BeiGene

2022 ASH Late Breaker Data Discussion

DECEMBER 13, 2022

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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.

AGENDA & SPEAKERS

- **Introduction:** John V. Oyler
- **BRUKINSA ALPINE Overview:** Jennifer R. Brown, M.D., Ph.D.
- **BRUKINSA Data:** Mazyar Shadman, M.D., M.P.H.
- **Key Takeaways:** Mehrdad Mobasher, M.D., M.P.H.
- **Q&A**

Introduction

John V. Oyler
Co-Founder, Chairman, and CEO

BeiGene

At A Glance

@BeiGeneGlobal BeiGene

Founded
2010

Co-Founder, Chairman, and CEO
John V. Oyler

30 Offices, **9,000+** Colleagues on **5** Continents

900+ Oncology Research Team

3,300+ Clinical Development & Medical Affairs Team

3,500+ Commercial Team in China, North America and Europe

60+ Pre-clinical programs, the majority with first-in-class potential

~50+ Assets in clinical and commercial stages

~20 Industry Collaborations

TRANSLATING SCIENCE TO IMPROVE ACCESS AND AFFORDABILITY BY CHALLENGING THE STATUS QUO

Trials Span

45+

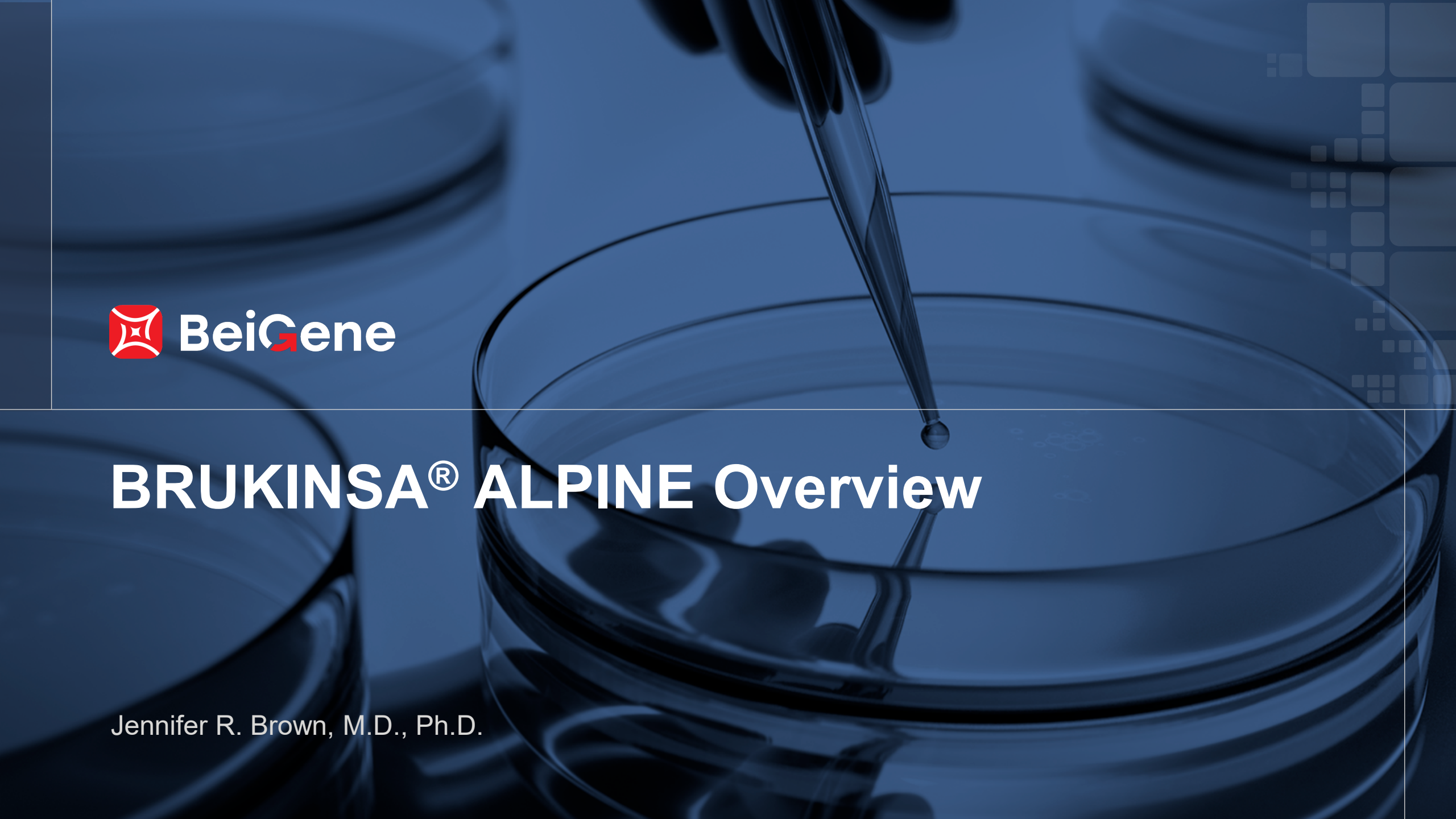
Countries & Regions

20K+

People Enrolled in

110+

Clinical Trials



BRUKINSA® ALPINE Overview

Jennifer R. Brown, M.D., Ph.D.

Jennifer R. Brown, M.D., Ph.D.

Director, Chronic Lymphocytic Leukemia (CLL) Center at the Dana Farber Cancer Institute

- Institute Physician

- Worthington and Margaret Collette Professor of Medicine in the Field of Hematologic Oncology, Harvard Medical School

- Clinical interests include chronic lymphocytic leukemia, lymphoma, stem cell/bone marrow transplant

- Education:

- Fellowship: Dana-Farber/Partners CancerCare, Medical Oncology

- Residency: Massachusetts General Hospital, Internal Medicine

- Medical School: Harvard Medical School

Zanubrutinib Demonstrates Superior Progression Free Survival Compared with Ibrutinib for Treatment of Relapsed/Refractory Chronic Lymphocytic Leukemia and Small Lymphocytic Lymphoma: Results from Final Analysis of ALPINE Randomized Phase 3 Study

Jennifer R. Brown, MD, PhD[1], Barbara Eichhorst, MD[2], Peter Hillmen, MD PhD[3], Nicole Lamanna, MD[4], Susan M. O'Brien, MD[5], Constantine S. Tam, MBBS, MD[6,7], Lugui Qiu, MD[8], Maciej Kaźmierczak, MD, PhD[9], Wojciech Jurczak, MD, PhD[10], Keshu Zhou, MD, PhD[11], Martin Simkovic MD, PhD[12,13], Jiri Mayer, MD[14], Amanda Gillespie-Twardy, MD[15], Alessandra Ferrajoli, MD[16], Peter S. Ganly, BMBCh, PhD[17], Robert Weinkove, MBBS, PhD[18,19], Sebastian Grosicki, MD, PhD[20], Andrzej Mital, MD, PhD[21], Tadeusz Robak, MD, PhD[22], Anders Osterborg, MD, PhD[23,24], Habte A. Yimer, MD[25], Tommi Salmi, MD[26], Megan (Der Yu) Wang, PharmD[26], Lina Fu, MS[26], Jessica Li, MS[26], Kenneth Wu, PhD[26], Aileen Cohen, MD, PhD[26], Mazyar Shadman, MD, MPH[27,28]

