *Clin Pharmacokinet* 2019;58:659-72. Ou et al. *Leuk Lymphoma* in press. Ibrutinib Clin Pharm and Biopharmaceutics Review; FDA 205552Org2s000. The concentration time profiles for ibrutinib major active metabolite (PCI-45227) at 560 mg are not available, thus not summarized here. It has been noted that PCI-45227 is ~15-fold less potent compared to the parent molecule.

Strong Long-Term R/R CLL Data



- Median follow up 39.4 months
- 5.8% a-fib/flutter at median follow up

Source: Data on file.

ASPEN: Differentiated Efficacy and Safety vs. Ibrutinib

Primary endpoint: CR+VGPR

IRC

Zanubrutinib	Ibrutinib
28.4%	19.2%
CR+VGPR Rate difference = 10.2† (-1.5, 22.0) ***p*-value = 0.0921**	

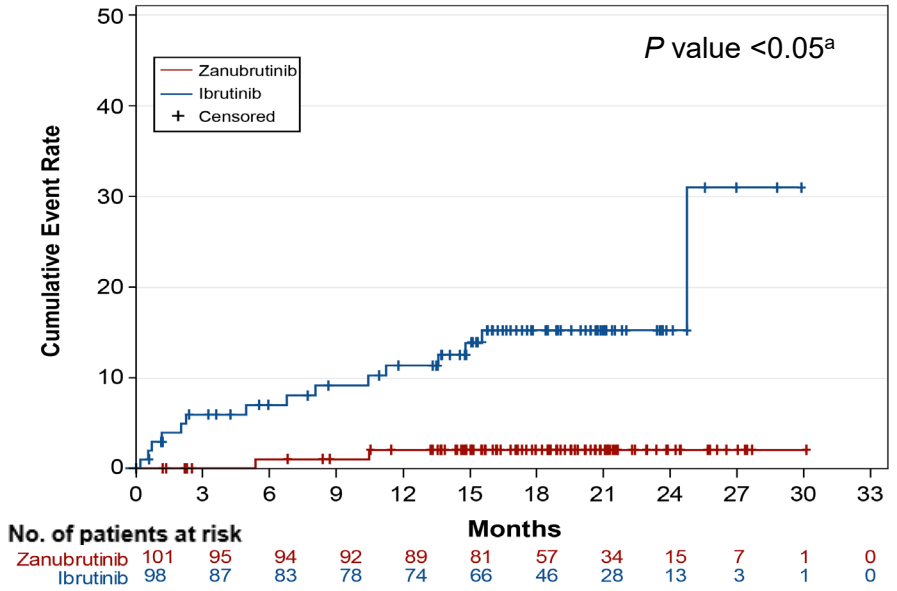
INVESTIGATOR

Zanubrutinib	Ibrutinib
28.4%	17.2%
CR+VGPR Rate difference = 12.1 † † (0.5, 23.7) ***p*-value = 0.0437**	

