BeiGene ASCO Data Review

Friday, May 29th, 2020 – 8:00 p.m. ET

BeiGene

Today's Participants

Constantine Tam, M.D.
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John V. Oyler
Chairman, Co-Founder, & CEO

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General Manager of China & President of BeiGene, Ltd.

Howard Liang, Ph.D.
CFO & Chief Strategy Officer

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Chief Advisor

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Chief Medical Officer, Immuno-Oncology

Jane Huang, M.D.
CMO, Hematology

Josh Neiman
SVP, Commercial North America

BeiGene

Howard Liang, Ph.D.

CFO and Chief Strategy Officer

BeiGene

Agenda

- Welcome – *Howard Liang, Ph.D.*[1]
- Introduction – *John V. Oyler*[1]
- Zanubrutinib ASPEN Study – *Constantine Tam, M.D.*[2]
- BOVen Study – *Andrew Zelenetz, M.D.*[3]
- Tislelizumab 1L Squamous NSCLC – *Yong (Ben) Ben, M.D.*[1]
- Program Status and Key Takeaways – *Eric Hedrick, M.D.*[1]
- Q&A

[1] BeiGene; [2] Peter MacCallum Cancer Centre, Melbourne, Victoria, Australia; St Vincent's Hospital, Fitzroy, Victoria, Australia; University of Melbourne, Parkville, Victoria, Australia; Royal Melbourne Hospital, Parkville, Victoria, Australia; [3] Memorial Sloan Kettering Cancer Center, New York, NY

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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 recent clinical data for BeiGene's product candidates and approvals of its products; the conduct of late-stage clinical trials and expected data readouts; additional planned commercial product launches; the advancement of and anticipated clinical development, regulatory milestones and commercialization of BeiGene's products and drug candidates. Actual results may differ materially from those indicated in the forward-looking statements as a result of various important factors, including 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 products and drug candidates, if approved; BeiGene's ability to obtain and maintain protection of intellectual property for its technology and drugs; BeiGene's reliance on third parties to conduct drug development, manufacturing and other services; BeiGene's limited operating history and BeiGene's ability to obtain additional funding for operations and to complete the development and commercialization of its drug candidates; the impact of the COVID-19 pandemic on the Company's clinical development, 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 press release is as of the date of this press release, 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 early phase, single-arm trials. When such data or data from later stage trials are presented in relation to other investigational or marketed drug products, the presentation and discussion are not based on head-to-head trials between BeiGene's investigational drug candidates and other products unless specified in the trial protocol. BeiGene is still conducting clinical trials and, as additional patients are enrolled and evaluated, data on BeiGene's investigational drug candidates may change.
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John V. Oyler

Chairman, Co-Founder, and CEO

BeiGene

Science Is Translating to Impact for Cancer Patients… Yet Medicines Remain Unaffordable

Clinical trials

- Consume **vast majority of cost and time**
- Are the single greatest challenge of our time

Excellence in clinical trials requires:

- Ability to truly run global trials highly inclusive of China and beyond
- Applying best practices in operational excellence and technology
- Building real world data sets

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BeiGene Capabilities

Global Clinical Development

- **1,200+** people on **four** continents
- Running **60+** clinical trials, including **26** potentially registration-enabling trials
- Over **7,000** patients enrolled by BeiGene in over **35** countries or regions

Commercial

- Commercial footprint in **two largest** markets
- China team of over **1,200** with **science and medicine focus** and track record of successfully commercializing **Abraxane, Revlimid, and Vidaza** and **launching tislelizumab**
- U.S. hematology commercial team

Research Platform

- Majority of our team is working on **novel mechanisms** or **potential first-in-class medicines**
- Internally-developed approved medicines or clinical programs include: BTK, PD-1, PARP, TIGIT, OX-40, Bcl2, and TIM3

Manufacturing

- Experienced high-quality manufacturing partners: Boehringer Ingelheim and Catalent
- Internal team of **200+** people and a **50,000-liter** biologics manufacturing facility

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Recent Accomplishments and Drivers for Growth

BeiGene's late-stage programs and assets

China

Global

1 NDA Filing

- Tislelizumab 1L Sq NSCLC

4 Preclinical Assets Advanced into Clinic

- BGB-A445 anti OX40
- BGB-11417 Bcl-2 inhibitor
- BGB-3245 B-RAF inhibitor

3 Approvals & Launch

- BRUKINSA MCL
- Tislelizumab cHL
- Tislelizumab UBC

3 Phase 3 Data Readouts

- BRUKINSA HTH in WM
- Tislelizumab 1L Sq NSCLC
- Tislelizumab 1L Nsq NSCLC

27 Assets Added Through Collaborations

4 Trial Enrolled

- BRUKINSA MZL
- Tislelizumab 2/3L NSCLC
- Tislelizumab 2L ESCC
- Pamiparib Breast cancer

AMGEN

SeattleGenetics

leaptherapeutics

EUSAPharma

6 Phase 3* Data Readouts

- BRUKINSA 1L CLL/SLL
- BRUKINSA HTH r/r CLL/SLL
- Tislelizumab 2/3L NSCLC
- Tislelizumab 2L ESCC
- Tislelizumab dMMR / MSI-H
- Pamiparib Pt-sensitive OC

7 Potential NDA Filing

- BRUKINSA WM
- BRUKINSA WM
- Tislelizumab 1L Nsq NSCLC
- Tslelizumab 2/3L HCC
- Pamiparib OC
- Sylvant Castleman disease
- QARZIBA neuroblastoma

Up to 11 Commercial Products

- Brukinsa™ 80mg zanubrutinib capsules
- tislelizumab 百泽安®
- pamiparib
- Abraxane® (nanoparticle albumin-bound paclitaxel)
- Revlimid® (lenalidomide) capsules
- Vidaza® azacitidine for injection
- XGEVA® (denosumab)
- Kyprolis™ (carfilzomib) for injection
- BLINCYTO® (blinatumomab) for injection 35 mcg single-dose vial
- sylvant® siltuximab
- QARZIBA (dinutuximab beta)

Past 6 months (from 4Q19 - 1Q20)

Next 12 - 18 months

* Phase 3 or registrational enabling trials.

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Constantine Tam, M.D.

Peter MacCallum Cancer Centre, Melbourne, Victoria, Australia; St Vincent's Hospital, Fitzroy, Victoria, Australia; University of Melbourne, Parkville, Victoria, Australia; Royal Melbourne Hospital, Parkville, Victoria, Australia

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Aspen: Results of a Phase 3 Randomized Trial of Zanubrutinib Versus Ibrutinib for Patients with Waldenström Macroglobulinemia (WM)

Presented at the 2020 Annual Meeting of the American Society of Clinical Oncology (ASCO), May 29 – May 31, 2020
Abstract: 8007

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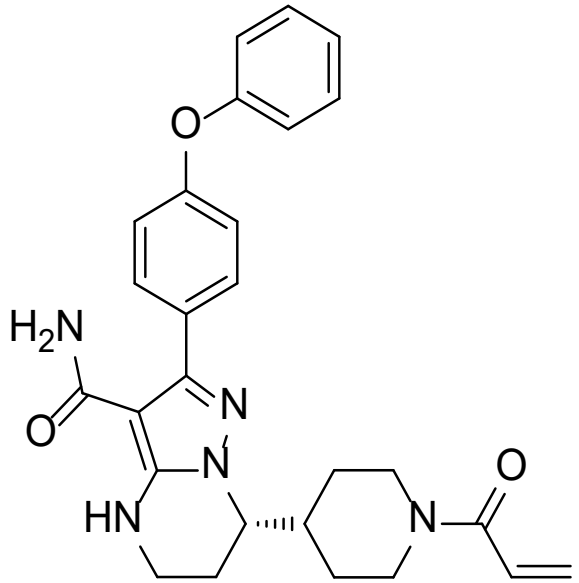
BTK Inhibition in WM

- BTK plays a critical role in B-cell receptor signaling; this pathway is constitutively activated in WM (> 90% with *MYD88* mutations), leading to malignant cell survival[1, 2]
- BTK inhibition is an emerging standard of care for WM[3]
- Zanubrutinib is a next-generation BTK inhibitor designed to maximize BTK occupancy and minimize off-target inhibition of TEC- and EGFR-family kinases
  - **Potent, selective, irreversible**
  - **Zanubrutinib generally equipotent against BTK compared to ibrutinib, based on non-clinical data;** higher selectivity vs EGFR, ITK, JAK3, HER2 and TEC[4]
  - **Advantageous PK, PD properties:** complete and sustained BTK occupancy in PBMC and lymph nodes[5]
  - **Favorable drug-drug interaction properties:** can be co-administered with strong/moderate CYP3A inhibitors at a reduced dose, proton pump inhibitors, acid-reducing agents, and anti-thrombotic agents.[6, 7]
  - **Approved for patients with R/R MCL in the United States Nov 2019**



BTK, Bruton tyrosine kinase; EGFR, epidermal growth factor receptor; HER2, human epidermal growth factor receptor 2; ITK, IL2-inducible T-cell kinase; JAK3, Janus tyrosine kinase 3; PD, pharmacodynamic; PK, pharmacokinetic; WM, Waldenström Macroglobulinemia.

[1]Rickert RC. *Nat Rev Immunol*. 2013;13:578-591. [2]Argyropoulos KV, et al. *Leukemia*. 2016;30:1116-1125. [3]Treon SP et al, *J Clin Oncol*. 2020;38:1198-1208 . [4]Guo Y, et al. *J Med Chem*. 2019;62:7923-7940. [5]Tam CS, et al. *Blood*. 2019;134:851-859. [6]Mu S et al. *Cancer Chemother Pharmacol*. 2020; 85, 391–399. [7]Data on file.

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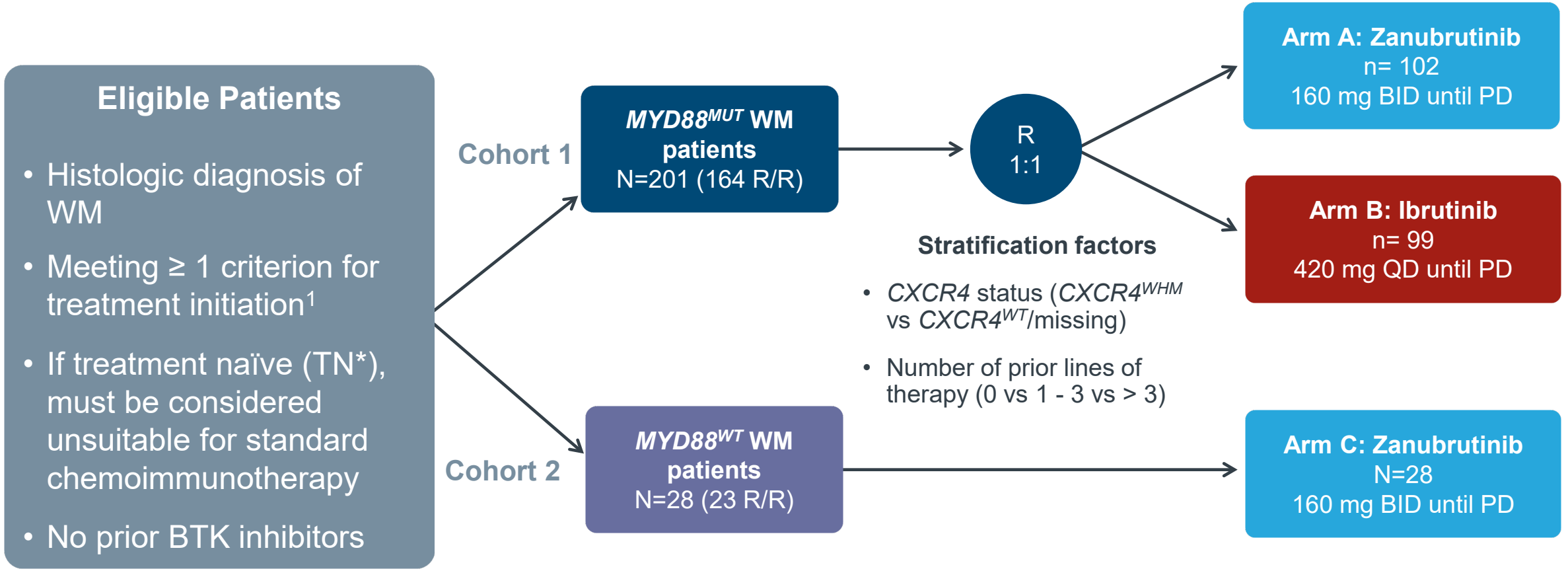
ASPEN Study Design: Zanubrutinib vs Ibrutinib in *MYD88^{MUT}* WM



Abstract: e20056

EUDRACT 2016-002980-33; NCT03053440

BID, twice daily; BTK, Bruton tyrosine kinase; CXCR4, C-X-C Motif Chemokine Receptor 4; MYD88^{MUT}, myeloid differentiation primary response gene 88 mutant; PD, progressive disease; QD, daily; R, randomization; R/R, relapsed/refractory; TN, treatment naïve; WM, Waldenström Macroglobulinemia; WT, wild-type.
*Up to 20% of the overall population.
[1]Dimopoulos MA, et al. *Blood*. 2014;124:1404-1411.

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ASPEN: Demographics and Disease Characteristics

Characteristics, n (%)	Overall ITT	
	Ibrutinib (n = 99)	Zanubrutinib (n =102)
Age, years median (range)	70.0 (38, 90)	70.0 (45, 87)
> 65 years	**70 (70.7)**	61 (59.8)
> 75 years	22 (22.2)	**34 (33.3)**
Gender, n (%)		
Male	65 (65.7)	69 (67.6)
Female	34 (34.3)	33 (32.4)
Prior Lines of Therapy, n (%)		
0	18 (18.2)	19 (18.6)
1 - 3	74 (74.7)	76 (74.5)
> 3	7 (7.1)	7 (6.9)
Genotype by central lab*, n (%)		
MYD88^{L265P}/*CXCR4*^{WT}	90 (90.9)	91 (89.2)
MYD88^{L265P}/*CXCR4*^{WHIM}	8 (8.1)	11 (10.8)
IPSS WM[1]		
Low	13 (13.1)	17 (16.7)
Intermediate	42 (42.4)	38 (37.3)
High	44 (44.4)	47 (46.1)
Hemoglobin ≤ 110 g/L	53 (53.5)	**67 (65.7)**

CXCR4, C-X-C Motif Chemokine Receptor 4; ITT, intention-to-treat; IPSS WM, International Prognostic Scoring System for Waldenström macroglobulinemia; MYD88, myeloid differentiation primary response gene 88; NGS, next-generation sequencing.

*"Wildtype-blocking PCR" for *MYD88* and Sanger sequencing for *CXCR4* using bone marrow aspirates. One patient had local NGS testing results of *MYD88 L265P/ CXCR4* Unknown.

[1]Morel et al, *Blood*. 2009;113:4163-4170.