1Dana-Farber Cancer Institute, Boston, MA, USA; 2University of Cologne, Cologne, Germany; 3St James's University Hospital, Leeds, United Kingdom; 4Columbia University, New York, NY, USA; 5University of California, Irvine, CA, USA; 6The Alfred Hospital, Melbourne, Victoria, Australia; 7Monash University, Melbourne, Victoria, Australia; 8National Clinical Research Center for Hematological Disorders, Institute of Hematology and Blood Diseases Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Tianjin, China; 9Department of Hematology and Bone Marrow Transplantation, Poznan University of Medical Sciences, Poznan, Poland; 10Maria Sklodowska-Curie National Research Institute of Oncology, Krakow, Poland; 11Affiliated Cancer Hospital of Zhengzhou University, Henan Cancer Hospital, Zhengzhou, China; 124th Department of Internal Medicine - Hematology, University Hospital, Hradec Kralove, Czech Republic; 13Faculty of Medicine, Charles University, Prague, Czech Republic; 14Department of Internal Medicine-Hematology and Oncology, Masaryk University and University Hospital, Brno, Czech Republic; 15Blue Ridge Cancer Care, Roanoke, VA, USA; 16Department of Leukemia, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; 17Department of Haematology, Christchurch Hospital, Christchurch, New Zealand; 18Te Rerenga Ora Blood and Cancer Centre, Te Whatu Ora Health New Zealand Capital Coast & Hutt Valley, Wellington, New Zealand; 19Cancer Immunotherapy Programme, Malaghan Institute of Medical Research, Wellington, New Zealand; 20Department of Hematology and Cancer Prevention, Health Sciences Faculty, Medical University of Silesia, Katowice, Poland; 21Department of Hematology and Transplantology, Medical University of Gdańsk, Gdańsk, Poland; 22Medical University of Lodz, Lodz, Poland; 23Department of Oncology-Pathology, Karolinska Institutet, Stockholm, Sweden; 24Department of Hematology, Karolinska University Hospital, Stockholm, Sweden; 25Texas Oncology-Tyler/US Oncology Research, Tyler, TX, USA; 26BeiGene (Beijing) Co., Ltd., Beijing, China and BeiGene USA, Inc., San Mateo, CA, USA; 27Fred Hutchinson Cancer Center, Seattle, WA, USA; 28University of Washington, Seattle, WA, USA

Tuesday, December 13, 2022: 9:00-10:30 AM
Late-Breaking Abstracts Session

64th ASH Annual Meeting and Exposition,
December 10-13, 2022 **LBA #6**

Bruton Tyrosine Kinase Inhibition in CLL: Background

- B-cell antigen receptor (BCR) signaling is required for tumor expansion and proliferation in CLL and B-cell lymphomas[1]
  - BCR signaling is dependent on BTK (Bruton's Tyrosine Kinase)
- Ibrutinib, a first-in-class, covalent BTK inhibitor, has transformed CLL therapy; however, it has properties that limit use
  - Treatment discontinuation from toxicities has been reported in 16%-23% of patients[3-6]
  - Exposure coverage between dosing intervals falls below IC_{50} and variable BTK occupancy at trough has been observed

Ibrutinib concentration-time profile

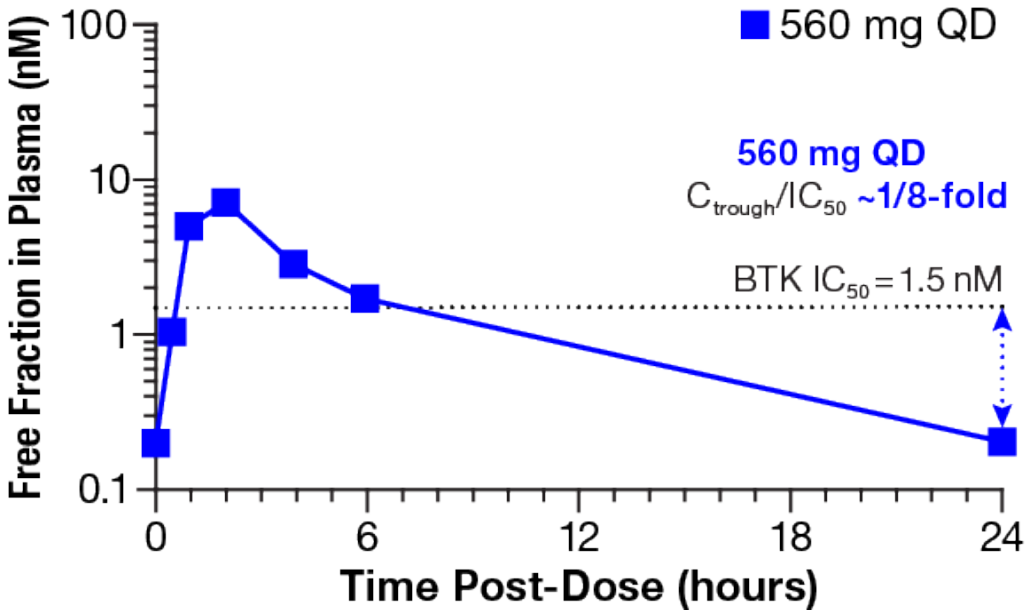


Figure adapted from Tam CS et al. *Expert Rev Clin Pharmacol*. 2021;14:11, 1329-1344

1. Singh SP, Dammeijer F and Hendriks RW. *Molecular Cancer.* 2018; 17:57.; 2. Molis S, Matures E, Tam C, Polliack A. *Hematol Oncol*. 2020; 38: 129-136; 3. Sharman JP, Black-Shinn JL, Clark J, et al. *Blood*. 2017;130(suppl 1):4060; 4. Mato AR, Nabhan C, Thompson MC, et al. *Haematologica*. 2018;103(5):874-879; 5. Munir T, Brown JR, O'Brien S, et al. *Am J Hematol*. 2019;94(12):1353-1363; 6. Ghia P, Owen C, Robak T, et al. EHA Abstract EP636 2021.

Zanubrutinib: Differentiating Features and Background

- Zanubrutinib is a second-generation Bruton tyrosine kinase inhibitor (BTKi)
  - Zanubrutinib was designed to have greater BTK specificity than ibrutinib
  - Zanubrutinib has exposure coverage above its IC_{50}
  - Higher drug-concentration/IC_{50} ratios would be expected to lead to more sustained and complete BTK inhibition to improve efficacy
- Zanubrutinib has demonstrated superior PFS by IRC over chemoimmunotherapy in treatment-naive CLL/SLL patients without del(17p)[1]

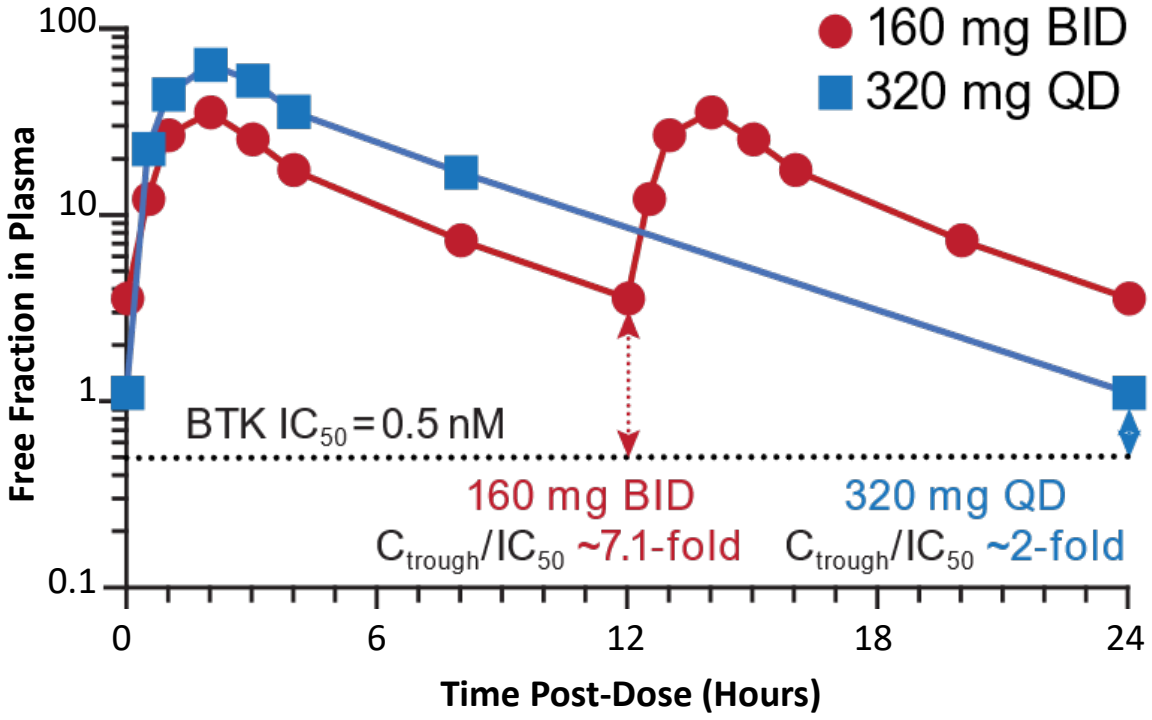


Figure modified from Ou YC, Tang Z, Novotny W, et al *Leukemia & Lymphoma.* 2021; 62(11):2612-2624.