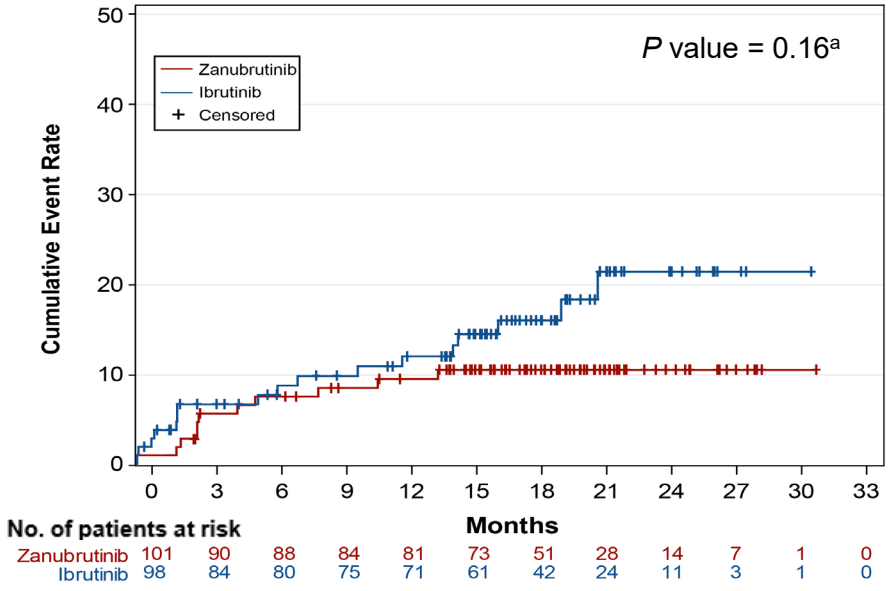
IRC – COHORT 2 *MYD88^{WT}*

Zanubrutinib
26.9%*

Kaplan-Meier Curve: Time to **Atrial Fibrillation / Flutter**



Kaplan-Meier Curve: Time to **Hypertension**

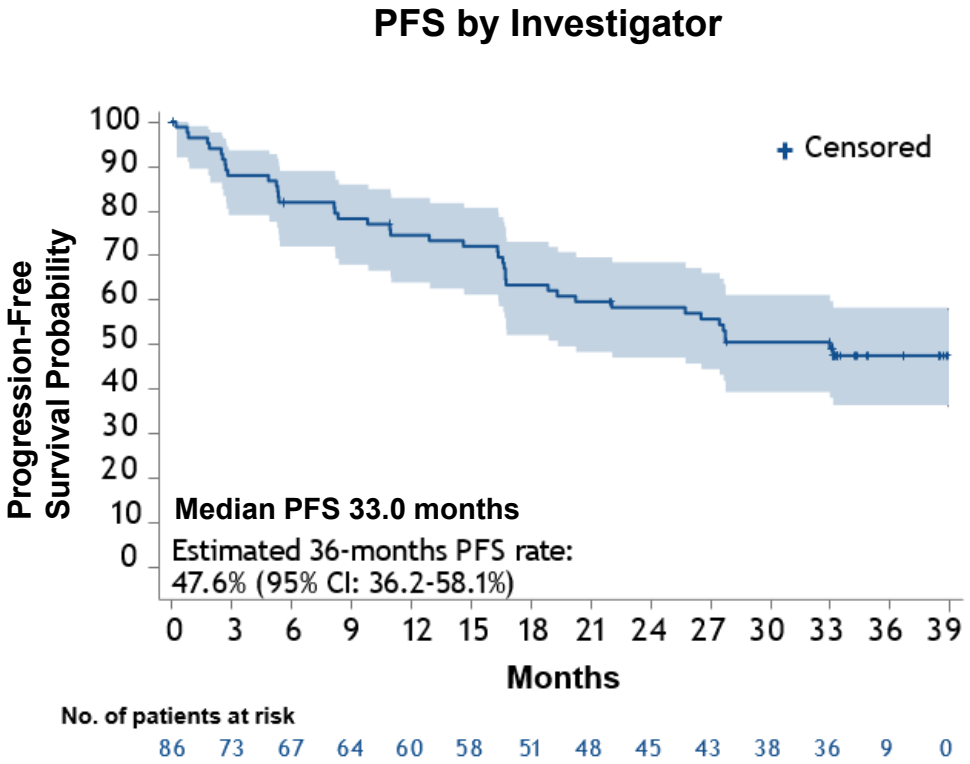


Source: Tam et. al., ASCO 2020. Garcia-Sanz et. al. ASCO 2020. AE, adverse event. a Descriptive purpose only. †Adjusted for stratification factors and age group. †† Adjusted for stratification factors and age group. p-value is for descriptive purpose only. * Non-controlled arm for ethical reasons.

Long-Term Data in R/R MCL Show Sustained Benefit

Median PFS of 33 months

Best Response	N=86
ORR (CR + PR), % (95% CI)	83.7 (74.2-90.8)
Best response, n (%)	
CR	67 (77.9)
PR	5 (5.8)
SD	1 (1.2)
PD	8 (9.3)
Discontinued prior to first assessment	5 (5.8)
Median time to response, months (range)	2.73 (2.5-3.0)
Median time to CR, months (range)	2.79 (2.5-16.7)
Median DOR, months (95% CI)	NE (24.9-NE)
Event-at risk free rate at 30 months, % (95% CI)	57.3 (44.9-67.9)

