BeiGene Investor Presentation Updates from ASH and SABCS

December 16, 2024

TODAY'S SPEAKERS

Lai Wang

Global Head
of R&D

Mark Lanasa

Chief Medical Officer
Solid Tumors

Mehrdad Mobasher

Chief Medical Officer
Hematology

John V. Oyler

Co-Founder,
Chairman & CEO

Aaron Rosenberg

Chief Financial Officer

Disclosures

Certain statements contained in this presentation and in any 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 overall R&D strategy; BeiGene's ability to grow leadership in CLL; the safety profile of BGB-43395; the ability of BeiGene to transform the lives of CLL patients; 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; the conduct of late-stage clinical trials and expected data readouts; the advantages of BTK degradation over non-covalent BTK inhibition; future pricing pressures on our medicines; and 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 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 technology and medicines; BeiGene's reliance on third parties to conduct drug development, manufacturing, commercialization, and other services; BeiGene's limited experience in obtaining regulatory approvals and commercializing pharmaceutical products; BeiGene's ability to obtain additional funding for operations and to complete the development of its drug candidates and achieve and maintain profitability; and those risks more fully discussed in the section entitled "Risk Factors" in BeiGene's most recent periodic report filed with the SEC, as well as discussions of potential risks, uncertainties, and other important factors in BeiGene's subsequent filings with the SEC. 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 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 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 any 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

December 16, 2024

Welcome, Safe Harbor and Agenda	**Dan Maller** Head of Investor Relations
Opening Remarks	**Lai Wang, Ph.D.** Global Head of R&D
SABCS Update and Solid Tumor Programs	**Mark Lanasa, M.D., Ph.D.** Chief Medical Officer - Solid Tumors
ASH Update and Hematology Programs	**Mehrdad Mobasher, M.D., M.P.H** Chief Medical Officer - Hematology
Closing Remarks	**John V. Oyler** Co-Founder, Chairman and CEO
Q&A	**BeiGene Team**

OPENING REMARKS

Lai Wang, Ph.D.

Global Head of R&D

BeiGene R&D Strategy to Transform Patients' Lives

Develop a **deep & impactful portfolio**

Execute **fast-to-PoC for value maximization**

BEIGENE

R&D

OVERALL STRATEGY

Initiate **combination therapies early** to win

Advance **only transformative medicines to late-stage** development

ENABLED BY:

1,100 researchers covering **diverse modalities**, advancing science with **urgency and agility**

Maximizing clinical **trial efficiency** with **CRO-free model**, powered by **automation** and **AI technologies**

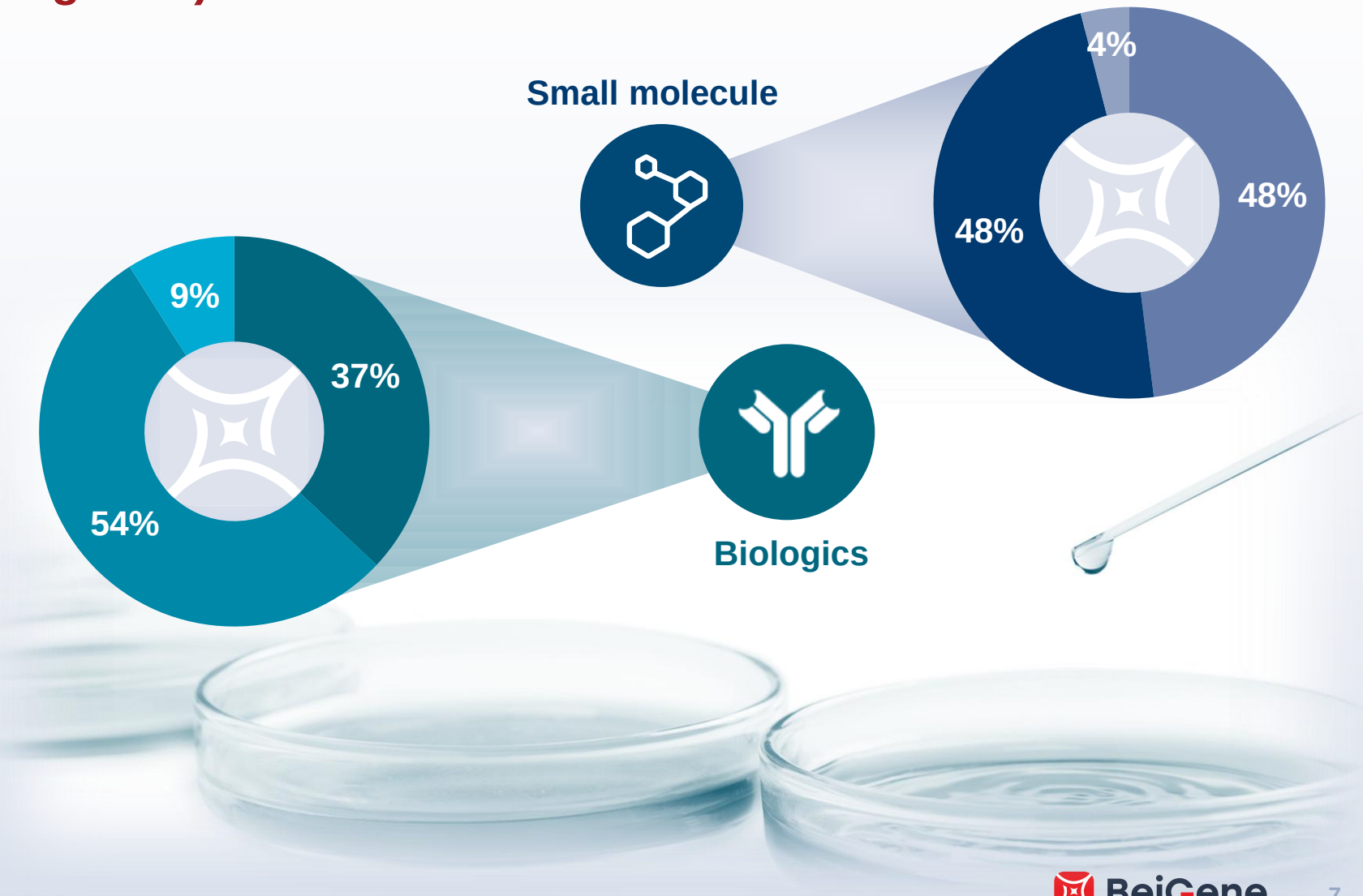
Extensive Investment on Innovative Platforms to Support Robust and Sustainable Pipeline Growth

Preclinical pipeline (69 programs)

Small Molecule, 29 (43%)
- CDAC, 14
- Traditional small molecule, 14
- Others, 1

Biologics, 35 (51%)
- Bi/multi-specific, 13
- ADC, 19
- Others, 3

Cell Therapy and mRNA, 4 (6%)
- Cell therapy, 2
- mRNA, 2



CDAC –Chimeric Degradation Activating Compound
ADC – Antibody Drug Conjugate
Cut-off date: 2024 Nov

Transforming Our Pipeline With the Next Wave of Innovation

Significant Portfolio Evolution in Three Years

Heme leadership with 3 cornerstone assets
Solid Tumor diversification from IO to disease-focused pipeline
POC data readouts for many NMEs in the next 1-2 years

Prior to 2022

- Zanubrutinib
- Sonrotoclax

- Tislelizumab
- Pamiparib
- Zanidatamab
- Ociperlimab
- TIM-3 mAb
- LAG-3 mAb
- HPK1
- DLL3 x CD3 BsAb
- STEAP1 x CD3 BsAb

2022

- BTK CDAC

- SMAC mimetics
- CEA x 4-1BB

2023

- Novel BCL-2i
(complementary to sonro)

- CDK4i
- DGKζi
- HPK1 (2G)
- CCR8 mAb

2024

Lung
- EGFR x MET TsAb
- EGFR CDAC
- MTA coop PRMT5i
- B7H3 ADC
- PanKRASi

Breast / Gynecologic
- B7H4 ADC
- CDK2i

GI
- MUC1 x CD16a BsAb
- GPC3 x 4-1BB BsAb
- CEA ADC
- FGFR2b ADC

Other
- IL-15 prodrug

2025 and beyond

New molecules
- CDACs
- Bispecific ADCs
- TCR-like TCEs
- Switch cytokine
- Cell therapy
- mRNA
- etc.

● Heme ● Solid Tumor

SABCS UPDATE
and SOLID TUMOR PROGRAMS

Mark Lanasa M.D., Ph.D.

Chief Medical Officer, Solid Tumors

Our Breast Cancer/Gynecologic Portfolio with CDK4i as a Backbone Across Lines of Therapy and for Combinations