[1]Tam CS, Brown JB, Kahl BS, et al. *Lancet Oncol*. 2022. https://doi.org/10.1016/S1470-2045(22)00293-5

ALPINE Study Design

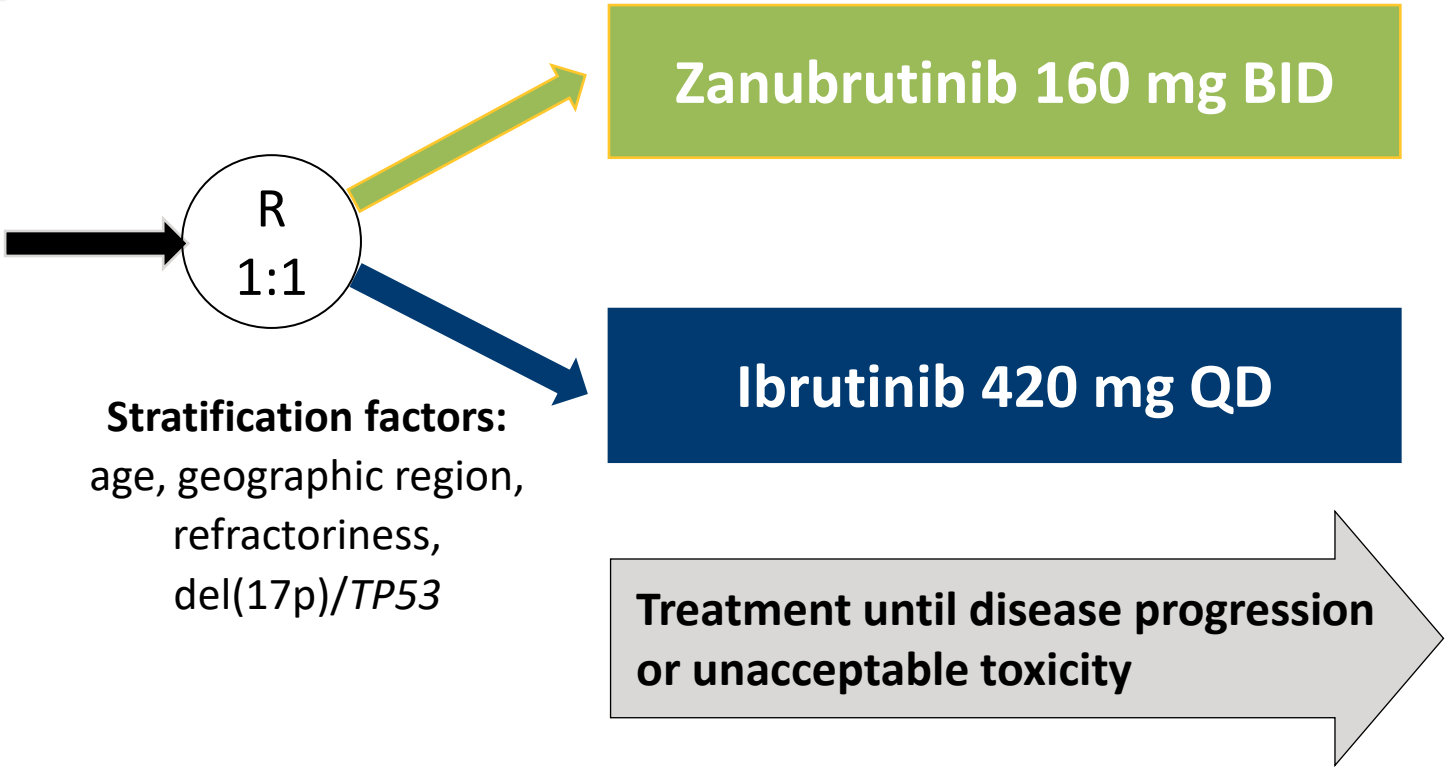
R/R CLL/SLL with ≥ 1 prior treatment
(Planned N=600, Actual N=652)

Key Inclusion Criteria

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

Key Exclusion Criteria

- Prior BTK inhibitor therapy
- Treatment with warfarin or other vitamin K antagonists



Endpoints and Statistical Design

Primary Endpoint

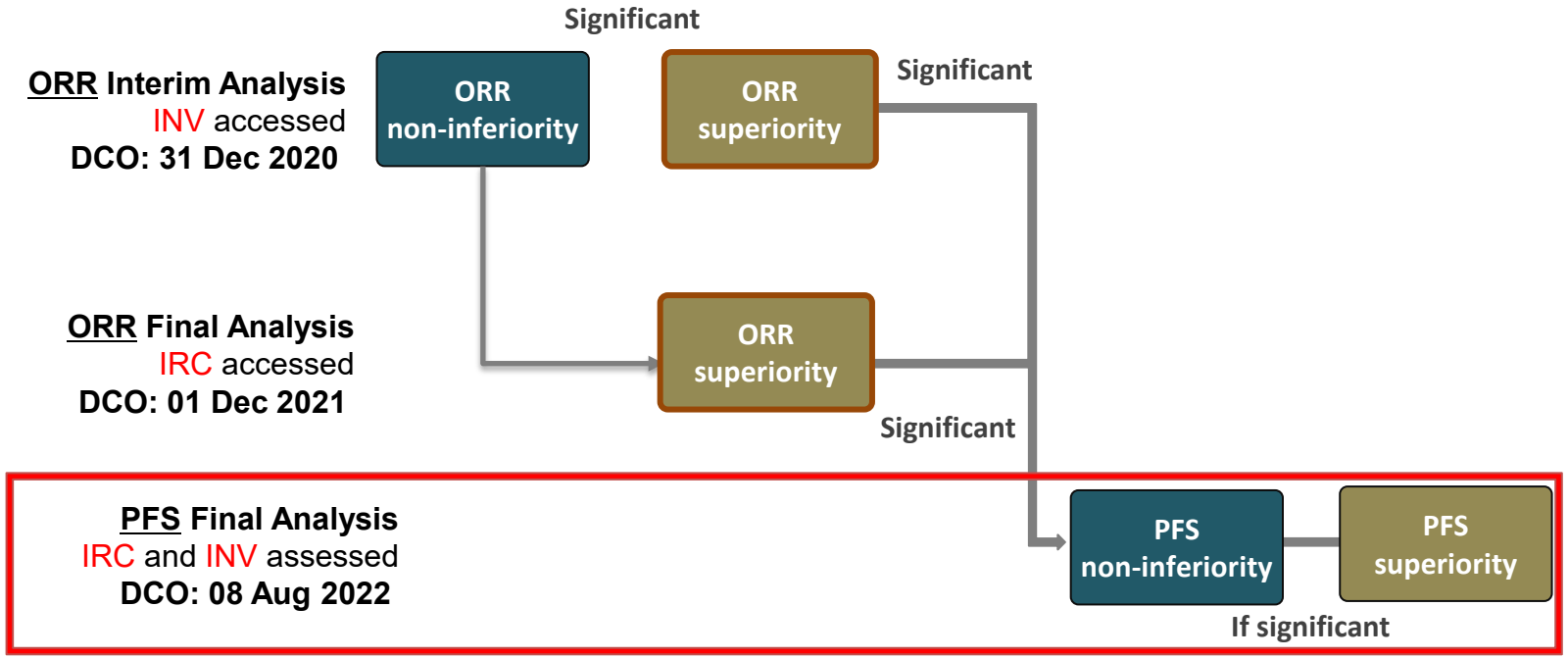
- ORR (PR+CR) noninferiority and superiority (by investigator)