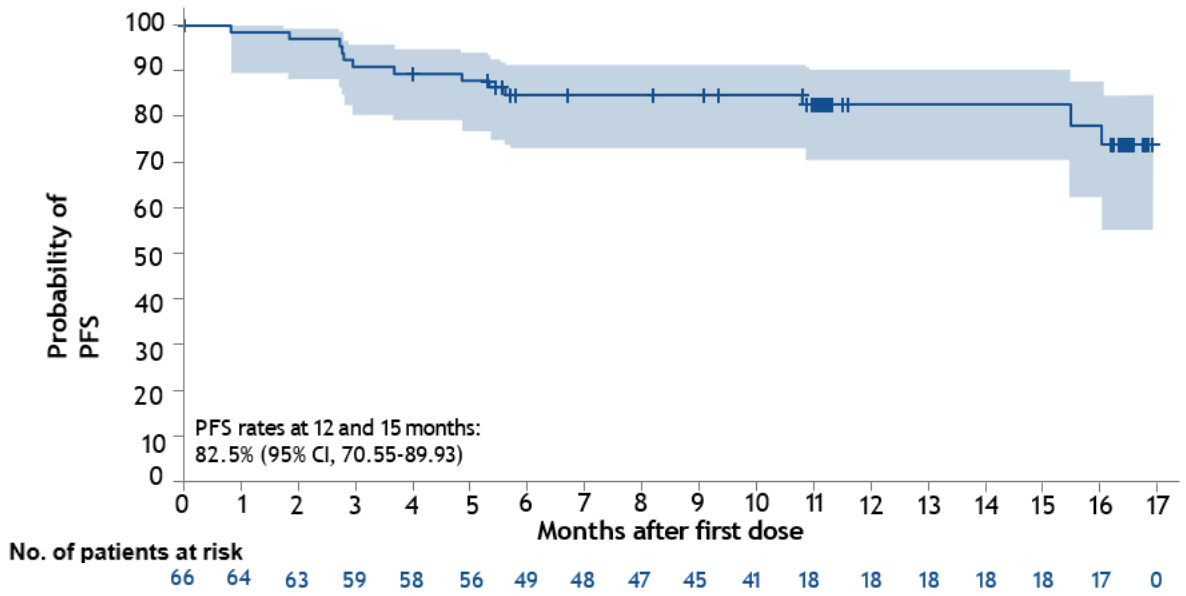


Safety summary, N=86 patients: Data as: 18.4 months follow-up, n (%), and 35.3 months follow-up, n (%). Grade ≥3 TEAEsa, 36 (41.9), 43 (50.0), Serious TEAEs, 21 (24.4), 25 (29.1), TEAEs leading to study drug discontinuation, 8 (9.3), 8 (9.3), TEAEs leading to study drug interruption, 13 (15.1), 16 (18.6), TEAEs leading to study drug reduction, 2 (2.3), 2 (2.3), Death due to TEAE[b], 5 (5.8)[c], 5 (5.8)[c]

Source: Song et. al. EHA 2021. CR, complete response; DOR, duration of response; NE, not estimable; ORR, overall response rate; PD, progressive disease; PR, partial response; SD, stable disease.
[a]Adverse event grades are evaluated based on National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE, version 4.03). [b]Death within 30 days of the last dose of zanubrutinib. [c]The 5 deaths due to TEAE included pneumonia, cerebral hemorrhage, traffic accident, and 2 deaths with unknown reason.

High ORR and CR Rates in R/R MZL

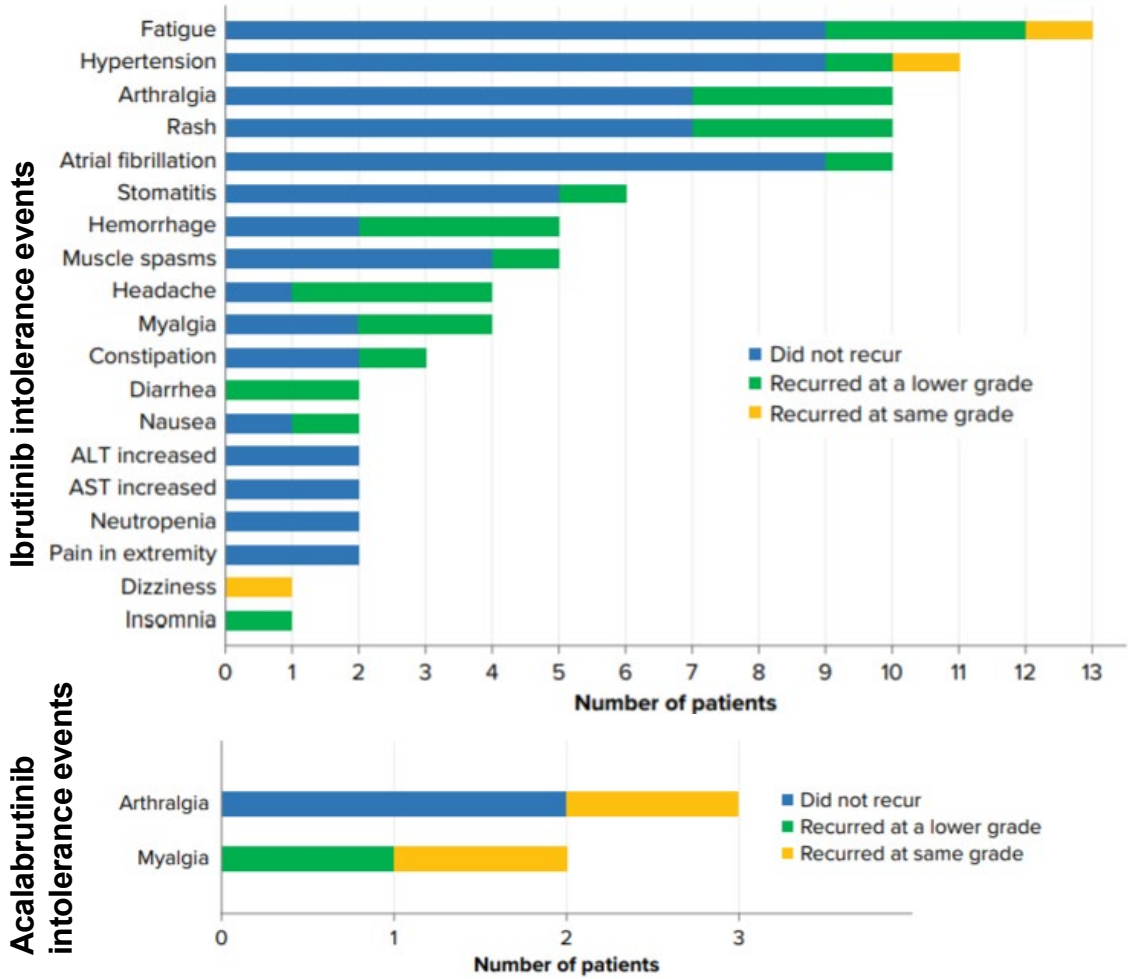
Best response by Investigator	Total (N=66[a])
ORR (CR or PR), n(%) 95% CI[b]	45 (68.2) (55.56-79.11)
Complete response	17 (25.8)
Partial response	28 (42.4)
Stable response	13 (19.7)
Nonprogressive disease	1 (1.5)
Progressive disease	6 (9.1)
Discontinued prior to first assessment	1 (1.5)