$HR^{+}/HER2^{low/neg}$ Breast Cancer

Stage I-III
Neoadjuvant/adjuvant therapy

CDK4i+ET

Recurrent unresectable or Stage IV

1L CDK4i+ET
2L+ CDK4i+ET

Recurrent unresectable or Stage IV - Combo

2L+ CDK2i+CDK4i+ET
2L+ novel BCL2i+CDK4i+ET

Endometrial

CDK4i + ET
CDK2i
B7H4 ADC

Ovarian

CDK2i
B7H4 ADC

TNBC

1L B7H4 ADC + Tislelizumab
2L+ B7H4 ADC

ET – Endocrine Therapy

San Antonio Breast Cancer Symposium (SABCS) 2024 Presentations

Topic	Title	Lead author	Key takeaways	Status
BGB-43395-101	First-in-human phase 1a, dose-escalation study of BGB-43395 (CDK4-selective inhibitor) as monotherapy and in combination with fulvestrant or letrozole in patients with metastatic HR+/HER2− breast cancer and other advanced solid tumors	Timothy A. Yap	• Preliminary safety/tolerability profile for BGB-43395 supports continued development with the most commonly reported AEs being diarrhea and nausea • No DLTs or AEs leading to discontinuation or death were reported • BGB-43395 absorption is rapid (median T_{max}=2 hr); exposure increased ~dose proportionately	Poster Number: **P4-10-20** Session Date and Time: **Thursday Dec 12, 2024** **5:30 - 7:00 PM CDT**
Preclinical (CDK4i)	Preclinical characterization of BGB-43395, a potential best-in-class CDK4 selective inhibitor with potent pharmacodynamic and anti-tumor activity in HR+HER2- breast cancer Models	Hengrui Zhu	• BGB-43395, a highly potent CDK4-selective kinase inhibitor that translates into a desirable toxicity profile, notably minimizing neutropenia and GI toxicity • BGB-43395 exhibits superior kinase inhibition against CDK4 compared with palbociclib, ribociclib and abemaciclib as well as investigational CDK4 inhibitor PF-07220060	Poster Number: **P4-10-06** Session Date and Time: **Thursday Dec 12, 2024** **5:30 - 7:00 PM CDT**
BGB-43395-102 (TiP)	Trial in progress: First-in-human phase 1a/1b, dose-escalation/expansion study of BGB-43395 (CDK4 selective inhibitor) as monotherapy or combination therapy in Chinese patients with metastatic HR+/HER2− breast cancer and other advanced solid tumors	Jian Zhang	TiP abstract describing the CDK4-102, FiH dose-escalation/ expansion trial in patients from China with metastatic HR+/HER2- BC and other solid tumors	Poster Number: **P4-08-26** Session Date and Time: **Thursday Dec 12, 2024** **5:30 - 7:00 PM CDT**
BG-68501-101 (TiP)	Trial in progress: A first-in-human phase 1a/b, dose-escalation/expansion study of BG-68501/ETX-197 (CDK2 inhibitor) as monotherapy or in combination for patients with HR+/HER2− breast cancer and other advanced solid tumors	Minal Barve	TiP abstract describing the CDK2-101, FiH dose-escalation/ expansion trial in patients with HR+/HER2- BC and other solid tumors	Poster Number: **P4-08-20** Session Date and Time: **Thursday Dec 12, 2024** **5:30 - 7:00 PM CDT**
ETX-197/ BG-68501	ETX-197/BG-68501, a potential best-in-class potent, selective, oral, small molecule CDK2 inhibitor, has anti-tumor activity in cancer models with Cyclin E amplification or deficiency in the Retinoblastoma 1 gene	Daliya Banerjee	• Abstract details the discovery and preclinical characterization of ETX-197, a highly potent and selective small molecule inhibitor of CDK2 activity • ETX-197 is in a first-in-human (FIH), Phase 1a/1b study to assess the safety, tolerability, pharmacokinetics (PK), pharmacodynamics, and preliminary antitumor activity in patients with advanced, nonresectable, or metastatic solid tumors (NCT06257264)	Poster Number: **P4-12-29*** Session Date and Time: **Thursday Dec 12, 2024** **5:30 - 7:00 PM CDT**

*Developed by Ensem

Poster number: P4-10-20
Presented at: San Antonio Breast Cancer Symposium

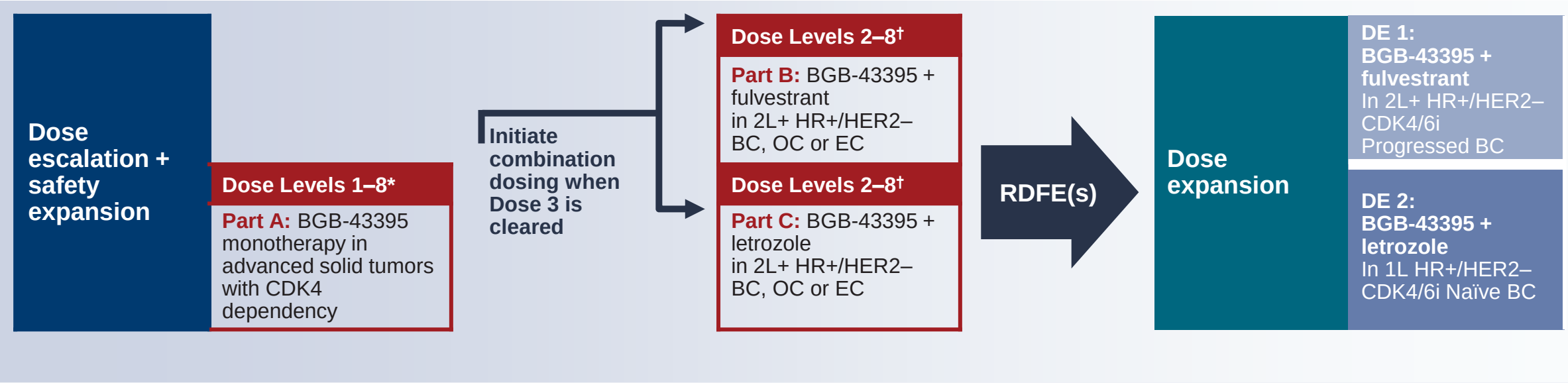
First-in-human phase 1a, dose-escalation study of BGB-43395 (CDK4-selective inhibitor) as monotherapy and in combination with fulvestrant or letrozole in patients with metastatic HR+/HER2− breast cancer and other advanced solid tumors

Timothy A. Yap,[1] Gerald Falchook,[2] Jennifer Man,[3] Dhanusha Sabanathan,[4] Robert Wesolowski,[5] Ildefonso Rodriguez-Rivera,[6] Hui Gan,[7] Gilbert Y. Wong,[8] Marion Carrigan,[8] Erqian Yu,[9] Hao Zheng,[8] Shom Goel[10]

[1]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Sarah Cannon Research Institute (SCRI) at Health One, Denver, CO, USA; [3]Blacktown Cancer and Haematology Centre, Blacktown, NSW, Australia; [4]Macquarie University, Macquarie Park, NSW, Australia; [5]The James Cancer Hospital and Solove Research Institute, Columbus, Ohio, USA; [6]NEXT Oncology, San Antonio, TX, USA; [7]Austin Hospital, Heidelberg, VIC, Australia; [8]BeiGene USA, Inc, San Mateo, CA, USA; [9]Clinical Pharmacology, BeiGene (Shanghai) Co., Ltd. Shanghai, China; [10]Peter MacCallum Cancer Centre, Melbourne, VIC, Australia

Poster number: P4-10-20
Presented at: San Antonio Breast Cancer Symposium
Date: December 12, 2024

CDK4i (BGB-43395) – Dose Escalation in Monotherapy and in Combination with ET in Both 1L and 2L+ Breast Cancer Patients



Study endpoints

Dose escalation (Phase 1a)

Primary	Secondary	Exploratory
• Safety and tolerability	• ORR, DOR and TTR	• PFS, DCR and CBR
• MTD and MAD	• PK	• PD biomarkers
• RDFE		

Study endpoints

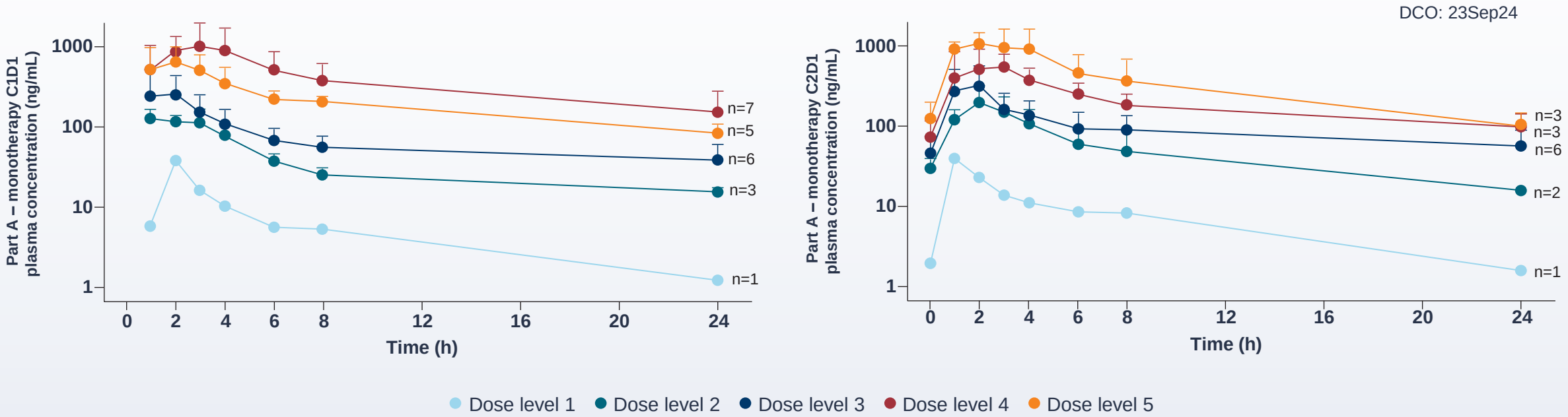
Dose expansion (Phase 1b)

Primary	Secondary	Exploratory
• ORR	• DOR, TTR, DCR, CBR and PFS	• OS
	• Safety	• PD biomarkers
	• PK	

BC – Breast Cancer
OC – Ovarian Cancer
EC – Endometrial Cancer
* Data for dose levels 1-5 are presented
† Data for dose levels 2-4 are presented

CDK4i (BGB-43395) Shows Expected PK Characteristics Across Dose Levels Tested

BGB-43395 observed plasma concentration in FIH study



- Rapid absorption after oral administration with median T_{max} occurring ~after 2 hours
- Half-life approximately 13 hours
- Exposures increased approximately dose proportionately
- Exposures were not impacted by co-administration with either fulvestrant or letrozole
- No significant differences in exposure observed in different regions or ethnic groups

Only the PK data of patients who received once daily dosing in Part A are shown

PK data have fewer dose levels than the study schema because not all dose levels have been explored yet.

CDK4i (BGB-43395) Safety as Single Agent and in Combination with Endocrine Therapy, All Dose Levels Safe and Tolerable