Key Secondary Endpoints

- PFS
- Incidence of atrial fibrillation

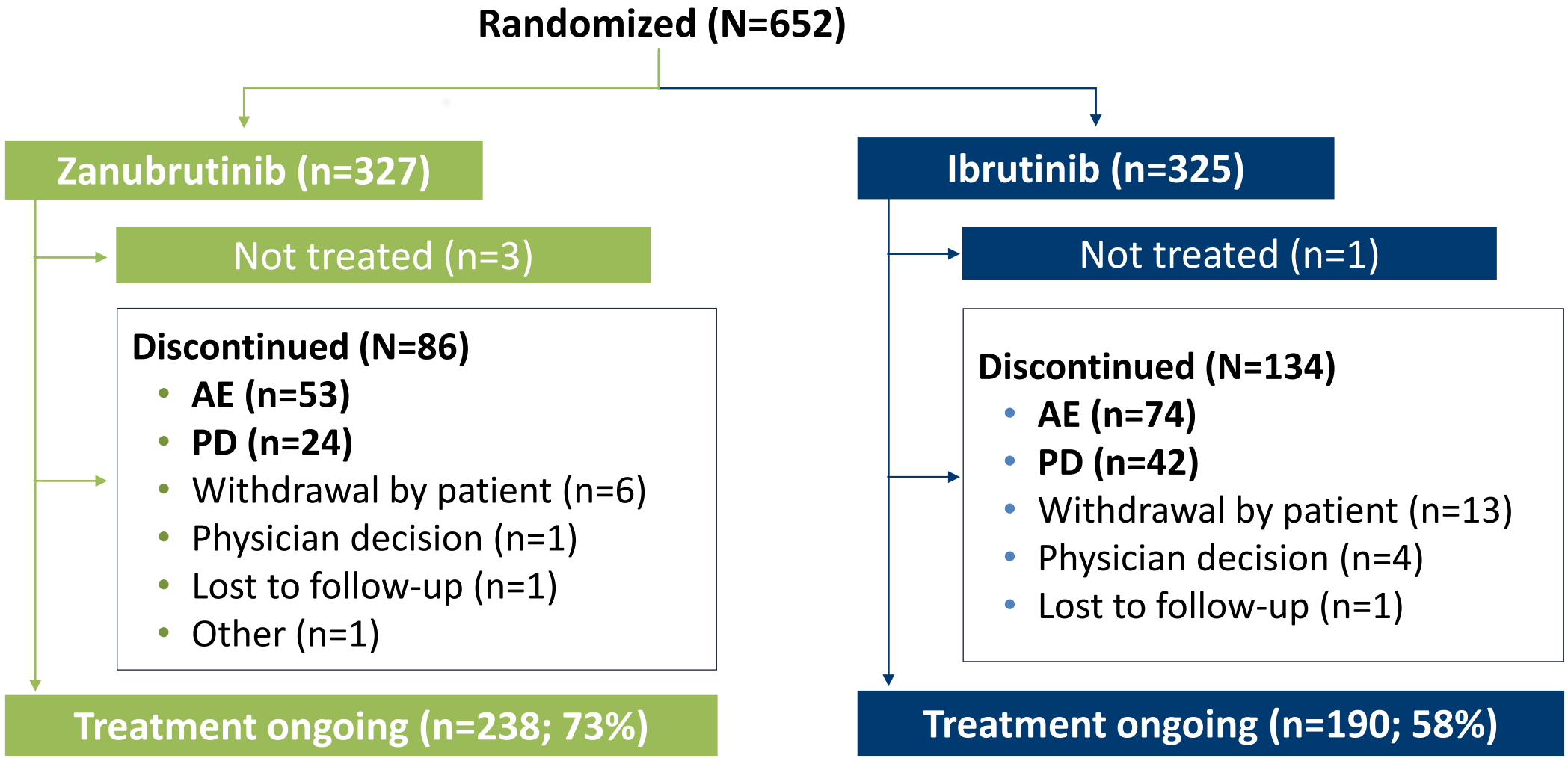
Other Secondary Endpoints

- DoR, OS
- Time to treatment failure
- PR-L or higher
- Patient-reported outcomes
- Safety



Overall response rate noninferiority and superiority were demonstrated in the ORR interim and final analyses; PFS was tested for noninferiority under hierarchical testing when 205 events had occurred

Patient Disposition



AE, adverse event; PD, progressive disease.

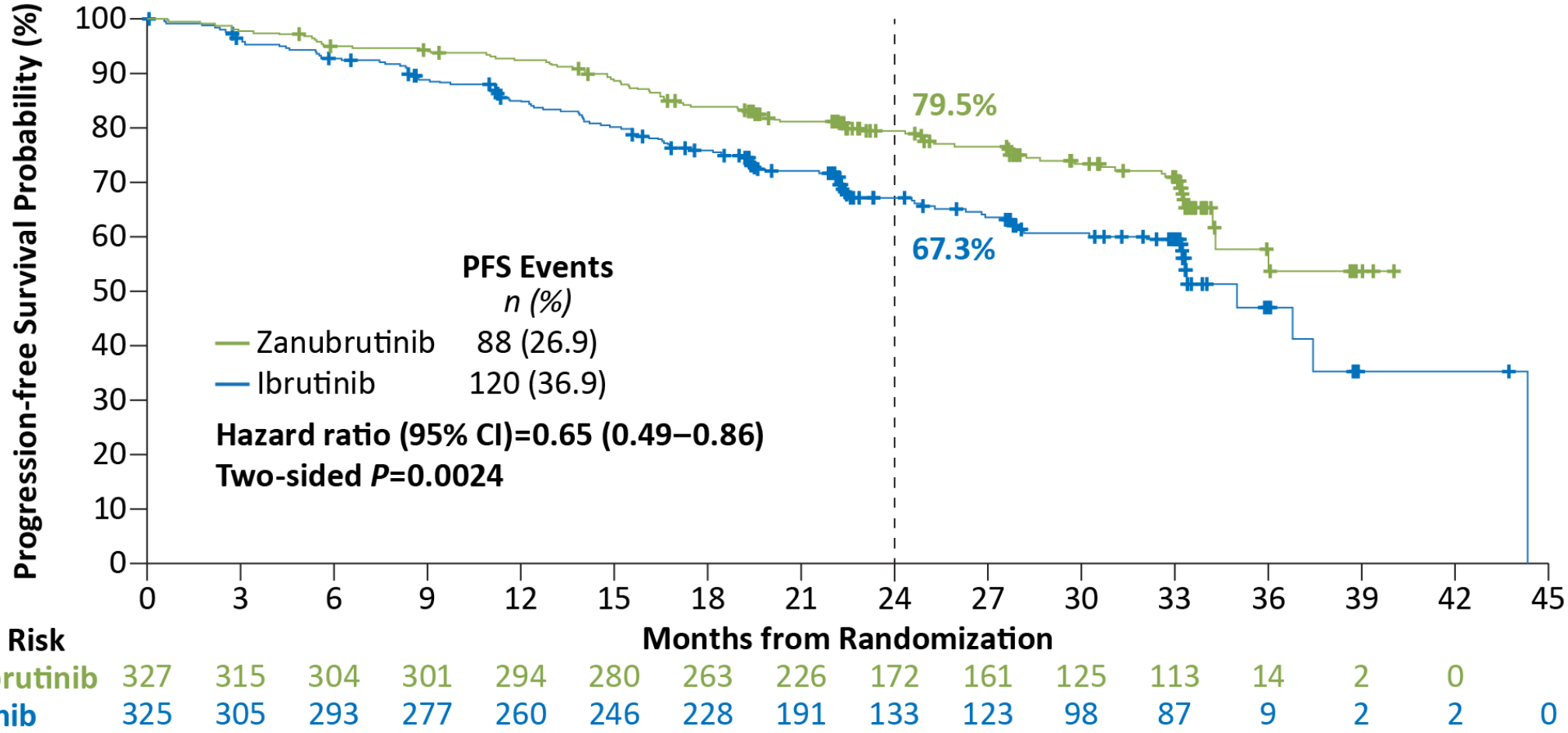
Balanced Demographics and Disease Characteristics

	Zanubrutinib (n=327)	Ibrutinib (n=325)
Age, median (range)	**67 (35-90)**	**68 (35-89)**
≥65 years, n (%)	201 (61.5)	200 (61.5)
Male, n (%)	**213 (65.1)**	**232 (71.4)**
ECOG PS ≥1, n (%)	**198 (60.6)**	**203 (62.5)**
Prior lines of systemic therapy, median (range)	**1 (1-6)**	**1 (1-12)**
>3 prior lines, n (%)	24 (7.3)	30 (9.2)
del(17p) and/or *TP53*^{mut}, n (%)	**75 (22.9)**	**75 (23.1)**
del(17p)	45 (13.8)	50 (15.4)
TP53^{mut} without del(17p)	30 (9.2)	25 (7.7)
del(11q), n (%)	**91 (27.8)**	**88 (27.1)**
IGHV mutational status, n (%)		
Mutated	79 (24.2)	70 (21.5)
Unmutated	**239 (73.1)**	**239 (73.5)**
Complex karyotype*	**56 (17.1)**	**70 (21.5)**
Bulky disease (≥5 cm), n (%)	**145 (44.3)**	**149 (45.8)**

*Complex karyotype is defined as having ≥3 abnormalities.