Safety summary: Category, n (%), Overall (n=68): Patients with ≥ 1 TEAE , 65 (95.6), Grade ≥3 TEAE, 27 (39.7), Serious TEAE, 26 (38.2), TEAE leading to dose interruption, 20 (29.4), AE leading to treatment discontinuation, 4 (5.9)[a], AE leading to death, 3 (4.4)[a], AE leading to dose reduction, 0. a. One patient discontinued due to pyrexia (later attributed to disease progression);

Source: Opat et. al. EHA 2021. Data cutoff: January 18, 2021.
[a]Two patients were excluded due to lack of central confirmation of MZL.
[b]Two-sided Clopper-Pearson 95% CI.
[c]One patient with FDG-avid disease missed the PET scan at Cycle 3 and was assessed as having nonprogressive disease by independent review due to missing PET scan. CT scan results showed stable disease at Cycle 3.
[d]One patient (extranodal MZL) withdrew consent prior to the first disease assessment.
CR, complete response; CT, computed tomography; FDG, fludeoxyglucose; MZL, marginal zone lymphoma; ORR, overall response rate; PET, positron emission tomography; PR, partial response.

Low Recurrence of BTKi Intolerance on Zanubrutinib



Conclusions

- Intolerable AEs experienced on Ibrutinib or Acalabrutinib were unlikely to recur with Zanubrutinib
  - 75% of Ibrutinib and Acalabrutinib intolerance events did not recur with Zanubrutinib
  - No recurrence of a prior intolerance event led to Zanubrutinib discontinuation
- Zanubrutinib was effective; 90% of patients' disease was controlled or responded to therapy

Source: Shadman et. al. EHA 2021. Data cutoff: 01 Mar 21. ALT, alanine aminotransferase; AST, aspartate transaminase.[a] Intolerance events occurring in ≥2 patients or recurring in ≥1 patient shown here. BOR, best overall response; DCR, disease control rate; CR, complete response; ORR, overall response rate; PR, partial response; PR-L, PR with lymphocytosis; SD, stable disease; VGPR, very good partial response.1. Disease parameters performed at study entry were used as baseline for response assessment. 2. IgM values were not measured for Waldenström macroglobulinemia patient. 3. One patient withdrew from study before first assessment timepoint because of syncope; 1 patient died from COVID-19 pneumonia before first response assessment. AE, adverse event. 4. Pain in jaw (grade 2), COVID-19 pneumonia (grade 5), anemia (grade 2). 5. Febrile neutropenia (grade 3) and gastroenteritis salmonella (grade 3), COVID-19 (grade 3). 6. Penile bleed (grade 2), COVID-19 pneumonia (grade 5), increased alanine aminotransferase and aspartate transaminase (grade 3). 7. COVID-19 pneumonia.