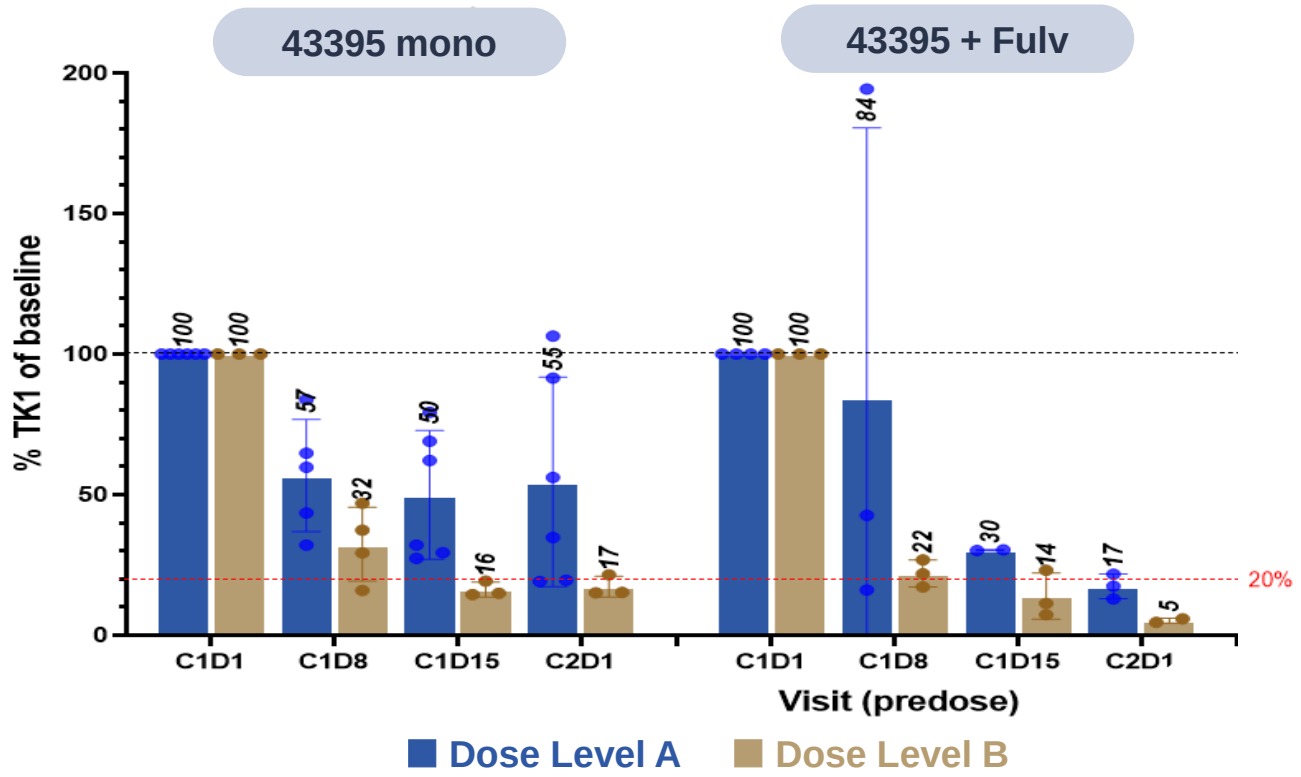
	Part A (BGB-43395 monotherapy)				Part B BGB-43395 + fulvestrant (n=17)		Part C BGB-43395 + letrozole (n=15)		Total (N=65)	
	All (n=33)		BC (n=6)							
Tolerability Summary										
Any AE	33 (100.0)		6 (100.0)		15 (88.2)		13 (86.7)		61 (93.8)	
Grade ≥3 AEs	10 (30.3)		2 (33.3)		4 (23.5)		1 (6.7)		15 (23.1)	
Treatment-related AE	31 (93.9)		6 (100.0)		14 (82.4)		12 (80.0)		57 (87.7)	
Grade ≥3 treatment-related AEs	9 (27.3)		1 (16.7)		1 (5.9)		0		10 (15.4)	
Any SAEs	3 (9.1)		1 (16.7)		2 (11.8)		1 (6.7)		6 (9.2)	
Fatal SAEs	1 (3.0)*		0		0		0		1 (1.5)	
Leading to study treatment discontinuation	2 (6.1)		1 (16.7)		0		1 (6.7)		3 (4.6)	
Treatment-Related† AEs Occurring in >10% of Pts	**All grades**	**Grade ≥3**	**All grade**	**Grade ≥3**	**All grade**	**Grade ≥3**	**All grade**	**Grade ≥3**	**All grade**	**Grade ≥3**
Diarrhea	24 (72.7)	2 (6.1)	2 (33.3)	0	9 (52.9)	0	9 (60.0)	0	42 (64.6)	2 (3.1)
Nausea	18 (54.5)	1 (3.0)	3 (50.0)	0	4 (23.5)	0	5 (33.3)	0	27 (41.5)	1 (1.5)
Vomiting	9 (27.3)	1 (3.0)	0	0	2 (11.8)	0	1 (6.7)	0	12 (18.5)	1 (1.5)
Neutrophil count decreased	4 (12.1)	2 (6.1)	1 (16.7)	0	5 (29.4)	0	1 (6.7)	0	10 (15.4)	2 (3.1)
Decreased appetite	6 (18.2)	0	0	0	1 (5.9)	0	1 (6.7)	0	8 (12.3)	0
Fatigue	4 (12.1)	0	2 (33.3)	0	2 (11.8)	0	2 (13.3)	0	8 (12.3)	0

DCO: 23Sep24

AEs per NCI-CTCAE v5.0 by type, frequency, severity, timing, seriousness and relationship to drug.
*One patient had treatment-emergent sepsis (not treatment-related) which led to death.
AE, adverse event; BC, breast cancer; SAE, treatment-emergent serious adverse event.

Data Update: Substantial PD Activity in Breast Cancer at Dose Levels A and B

TK1 activity change after BGB-43395-based treatment
(BC-only)



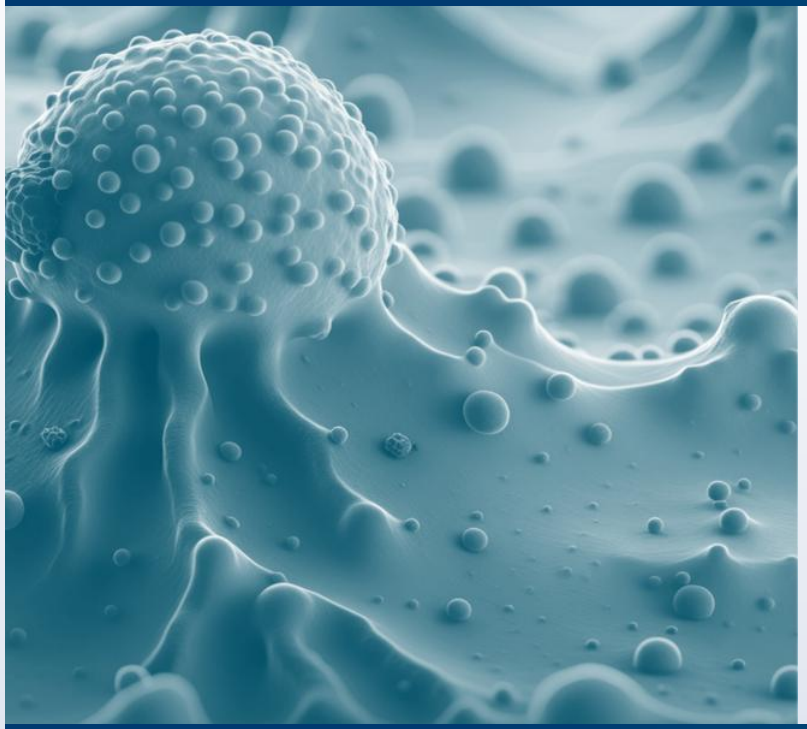
Pronounced TK1 reduction observed at Dose Level B (≥80% inhibition)

- For monotherapy cohort, **Dose Level B** showed stronger and more sustained TK1 inhibition as compared with **Dose Level A**
- For fulvestrant combo cohorts, **Dose Level B** and **Dose Level A** also show dose dependent PD effect and are in the expected clinically efficacious range based on biomarker effect.
- **Dose Level A** and **Dose Level B** in combination with fulvestrant achieved a similar level of TK1 inhibition as RP2D of atirmociclib (PF-07220060) + ET

TK1 – Thymidine Kinase 1
BC – Breast Cancer
ET – Endocrine Therapy

BGB-43395 is a Novel, Potential Best-in-class, CDK4 Inhibitor

Preclinical differentiation and accelerated development to maximize patient impact



- BGB-43395 is a potent CDK4 inhibitor with strong selectivity for CDK4 over CDK6 and clean kinome profile
- In the first year of clinical investigation, over 120 patients have been enrolled, substantially closing the development gap with atirmociclib
- Clinical investigation has revealed low rates of hematologic toxicity, encouraging PD data, as well as preliminary clinical efficacy. Additional study data updates will be reported at a future medical conference in 2025
- Planning is underway for Phase 3 studies in 1L and 2L HR+ breast cancer

Deep and Differentiated Disease Franchises Established in 2024

Building Momentum in Breast, Lung and GI into 2025

Lung

- PanKRASi*
- MTA Cooperative PRMT5i
- MAT2Ai*
- CEA ADC*
- B7H3 ADC*
- EGFR CDAC*
- EGFR x MET Tsp*

Breast/Gynecologic

- **CDK4i*** Combo RDFE 4Q24
- **CDK2i*** CDK4 combo 1Q25
- **Novel BCL2i*** CDK4 combo 2H25
- **B7H4 ADC*** RDFE 1Q25

GI

- PanKRASi*
- MTA Cooperative PRMT5i
- MAT2Ai*
- FGFR2b ADC
- CEA ADC*
- GPC3 x 4-1BB*
- MUC1 x CD16A*

Pan-Tumor

- DGKζi*
- HPK1i*
- CCR8*
- IL-15 prodrug*

Small molecule | Protein degrader | Bi/Tri-specific | mAb | ADC | Cytokine therapy

BeiGene has global rights for CDK2 (Ensem partnership), B7H4 ADC (DualityBio partnership), MAT2A (CSPC Zhongqi Pharmaceutical Technology); * In the clinic

ASH UPDATE
and HEMATOLOGY PROGRAMS

Mehrdad Mobasher, M.D., M.P.H.

Chief Medical Officer, Hematology

Transforming Lives of All CLL Patients and Other Hematological Cancer Patients with Our Current and Future Medicines

BTKi — BRUKINSA (zanubrutinib)

Only BTKi to show PFS superiority vs. ibrutinib in H2H study in **CLL**

Leader-in-class with broadest BTKi label with CLL/SLL, WM, MCL, MZL, FL

Approved in **72 countries** with high reimbursement / market access rate

Expand lifecycle as cornerstone asset with novel combinations including **MANGROVE (1L MCL), MAHOGANY (RR FL and RR MZL), CELESTIAL-TNCLL, (FD 1L CLL), CELESTIAL-RRMCL (RR MCL)**

BCL2i — SONROTOCLAX

Best-in-class potential with higher efficacy, safety and broader usability

1,600+ patients with **compelling** data across indications

Phase 3 in **TN CLL (CELESTIAL-TNCLL)** and **fast-to-market** studies **in MCL / WM / CLL** ongoing**.** Phase 3 studies in **RR CLL and RR MCL** in H1 2025

Differentiated opportunity in **AML / MDS and Multiple Myeloma**

BGB-21447 is a **novel BCL2 inhibitor** specifically designed to be complementary and target additional B-cell malignancies

BTK CDAC — BGB-16673

Most advanced BTK degrader, with **400+ patients** treated in monotherapy. **Strong clinical efficacy seen in a variety of B-cell malignancies including BTKi-resistant CLL patients. Combinations** have started**.**

Distinct MOA, potential to be **more potent**, **overcome and/or prevent emerging resistance mutations, and penetrate blood brain barrier**

With first and best-in-class potential, Ph2 expansion in R/R CLL with pivotal intent and Fast Track Designation ongoing and **Ph3(s) planned for 2025**

Development beyond R/R CLL in parallel with vision to expand **into earlier lines as monotherapy and in novel combinations**

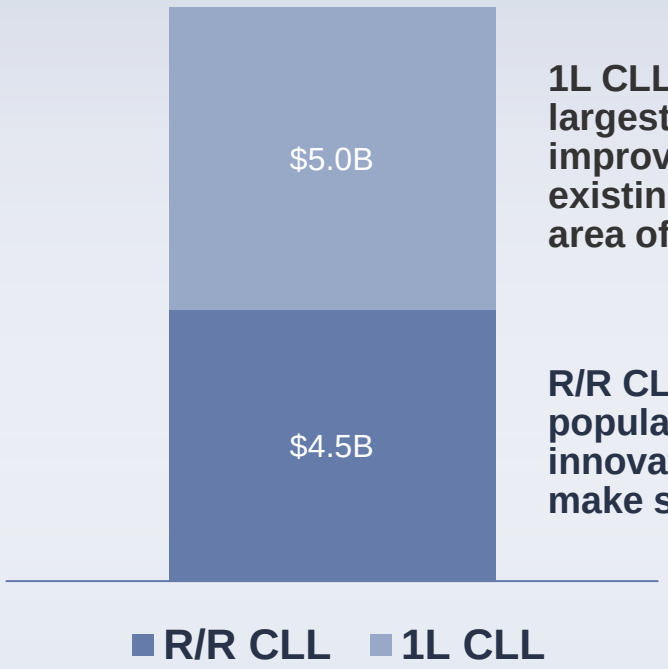
CLL/SLL - Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma
WM - Waldenström's Macroglobulinemia
MCL - Mantle Cell Lymphoma
MZL – Marginal Zone Lymphoma
FL- Follicular Lymphoma