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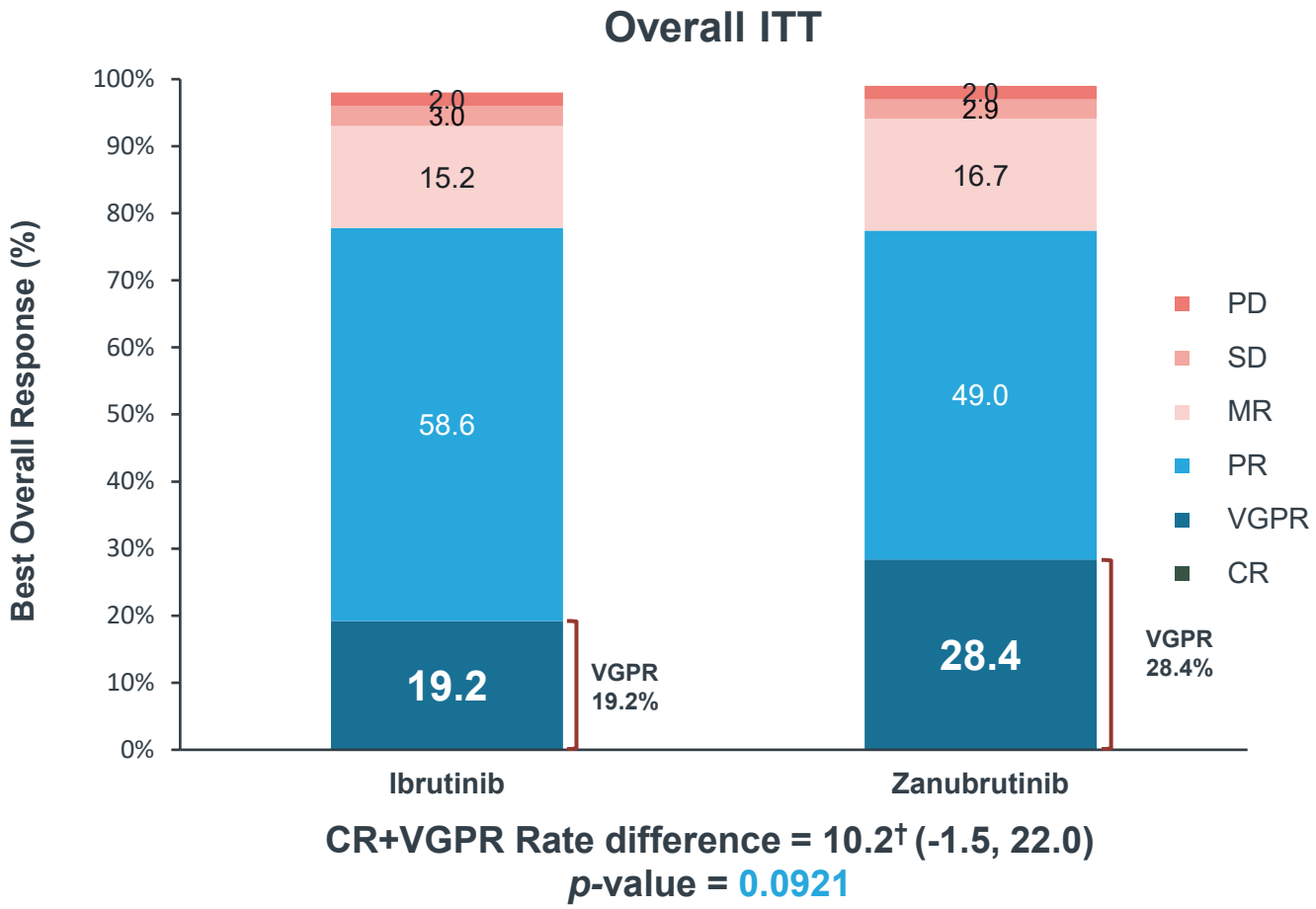
ASPEN: Efficacy – Response by IRC

(Data cutoff: August 31, 2019)

Superiority in CR+VGPR rate compared to ibrutinib in relapsed/refractory population (primary study hypothesis) was not statistically significant*



CR, complete response; IRC, independent review committee; ITT, intention-to-treat; MRR, major response rate; MR, minor response; ORR, overall response rate; PD, progressive disease; PR, partial response; R/R, relapsed/refractory; SD, stable disease; VGPR, very good PR.
Overall concordance between Independent review and investigators = 94%
*All other *p*-values are for descriptive purposes only. †Adjusted for stratification factors and age group.

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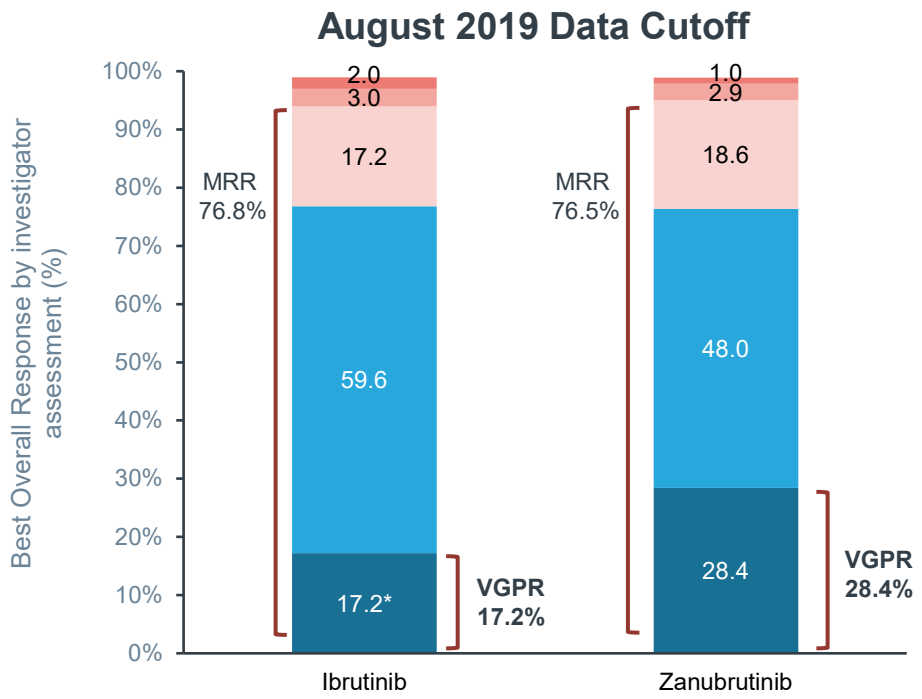
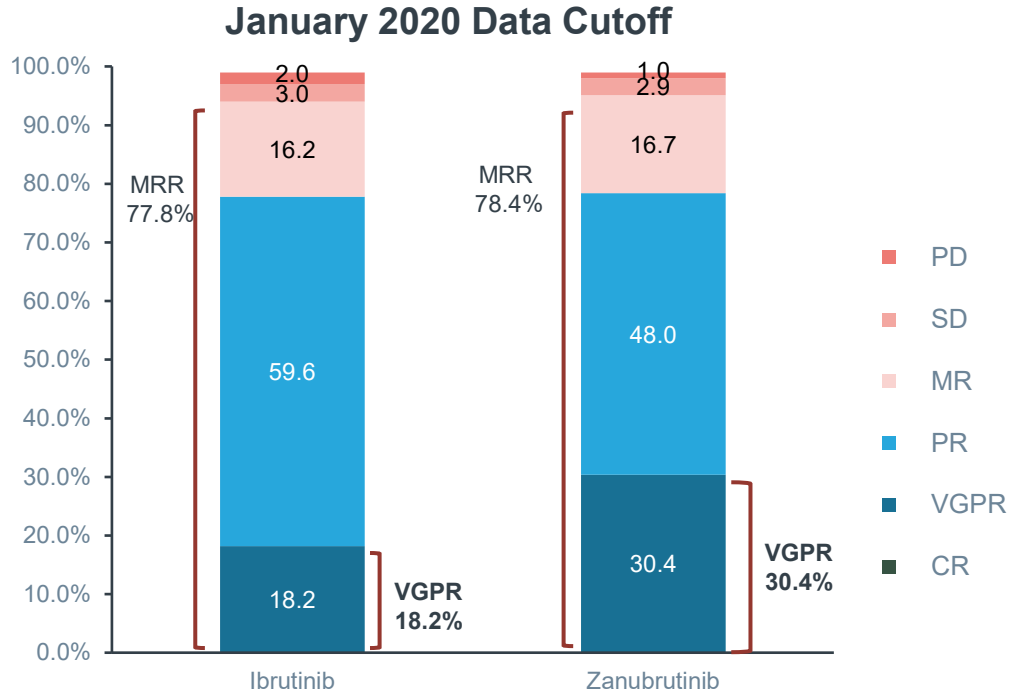
ASPEN: Secondary Efficacy Endpoints

Assessment of response according to investigator and IgM analysis

Investigator-Assessed Response



CR+VGPR Rate difference = 12.1† (0.5, 23.7)
***p*-value = 0.0437**



CR+VGPR Rate difference = 13.2† (1.4, 25.1)
***p*-value = 0.0302**

IgM Reduction

Area-under-the-curve (AUC) for IgM reduction over time was significantly greater for zanubrutinib vs ibrutinib (p=0.037)

CR, complete response; EMD, extramedullary disease; IgM, Immunoglobulin M; IRC, independent review committee; MRR, major response rate; MR, minor response; ; ORR, overall response rate; PD, progressive disease; PR, partial response; SD, stable disease; SPEP, serum protein electrophoresis; VGPR, very good PR.
*Excluded two patients with VGPR by IRC: MR (EMD present) and PR (IgM assessment by local SPEP M-protein)
†Adjusted for stratification factors and age group. *p*-value is for descriptive purpose only.

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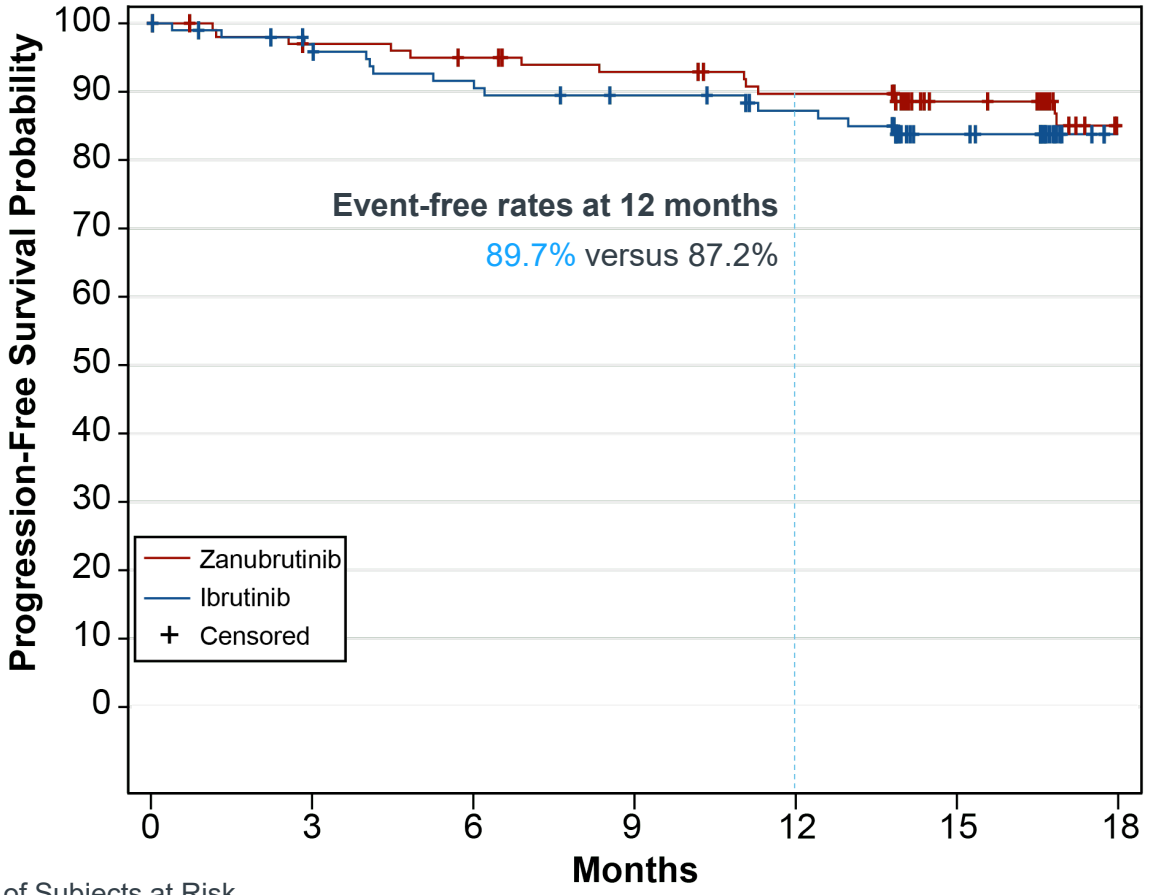
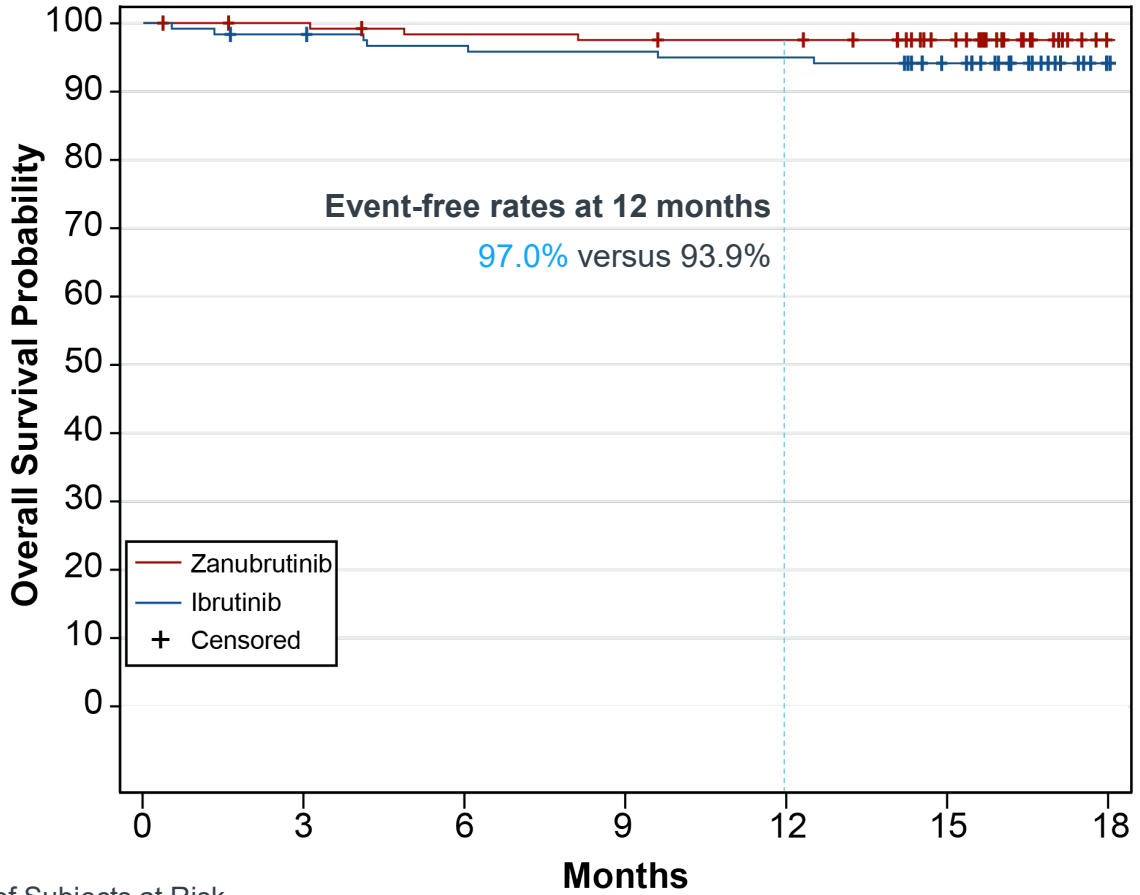
ASPEN: Progression-Free and Overall Survival in ITT population



No. of Subjects at Risk

Zanubrutinib	102	96	93	89	84	63	43
Ibrutinib	99	92	86	82	77	62	42



No. of Subjects at Risk

Zanubrutinib	102	100	97	96	95	86	62
Ibrutinib	99	96	93	92	91	83	61

IRC, independent review committee; VGPR, very good partial response.
Disease progression determined by IRC.