Zanubrutinib PFS by IRC Significantly Superior to Ibrutinib

Median study follow-up of **29.6** months

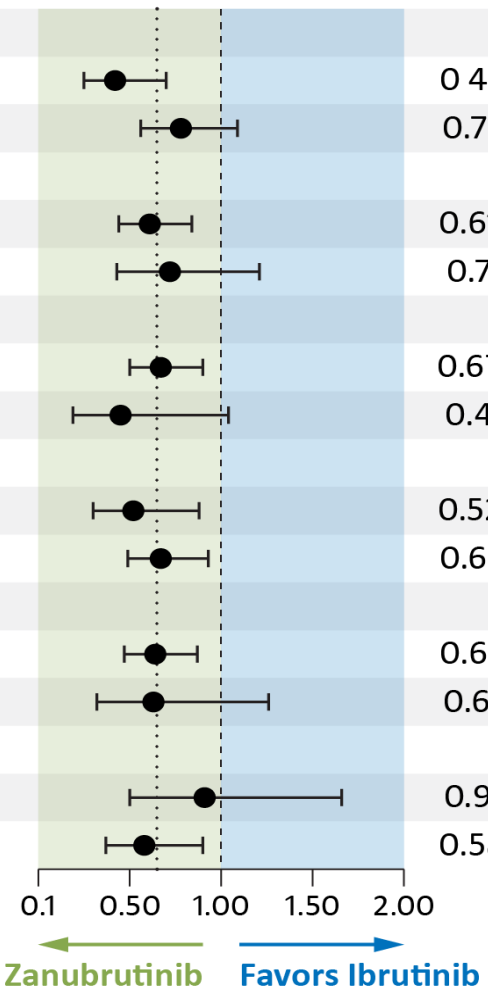


No. at Risk															
Zanubrutinib	327	315	304	301	294	280	263	226	172	161	125	113	14	2	0
Ibrutinib	325	305	293	277	260	246	228	191	133	123	98	87	9	2	2	0

Data cutoff: 8 Aug 2022

PFS Favored Zanubrutinib Across Subgroups

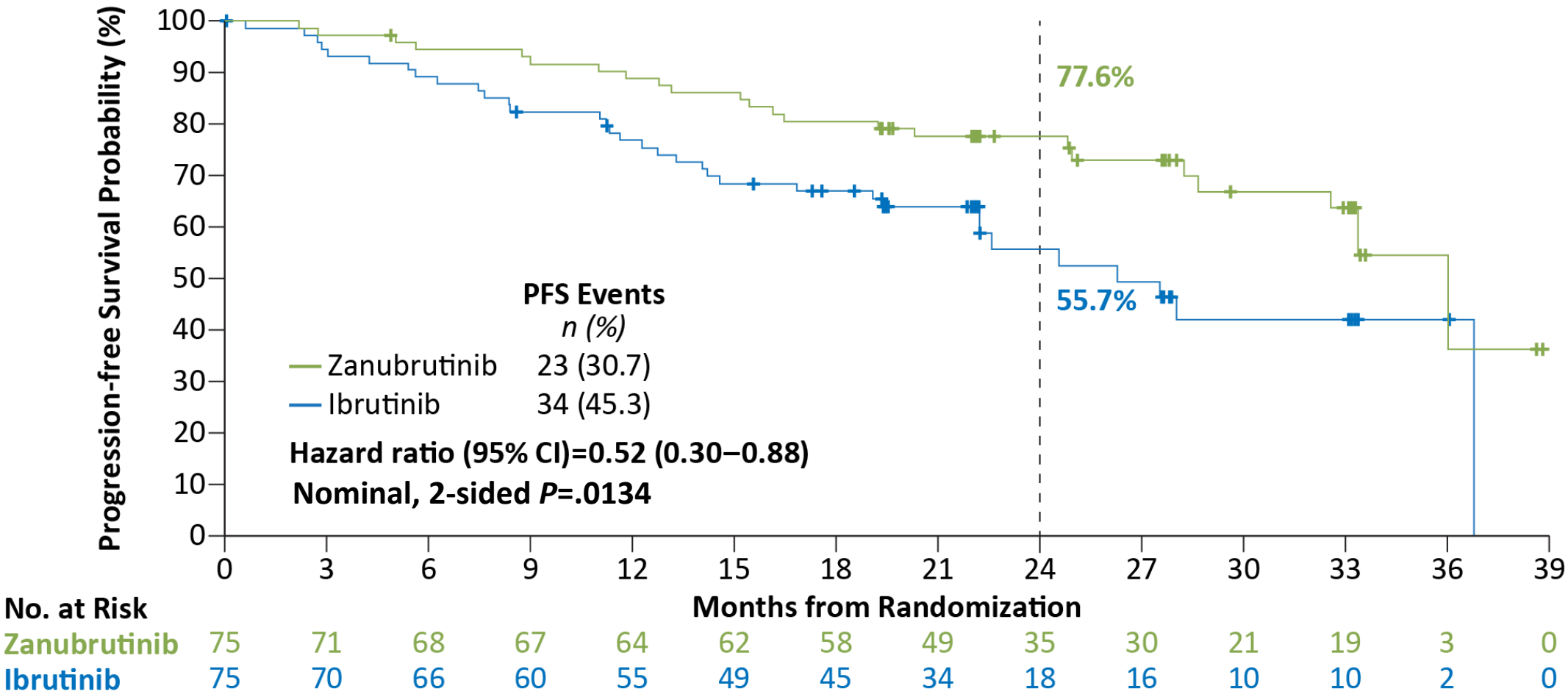
Subgroup	Zanubrutinib Response/Patients	Ibrutinib Response/Patients	Hazard Ratio (95% CI)[a]
Age group			
<65 years	23/126	43/125	0 42 (0.25, 0.70)
≥65 years	65/201	77/200	0.78 (0.56, 1.09)
Sex			
Male	59/213	91/232	0.61 (0.44, 0.84)
Female	29/114	29/93	0.72 (0.43, 1.21)
Prior lines of therapy			
1–3	80/303	102/295	0.67 (0.50, 0.90)
>3	8/24	18/30	0.45 (0.19, 1.04)
Baseline *del*(17p)/*TP53* mutation status			
Present	23/75	34/75	0.52 (0.30, 0.88)
Absent	65/251	86/250	0.67 (0.49, 0.93)
Baseline IGHV mutation status			
Unmutated	72/239	98/239	0.64 (0.47, 0.87)
Mutated	15/79	18/70	0.63 (0.32, 1.26)
Complex karyotype			
Yes	20/56	24/70	0.91 (0.50, 1.66)
No	37/153	45/130	0.58 (0.37, 0.90)



Data cutoff: 8 Aug 2022

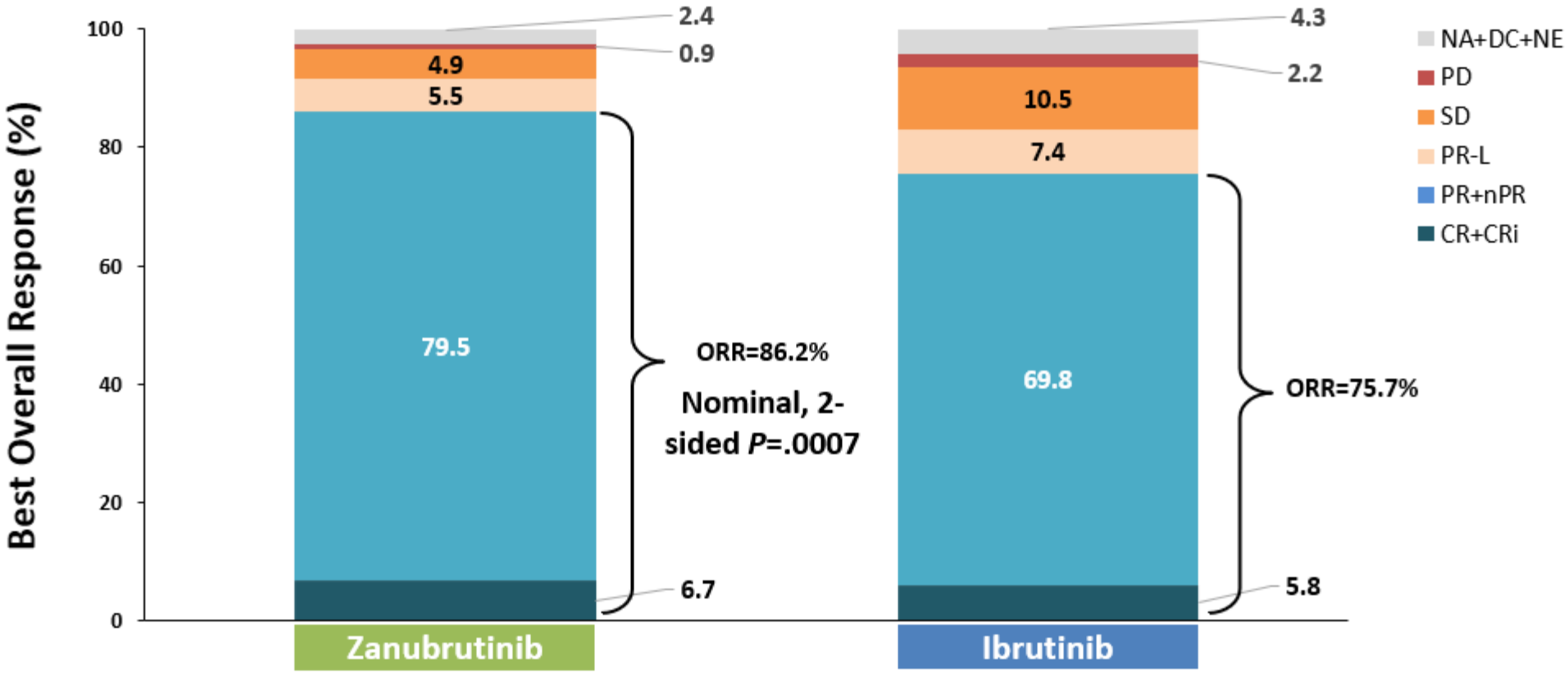
[a]Hazard ratio and 95% CI were unstratified for subgroups.