R/R – Relapsed Refractory
TN – Treatment Naive
AML - Acute Myeloid Leukemia
MDS – Myelodysplastic Syndrome
MM - Multiple Myeloma

Success of Brukinsa and BeiGene's Wholly-Owned Innovative Pipeline Enables Impactful Growth in Our CLL Leadership

CLL prevalence and market opportunity remains significant and growing

2023 Global CLL revenue: BTKi and BCL2i[1]



1L CLL remains the largest segment and improvement upon existing outcomes is an area of high unmet need

R/R CLL is a growing population where innovative therapies can make substantial impact

BeiGene has a robust pipeline to develop optimal therapies for all impacted by CLL

BRUKINSA is a **proven** and best-in-class BTKi for 1L and R/R settings

- Only BTKi to demonstrate superiority vs. ibrutinib, showing clear differentiation
- **Long-term follow-up** shows highest CRs **sustained efficacy regardless of risk status and patient characteristics**

Development of BRUKINSA + sonrotoclax in 1L CLL can provide a **best-in-disease fixed-duration combination**, delivering exceptional efficacy, safety, and convenience

The BTK degrader (BGB-16673) can **disrupt the CLL treatment paradigm** as monotherapy or combinations

CLL - Chronic Lymphocytic Leukemia
RR – Relapsed Refractory
[1] Source: IQVIA Analytics: split of 1L and R/R CLL and the actual revenues from FY 2023 company filings.

ASH 2024 BeiGene's Presentations

21 abstracts presented

- **Black:** zanubrutinib
- **Blue:** Real-world evidence/ health economic outcomes research
- **Pink:** sonrotoclax
- **Green:** CDAC
- **Purple:** CAR-T




Friday
December 6

Saturday
December 7

5:30 - 7:30 PM

- Preferences of Patients with CLL
- BTKi Treatment Patterns in CLL
- BGB-11417-203 Study Design
- iNHL Data from CaDAnCe-101
- iPSC-Derived CAR-T

Sunday
December 8

6:00 - 8:00 PM

- 60 mo mFU Data from SEQUOIA Study (CLL)
- 78 mo mFU Data from the Long-Term Extension Study (CLL Patients)
- 73 mo Data from the Long-Term Extension Study (WM Patients Originally in ASPEN)
- 3111-212 Growth Modulation Index (FL)
- Preferences of Patients with FL
- Comparative Effectiveness MCL
- CELESTIAL-TNCLL Study Design

Monday
December 9

2:45 PM - 4:15 PM
4:30 PM - 6:00 PM
6:00 PM - 8:00 PM

- WM Data from CaDAnCe-101- (3:00 PM)
- CLL Data from CaDAnCe-101 (3:15 PM)
- 3111-110 Zanu + lenalidomide in R/R DLBCL (4:45 PM)
- Sonro+ Zanu in Patients with TN CLL Data From BGB-11417-101 (5:15 PM)


(x4)

- Effects of Zanu Dose Interruption During Treatment of WM
- Data from BGB-3111-215 in Acala-intolerant Patients

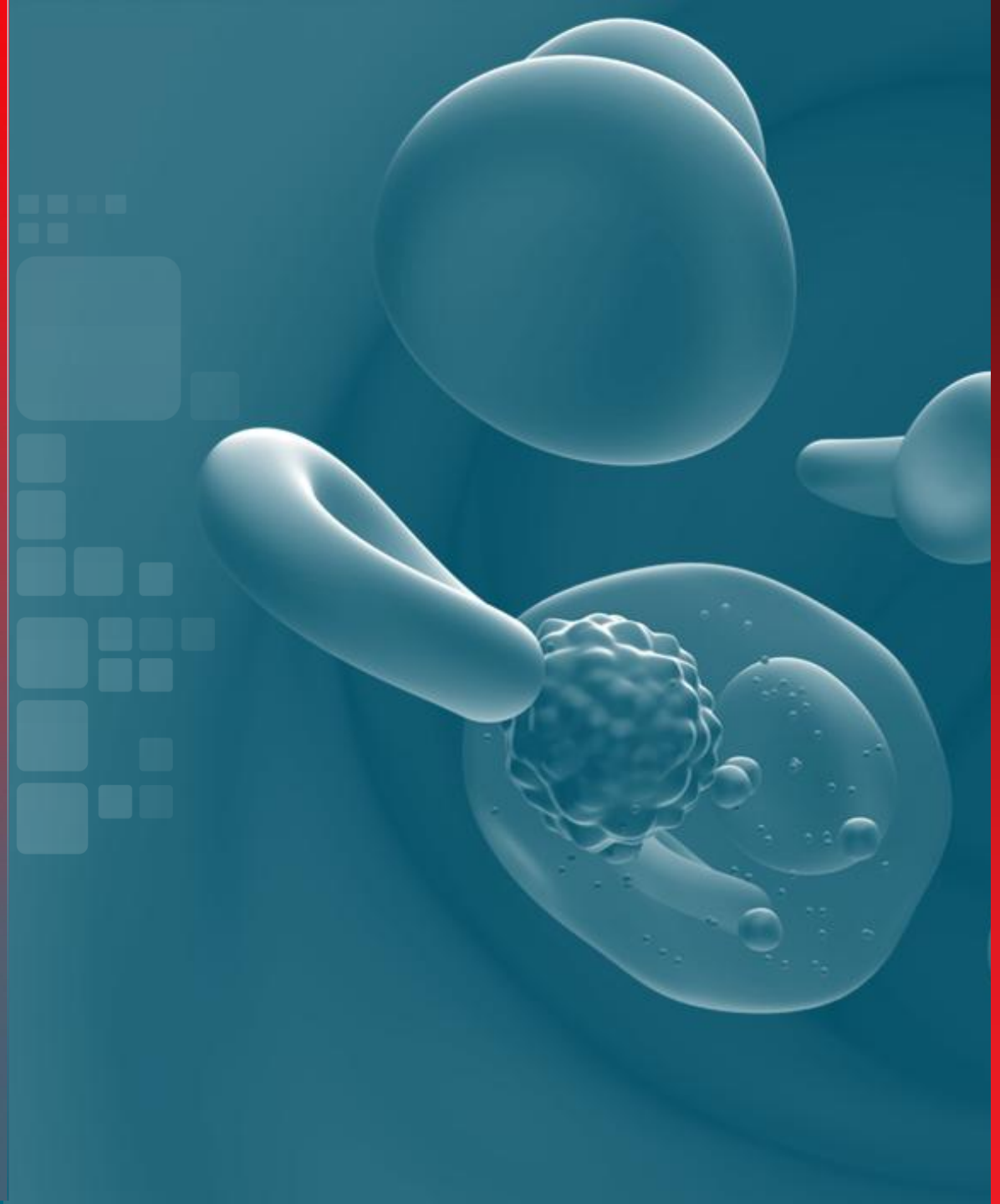
- Impact of Novel Therapies MCL

Tuesday
December 10

Abstract only:

- CLL Switch (Ontada)
- CDAC in Preclinical MCL Models

BTKi: Bruton tyrosine kinase inhibitor; CART: chimeric antigen receptor T-cell; CDAC: chimeric degradation activation compounds; CLL: chronic lymphocytic leukemia; DI: dose interruptions; FL: follicular lymphoma; GMI: growth modulation index; HEOR: health economics and outcome research; iPSC: induced pluripotent stem cell; LTE: long term extension; LTFU: long term follow up; MCL: mantle cell lymphoma; NHL: non-Hodgkin's lymphoma; RWE: real world evidence; S+Z: sonrotoclax+zanubrutinib; TN: treatment naïve; WM: Waldenstrom's macroglobulinemia



BRUKINSA (zanubrutinib)

Sonrotoclax

BGB-16673 (BTK CDAC)

BRUKINSA, a Next Generation BTKi with Broadest Label Globally and Leader in New Patient Starts in CLL

Specific, potent and sustained BTK inhibition

Designed to succeed where competitors have not

Greater BTK specificity and increased potency[1]

Bioavailability that provides near complete target occupancy in all disease relevant tissues

Consistently demonstrated superior efficacy

Only BTKi to demonstrate PFS superiority to ibrutinib in **R/R CLL/SLL in all patient segments, including high-risk (17p / *TP53*)**[2]

Sustained PFS superiority in both TN and R/R CLL in all patient segments regardless of risk and patient characteristics at extended follow-up[3,4]

Distinct safety advantages

Lowest rate of atrial fibrillation across multiple studies in an independent meta-analysis[5]

Lower rate of infections vs acalabrutinib[6]

Lower rates of AEs that limit activities of daily living vs acalabrutinib, including headache and GI toxicities[6]

BTKi with the broadest label

Only BTKi approved in 5 B-cell malignancies with deep and durable responses:

- CLL/SLL, WM. MCL, MZL
- FL, only BTKi approved

Four Ph 3 studies to maximize lifecycle: TN MCL (MANGROVE) 2L FL and MZL (MAHOGANY) TN CLL FTD (CELESTIAL-TNCLL) RR MCL (CELESTIAL-RRMCL)

Dosing optimized for efficacy, safety, and convenience

Only BTKi with QD and BID dosing allowing adjustment flexibility

Only BTKi without dose reductions in severe hepatic impairment

New tablet formulation expected in 2025 with reduced pill number and size

Brukinsa® zanubrutinib

RR – Relapsed Refractory
CLL/SLL - Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma
PFS – Progression Free Survival
TN – Treatment Naïve
AE – Adverse Events
WM - Waldenström's Macroglobulinemia
MCL - Mantle Cell Lymphoma
MZL - Marginal Zone Lymphoma
FL - Follicular Lymphoma
FTD – Fixed Treatment Duration