Incidence of Any-Grade Atrial Fibrillation/Flutter Significantly Lower With Zanubrutinib

Key secondary endpoint

	ALPINE		ASPEN	
	Zanubrutinib (n=204)	Ibrutinib (n=207)	Zanubrutinib (n=101)	Ibrutinib (n=98)
Afib/flutter	**5 (2.5)**	**21 (10.1)**	**2 (2.0)**	**15 (15.3)**
Events/100 person-months	0.16	0.76	0.1	1
Afib/flutter incidence among patients without prior history of afib/flutter	4 / 193 (2.1)	18 / 194 (9.3)	2/91 (2.2)	12/90 (13.3)

Key Takeaways from EHA Presentations

- EHA data supportive of the underlying hypothesis that sustained target occupancy may produce meaningful improvement in efficacy and selective BTK inhibition offers better safety
- CLL
  - ALPINE trial, second head-to-head trial against Ibrutinib, interim analysis data continue to show advantages of Zanubrutinib in efficacy and safety, including superiority by investigator assessment in ORR, improved PFS* and significantly lower atrial fibrillation rate
- MCL
  - Long-term follow-up data from Phase 2 R/R MCL further demonstrates high CR rate translates into prolonged PFS
- MZL
  - Phase 2 MAGNOLIA trial in MZL showed high ORR and CR rate relative to ibrutinib studies
- Consistent data across multiple indications including long-term follow-up data and activity in hard-to-treat populations

*Not a prespecified analysis. PFS data were early at the time of interim analysis and formal analysis will be performed when the target number of events is reached.

BRUKINSA Global Development – Near-Term Events

- Broad global program with over 25 trials in 8 indications with more than 3,100[1] subjects in trials, with best-in-class hypothesis (safety and efficacy) consistently demonstrated across the board
- Filed over 30 applications covering countries in the EU and over 20 other countries
- Near-term events:
  - Topline data from SEQUOIA as early as 2H21
  - Have regulatory discussions based on SEQUOIA and ALPINE
  - Complete patient enrollment for Phase 2 ROSEWOOD trial in R/R FL in 2021
  - Potential approvals in 2021 for:
    - WM in the U.S. (PDUFA date on October 18), EU, China, and Australia
    - MZL in the US (PDUFA date September 19)
    - MCL in Canada, Australia, Russia, Middle East, and South America

Regions and countries with marketing application filed

1 As of January 2021.

Concluding Remarks

John V. Oyler

Co-Founder, Chairman, and CEO

BRUKINSA

- BRUKINSA is the only second generation BTK to:
  - Run two head-to-head studies against BTK in two indications
  - Show improved efficacy and safety in head-to-head
  - File in MZL and WM
  - Offer BID/QD dosing flexibility and useability with PPIs
- Consistent results across broad, global program
- Substantial long-term follow-up data (e.g., R/R CLL study above)
- Supports our mechanistic hypothesis that complete and sustained inhibition will result in superior efficacy
- Encouraging share penetration
- Working towards vision of bringing this medicine to more people around the world
  - Approved for MCL in U.S., China, and UAE; CLL/SLL in China; and for WM in Canada[1]
  - More than 30 marketing authorization applications covering the EU and more than 20 countries outside of the U.S. and China
- BRUKINSA is the cornerstone of hematology franchise that includes our Bcl-2 inhibitor

1. China approvals for R/R MCL and R/R CLL/SLL under accelerated pathway. US approval for R/R MCL under accelerated pathway. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

Conclusion

1. BRUKINSA's totality of evidence supports our best-in-class hypothesis
2. Development of BRUKINSA exemplifies power of our unique strategic competitive advantages
3. Our portfolio includes over 40 potential medicines, 8 approved medicines, 4 more filed
4. We are striving to bring better medicines to more patients, more affordably