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ASPEN: Safety and Tolerability

Category, n (%)	Overall	
	Ibrutinib (n = 98)	Zanubrutinib (n = 101)
Patients with ≥ 1 AE	97 (99.0)	98 (97.0)
Grade ≥3	62 (63.3)	59 (58.4)
Serious	40 (40.8)	40 (39.6)
AE leading to death	4 (4.1) [a]	1 (1.0) [b]
AE leading to treatment discontinuation	9 (9.2) [c]	4 (4.0) [d]
AE leading to dose reduction	23 (23.5)	14 (13.9)
AE leading to dose held	55 (56.1)	47 (46.5)
Patients with ≥ 1 treatment-related AE	84 (85.7)	80 (79.2)
Patients with ≥ 1 AE of interest	81 (82.7)	86 (85.1)

AE, adverse event (treatment-emergent); G, grade.
[a] cardiac failure acute; sepsis (n=2); unexplained death.
[b] cardiac arrest after plasmapheresis
[c] G5 sepsis (n=2); G5 unexplained death; G3 acute myocardial infarction; G3 hepatitis ; G3 pneumonia; G2 drug-induced liver injury; G2 pneumonitis; G1 pneumonitis.
[d] G5 cardiac arrest after plasmapheresis; G4 neutropenia; G4 subdural hemorrhage ; G2 plasma cell myeloma.

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Aspen: AE Categories of Interest (BTKi Class AEs) with Additional Five Months Follow-Up (Data Cutoff: 31 January 2020)

An additional 5 patients had discontinued ibrutinib treatment due to AEs versus zero in the zanubrutinib arm (14% vs 4%)

AE *Categories*, n (%) *(pooled terms)*	All Grades		Grade ≥ 3	
	Ibrutinib (n = 98)	Zanubrutinib (n = 101)	Ibrutinib (n = 98)	Zanubrutinib (n = 101)
Atrial Fibrillation / Flutter†	**18 (18.4)**	3 (3.0)	**7 (7.1)**	0 (0.0)
Diarrhea (PT)	**32 (32.7)**	22 (21.8)	2 (2.0)	3 (3.0)
Hemorrhage	**59 (60.2)**	51 (50.5)	9 (9.2)	6 (5.9)
Major Hemorrhage[a]	10 (10.2)	6 (5.9)	9 (9.2)	6 (5.9)
Hypertension	20 (20.4)	13 (12.9)	**15 (15.3)**	8 (7.9)
Neutropenia[b] †	15 (15.3)	**32 (31.7)**	8 (8.2)	**23 (22.8)**
Infection	70 (71.4)	70 (69.3)	23 (23.5)	19 (18.8)
Second Malignancy	12 (12.2)	13 (12.9)	1 (1.0)	3 (3.0)

Higher AE rate in bold blue with ≥ 10% difference in any grade or ≥ 5% difference in grade 3 or above.
[a] Defined as any grade ≥ 3 hemorrhage or any grade central nervous system hemorrhage.
[b] Including PT terms of neutropenia, neutrophil count decreased, febrile neutropenia, agranulocytosis, neutropenic infection and neutropenic sepsis.
† Descriptive two-sided *P*-value < 0.05.

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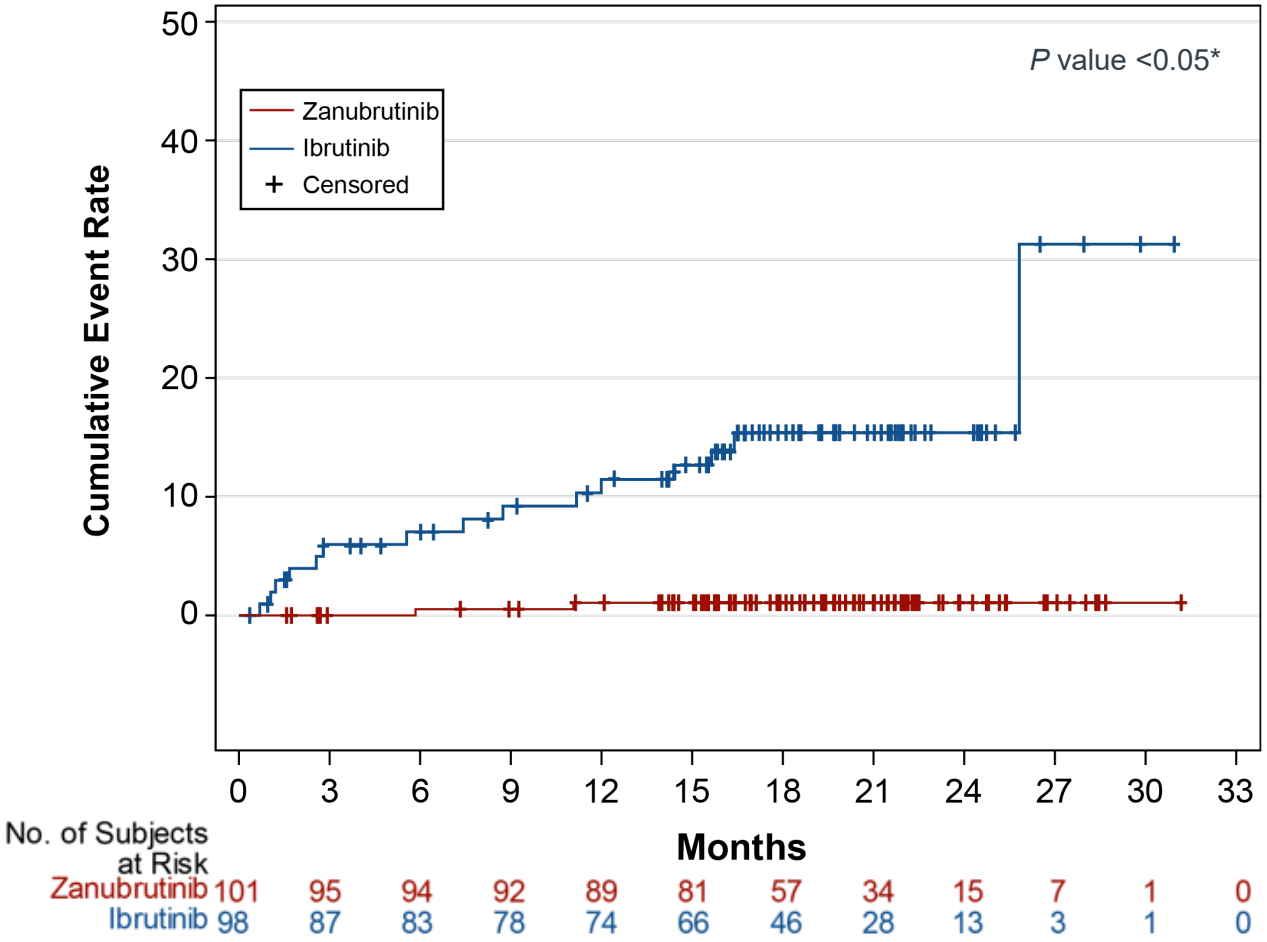
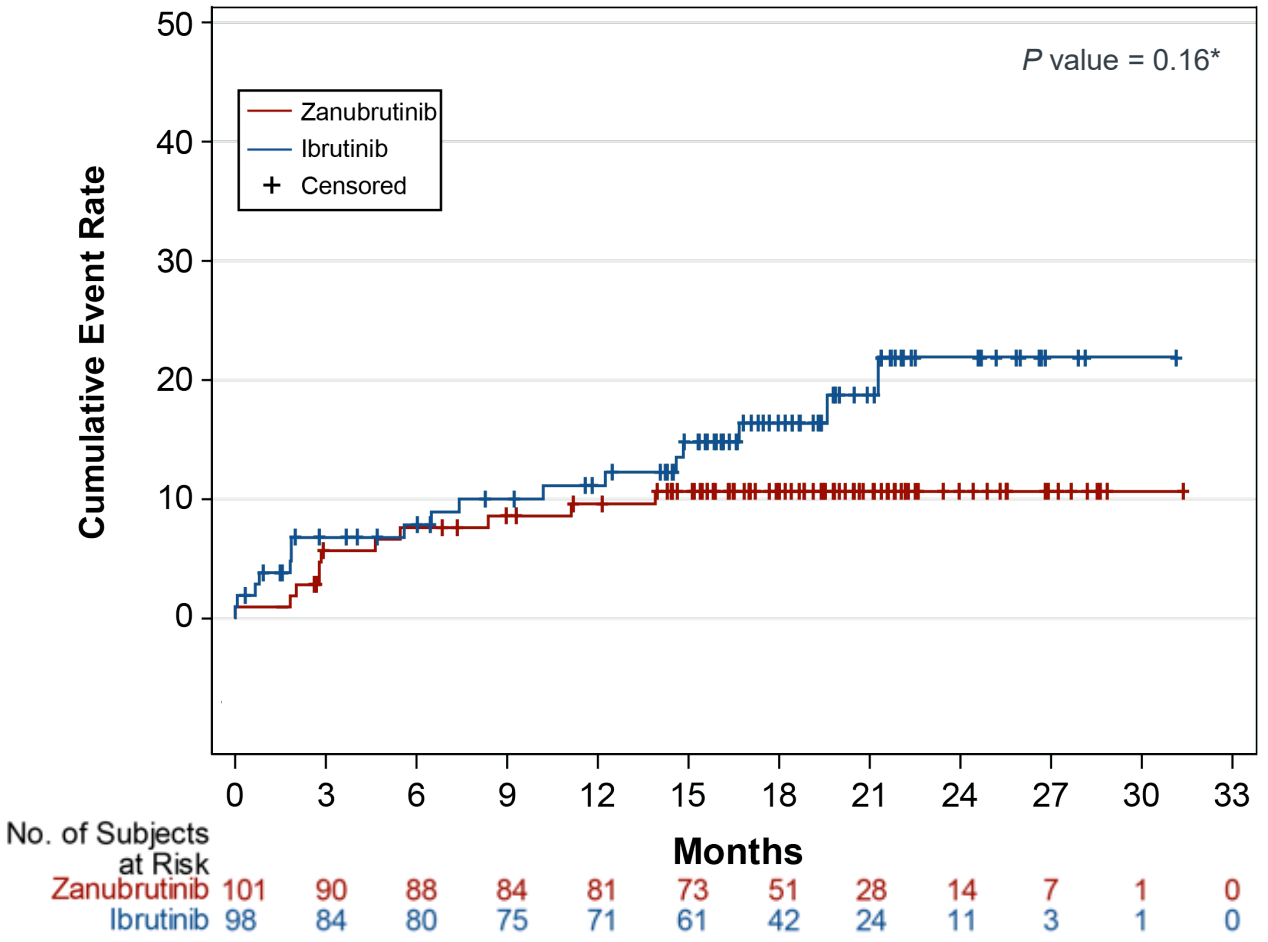
ASPEN: Time to AE – Risk Analysis Over Duration of Treatment

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



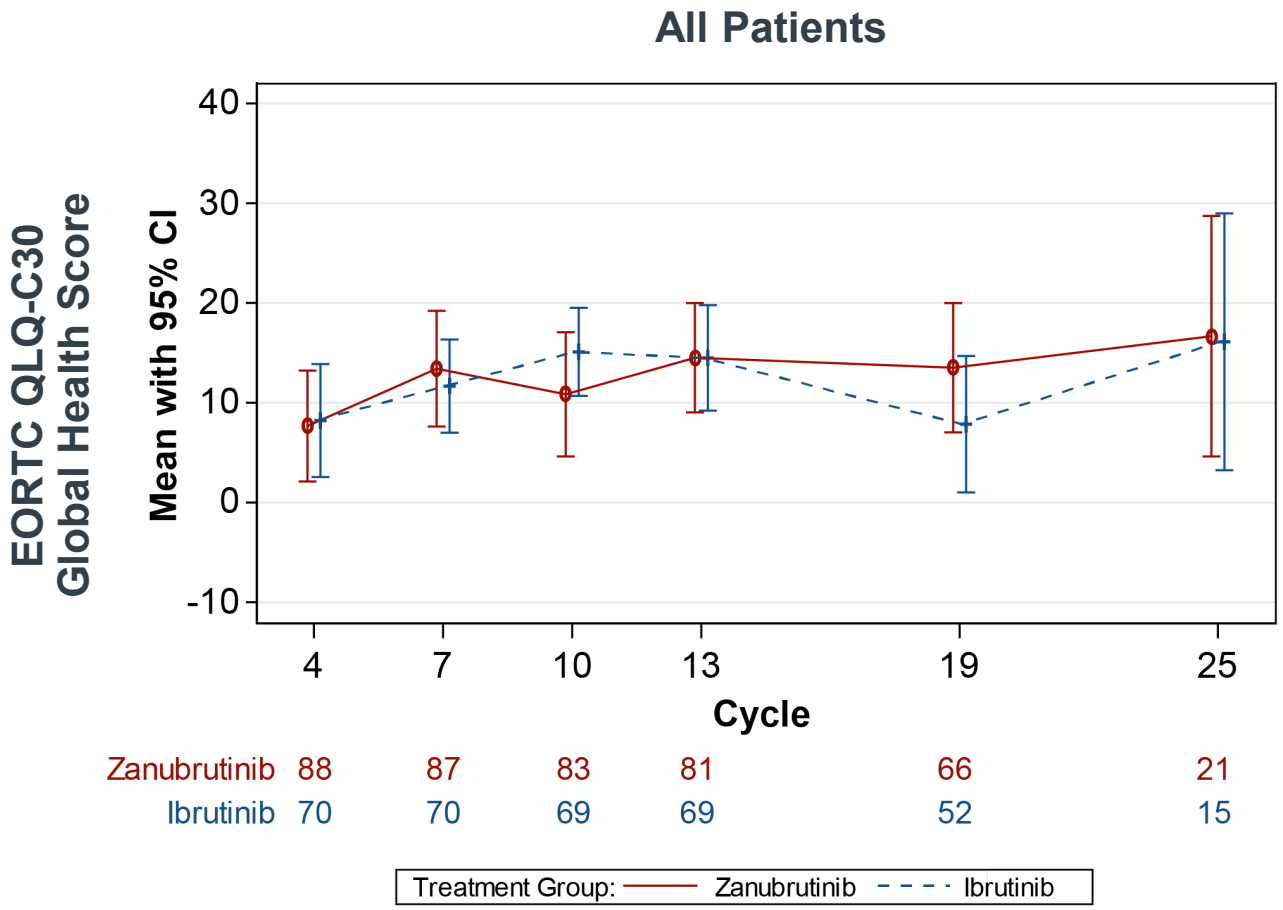
Kaplan-Meier Curve: Time to **Hypertension**