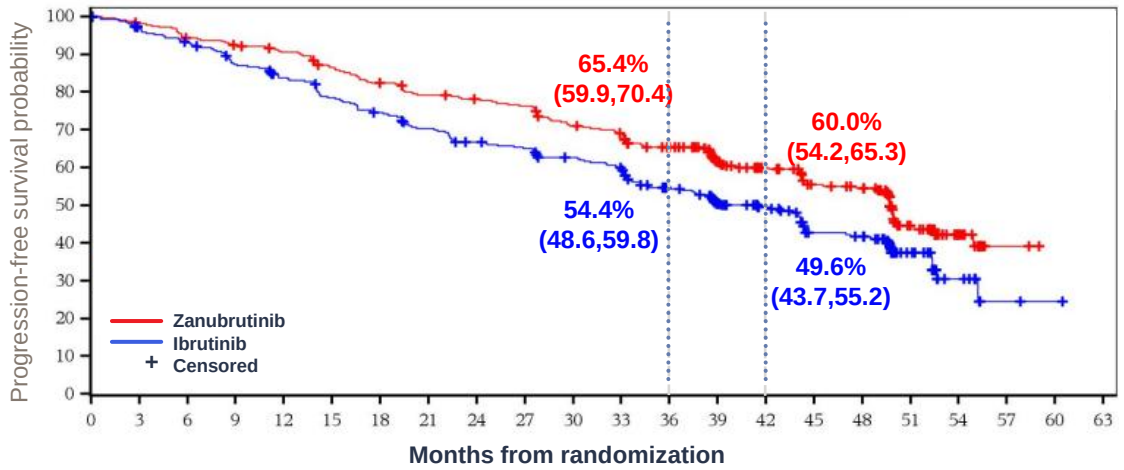
[1] Guo et al. J Med Chem 2019
[2] Brown et al. Blood 2024
[3] Brown et al. ASH 2023
[4] Shadman et al. ICHM 2024
[5] Hwang et al. EHA 2023
[6] Brown et al. Haematologica 2024

2024 ASH BeiGene Key Presentations
Zanubrutinib (Clinical)

Topic	Title	First author / significance	Status
SEQUOIA Long Term Follow-up	Sustained Superiority of Zanubrutinib vs Bendamustine + Rituximab in Treatment-Naive Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (TN CLL): 5-Year Follow-Up of Cohort 1 from the SEQUOIA Study	**Mazyar Shadman** PFS superiority, regardless of risk status, is maintained with BRUKINSA vs BR with an extended median follow-up of 5 years. High CR rates were seen. BRUKINSA was well tolerated with low rate of AEs including afib/flutter, infections.	**Poster 3249**
Long Term Extension (LTE1) Study - CLL	Deep and sustained responses in patients with CLL treated with zanubrutinib or zanubrutinib + obinutuzumab in phase 1/2 AU-003 and phase 1b GA-101 studies: A report from the zanubrutinib extension study	**Constantine S. Tam** With longer follow up (now median 6.5y) unprecedented CR rates for a BTKi were observed with zanubrutinib +/- obinutuzumab and impressive sustained PFS achieved in CLL. Tolerability and safety profile of zanubrutinib +/- obinutuzumab remained favorable	**Poster 3255**
BOVen 5-Year Data IIS	Multicenter Phase II Trial of Zanubrutinib, Obinutuzumab, and Venetoclax (BOVen) in Treatment-Naïve Chronic Lymphocytic Leukemia: 5-Year Follow up, Retreatment Outcomes, and Impact of MRD Kinetics (ΔMRD400)	**Jacob D. Soumerai** Five-year follow up of the BOVen study evaluating time limited uMRD guided treatment with ZVO in all comer TN CLL demonstrates high rates of uMRD4 with median 10 cycles (8-12) before stopping treatment BOVen was well tolerated.	**Oral 1867**

R/R CLL - BRUKINSA Demonstrates Sustained Superiority Over Ibrutinib in ALPINE H2H Study with 42.5 Months Follow-up

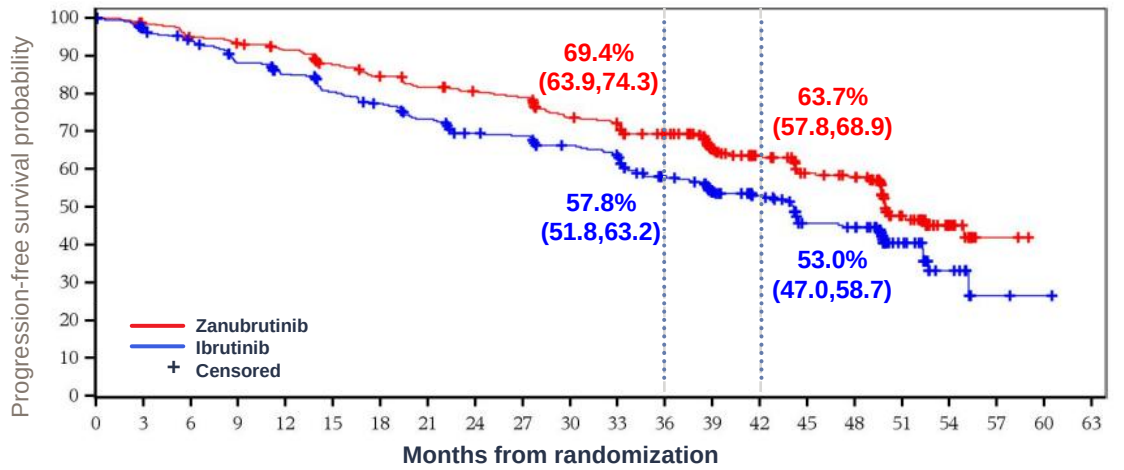
PFS superiority sustained in ALPINE



0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51	54	57	60	63
327	315	302	295	287	272	258	247	242	236	218	210	189	151	128	109	104	43	19	2	0	
325	305	293	273	258	241	228	213	200	194	183	173	148	116	101	77	74	30	10	2	1	0

No. subjects at risk

Superiority with COVID-19 adjustment



0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51	54	57	60	63
327	313	301	295	286	268	257	247	241	236	214	208	189	151	128	108	103	43	19	2	0	
325	304	292	271	256	238	227	213	197	194	182	173	147	116	101	76	73	30	10	2	1	0

No. subjects at risk

	Zanubrutinib	Ibrutinib
# of events (%)	150 (45.9%)	177 (54.5%)
HR (95% CI):	0.68 (0.54, 0.84)	
nominal *p*-value	0.0005	

	Zanubrutinib	Ibrutinib
# of events (%)	134 (41.0%)	160 (49.2%)
HR (95% CI):	0.66 (0.52, 0.84)	
nominal *p*-value	0.0005	

blood

Brown et al., Blood, 2024

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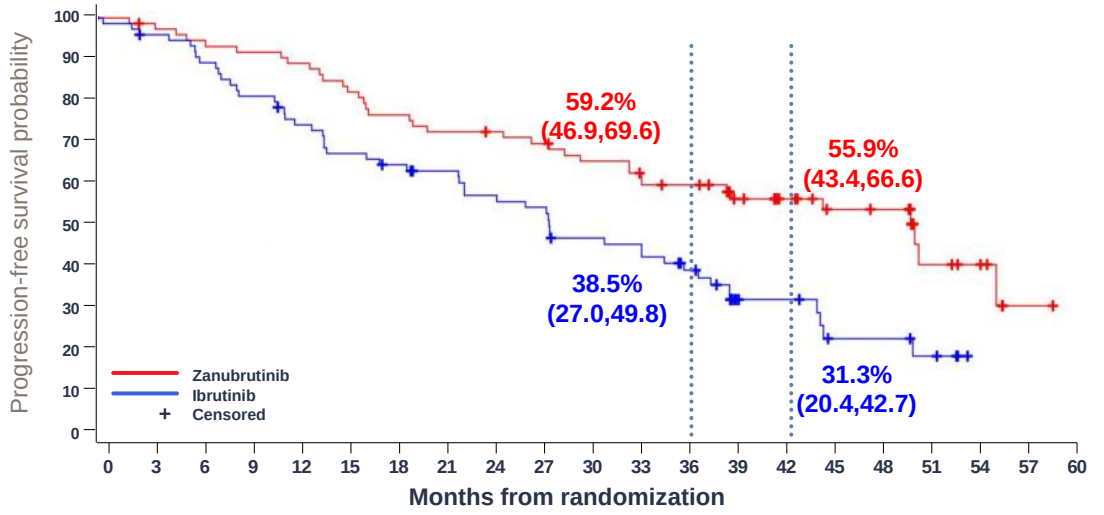
R/R CLL - Sustained Superiority and Risk Reduction in *TP53*/Del17p Population, Clear Evidence of Differentiation

PFS in del(17p)/TP53 subset consistent with IIT patient population

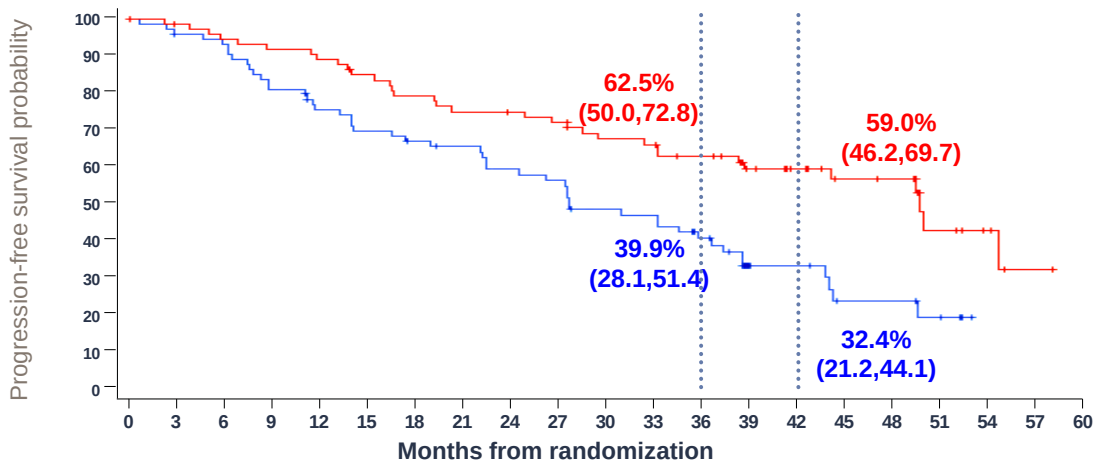


0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51	54	57	60
75	71	68	66	64	61	55	52	51	49	45	43	39	31	25	20	19	8	5	1	0
75	70	68	59	54	48	45	42	38	36	30	29	23	13	11	6	6	4	0		

No. subjects at risk

	Zanubrutinib	Ibrutinib
# of events (%)	36 (48.0%)	51 (68.0%)
HR (95% CI):	0.51 (0.33, 0.78)	
nominal *p*-value	0.0019	

PFS in ALPINE Del17p/*TP*53 Population with COVID-19 adjustment



0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51	54	57	60
75	71	68	66	64	59	55	52	51	49	44	43	39	31	25	20	19	8	5	1	0
75	70	68	59	52	48	45	42	38	36	30	29	23	13	11	6	6	4	0		

No. subjects at risk

	Zanubrutinib	Ibrutinib
# of events (%)	33 (44)	49 (65.3)
HR (95% CI):	0.48 (0.31, 0.75)	
nominal *p*-value	0.0011	