Zanubrutinib Improved PFS in Patients with del(17p)/*TP53*^{mut}



PFS data assessed by IRC
Data cutoff: 8 Aug 2022

Zanubrutinib Showed Higher ORR Assessed by IRC

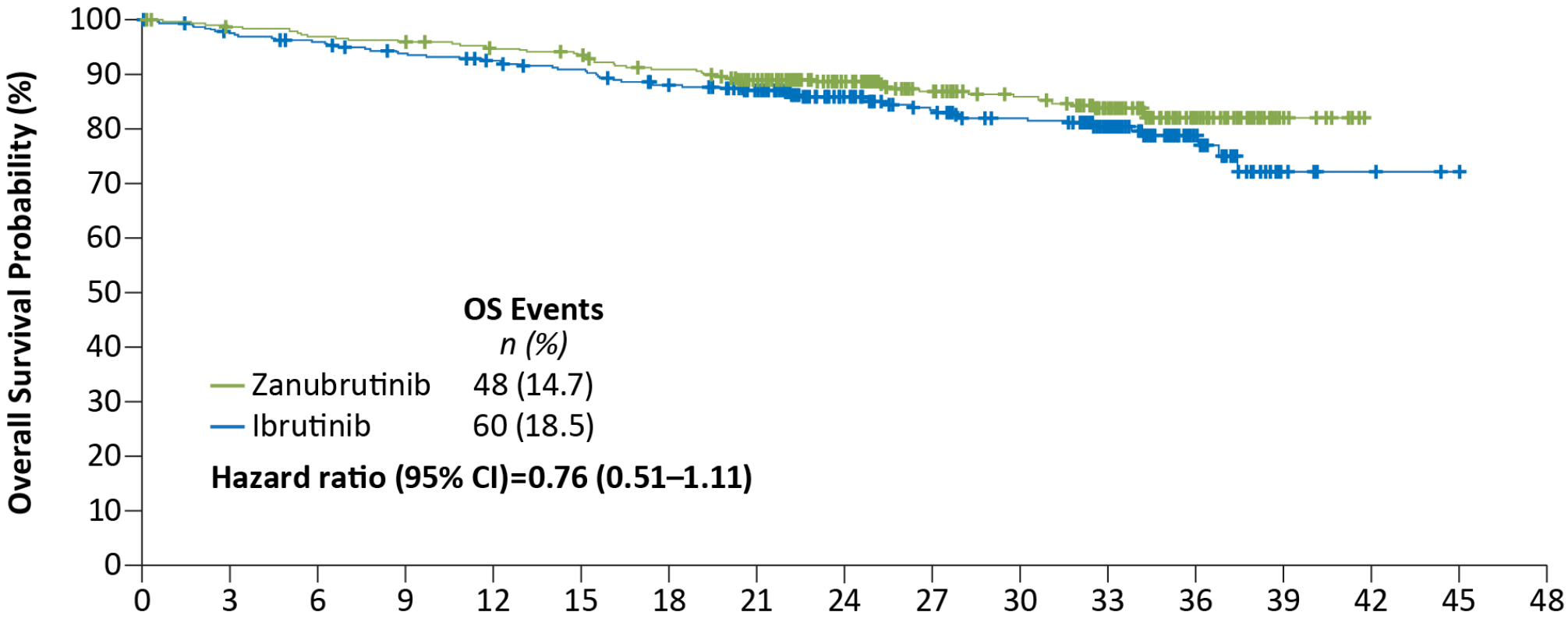


CR, complete response; CRi, complete response with incomplete bone marrow recovery; nPR, nodular partial response; PR, partial response; PR-L, partial response with lymphocytosis; SD, stable response; PD, progressive disease; NA, not assessed; DC, discontinued prior to first assessment; NE, not evaluable.

Data cutoff: 8 Aug 2022

Overall Survival

Fewer deaths with zanubrutinib compared with ibrutinib



No. at Risk																	
Zanubrutinib	327	319	313	310	303	298	287	268	224	185	169	134	56	8	0		
Ibrutinib	325	314	307	297	290	283	271	255	200	171	156	124	50	7	3	1	0

Data cutoff: 8 Aug 2022

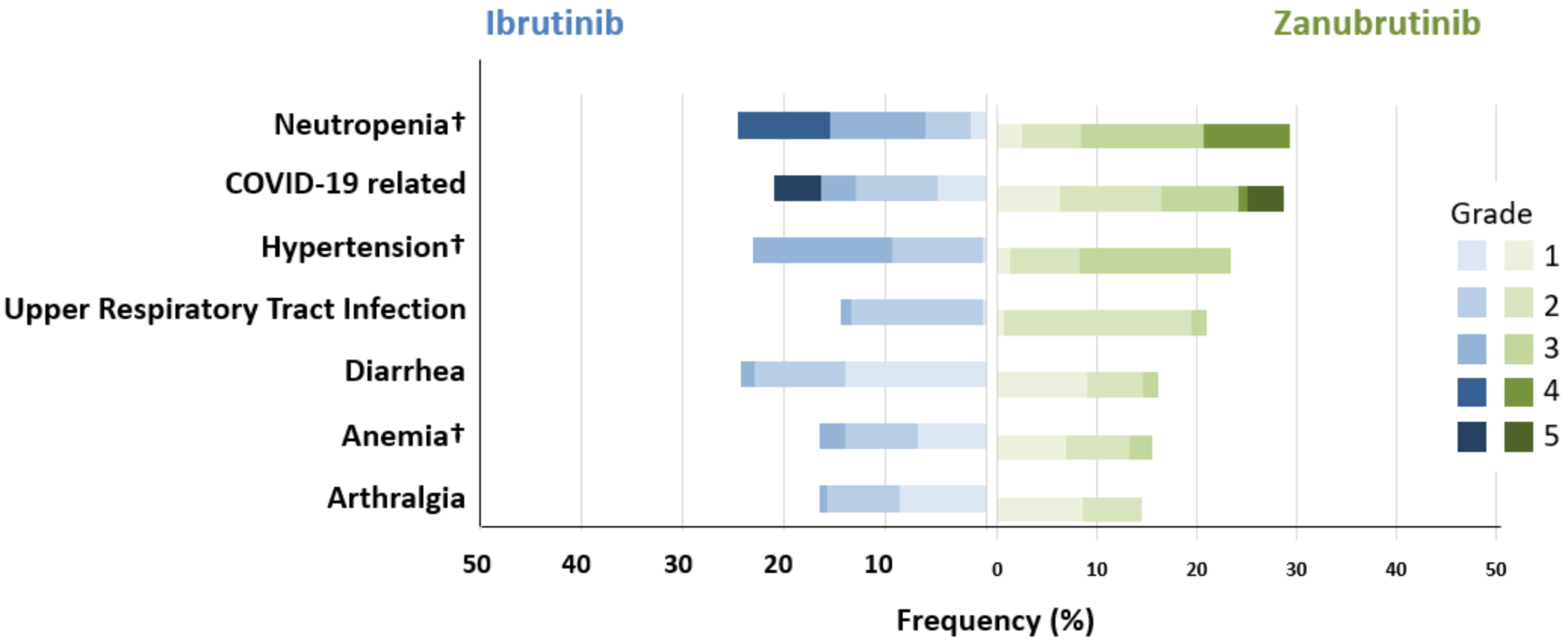
Overall Safety/Tolerability Summary

Zanubrutinib safety profile was favorable to ibrutinib

	Zanubrutinib (n=324)	Ibrutinib (n=324)
Median treatment duration, months	**28.4**	**24.3**
Any grade adverse event	**318 (98.1)**	**321 (99.1)**
Grade 3 to 5	218 (67.3)	228 (70.4)
Grade 5	33 (10.2)	36 (11.1)
Serious adverse event	**136 (42.0)**	**162 (50.0)**
Adverse events leading to		
Dose reduction	**40 (12.3)**	**55 (17.0)**
Dose interruption	**162 (50.0)**	**184 (56.8)**
Treatment discontinuation	**50 (15.4)**	**72 (22.2)**