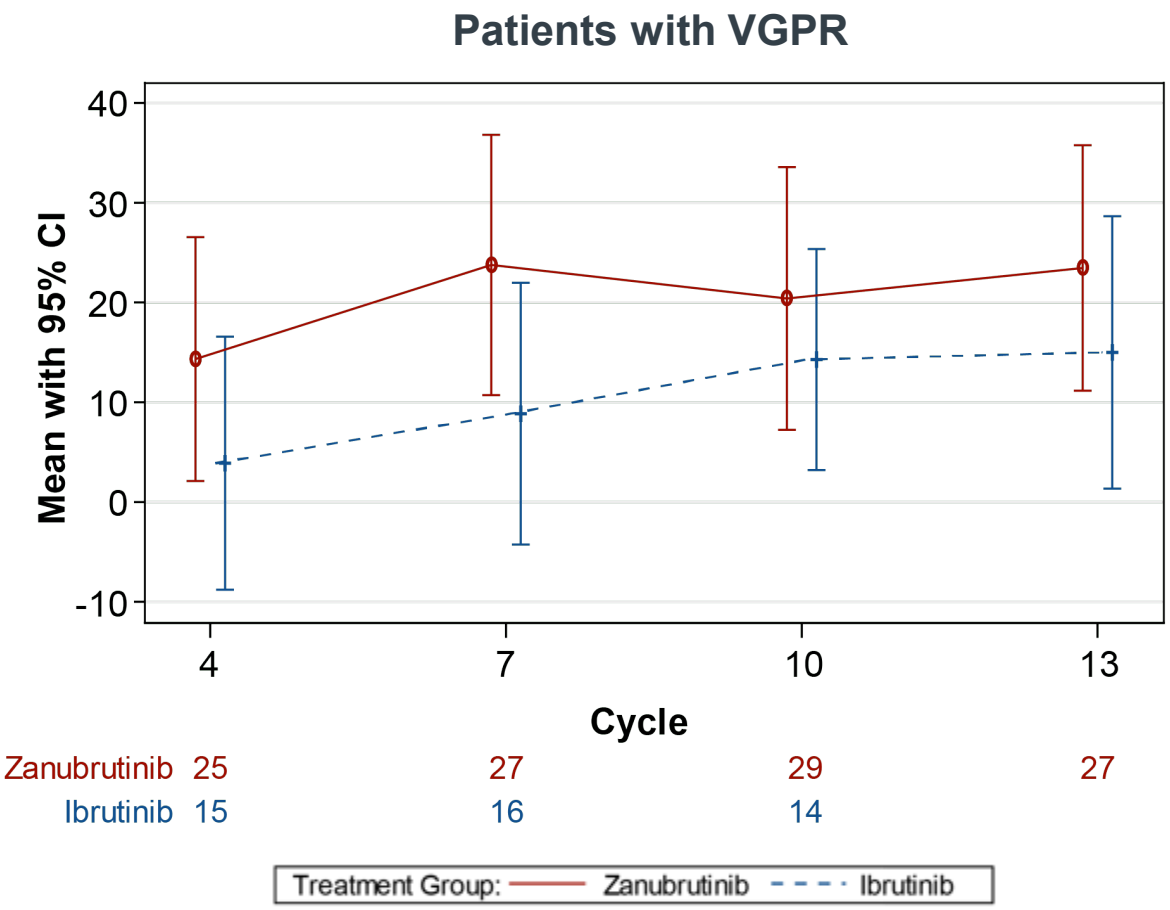


AE, adverse event. *Descriptive purpose only.

Aspen: Quality of Life – Change From Baseline Over Time

EORTC quality of life questionnaire - core questionnaire[1]





[1] EORTC QLQ-C30; VGPR, very good partial response

ASPEN Conclusions

Zanubrutinib was associated with a CR+VGPR response rate of 28.4% compared to ibrutinib of 19.2% (p= 0.0921)

- The primary hypothesis of superiority in CR+VGPR rate (by IRC) was not met with statistical significance
- Greater CR+VGPR response rate difference by investigator assessment (ITT: 28.4% vs 17.2%, *P*=0.04*)
- Deeper and sustained IgM reduction over time (*P*=0.04*)
- Major response rates were comparable, with directionally favorable PFS, OS, and QoL

Zanubrutinib demonstrated clinically meaningful advantages in safety and tolerability

- A reduction in the risk of atrial fibrillation/flutter (2.0% vs 15.3%, *P*= 0.0008*)
- Lower rates of major bleeding (5.9% vs 9.2%), diarrhea (20.8% vs 32.7%), and hypertension (10.9% vs 17.3%)
- There was no difference in the rate of infection despite higher rates of neutropenia with zanubrutinib
- Fewer AEs leading to death, treatment discontinuation or interruption with zanubrutinib

AEs, (treatment-emergent) adverse events; CR, complete response; IgM, Immunoglobulin M; IRC, independent review committee; ITT, intention-to-treat; OS, overall survival; PFS, progression-free survival; QoL, quality of life; VGPR, very good partial response.
*Descriptive purpose only.

BeiGene

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[1]Massachusetts General Hospital, Boston, MA; and [2]Memorial Sloan Kettering Cancer Center, New York, NY

The BOVen study = Brukinsa + Obinutuzumab + Venetoclax

Initial Results of a Multicenter, Investigator-Initiated Study of MRD Driven, Time-Limited Therapy with Zanubrutinib, Obinutuzumab, and Venetoclax in Patients with Previously Untreated CLL

Presented at the 2020 Annual Meeting of the American Society of Clinical Oncology (ASCO), May 29 – May 31, 2020
Abstract: 8007

BeiGene

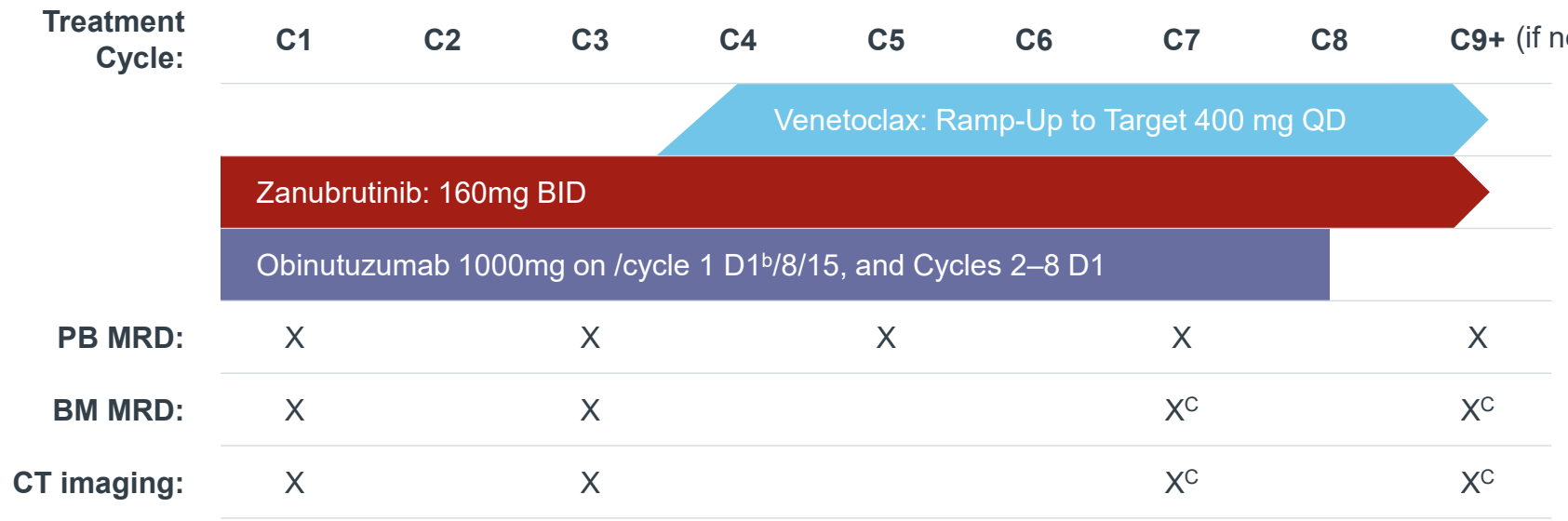
BOVen: BTK-BCL2 Combination Promising as Initial CLL Therapy

	CAPTIVATE-MRD (n=164)[1]	Jain IIT (n=80)[2,3]
Treatment	Ibrutinib-Venetoclax	Ibrutinib-Venetoclax
Age	58 (28-69)	65 (26-83)
IGHV unmutated	59%	83%
TP53 aberration	20% 17p del and/or TP53M	18% 17p del; 14% TP53M
PB / BM uMRD (10^{-4})	PB: 73% at 1y* (n=153) BM: 72% at best (n=155) * Plus 3 mo. Ibr lead-in	BM: 65% at 1y* (n=80) 75% at best (n=80) * Plus 3 mo. Ibr lead-in
AF (any grade)	6%	15%
Hemorrhage (grade ≥3)	1%	0%
Neutropenia (grade ≥3)	35%	51%
Febrile neutropenia (grade ≥3)	6%	5%

[1]Tam et al, ASH Proc 2019; [2]Jain et al, N Eng J Med 2019; [3]Jain et al, ASH Proc 2019.

BeiGene

BOVen: Treatment Schema



BOVen discontinued if:

- Prespecified uMRD end point[a]
- Min 8 cycles; Max 24 cycles

a. Once peripheral blood (PB) uMRD is determined and confirmed in bone marrow (BM), patients complete 2 additional cycles followed by confirmatory MRD peripheral blood testing; if PB uMRD x 2 and BM uMRD x 1, therapy is discontinued.

b. Obinutuzumab split over days 1-2 of cycle 1 if ALC >25,000.

c. BM biopsy obtained at Screening and C3D1; thereafter BM is only obtained if PB-uMRD. CT imaging obtained at Screening, C3D1, C7D1, EOT, then every 6 months during post-treatment surveillance.

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BOVen: Baseline Clinical Characteristics

	N=39
Enrollment period	March 2019 to October 2019
Median follow-up (months)	11 months (2–14+)
Age (years)	59 years (23–73)
Sex (Male:Female)	3:1
CLL-IPI high or very high risk(%)	72% (28/39)

- 72% had unmutated IGHV
- 15% had TP53 aberration

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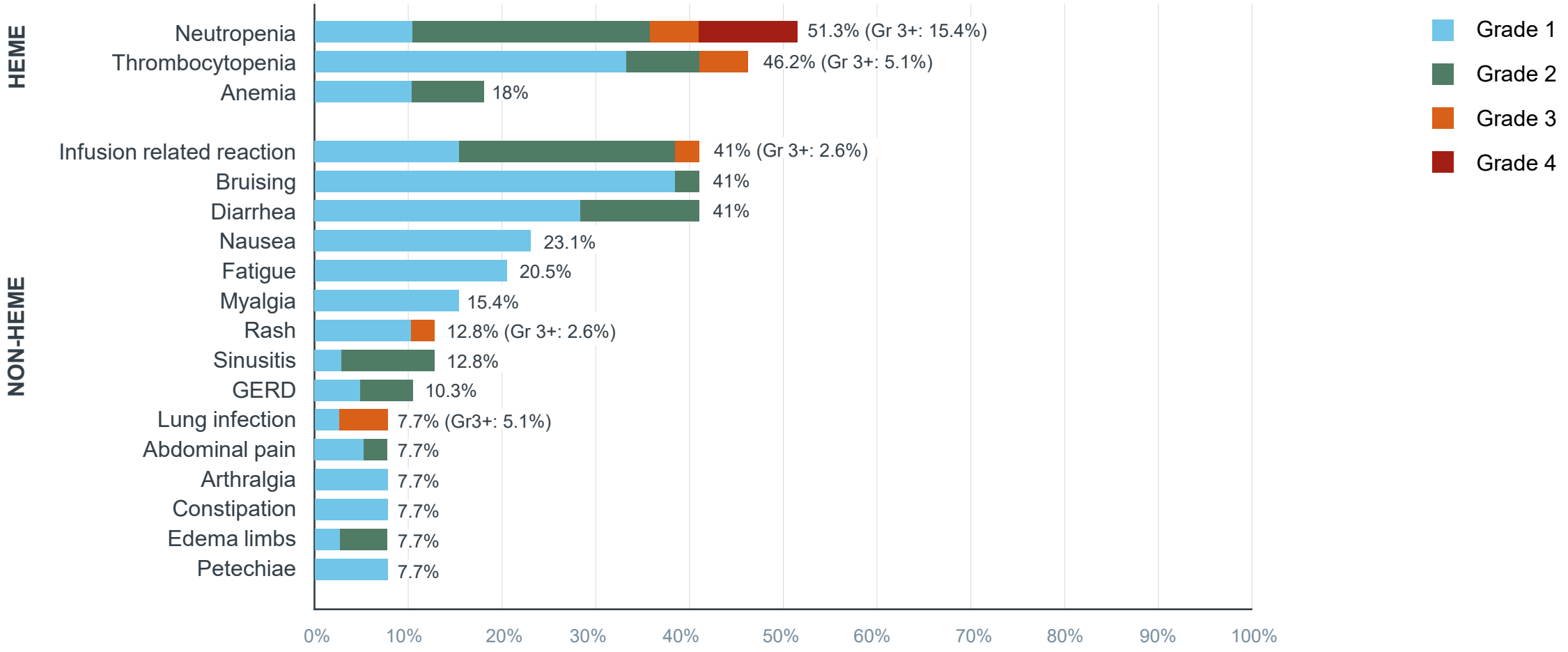
BOVen: Treatment Emergent Adverse Events



- Treatment emergent hematologic and non-hematologic adverse events occurring in ≥5% of patients are shown

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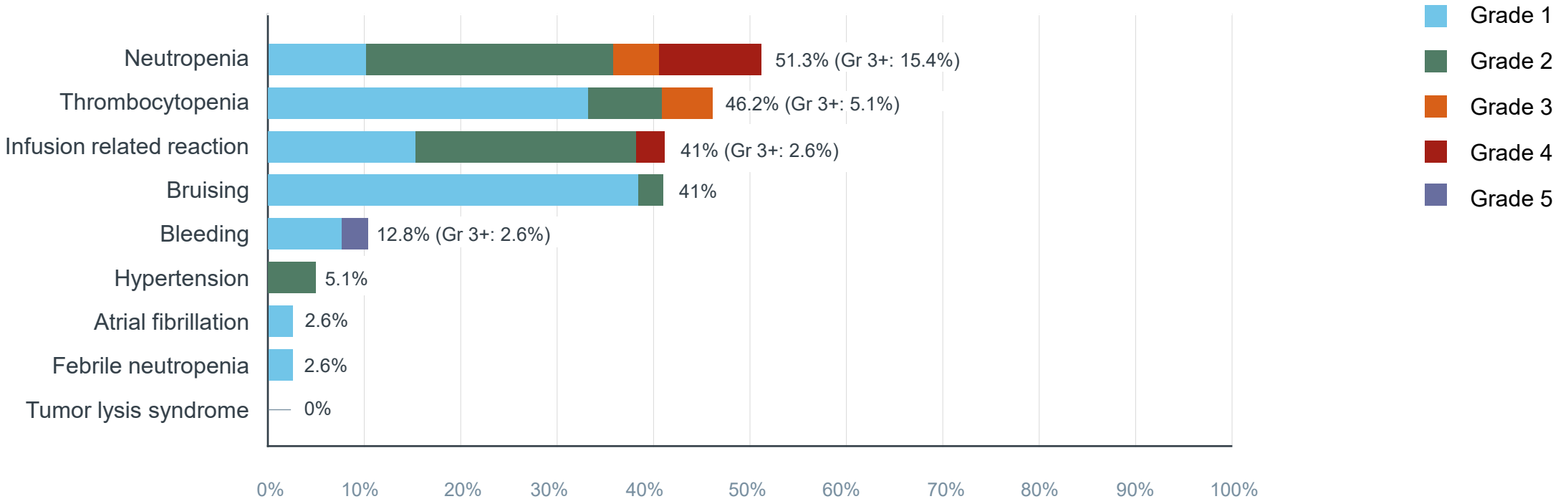
BOVen: Adverse Events of Special Interest