BEIGENE

Q&A

Q&A Participants

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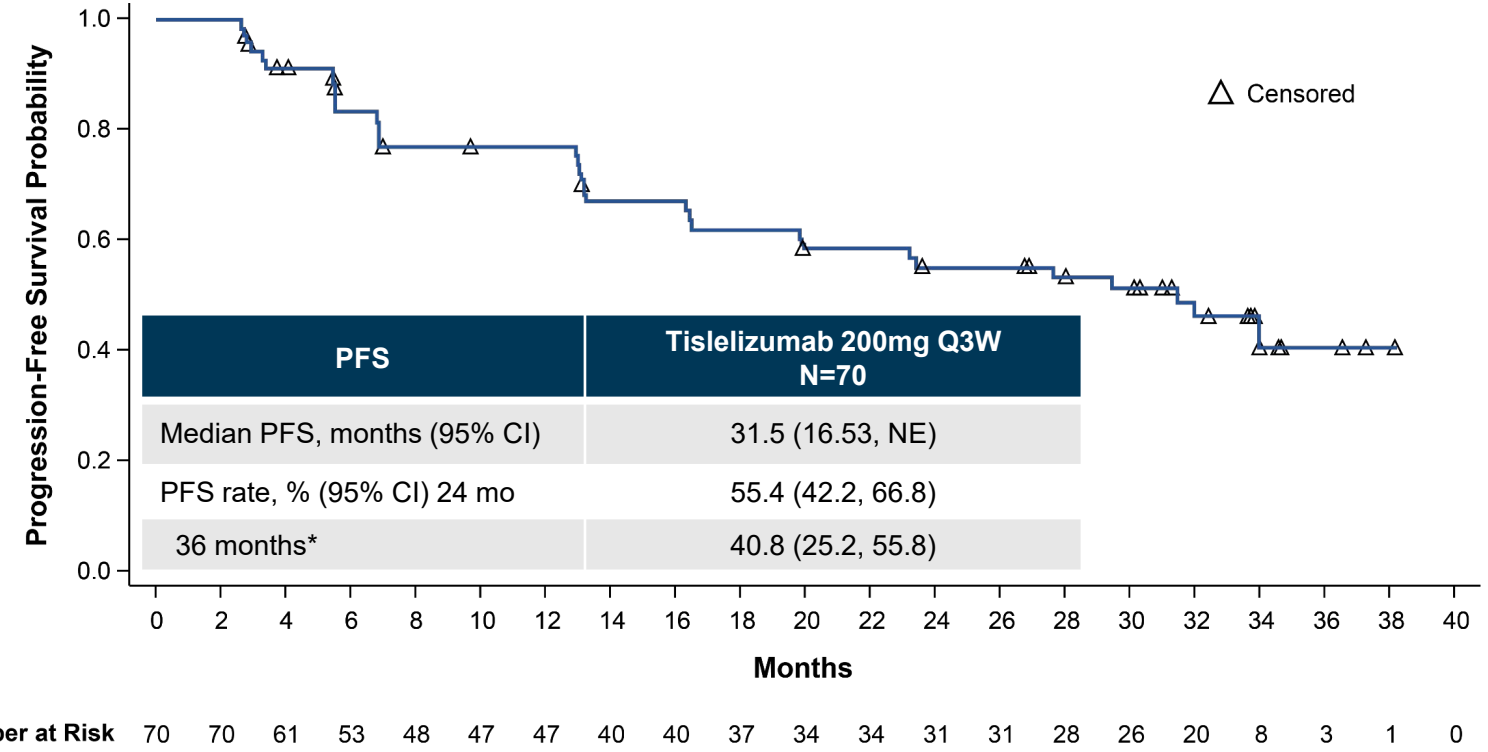
Xiaobin Wu, Ph.D.
President, Chief Operating Officer, and General Manager of China

Josh Neiman
SVP, Chief Commercial Officer, North America and Europe

BEIGENE

Backup

Tislelizumab: cHL Long-Term PFS and Safety



PFS	Tislelizumab 200mg Q3W N=70
Median PFS, months (95% CI)	31.5 (16.53, NE)
PFS rate, % (95% CI) 24 mo	55.4 (42.2, 66.8)
36 months*	40.8 (25.2, 55.8)

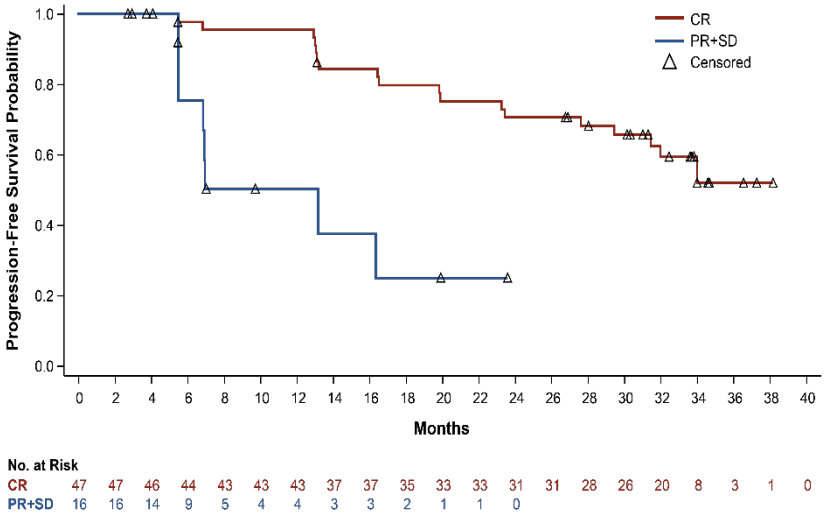
Best response[a], n (%)	N=70
ORR	**61 (87.1)**
(95% CI[b])	**(77.0–93.9)**
CR	47 (67.1)
(95% CI[b])	(54.9–77.9)
PR	14 (20.0)
SD	2 (2.9)
PD	6 (8.6)
Died before any post baseline tumor assessment[c]	1 (1.4)