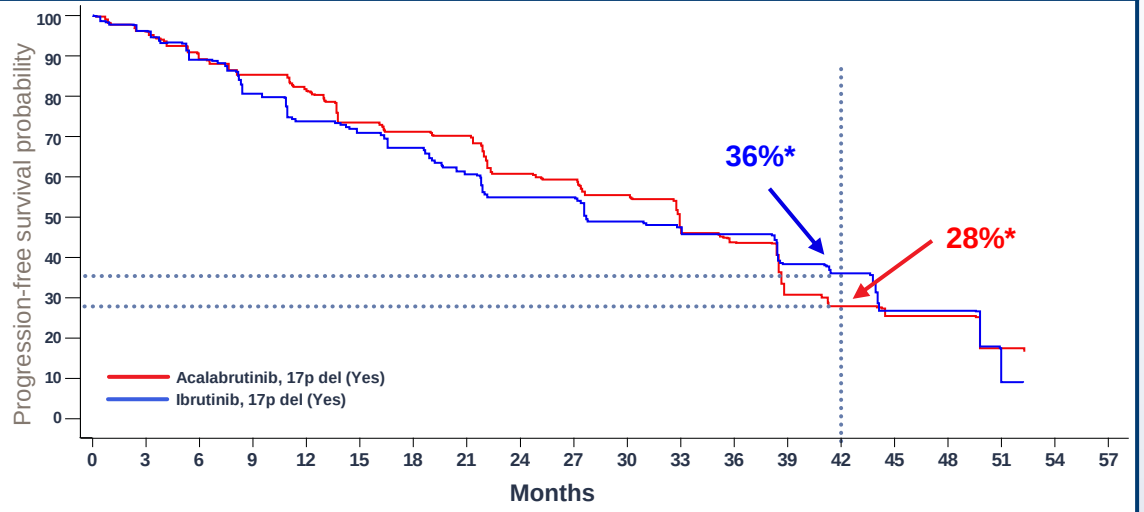
blood

Brown et al., Blood, 2024

BeiGene

R/R CLL – Cross Trial Comparison of ELEVATE-RR Del17p Population and ALPINE *TP53*/Del17p Population

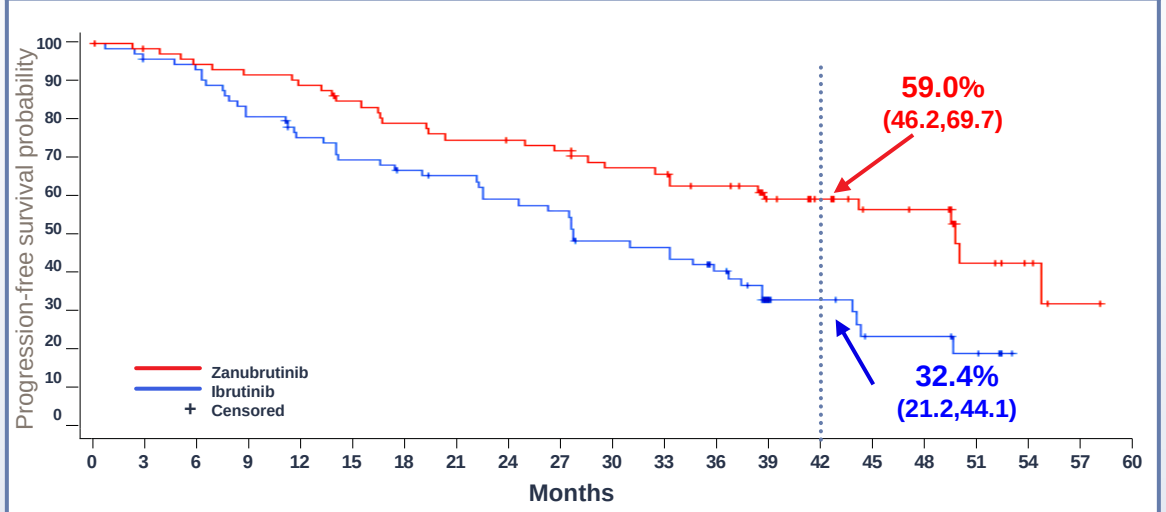
PFS in ELEVATE-RR Del17p Population



	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51	54	57
Acalabrutinib, 17p del	124	113	104	100	94	84	79	78	66	63	58	43	35	23	14	10	7	1	0	
Ibrutinib, 17p del	121	112	100	89	80	75	71	64	57	56	49	43	38	29	16	11	7	2	0	

No. at risk

PFS in ALPINE Del17p/*TP*53 Population with COVID-19 adjustment



	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51	54	57	60
Zanubrutinib	75	71	68	66	64	59	55	52	51	49	44	43	39	31	25	20	19	8	5	1	0
Ibrutinib	75	70	68	59	52	48	45	42	38	36	30	29	23	13	11	6	6	4	0		

No. subjects at risk

	Acalabrutinib, 17p del	Ibrutinib, 17p del
# of events (%)	76 (61)	72/121 (60)
HR (95% CI):	1.00 (0.73, 1.38)	

	Zanubrutinib	Ibrutinib
# of events (%)	33 (44)	49 (65.3)
HR (95% CI):	0.48 (0.31, 0.75)	
nominal *p*-value	0.0011	

Byrd et al, JCO, 2021
*42-month PFS estimated from JCO paper
CI, Confidence interval

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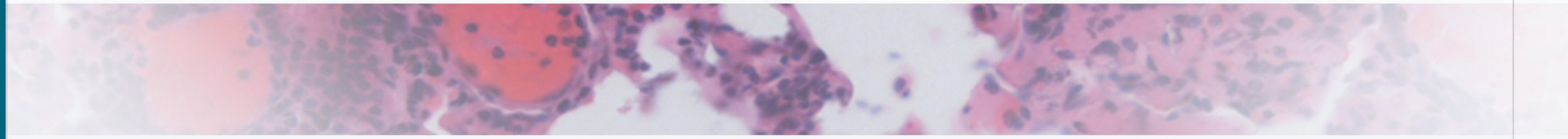


Sustained Superiority of Zanubrutinib vs Bendamustine + Rituximab in Treatment-Naive Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma: 5-Year Follow-Up of Cohort 1 From the SEQUOIA Study

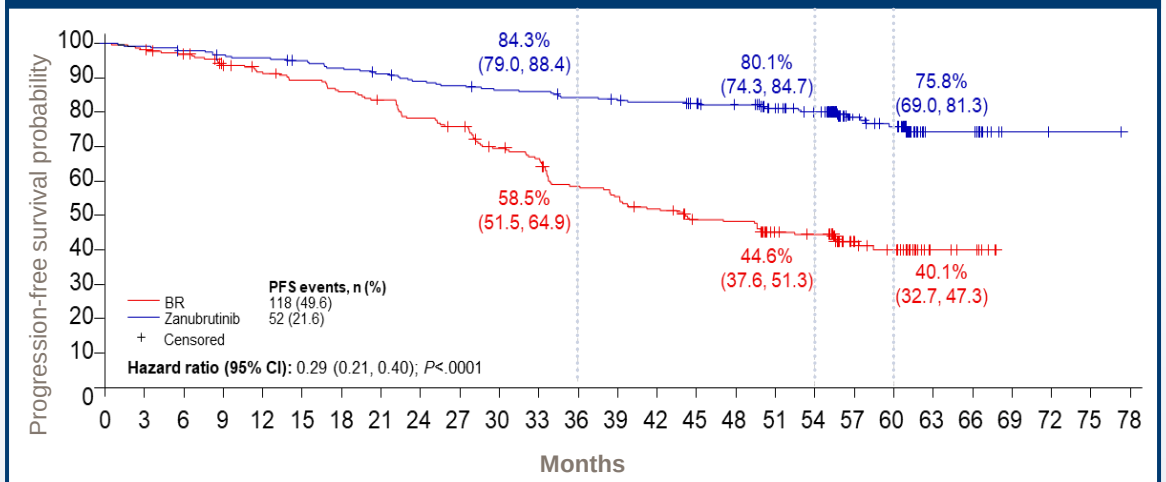
Mazyar Shadman,[1,2] Talha Munir,[3] Tadeusz Robak,[4] Jennifer R. Brown,[5] Brad S. Kahl,[6] Paolo Ghia,[7,8] Tian Tian,[9] Andy Szeto,[9] Roman Korolkiewicz,[9] Constantine S. Tam,[10] Wojciech Jurczak[11]

[1]Fred Hutchinson Cancer Center, Seattle, WA, USA; [2]University of Washington, Seattle, WA, USA; [3]Leeds Teaching Hospitals NHS Trust, Leeds, UK; [4]Copernicus Memorial Hospital, Medical University of Łódź, Łódź, Poland; [5]Dana-Farber Cancer Institute, Boston, MA, USA; [6]Siteman Cancer Center, Washington University School of Medicine, St Louis, MO, USA; [7]Università Vita-Salute San Raffaele, Milano, Italy; [8]IRCCS Ospedale San Raffaele, Milano, Italy; [9]BeiGene USA, Inc, San Mateo, CA, USA; [10]Alfred Hospital and Monash University, Melbourne, VIC, Australia; [11]Maria Sklodowska-Curie National Research Institute of Oncology, Kraków, Poland

BeiGene

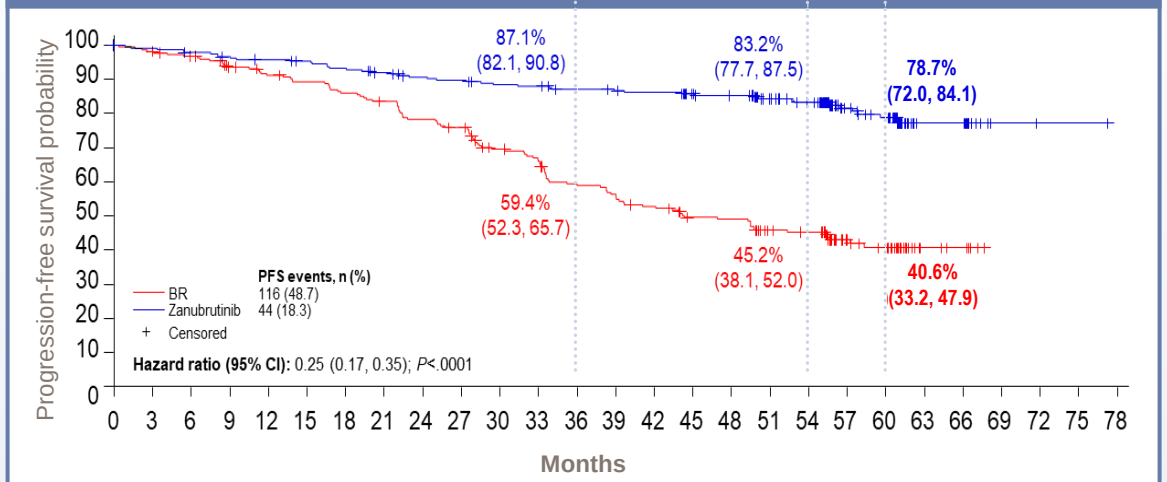
TN CLL (unfit*) - Sustained PFS Benefit Demonstrated with Zanubrutinib with Follow-up of 61.2 Months of SEQUOIA