- Bleeding included one grade 5 ICH on cycle 1 day after initiating intravenous heparin for pulmonary emboli, one grade 1 conjunctival hemorrhage, and one grade 1 vaginal bleeding
- Atrial fibrillation occurred in one patient who had a history of prior paroxysmal atrial fibrillation

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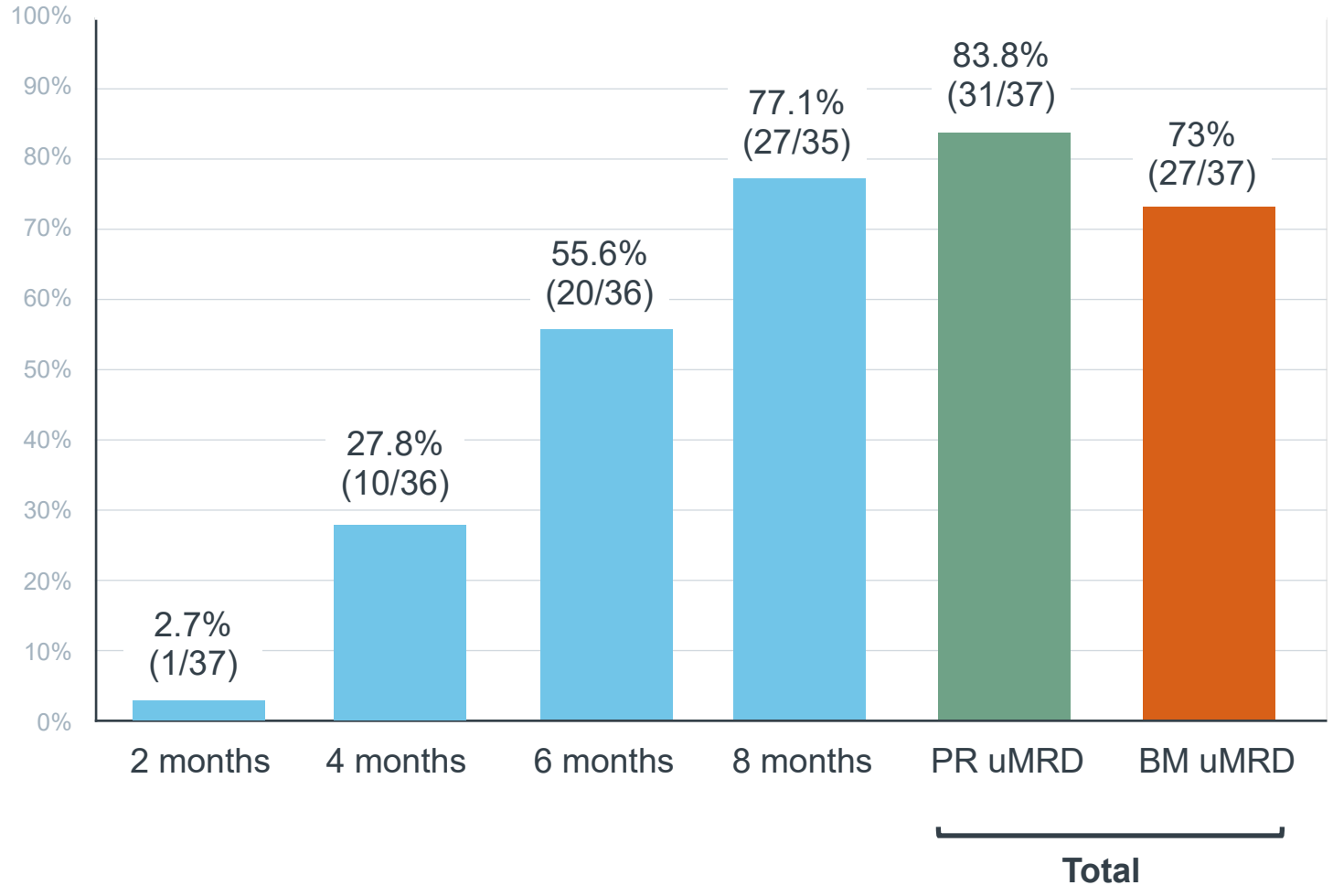
BOVen: Achieved Rapid Undetectable MRD



- Follow up: 11 months (2-14+)
- Median time to uMRD in marrow: 6 months (2-14+)
- 62% (23/37) met the uMRD endpoint and have stopped therapy at median 8 months (6 months of triplet)

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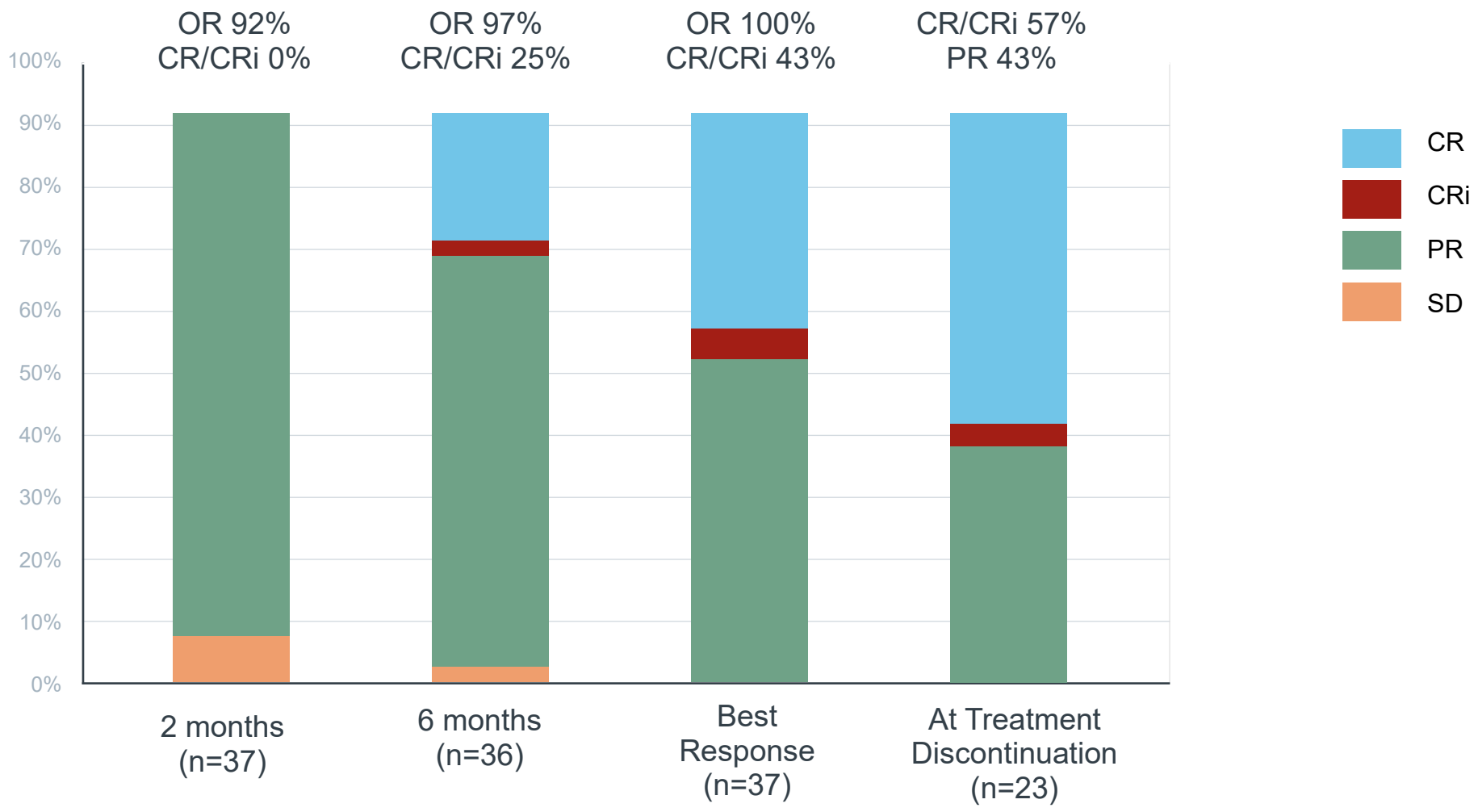
BOVen: iwCLL Response



BOVen: Conclusions

- The study demonstrated that BOVen was generally well tolerated with low rate of grade 3/4 neutropenia (15%)
- Zanubrutinib and obinutuzumab lead-in reduced TLS risk prior to venetoclax initiation, and no cases of laboratory or clinical TLS were observed
- BOVen achieved rapid undetectable MRD
  - 84% uMRD in blood and 73% uMRD in marrow (median follow up of 11 months)
  - Median time to uMRD in marrow of 6 months (4 months of triplet)
  - 62% have achieved the prespecified MRD endpoint and stopped therapy after a median of 8 months (6 months of triplet)
- The value of MRD-directed treatment duration will be evaluated with continued post-discontinuation follow up

BeiGene

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Chief Medical Officer, Immuno-Oncology

BeiGene

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[1]National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China; [2]Zhejiang Cancer Hospital, Hangzhou, China; [3]Shanghai Chest Hospital, Shanghai, China; [4]Hubei Cancer Hospital, Wuhan, China; [5]Jinan Central Hospital, Shandong, China; [6]Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education, Beijing), Department of Thoracic Medical Oncology, Peking University Cancer Hospital & Institute, Beijing, China; [7]Harbin Medical University Cancer Hospital, Harbin, China; [8]The Second Hospital of Central South University, Changsha, China; [9]Union Hospital Tongji Medical College Huazhong University of Science and Technology, Hubei, China; [10]The People's Hospital of Guangxi Zhuang Autonomous Region, Nanning, China; [11]Sir Run Shaw Hospital, Zhejiang University, School of Medicine, Zhejiang, China; [12]Fujian Tumor Hospital, Fuzhou, China; [13]The First Affiliated Hospital, Zhejiang University, Zhejiang, China; [14]The First Affiliated Hospital of Xiamen University, Fujian, China; [15]BeiGene (Beijing) Co., Ltd., Beijing, China; and [16]Hunan Cancer Hospital, Hunan, China

Phase 3 Study of Tislelizumab Plus Chemotherapy Versus Chemotherapy Alone as First-Line Treatment for Advanced Squamous Non-Small Cell Lung Cancer

Presented at the 2020 Annual Meeting of the American Society of Clinical Oncology (ASCO), May 29 – May 31, 2020
Abstract: 8007

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Tislelizumab in 1L Sq NSCLC

- In China, lung cancer is the most commonly diagnosed cancer and is the leading cause of cancer-related death[1]
- First-line treatment for advanced squamous NSCLC in China historically has been platinum-doublet chemotherapy
  - Prognosis for patients remains poor[2]
- Tislelizumab:
  - A humanized monoclonal IgG4 antibody with high affinity and specificity for PD-1
  - Engineered to minimize binding to FcγR on macrophages, thereby abrogating antibody-dependent phagocytosis, a potential mechanism of T-cell clearance, which may minimize potentially negative interactions with other immune cells based on preclinical data[3, 4])
- Phase 2 study[5] suggested tislelizumab plus platinum-doublet chemotherapy was generally well tolerated and demonstrated antitumor activity in Chinese patients with squamous NSCLC[6]

[1]Bray F, Ferlay J, Soerjomataram I, et al. CA Cancer J Clin. 2018:68(66):394-424. [2]Shi Y, Sun Y, Yu J, et al. Asia Pac J Clin Oncol. 2017;13(1):87-103. [3]Lee A, Keam SJ. Tislelizumab: first approval. Drugs. 2020;80:617-624. [4]Dahan R, Sega E, Engelhardt J, Selby M, Korman AJ, Ravetch JV. *Cancer Cell.* 2015;28(3):285-295. [5](NCT03432598). [6]Wang Z, Zhao J, Ma Z, et al. Lung Cancer. Under review.

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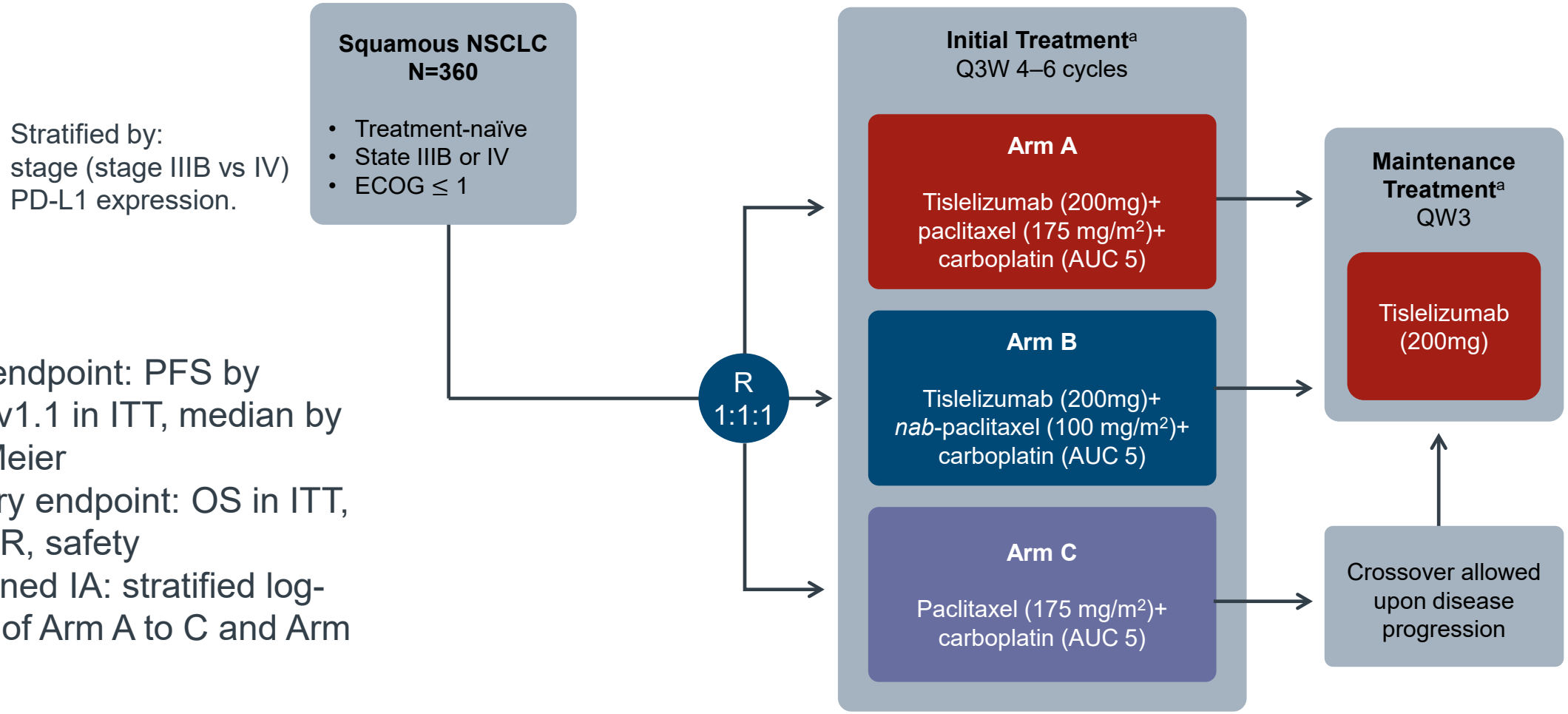
Tislelizumab in 1L Sq NSCLC: Study Schema



- Primary endpoint: PFS by RECIST v1.1 in ITT, median by Kaplan-Meier
- Secondary endpoint: OS in ITT, ORR, DoR, safety
- One planned IA: stratified log-rank test of Arm A to C and Arm B to C

[a] Paclitaxel, nab-paclitaxel, and carboplatin were administered for four to six cycles, and tislelizumab was administered until disease progression, intolerable toxicity, or treatment discontinuation.
Abbreviations: D, day; ECOG, Eastern Cooperative Oncology Group; nab, nanoparticle albumin-bound; NSCLC, non-small cell lung cancer; PD-L1, programmed death ligand-1; Q3W, every 3 weeks; R, randomized.