Data cutoff: 8 Aug 2022

Most Common Adverse Events*



*Adverse events occurring in ≥15% of patients in either arm.
†Pooled terms.
Data cutoff: 8 Aug 2022

Zanubrutinib Had A Favorable Cardiac Profile

Lower rate of cardiac events, serious cardiac events, treatment discontinuation, and deaths

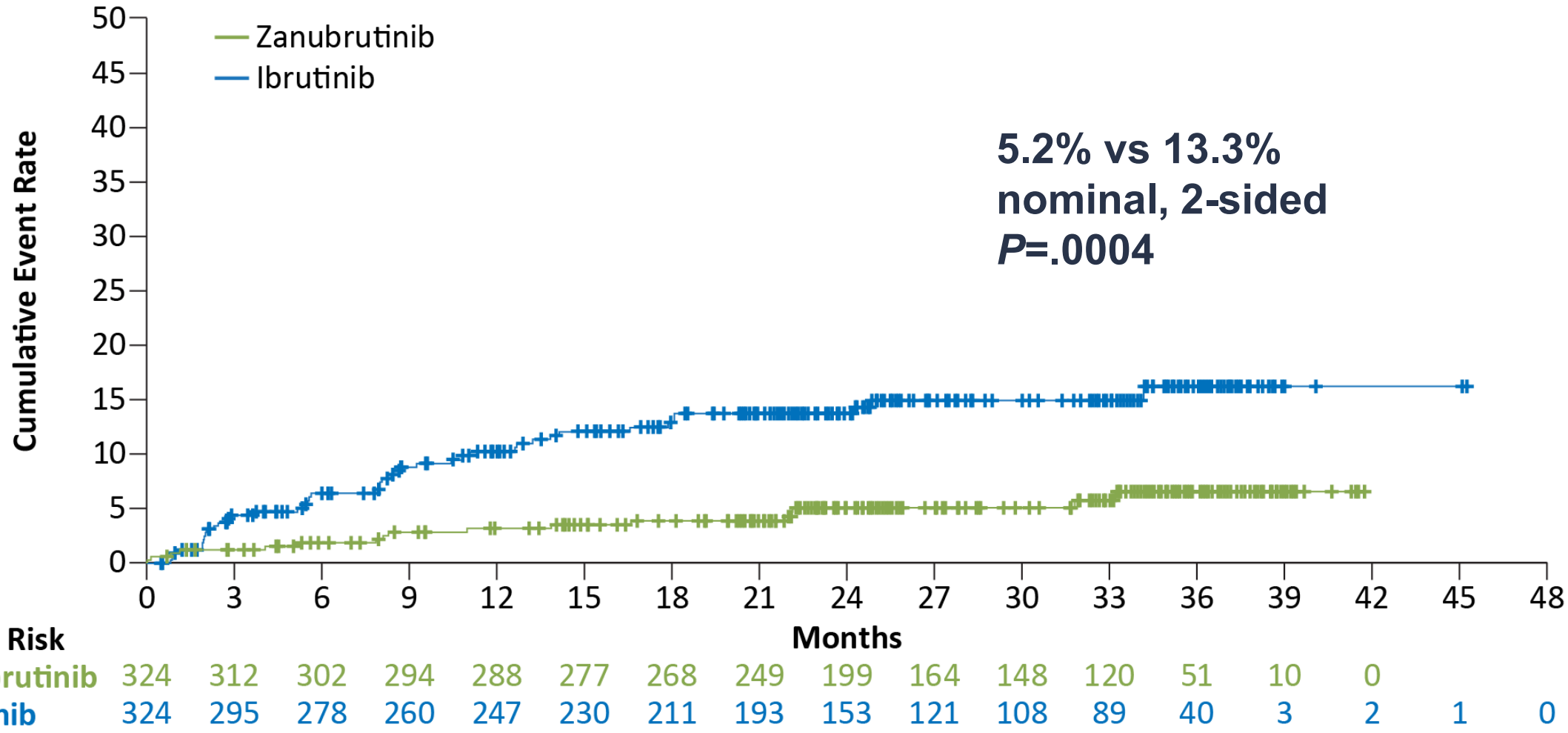
- Lower rate of serious cardiac adverse events reported with zanubrutinib
  - A fib/flutter (n=2)
  - MI/ACS (n=2)
  - CHF (n=2)

- **Fatal cardiac events:**
  - **Zanubrutinib, n=0 (0%)**
  - **Ibrutinib, n=6 (1.9%)**

	Zanubrutinib (n=324)	Ibrutinib (n=324)
Cardiac adverse events	**69 (21.3%)**	**96 (29.6%)**
Serious cardiac adverse events	**6 (1.9%)**	**25 (7.7%)**
Cardiac adverse events leading to treatment discontinuation	**1 (0.3)**	**14 (4.3)**
Ventricular extrasystoles	1 (0.3)	0
Atrial fibrillation	0	5 (1.5)
Cardiac arrest	0	2 (0.6)*
Cardiac failure	0	2 (0.6)
Cardiac failure acute	0	1 (0.3)*
Congestive cardiomyopathy	0	1 (0.3)*
Myocardial infarction	0	1 (0.3)*
Palpitations	0	1 (0.3)
Ventricular fibrillation	0	1 (0.3)

*Cardiac deaths. One death not listed due to myocardial infarction with ibrutinib discontinuation due to diarrhea 14 days prior to the fatal event.
Data cutoff: 8 Aug 2022

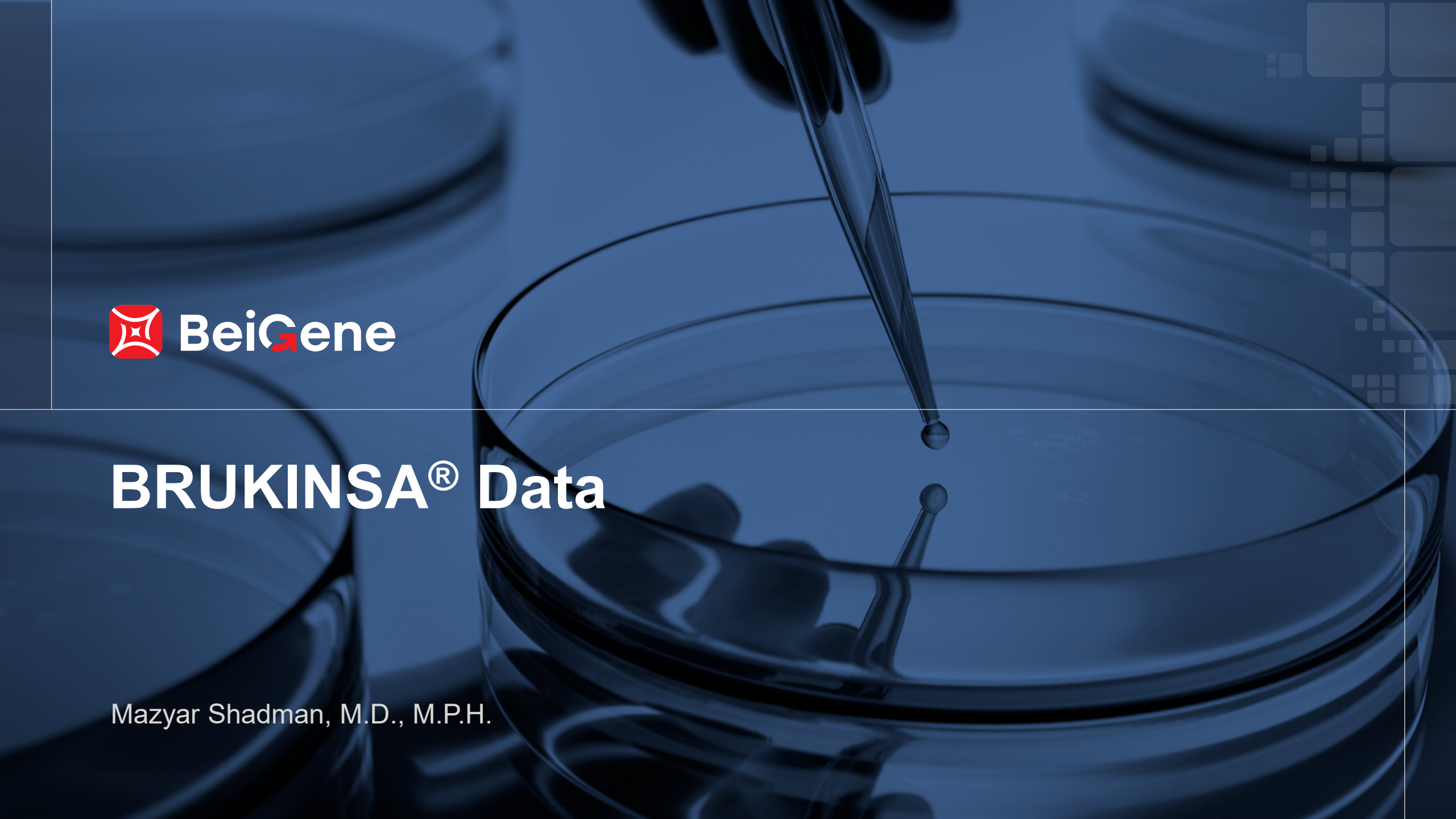
Fewer Atrial Fibrillation/Flutter Events With Zanubrutinib