PFS ITT



No. at risk																											
0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51	54	57	60	63	66	69	72	75	78
238	218	212	201	192	187	180	174	163	157	141	134	116	110	102	92	91	77	74	38	32	8	6	0			
241	238	234	230	228	224	219	214	208	205	201	200	195	192	190	183	178	164	153	89	81	19	19	2	1	1	0

PFS Covid-Adjusted



No. at risk																											
0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51	54	57	60	63	66	69	72	75	78
238	218	212	201	192	187	180	174	163	157	139	133	116	110	102	92	91	77	74	38	32	8	6	0			
241	238	234	230	227	224	219	213	207	205	200	199	194	192	190	183	178	164	153	89	81	19	19	2	1	1	0

ASH 2024 presentation

■ BR ■ Zanubrutinib

* In SEQUOIA, patients with TN CLL were 65 years or older or 18-64 years of age with one of the following factors: CIRS score >6, creatinine clearance <70 mL/min, history of previous serious infection or multiple infections in the past 2 years

Presented at the 2024 66th ASH Annual Meeting and Exposition

Shadman et al., JCO, 2024.
DOI: https://doi.org/10.1200/JCO-24-02265

TN CLL (unfit) – Hypertension and Atrial Fibrillation/Flutter Rates Were Low

Exposure-adjusted Incidence Rate[a] for Select AEIs[b]

	Arm A: zanubrutinib (n=240)	Arm B: BR (n=227)
Atrial fibrillation and flutter	0.13	0.09
Hemorrhage	1.66	0.35
Major hemorrhage	0.18	0.05
Hypertension	0.50	0.37

[a] EAIR was calculated as the number of patients with an event in each TEAE category divided by the total time from the first dose date to the first event date or the exposure time if no event occurred.

[b]Adverse events of interest for zanubrutinib are defined in Tam et al, 2022.[1]

1. Tam CS, et al. Lancet Oncol. 2022;23:1031-1043.

Presented at the 2024 66th ASH Annual Meeting and Exposition

Shadman et al., JCO, 2024.
DOI:https://doi.org/10.1200/JCO-24-02265

TN CLL - Zanubrutinib Authors' Conclusions:

Sustained PFS benefit regardless of risk status and low rates of AEs with 5-year follow-up

- With a median study follow-up of 61.2 months, zanubrutinib has been shown to offer a sustained PFS benefit vs BR in treatment naive patients with CLL/SLL, with a **71% reduction in risk** of progression or death
- Superior PFS benefit was consistent **irrespective of IGHV status**. Similarly, in prior reports, data from SEQUOIA cohort 2 in patients with **del(17p)/*TP53* mutation** showed an estimated 42-month rate of 79.4% were similar to PFS rates in those without this high-risk feature.[1] **This suggests that treatment with zanubrutinib may overcome negative prognostic factors such as IGHV and del(17p)/*TP53***
- **High CR/CRi rates in the zanubrutinib arm, 20.7% (95% CI: 15.8, 26.4),** that increased over the course of the study are the highest reported with BTK inhibitor monotherapy
- Zanubrutinib was well tolerated over this extended treatment period, with **low rates of atrial fibrillation/flutter, infections, and AEs that limit daily living activities such as GI toxicities**
- The cumulative incidence of hypertension and atrial fibrillation/flutter remain low and are comparable to the background incidence in this patient population, which was observed in the BR arm
- The results of this extended follow-up in the SEQUOIA study support the use of zanubrutinib as a standard first-line treatment option for patients regardless of disease risk status

1. Munir T, et al. EHA 2023. Abstract P639.

Presented at the 2024 66th ASH Annual Meeting and Exposition

Shadman et al., JCO, 2024.
DOI:https://doi.org/10.1200/JCO-24-02265

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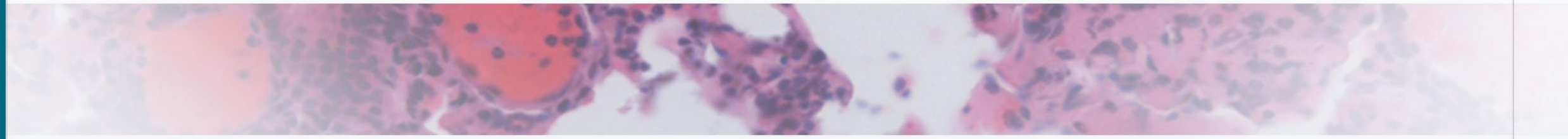

Deep and Sustained Responses in Patients With CLL Treated With Zanubrutinib or Zanubrutinib + Obinutuzumab in Phase 1/2 AU-003 and Phase 1b GA-101 Studies: A Report From the Zanubrutinib Extension Study

Constantine S. Tam,[1] Stephen S. Opat,[2] Eileen Merriman,[3] Jan A. Burger,[4] Emma Verner,[5,6] Paula Marlton,[7] David J. Gottlieb,[8] Ian W. Flinn,[9] Sumit Madan,[10] Matthew Ku,[11] Radha Prathikanti,[12] Heather Allewelt,[12] Tian Tian,[12] Remus Vezan,[12] Gavin Cull[13]

[1]Alfred Hospital and Monash University, Melbourne, VIC, Australia; [2]Lymphoma Research Group, School of Clinical Sciences at Monash Health, Monash University, Clayton, VIC, Australia; [3]North Shore Hospital, Auckland, New Zealand; [4]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [5]Concord Repatriation General Hospital, Concord, NSW, Australia; [6]University of Sydney, Sydney, NSW, Australia; [7]Princess Alexandra Hospital and University of Queensland, Brisbane, QLD, Australia; [8]8Department of Haematology, Westmead Hospital Sydney, Sydney, NSW, Australia; [9]Tennessee Oncology/OneOncology, Nashville, TN, USA; [10]Banner MD Anderson Cancer Center at Banner Gateway Medical Center, Gilbert, AZ, USA; [11]St Vincent's Hospital, Fitzroy, VIC, Australia; [12]BeiGene USA, Inc, San Mateo, CA, USA; [13]Sir Charles Gairdner Hospital, Nedlands, WA, Australia

BeiGene

TN and R/R CLL/SLL - Zanubrutinib and ZO Author's Conclusions:

Unprecedented CR/CRi rates and impressive PFS in CLL/SLL patients

- In patients with CLL/SLL, treatment with **zanubrutinib** in AU-003 and with **ZO** in GA-101 led to high rates of overall and complete responses, with **unprecedented CR/CRi rates for BTKi treatment in TN patients**
- With the longest follow-up to date (median 6.5 years), treatment with zanubrutinib or ZO resulted in durable responses **and impressive PFS in patients with both TN and R/R CLL/SLL**
- The tolerability/safety profile of zanubrutinib, alone and in combination with ZO, remained favorable, with decreasing prevalence of most TEAEs of interest from the initial treatment period

Mass General Brigham
Mass General Cancer Center

Memorial Sloan Kettering Cancer Center

Multicenter Phase II Trial of Zanubrutinib, Obinutuzumab, and Venetoclax (BOVen) in Treatment-Naïve Chronic Lymphocytic Leukemia: 5-Year Follow up, Retreatment Outcomes, and Impact of MRD Kinetics (ΔMRD400)

Jacob D. Soumerai[1], Ahmet Dogan[2], Venkatraman Seshan[2], Kelsey Flaherty[2], Natalie Slupe[2], Jason Carter[2], Ephraim Hochberg[1], Jeffrey A. Barnes[1], Jeremy S. Abramson[1], Audrey M. Hamilton[2], Ariela Noy[2], Colette N. Owens[2], M. Lia Palomba[2], Anita Kumar[2], Lindsey E. Roeker[2], Meghan Thompson[2], Ronald W. Takvorian[1], Zachary Epstein-Peterson[2], Mark Geyer[2], Gilles Salles[2], Robert Stuver[2], Philip Caron[2], Prioty Islam[2], Tamanna Haque[2], Paola Ghione[2], Raphael Steiner[2], Pallawi Torka[2], Kevin David[2],Jennifer Lue[2], Paul Hamlin[2], Alison Moskowitz[2], Lorenzo Falchi[2], J. Erika Haydu[1], P. Connor Johnson[1], Joanna Mi[2], Jessica Pendleton[2], Alyssa Labarre[2], Rosalba Martignetti[1], Sean Plummer[1], Maria Chabowska[2], Walter Ramos-Amador[2], Neena Mahajan[2], Morgan Choma[2], Clare Grieve[2], Rayna Garcia[1], Hailey Kelly[1], Ella Mallinger[1], James O'Grady[1], Bernadette Beatty[1], Michelle Adams[1], Athina Apazidis[1], Aileen Cohen[3], Mina Shahkarami[4], Allison Jacob[5], Omar Abdel-Wahab[2], and Andrew D. Zelenetz[2]

[1] Massachusetts General Hospital Cancer Center, Center for Lymphoma, Boston, MA, United States of America
[2] Memorial Sloan Kettering Cancer Center, New York, NY, United States of America
[3] Beigene Ltd., San Mateo, CA, United States of America
[4] Genentech Inc., South San Francisco, CA, United States of America
[5] Adaptive Biotechnologies Corp., Seattle, WA, United States of America

Presented at the 2024 66th ASH Annual Meeting and Exposition

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TN CLL - Adverse Events Occurring with BOVen Regimen (all-cause)