Safety Summary: Event, n (%), N=70: Patients with at least one TEAE, 68 (97.1), Grade ≥3 TEAE, 29 (41.4), Serious, 18 (25.7), Leading to treatment discontinuation, 6 (8.6), TRAE, 68 (97.1), Grade ≥3 TRAE, 22 (31.4), imAE, 32 (45.7), Most common: hypothyroidism (28.6%), skin adverse reaction (8.6%), pneumonitis (7.1%).
(imAE, immune-mediated adverse event; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event)

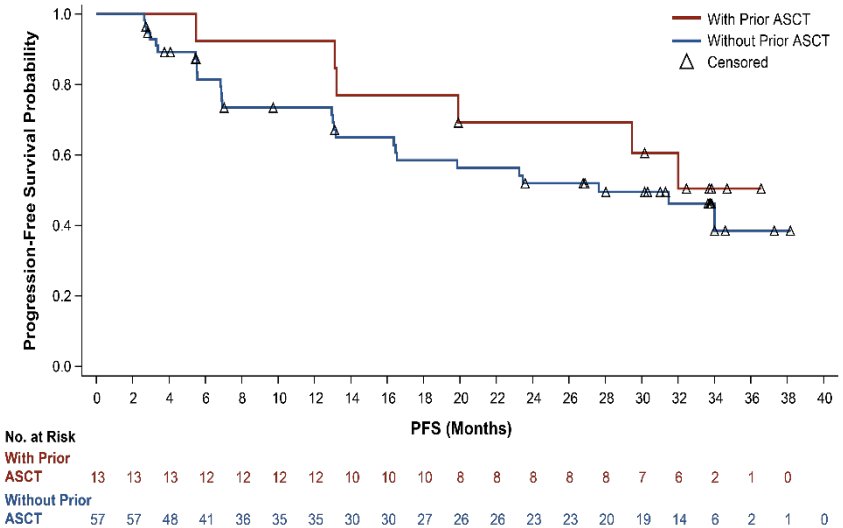
CR, complete response; IRC, independent review committee; NE, not estimable; ORR, overall response rate; PD, progressive disease; PFS, progression-free survival; PR, partial response; Q3W, every 3 weeks; SD, stable disease. *Note: Data to be interpretated with caution due to smaller subject number at risk. [a]Response assessment by IRC according to the Lugano Classification.[1] [b]1-sided Clopper-Pearson 95% CI. [c]Died due to disease progression, not related to study drug. 1. Cheson BD, et al. J Clin Oncol. 2014;32:3059-3067.