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Tislelizumab in 1L Sq NSCLC: Demographics And Baseline Characteristics

		Arm A Tislelizumab + PC (n=120)	**Arm B** Tislelizumab + *nab*-PC (n=119)	**Arm C** PC (n=121)	**Total** (N=360)
Median age, years (range)		60 (41–74)	63 (38–74)	62 (34–74)	62 (34–74)
Age group, n (%)	< 65	81 (67.5)	67 (56.3)	85 (70.2)	233 (64.7)
	≥ 65	39 (32.5)	52 (43.7)	36 (29.8)	127 (35.3)
Sex, n (%)	Male	107 (89.2)	112 (94.1)	111 (91.7)	330 (91.7)
	Female	13 (10.8)	7 (5.9)	10 (8.3)	30 (8.3)
Tobacco use, n (%)	Former	72 (60.0)	86 (72.3)	71 (58.7)	229 (63.6)
	Current	24 (20.0)	21 (17.6)	27 (22.3)	72 (20.0)
	Never	24 (20.0)	12 (10.1)	23 (19.0)	59 (16.4)
ECOG status, n (%)	0	31 (25.8)	22 (18.5)	32 (26.4)	85 (23.6)
	1	89 (74.2)	97 (81.5)	89 (73.6)	275 (76.4)
Solid tumor stage, n (%)	Stage IIIB	38 (31.7)	40 (33.6)	44 (36.4)	122 (33.9)
	Stage IV	82 (68.3)	79 (66.4)	77 (63.6)	238 (66.1)
PD-L1 expression on tumor cells, n (%)	< 1%	48 (40.0)	47 (39.5)	49 (40.5)	144 (40.0)
	1–49%	30 (25.0)	30 (25.2)	31 (25.6)	91 (25.3)
	≥ 50%	42 (35.0)	42 (35.3)	41 (33.9)	125 (34.7)
Confirmed distance metastatic site(s)[a], n (%)	Bone	24 (20.0)	16 (13.4)	21 (17.4)	61 (16.9
	Liver	15 (12.5)	15 (12.6)	14 (11.6)	44 (12.2)
	Brain	2 (1.7)	3 (2.5)	1 (0.8)	6 (1.7)

[a] [a]patient was counted only once within each category but may be counted in multiple categories.
Abbreviations: ECOG, Eastern Cooperative Oncology Group; ITT, intent-to-treat; nab, nanoparticle albumin-bound; PC, paclitaxel and carboplatin; PD-L1, programmed death ligand-1.

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Tislelizumab in 1L Sq NSCLC: Safety

Overall Summary

	Arm A Tislelizumab + PC (n=120)	**Arm B** Tislelizumab + *nab*-PC (n=119)	**Arm C** PC (n=121)
Patients with ≥ 1 TEAE	120 (100.0)	117 (99.2)	117 (100.0)
Serious TEAE	44 (36.7)	45 (38.1)	29 (24.8)
TEAE leading to permanent discontinuation of any study treatment component	15 (12.5)	35 (29.7)	18 (15.4)
TEAE leading to death	4 (3.3)	5 (4.2)	5 (4.3)

Data presented as n (%).

- Investigator-assessed TEAEs related to any study treatment were reported in 99.2%, 99.2%, and 100% of patients in Arms A, B, and C, respectively
- The most commonly reported treatment-related AEs (TRAEs) associated with any study component were mainly hematologic in nature

TRAEs Associated With Any Study Component and Occurring in ≥ 20% in Any Arm

Preferred Term, n (%)	**Arm A** Tislelizumab + PC (n=120)		**Arm B** Tislelizumab + *nab*-PC (n=119)		**Arm C** PC (n=121)	
	All Grades	Grades ≥3	All Grades	Grades ≥3	All Grades	Grades ≥3
Anemia	99 (82.5)	6 (5.0)	104 (88.1)	24 (20.3)	87 (74.4)	11 (9.4)
Alopecia	77 (64.2)	0	81 (68.6)	0	72 (61.5)	0
Neutrophil count decreased	75 (62.5)	62 (51.7)	72 (61.0)	54 (45.8)	68 (58.1)	53 (45.3)
White blood cell count decreased	63 (52.5)	26 (21.7)	68 (57.6)	32 (27.1)	62 (53.0)	28 (23.9)
Leukopenia	57 (47.5)	19 (15.8)	66 (55.9)	30 (25.4)	56 (47.9)	21 (17.9)
Neutropenia	51 (42.5)	40 (33.3)	50 (42.4)	32 (27.1)	55 (47.0)	47 (40.2)
Decreased appetite	50 (41.7)	1 (0.8)	49 (41.5)	1 (0.8)	35 (29.9)	1 (0.9)
ALT increased	48 (40.0)	2 (1.7)	40 (33.9)	2 (1.7)	27 (23.1)	0
Platelet count decreased	40 (33.3)	5 (4.2)	52 (44.1)	16 (13.6)	28 (23.9)	2 (1.7)
AST increased	39 (32.5)	0	38 (32.2)	1 (0.8)	13 (11.1)	0
Nausea	34 (28.3)	0	48 (40.7)	0	29 (24.8)	1 (0.9)
Thrombocytopenia	33 (27.5)	7 (5.8)	47 (39.8)	15 (12.7)	32 (27.4)	7 (6.0)
Pain in extremity	33 (27.5)	3 (2.5)	8 (6.8)	0	23 (19.7)	0
Blood bilirubin increased	27 (22.5)	0	14 (11.9)	0	15 (12.8)	0
Asthenia	26 (21.7)	0	19 (16.1)	0	23 (19.7)	1 (0.9)
Hypoesthesia	25 (20.8)	0	11 (9.3)	0	19 (16.2)	0
Vomiting	24 (20.0)	0	22 (18.6)	0	15 (12.8)	2 (1.7)

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; nab, nanoparticle albumin-bound; PC, paclitaxel and carboplatin; TEAE, treatment-emergent adverse event, TRAE, treatment-related adverse event.

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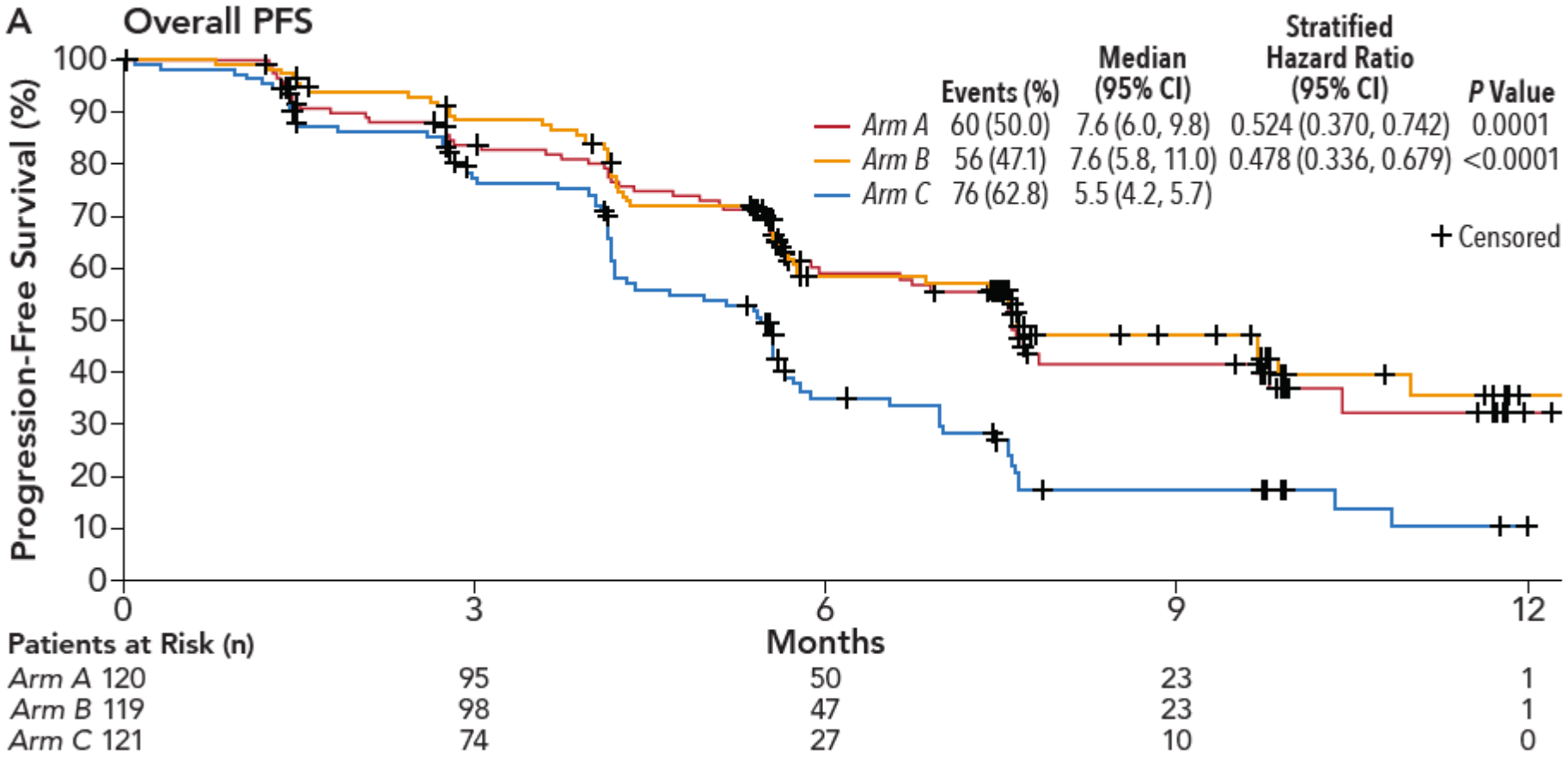
Tislelizumab in 1L Sq NSCLC: PFS by IRC



Abbreviations: CI, confidence interval; PD-L1, programmed death ligand-1; PFS, progression-free survival; TC, tumor cell.

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Tislelizumab in 1L Sq NSCLC: Response

		Arm A Tislelizumab + PC (n=120)	Arm B Tislelizumab + *nab*-PC (n=119)	Arm C PC (n=121)
BOR, n (%)	CR	5(4)	3 (3)	1 (< 1)
	PR	82 (68)	86 (72)	59 (49)
	SD	18 (15)	19 (16)	36 (30)
	Non-CR/non-PD	0	0	1 (< 1)
	PD	12 (10)	5 (4)	11 (9)
	NE/missing	3(3)	6 (5)	13 (11)
ORR, % (95% CI)		73 (63.6, 80.3)	75 (66.0, 82.3)	50 (40.4, 58.8)
DCR, % (95% CI)		88 (80.2, 92.8)	91 (84.1, 95.3)	80 (71.9, 86.9)
CBR, %* (95% CI)		81 (72.6, 87.4)	80 (71.5, 86.6)	56 (46.9, 65.2)
Median DoR, months (95% CI)		8.2 (5.0, NE)	8.6 (6.3, NE)	4.2 (2.8, 4.9)

DCR=CR+PR+SD. *Includes patients with BOR in CR or PR or ≥24 weeks SD.
Abbreviations: BOR, best overall response; CBR, clinical benefit rate; CI, confidence interval; CR, complete response; DCR, disease control rate; IRC, Independent Review Committee; ITT, intent-to-treat; nab, nanoparticle albumin-bound; NE, not evaluable; ORR, objective response rate; PC, paclitaxel and carboplatin; PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease.

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Tislelizumab in 1L Sq NSCLC: Conclusions

- Interim analysis of this Phase 3 trial showed that tislelizumab plus paclitaxel and carboplatin and tislelizumab plus nab-paclitaxel and carboplatin resulted in significantly improved PFS as well as higher ORR and longer DoR compared with carboplatin and paclitaxel alone in first-line patients with advanced squamous NSCLC
- With median study follow-up of 8.6 months, median OS has not been reached
- First-line treatment with tislelizumab in combination with paclitaxel and carboplatin or nab-paclitaxel and carboplatin was generally well tolerated
  - The incidence and frequency of observed AEs (including grade ≥3) were similar to paclitaxel and carboplatin alone
  - Most AEs were mild or moderate in severity and manageable
- Reported TRAEs were consistent with known tolerability profiles of doublet chemotherapy; no new safety signals were identified with the addition of tislelizumab to both chemotherapy backbones
- The results from this pivotal phase 3 study support tislelizumab in combination with paclitaxel and carboplatin or nab-paclitaxel and carboplatin as a potential new treatment option for patients with first-line advanced squamous NSCLC, irrespective of PD-L1 expression

BeiGene

Program Status and Key Takeaways

Eric Hedrick, M.D.