Data cutoff: 8 Aug 2022

Conclusions

- Zanubrutinib demonstrated superior PFS over ibrutinib in patients with relapsed/refractory CLL/SLL
  - PFS benefit seen across all major subgroups, including the del(17p)/*TP53*^{mut} population
- Zanubrutinib has a favorable safety profile compared with ibrutinib
  - Lower rate of grade ≥3 and serious AEs, fewer AEs leading to treatment discontinuation and dose reduction
  - Zanubrutinib has a better cardiac profile than ibrutinib with lower rates of atrial fibrillation, serious cardiac events, cardiac events leading to treatment discontinuation, and fatal cardiac events
- ALPINE is the first study to demonstrate PFS superiority in a head-to-head comparison of BTK inhibitors in patients with relapsed/refractory CLL/SLL; **Zanubrutinib has now proven superiority to ibrutinib in both PFS and ORR**



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BRUKINSA® Data

Mazyar Shadman, M.D., M.P.H.

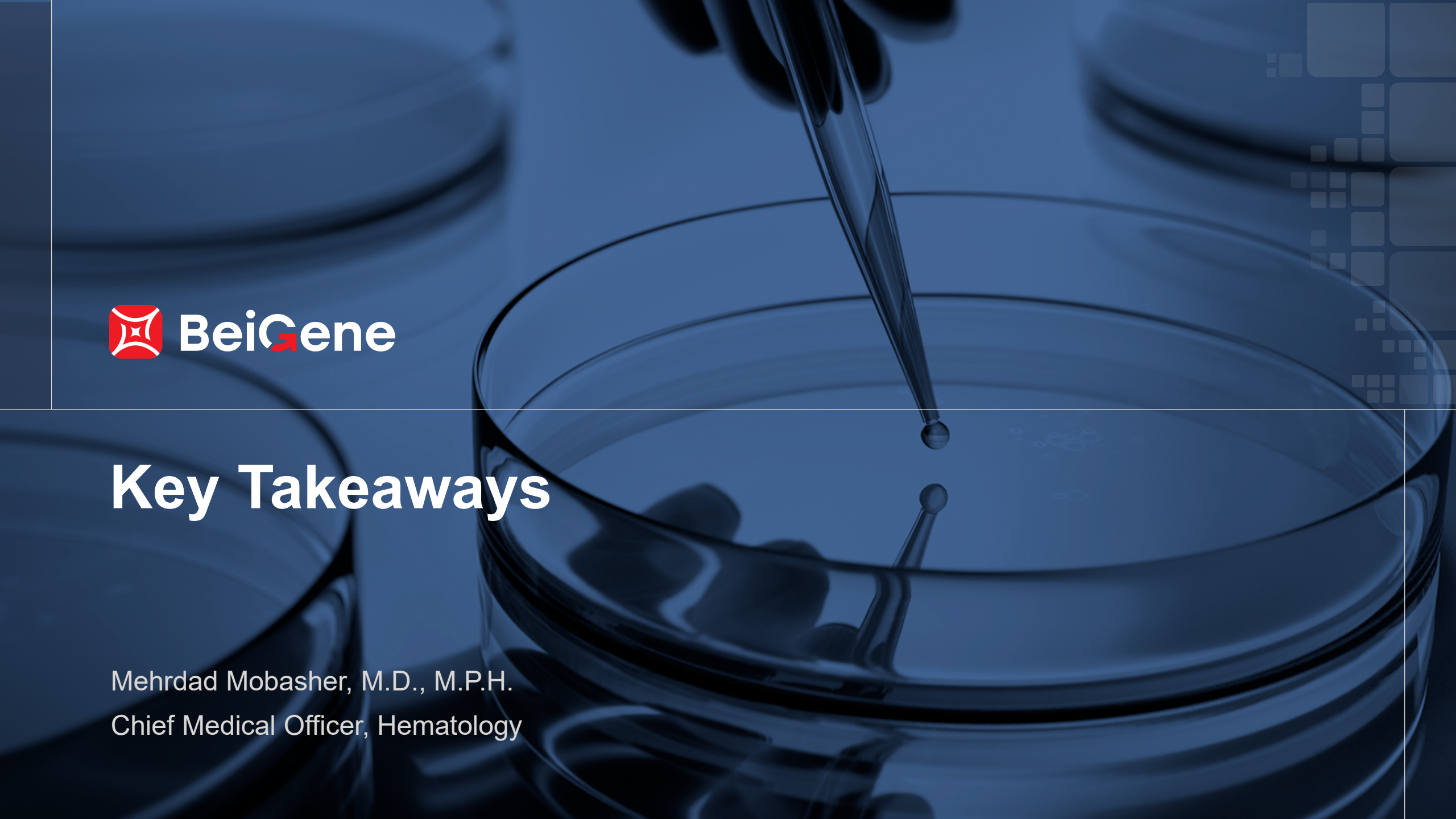
Mazyar Shadman, M.D., M.P.H

Associate Professor, Fred Hutch Cancer Center and University of Washington

- Dr. Shadman focuses on lymphoid malignancies with a clinical research goal to identify the best treatment sequence or combination for patients with high-risk lymphoma and CLL.
- Attending Physician, Hematologic Malignancies
  Fred Hutchinson Cancer Center
- Associate Professor, Medical Oncology Division
  University of Washington School of Medicine

Education

- Hematology and Medical Oncology fellowship, University of Washington/Fred Hutchinson Cancer Research Center, 2011-2014
- Internal Medicine Residency, Cleveland Clinic, 2008-2011
- M.P.H., Cancer Epidemiology, University of Washington, 2008
- M.D., Tehran University of Medical Sciences, 2004



Key Takeaways

Mehrdad Mobasher, M.D., M.P.H.
Chief Medical Officer, Hematology

Key Takeaways - BRUKINSA®

- Designed to be a best-in-class BTKi
  - Improve efficacy through targeted and sustained BTK inhibition
  - Improve safety by reducing inhibition of off-target tyrosine kinases
- Broad clinical development program with 4,700+ subjects enrolled in clinical trials in 30+ geographies, with 3,700+ outside of China
- Today, BRUKINSA® is the only BTKi demonstrating PFS superiority vs. IMBRUVICA® in a head-to-head study
- Approvals in 60+ markets and four indications
- sNDA in CLL based on ALPINE (ORR Superiority endpoint) and SEQUOIA (1L CLL) with PDUFA in January 2023

Q&A Participants

Dr. Jennifer Brown
Dana Farber Cancer Institute

Dr. Mazyar Shadman
Fred Hutch, University of Washington

John V. Oyler
Co-Founder, Chairman and Chief Executive Officer

Josh Neiman
Chief Commercial Officer, North America and Europe

Dr. Mehrdad Mobasher
Chief Medical Officer, Hematology

Julia Wang
Chief Financial Officer

Cancer has no borders.

Neither do we.


BeiGene
THANK YOU