Tislelizumab: cHL Long-Term PFS by Subgroup

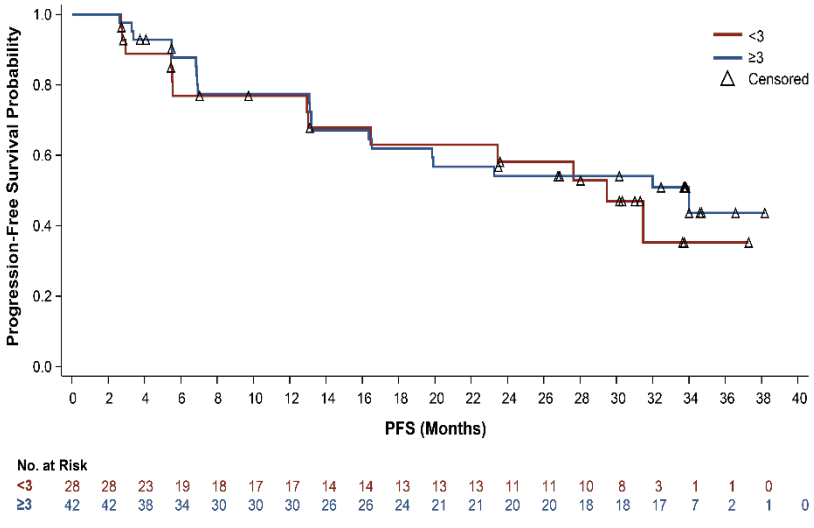
BOR



Prior ASCT



Prior lines of therapy



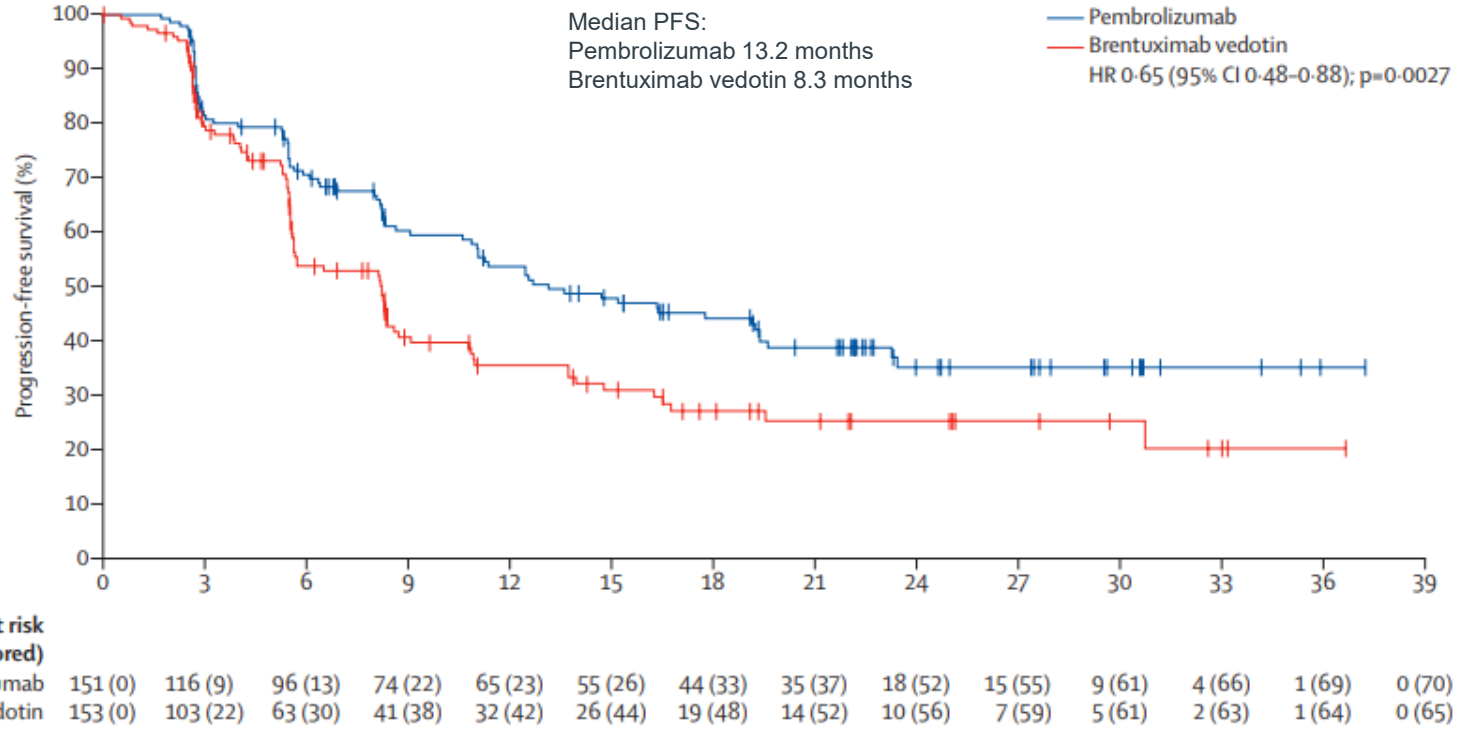
PFS	CR (n=47)	PR+SD (n=16)
Median PFS, months (95% CI)	NE (29.5, NE)	13.2 (5.5, NE)

PFS	Prior ASCT (n=13)	No prior ASCT (n=57)
Median PFS, months (95% CI)	NE (13.2, NE)	27.6 (16.4, NE)

PFS	<3 lines (n=28)	≥3 lines (n=42)
Median PFS months (95% CI)	29.5 (13.0, NE)	34.0 (16.4, NE)

ASCT, autologous hematopoietic stem cell transplant; BOR, best overall response; CR, complete response; No., number; PR, partial response; SD, stable disease; NE, not estimable; PFS, progression-free survival.

Pembrolizumab in R/R cHL



BOR by IRC	Pembro n=151	Brentuximab vedotin n=153
ORR (95% CI)	**66 (57-73)**	**54 (46-62)**
CR	25	24
PR	41	30
SD	14	24
PD	17	18

Source: Kuruvilla et. al. The Lancet Oncology 2021 https://doi.org/10.1016/ S1470-2045(21)00005-X. BOR, best overall response; CR, complete response; IRC, independent review committee; PR, partial response; SD, stable disease; NE, not estimable; PD, progressive disease PFS, progression-free survival.