Chief Advisor

BeiGene

ASCO Key Takeaways / Next Steps

Zanubrutinib

Zanubrutinib in WM

- ASPEN study data clearly defines distinctions between zanubrutinib and ibrutinib in the treatment of WM
  - Data in totality is consistent with our best-in-class development hypothesis
  - While primary endpoint (VGPR by IRC) not met, secondary efficacy analyses (VGPR by investigator, IgM reduction over time) clearly favor zanubrutinib
  - Clear safety advantages for zanubrutinib, including a lower cardiovascular toxicity risk compared with ibrutinib
- Ongoing discussions with FDA and EMA regarding filing for approval of zanubrutinib in WM

Zanubrutinib in CLL

- BOVen data is the first demonstration of efficacy and safety of zanubrutinib/venetoclax combination in initial treatment of CLL
  - High rate of MRD-negative responses and favorable safety profile (especially in respect to cardiovascular toxicity) offer promise for this triplet as a fixed-course treatment for 1L CLL
- Monotherapy Phase 3 trials in 1L CLL (vs BR) and R/R CLL (vs ibrutinib) are maturing
  - Data from Phase 3 1L CLL trial vs BR (SEQUOIA) as early as 2H 2020

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Brukinsa Broad Clinical Development Program

Nine filed or potentially registration-enabling studies

MCL	Pivotal Phase 2 (n=86) in R/R MCL zanu monotherapy, PE: ORR Initiated: Mar 2017, Enrollment complete: Sep 2017 NDA accepted by NMPA Aug. 2018, approved by U.S. FDA in Nov. 2019 under accelerated approval	Phase 3 (n=500) in 1L MCL R+zanu vs. R+chemo, PE: PFS Initiated: Nov 2019	Phase 1/2 cohort (n=45) in MCL zanu monotherapy, PE: Safety RP2D Initiated: Aug 2014, Enrollment complete: Jun 2019
WM	Phase 3 (n=229) in WM (ASPEN) zanu vs. ibrutinib, PE: VGPR/CR, Initiated: Jan 2017, Enrollment complete: Jul 2018, Top-line data: Dec 2019	Pivotal Phase 2 (n=44) in R/R WM zanu monotherapy, PE: MRR Initiated: Aug 2017, Enrollment complete: May 2018	Phase 1/2 (n=80) in WM zanu monotherapy, PE: Safety, RP2D Initiated: Aug 2014, Enrollment complete: Jun 2019
CLL/ SLL	Pivotal Phase 2 (n=91) in R/R CLL/SLL zanu monotherapy, PE: ORR Initiated: Mar 2017, Enrollment complete: Dec 2017 NDA accepted	Phase 3 (n=550) in 1L CLL/SLL (SEQUOIA) zanu vs. BR, PE: PFS, Initiated: Nov 2017, Enrollment complete^: Aug 2019	Phase 3 (n=600) in R/R CLL/SLL (ALPINE) zanu vs. ibrutinib, PE: ORR Initiated: Nov 2018
	Phase 1 cohort (n=125) in CLL/SLL zanu monotherapy, PE: Safety RP2D Initiated: Aug 2014, Enrollment complete: Jun 2019	Phase 2 (n=60) in previously treated CLL/SLL (ibrutinib intolerant) zanu monotherapy, PE: Frequency and severity of treatment-emergent AEs of interest Initiated: Nov 2019	**COVID-19** Phase 2 (n=42) in COVID-19 zanu monotherapy, 28 day respiratory-failure free survival Initiated: May 2020
FL	Pivotal phase 2 (n=210) in R/R FL Obinutuzumab ± zanu, PE: ORR Initiated: Nov 2017	**MZL** Phase 2[1] (n=65) in R/R MZL (MAGNOLIA) zanu monotherapy, PE: ORR Initiated: Feb 2019, complete^: 4Q19	Phase 1b: zanu + ME-401, in B-cell malignancies
DLBCL	Phase 2: Monotherapy, R/R Non-GCB DLBCL	Phase 1b/2: zanu + tislelizumab, B-cell malignancies	**CLL Combination** Phase 1b: zanu + obinutuzumab, R/R CLL Phase 2: zanu / venetoclax / obinutuzumab in 1L CLL (MSKCC study)
	Phase 1b: zanu + Revlimid, R/R DLBCL	Phase 1b: zanu + R-chemo, 1L and 2L DLBCL	Phase 2: zanu / venetoclax / obinutuzumab in 1L CLL (GCLLSG study) Phase 1 in hematologic malignancies Bcl-2 inhibitor BGB-11417 monotherapy and comb. with zanu Initiated: 1Q20

Approved
Filed, in NDA review
Enrollment complete
Enrolling
Planned
Filed or potentially registrational

China
Global

^Time of the announcement of the enrollment completion; 1L: First Line; CLL/SLL: Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma; CR: Complete Response; DLBCL: Diffuse Large B-Cell Lymphoma; FL: Follicular Lymphoma; GCB: Germinal Center B-cell-like; MCL: Mantle Cell Lymphoma; MRR: Major Response Rate; MZL: Marginal Zone Lymphoma; NHL: Non-Hodgkin's Lymphoma; ORR: Overall Response Rate; PCNSL: Primary Central Nervous System Lymphoma; PE: Primary endpoint; PFS: Progression-Free Survival; RP2D: Recommended Phase 2 Dose; R/R: Relapsed / Refractory; RT: Richter's Transformation; VGPR: Very Good Partial Response; WM: Waldenström's Macroglobulinemia. 1. global trial and potentially registration-enabling in certain countries.

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ASCO Key Takeaways / Next Steps

Tislelizumab

Tislelizumab in Lung Cancer

- In Phase 3 studies in both squamous and non-squamous NSCLC, the addition of tislelizumab to standard combination chemotherapy significantly prolongs PFS
- Interim analysis of Phase 3 study of tislelizumab in squamous NSCLC presented at ASCO
  - Robust, highly statistically significant improvement in PFS (HR of 0.52 and 0.48 respectively), DOR, and RR when added to either paclitaxel/carboplatin or nab-paclitaxel/carboplatin
  - Safety profile consistent with checkpoint inhibitor class
- Positive interim analysis of Phase 3 study in non-squamous NSCLC
- Additional ongoing Phase 3 studies in 2L NSCLC and 1L SCLC; Phase 3 in Stage II/IIIA NSCLC initiating

Tislelizumab Next Steps

- Filed with China NMPA for approval in 1L squamous NSCLC
  - 1st China-originated checkpoint inhibitor to be filed in this indication
- Anticipate 2020 filing with China NMPA for 1L non-squamous NSCLC indication
- Regulatory discussions with health authorities on filing for 2L/3L HCC, data to be presented at the ESMO World Congress on Gastrointestinal Cancer Virtual Symposium (July 1-4)
- In late 2020 or early 2021, Phase 3 read-outs anticipated in 2L NSCLC and 2L esophageal cancer

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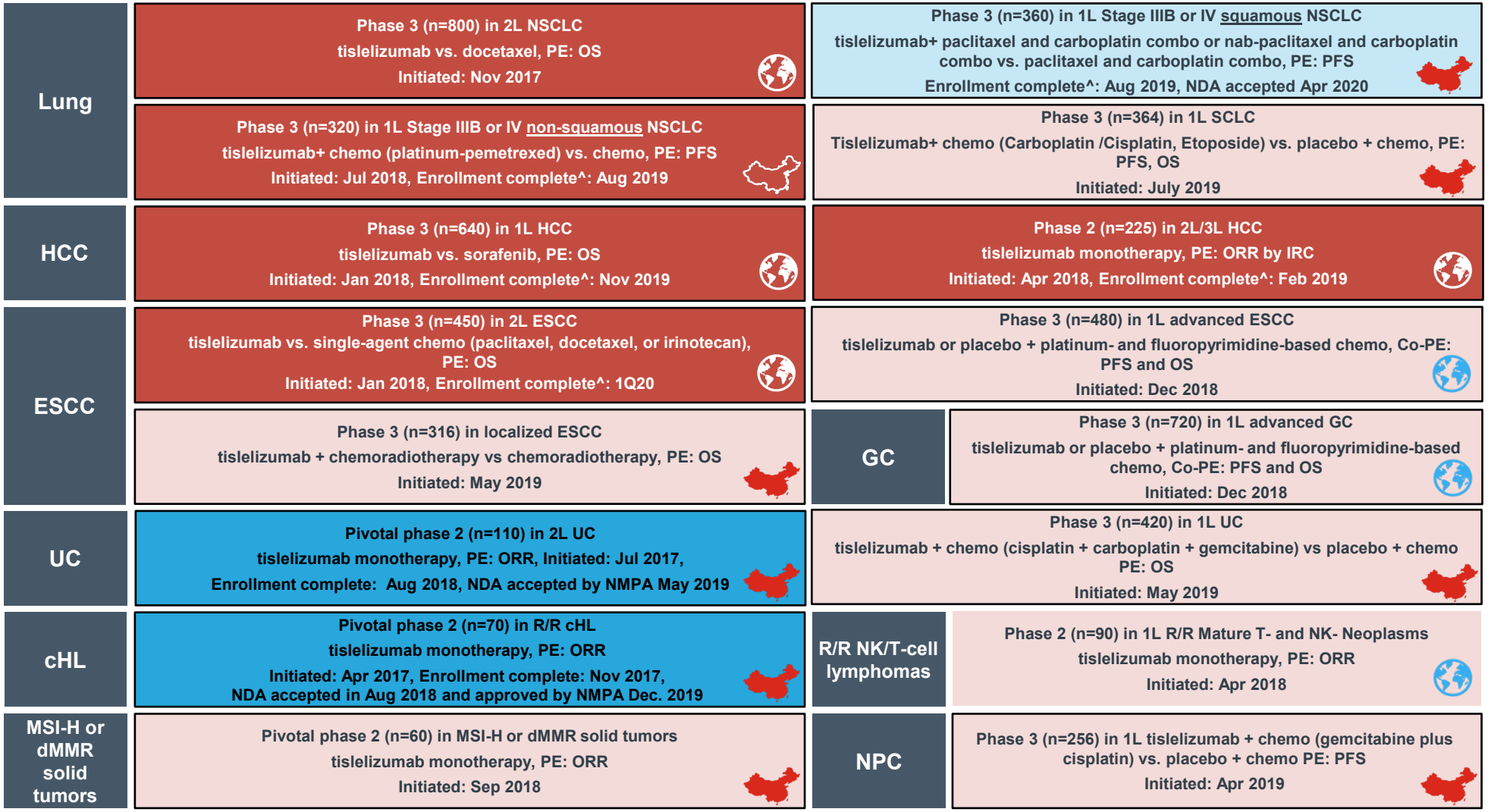
Tislelizumab Broad Late-stage Development Program

Fifteen filed or potentially registration-enabling studies



^Time of the announcement of the enrollment completion; *Tislelizumab dosage 200mg every three weeks, Q3W. Global Ph2 in R/R/ NK/T-cell lymphoma and Ph2 trial in MSI-H or dMMR solid tumors in China are potentially registrational-enabling trials. 1/2L: First/Second Line; cCRT: concurrent chemoradiotherapy; cHL: Classical Hodgkin's Lymphoma; ESCC: Esophageal Squamous-Cell Carcinoma; GC: Gastric Cancer; HCC: Hepatocellular Carcinoma; IRC: Independent Review Committee; ITT: Intent-to-treat; MSI-H or dMMR: Microsatellite Instability High or Deficient Mismatch Repair; NDA: New Drug Application; NK: Natural Killer; NSCLC: Non-Small Cell Lung Cancer; ORR: Overall response rate; OS: Overall survival; PE: Primary Endpoint; PFS: Progression-free survival; R/R: Relapsed / Refractory; UC: Urothelial Carcinoma;

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Tislelizumab Combination Studies

COMBINATION	MECHANISM OF ACTION	INDICATIONS	DOSE ESC.	DOSE EXPANSION	
			PH1a	PH1b	PH2
+ sitravatinib[1]	multi-kinase inhibitor	HCC or GEJ, NSCLC, RCC, OC, melanoma			
+ BGB-A333	PD-L1 antibody	Solid tumors			
+ BGB-A425	TIM-3 antibody	Solid tumors			
+ BGB-A1217	TIGIT antibody	Solid tumors			
+ BGB-A445	Non ligand-competing OX-40 antibody	Solid tumors			
+ zanubrutinib	BTK inhibitor	B-cell malignancies			
+ pamiparib	PARP inhibitor	Solid tumors			
+ ZW25[2]	bispecific HER2 antibody	BC, GC and GEJ			
+ BGB-10188	PI3K Delta inhibitor	Solid tumors			
+ lenvatinib	VEGFR inhibitor	HCC	*Phase 2 trial initiating*		
+ BA3071[3]	pH-dependent CTLA-4 antibody	Solid tumors	*Phase 1 trial planned*		
+ DKN-01[4]	Anti-DKK1 antibody	GC or GEJ	*Phase 2 trial planned*		
+ surufatinib[5]	VEGFR inhibitor	Solid tumors	*Phase 2 trial planned*		
+ fruquitinib[5]	VEGFR inhibitor	Solid tumors	*Phase 2 trial planned*		

*Clinical trials in Asia Pacific regions.1.Collaboration with Mirati Therapeutics, Inc., 2. Collaboration with Zymeworks; 3. Collaboration with BioAtla, LLC; 4. Collaboration with Leap Therapeutics; 5. Collaboration with Hutchison China MediTech Ltd. GEJ: gastroesophageal junction cancer. GC: gastric cancer. HCC: hepatocellular carcinoma. NSCLC: non-small cell lung cancer. RCC: renal cell carcinoma. OC: ovarian cancer. BC: breast cancer.

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Q&A

BeiGene Participants:

- John V. Oyler
- Xiaobin Wu, Ph.D.
- Howard Liang, Ph.D.
- Yong (Ben) Ben, M.D.
- Eric Hedrick, M.D.
- Jane Huang, M.D.
- Josh Neiman

Guest Participants:

- Constantine Tam, M.D.
- Andrew Zelenetz, M.D.

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Closing Remarks

Please join us on our ASCO20 microsite for more detailed overview of our current work

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Appendix

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Zanubrutinib: A Potent and Selective BTK Inhibitor[1,2]

Potent, selective, irreversible; minimize off-target inhibition

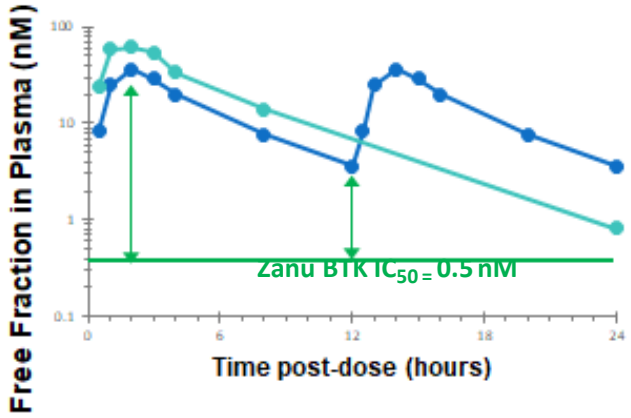
Targets	Assays	Zanubrutinib IC_{50} (nM)	Ibrutinib IC_{50} (nM)	Ratio (Zanubrutinib:Ibrutinib)
BTK	BTK-pY223 Cellular Assay	1.8	3.5	0.5
	Rec-1 Proliferation	0.36	0.34	1.1
	BTK Occupation Cellular Assay	2.2	2.3	1.0
	BTK Biochemical Assay	0.22	0.2	1.1
EGFR	p-EGFR HTRF Cellular Assay	606	101	6
	A431 Proliferation	3210	323	9.9
ITK	ITK Occupancy Cellular Assay	606	189	17
	p-$PLC_{\gamma1}$ Cellular Assay	3433	77	45
	IL-2 Production Cellular Assay	2536	260	9.8
	ITK Biochemical Assay	30	0.9	33
JAK3	JAK3 Biochemical Assay	200	3.9	51
HER2	HER2 Biochemical Assay	661	9.4	70
TEC	TEC Biochemical Assay	1.9	0.8	2.4

BID, twice daily; QD: once daily; BTK, Bruton tyrosine kinase; CLL, chronic lymphocytic leukemia; DLBCL, diffuse large B-cell lymphoma; EGFR, epidermal growth factor receptor; FL, follicular lymphoma; HER2, human epidermal growth factor receptor 2; HRRF, Homogeneous Time Resolved Fluorescence; IC_{50}, half maximal inhibitory concentration; ITK, IL2-inducible T-cell kinase; JAK3, Janus tyrosine kinase 3; MCL, mantle cell lymphoma; MZL, marginal zone lymphoma; PLC, phospholipase C; WM, Waldenström Macroglobulinemia; Zanu, zanubrutinib.

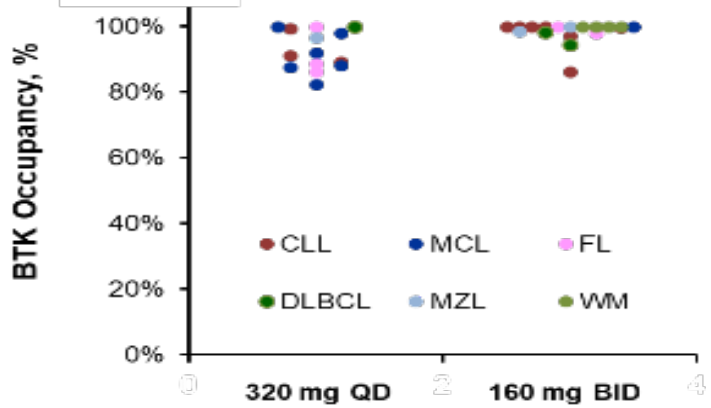
[1]Guo Y, et al. *J Med Chem.* 2019;62:7923-7940. [2]Tam CS, et al. *Blood*. 2019;134:851-859.

C_{max} and C_{trough} > BTK IC_{50} over 24 hours

160 mg BID and 320 mg QD



Complete, sustained BTK occupancy



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ASPEN: Study Objectives

Primary Objective

- To compare the efficacy of zanubrutinib vs ibrutinib
  - Primary endpoint was CR + VGPR rate in patients with activating mutations (*MYD88*^{MUT}) WM

Secondary Objective

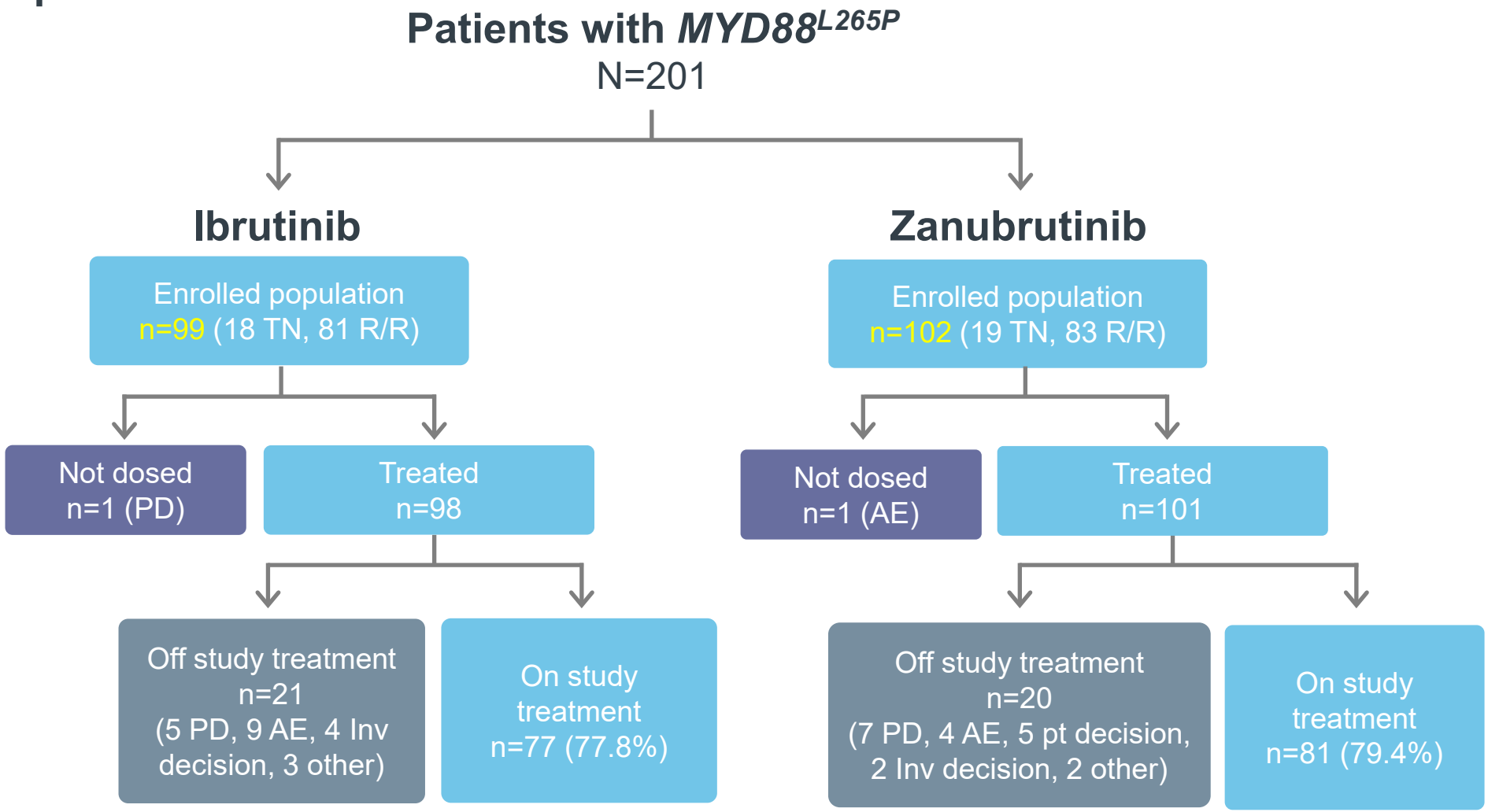
- To further compare the efficacy, clinical benefit, and anti-lymphoma effects of zanubrutinib vs ibrutinib
- To evaluate safety and tolerability of zanubrutinib versus ibrutinib as measured by the incidence, timing, and severity of TEAEs according to NCI-CTCAE (version 4.03)

Third Objective

- To characterize the PK of zanubrutinib in patients with WM
- To compare QoL by EORTC QLQ-C30 and EQ-5D

ASPEN: Patient Disposition

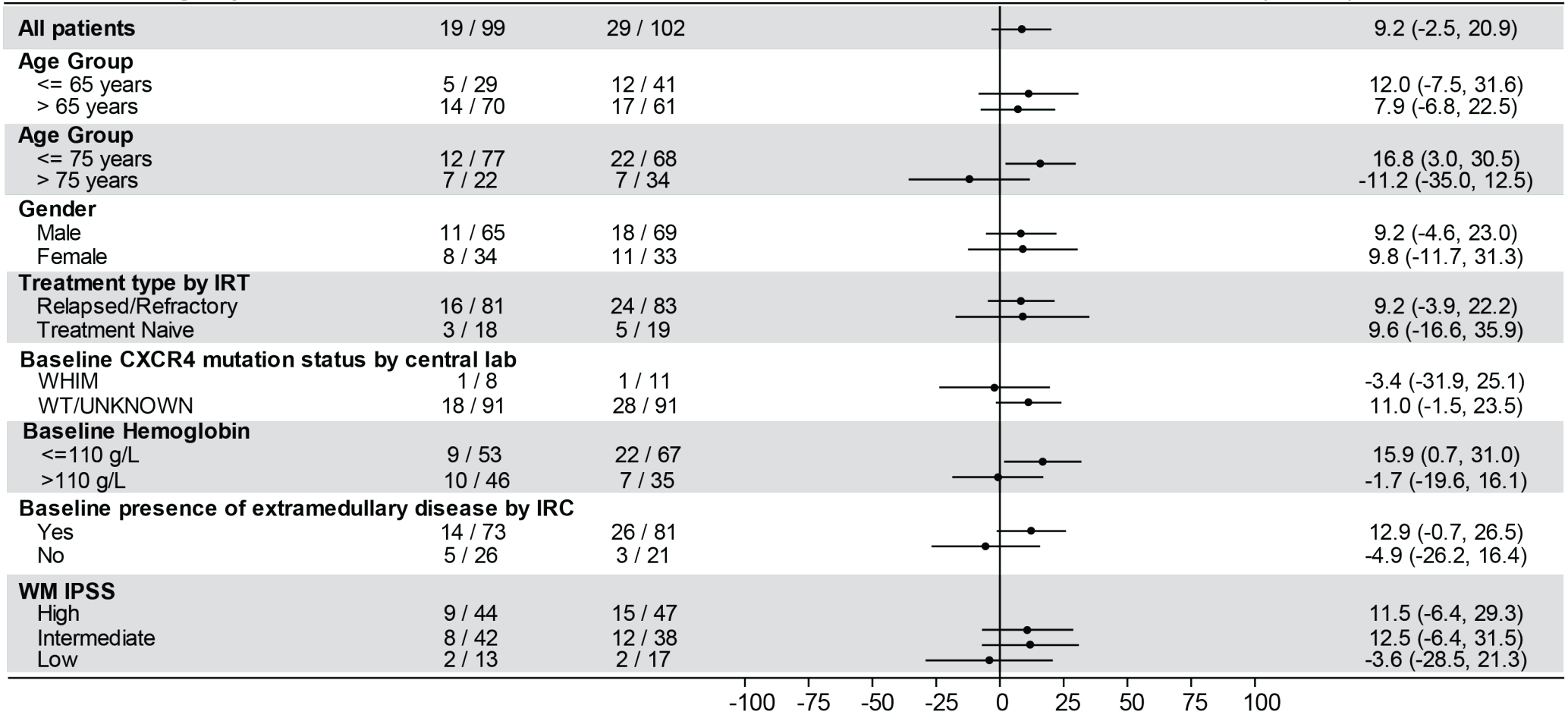
Median follow-up: 19.4 months



AE, adverse event; Inv, Investigator; MYD88, myeloid differentiation primary response gene 88; PD, progressive disease; pt, patient; R/R, relapsed/refractory; TN, treatment-naïve.

ASPEN: Forest Plot of CR+VGPR Response Rate Risk Difference by IRC, in Overall ITT Population

Subgroup	Response/Subject Ibrutinib	Response/Subject Zanubrutinib	Risk Difference (95% CI), % [a]
All patients	19 / 99	29 / 102	9.2 (-2.5, 20.9)
Age Group			
<= 65 years	5 / 29	12 / 41	12.0 (-7.5, 31.6)
> 65 years	14 / 70	17 / 61	7.9 (-6.8, 22.5)
Age Group			
<= 75 years	12 / 77	22 / 68	16.8 (3.0, 30.5)
> 75 years	7 / 22	7 / 34	-11.2 (-35.0, 12.5)
Gender			
Male	11 / 65	18 / 69	9.2 (-4.6, 23.0)
Female	8 / 34	11 / 33	9.8 (-11.7, 31.3)
Treatment type by IRT			
Relapsed/Refractory	16 / 81	24 / 83	9.2 (-3.9, 22.2)
Treatment Naive	3 / 18	5 / 19	9.6 (-16.6, 35.9)
Baseline CXCR4 mutation status by central lab			
WHIM	1 / 8	1 / 11	-3.4 (-31.9, 25.1)
WT/UNKNOWN	18 / 91	28 / 91	11.0 (-1.5, 23.5)
Baseline Hemoglobin			
<=110 g/L	9 / 53	22 / 67	15.9 (0.7, 31.0)
>110 g/L	10 / 46	7 / 35	-1.7 (-19.6, 16.1)
Baseline presence of extramedullary disease by IRC			
Yes	14 / 73	26 / 81	12.9 (-0.7, 26.5)
No	5 / 26	3 / 21	-4.9 (-26.2, 16.4)
WM IPSS			
High	9 / 44	15 / 47	11.5 (-6.4, 29.3)
Intermediate	8 / 42	12 / 38	12.5 (-6.4, 31.5)
Low	2 / 13	2 / 17	-3.6 (-28.5, 21.3)



CR, complete response; CXCR4, C-X-C Motif Chemokine Receptor 4; IRC, independent review committee; IRT, Interactive Response Technology; ITT, intention-to-treat; VGPR, very good PR; WM IPSS, Waldenström macroglobulinemia International Prognostic Scoring System.

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ASPEN: AE Categories of Interest (BTKi Class AEs)

AE *Categories*, n (%) (pooled terms)	All Grades		Grade ≥ 3	
	Ibrutinib (n = 98)	Zanubrutinib (n = 101)	Ibrutinib (n = 98)	Zanubrutinib (n = 101)
Atrial Fibrillation / Flutter†	**15 (15.3)**	2 (2.0)	4 (4.1)	0 (0.0)
Diarrhea (PT)	**31 (31.6)**	21 (20.8)	1 (1.0)	3 (3.0)
Hemorrhage	**58 (59.2)**	49 (48.5)	8 (8.2)	6 (5.9)
Major Hemorrhage[a]	9 (9.2)	6 (5.9)	8 (8.2)	6 (5.9)
Hypertension	17 (17.3)	11 (10.9)	**12 (12.2)**	6 (5.9)
Neutropenia[b] †	13 (13.3)	**30 (29.7)**	8 (8.2)	**20 (19.8)**
Infection	66 (67.3)	67 (66.3)	19 (19.4)	18 (17.8)
Second Malignancy	11 (11.2)	12 (11.9)	1 (1.0)	2 (2.0)

Higher AE rate in bold blue with ≥ 10% difference in any grade or ≥ 5% difference in grade 3 or above.
No tumor lysis syndrome was reported. Opportunistic infection ibrutinib (n=2), zanubrutinib (n=1).
AE, adverse event; BTKi, Bruton tyrosine kinase inhibitor; PT, preferred term.
[a]Defined as any grade ≥ 3 hemorrhage or any grade central nervous system hemorrhage.
[b]Including PT terms of neutropenia, neutrophil count decreased, febrile neutropenia, agranulocytosis, neutropenic infection and neutropenic sepsis.
† Descriptive two-sided *P*-value < 0.05.

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ASPEN: Most Common AEs

Event Preferred Term*, n (%)	All Grades (≥20%)		Grade ≥ 3 (≥5%)	
	Ibrutinib (n = 98)	Zanubrutinib (n = 101)	Ibrutinib (n = 98)	Zanubrutinib (n = 101)
Diarrhea	**31 (32)**	21 (21)	1 (1)	3 (3)
Upper respiratory tract infection	28 (29)	24 (24)	1 (1)	0
Contusion	**23 (24)**	13 (13)	0	0
Muscle spasms†	**23 (24)**	10 (10)	1 (1)	0
Peripheral edema†	**19 (19)**	9 (9)	0	0
Hypertension	16 (16)	11 (11)	**11 (11)**	6 (6)
Atrial fibrillation†	**14 (14)**	2 (2)	3 (3)	0
Neutropenia†	12 (12)	**25 (25)**	8 (8)	**16 (16)**
Pneumonia†	**12 (12)**	2 (2)	**7 (7)**	1 (1)
Anemia	10 (10)	12 (12)	5 (5)	5 (5)
Thrombocytopenia	10 (10)	10 (9)	3 (3)	6 (5)

*Including most common AEs, and AEs with ≥10% or ≥5% differentials respectively (higher frequency in **bold blue**).
AE, adverse event; PT, preferred term.
†Descriptive two-sided *P*-value < 0.05

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