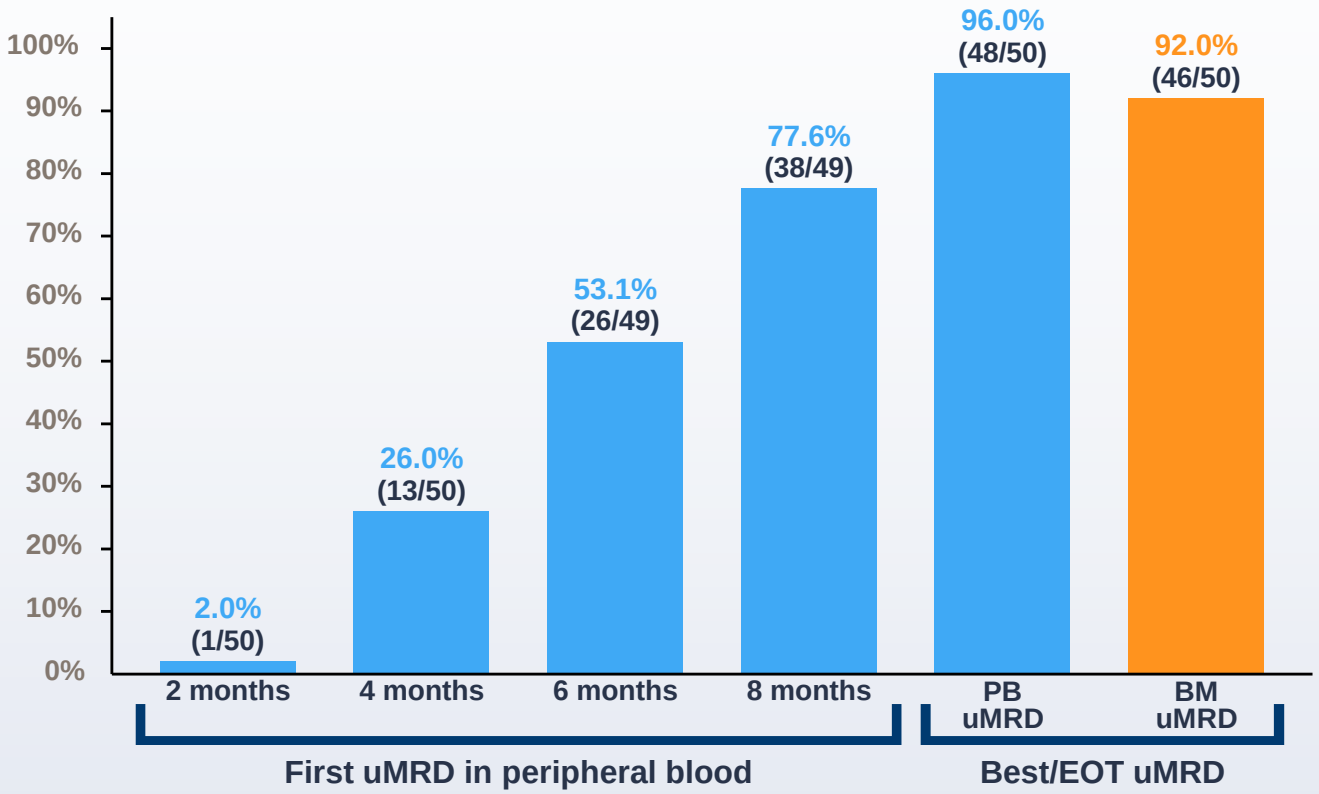
Mass General Brigham
Mass General Cancer Center

Any grade AEs in ≥15% pts	Grade 1-2 (%)	Grade 3 (%)	Grade 4 (%)
Platelet count decreased	27 (52%)	4 (8%)	
Fatigue	30 (58%)	1 (2%)	
Neutrophil count decreased	16 (31%)	4 (8%)	10 (19%)
Diarrhea	25 (48%)	2 (4%)	-
Bruising	25 (48%)	-	-
Cough	20 (39%)	-	-
Infusion related reaction	17 (33%)	2 (4%)	1 (2%)
Nausea	19 (37%)	-	-
Anemia	19 (37%)	-	-
Constipation	18 (35%)	-	-
Nasal congestion	15 (29%)	-	-
Rash	11 (21%)	2 (4%)	-
Insomnia	12 (23%)	-	-
Myalgia	12 (23%)	-	-
Gastroesophageal reflux disease	12 (23%)	-	-
Arthralgia	11 (21%)	-	-
Aspartate aminotransferase increased	10 (19%)	-	-
Dyspnea	10 (19%)	-	-
Dizziness	9 (17%)	-	-
Abdominal pain	9 (17%)	-	-
Alkaline phosphatase increased	7 (14%)	1 (2%)	-
Headache	7 (14%)	1 (2%)	-
Postnasal drip	8 (15%)	-	-
Sore throat	8 (15%)	-	-
Hypocalcemia	8 (15%)	-	-
Sinusitis	8 (15%)	-	-

Grade ≥3 AEs in ≥2 pts	Grade 3 (%)	Grade 4 (%)	Grade 5 (%)
Neutrophil count decreased	4 (8%)	10 (19%)	-
Platelet count decreased	4 (8%)	-	-
Lung infection	3 (6%)	-	-
Diarrhea	2 (4%)	-	-
Infusion related reaction	1 (2%)	1 (2%)	-
Rash	2 (4%)	-	-
Skin infection	2 (4%)	-	-
Fatigue	1 (2%)	-	-
Alkaline phosphatase increased	1 (2%)	-	-
Headache	1 (2%)	-	-
Mucositis oral	1 (2%)	-	-
Atrial fibrillation	-	1 (2%)	-
Hypophosphatemia	1 (2%)	-	-
Rash	1 (2%)	-	-
Blood bilirubin increased	1 (2%)	-	-
Heart failure	1 (2%)	-	-
Purpura	1 (2%)	-	-

- No laboratory or clinical tumor lysis syndrome (Howard criteria)
- Additional Grade ≥3 AEs occurring in 1 patient each are as follows: One grade 5 AE occurred in a patient with intracranial hemorrhage on cycle 1 day 1. One grade 3 febrile neutropenia. One Achilles tendon partial tear.`

TN CLL - BOVen High Rates of uMRD4 at End of Treatment



* One patient, initially ascertained as uMRD in peripheral blood at 8 mo, had subsequent serial testing which confirmed MRD positivity at the threshold of detection, so the patient was excluded from the proportion of patients achieving uMRD

- 96% (48/50) uMRD4 in PB
- 92% (46/50) uMRD4 in both PB and BM
  - All met **prespecified MRD endpoint/ treatment discontinuation criterion and stopped therapy after median of 10 mo (IQR 8-12 mo)**

** uMRD = MRD $<10^{-4}$ (14-color flow cytometry)
LOD: 10^{-4}
Cutoff: uMRD if $<10^{-4}$

BeiGene's Interpretation of AMPLIFY Data Presentation

We believe in fixed treatment duration, but AMPLIFY did not meet expectations

The study was conducted in **low-risk fit TN CLL** patients excluding 17p del/TP53 and CIRS >6 vs FCR/BR[1]

- **AV:**
  - With only 40 mo follow up time, modest risk reduction reported vs FCR/BR, a substandard control arm
  - **36 mo PFS estimate show no evidence of benefit vs current SoC** (BRUKINA and VO/VI) in cross-trial comparisons
    - Superiority even less noticeable after adjustment for COVID-19, with curves converging
    - Lower 36 mo PFS estimate is seen in uIGVH; numerically lower compared to SoC
  - **uMRD key secondary endpoint failed, favoring FCR/BR** (51%) vs only **29% uMRD4 in AV** (notably lower than those observed with **VI** and VO at similar timepoints in cross-trial comparisons).
  - **No claim of OS benefit can be made** as analysis of key secondary endpoint failed
  - Concerning number of deaths (all cause) over a short duration of follow up in a 1L fit population, a population that historically performed better than unfit

- **AVO**: Triplet is associated with major safety concerns with increased high-grade toxicity and death, with no benefit vs current Soc

Fixed treatment duration needs to be safe and **efficacious in all patients with any disease risk status or patient characteristics and feasible to deliver at any clinical practice**

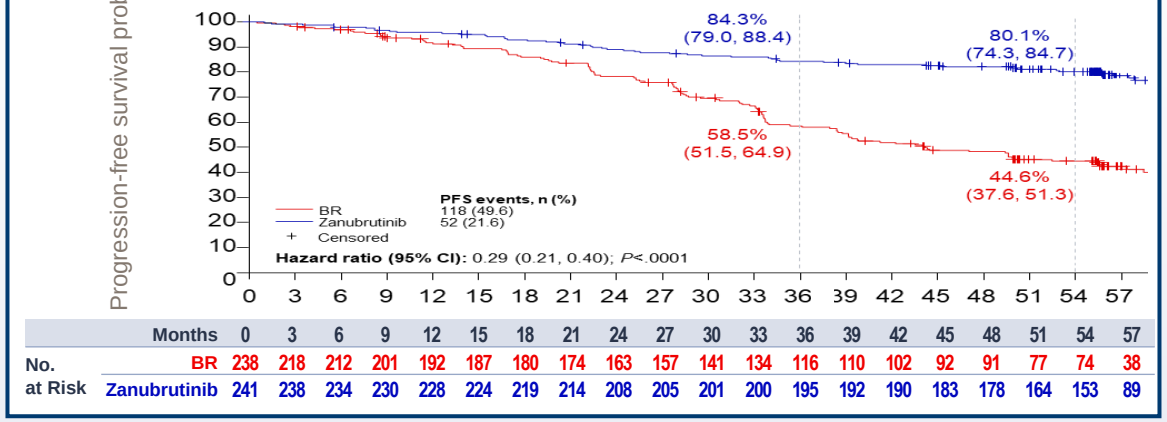
[1] Brown et al, ASH, 2024

TN – Treatment Naïve
CLL – Chronic Lymphocytic Leukemia
PFS – Progression Free Survival
SoC – Standard of Care
VO – Venetoclax/ Obinutuzumab
VI – Venetoclax/ Ibrutinib
MRD – Minimal Residual Disease
AV – Acalabrutinib/ Venetoclax
OS – Overall Survival
AVO- – Acalabrutinib/ Venetoclax/. Obinutuzumab

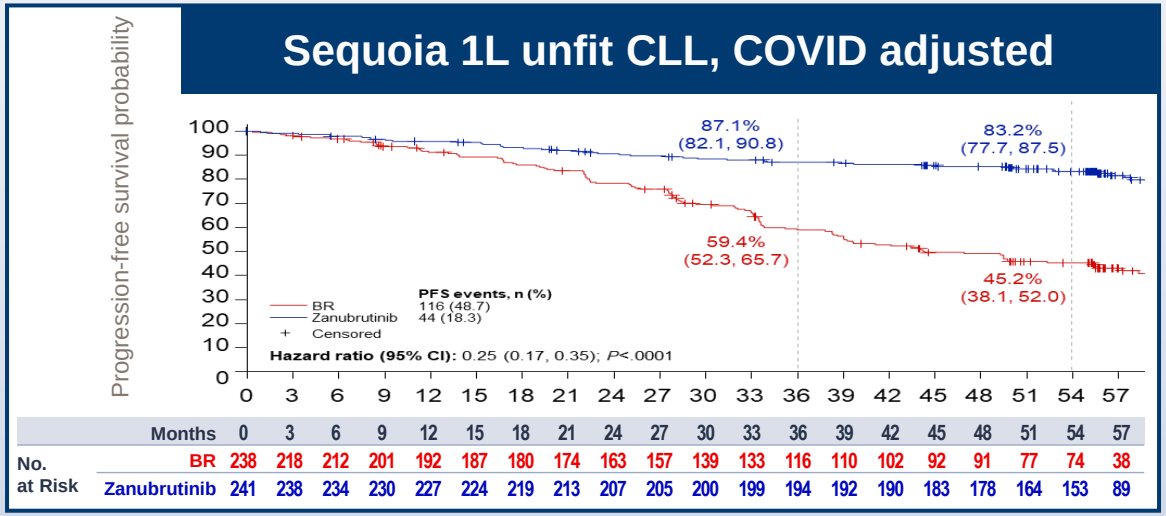
Cross Trial Comparison of SEQUOIA Study of 1L Unfit Vs. AMPLIFY Study of 1L Fit CLL

Median age =70

Sequoia 1L unfit CLL, ITT

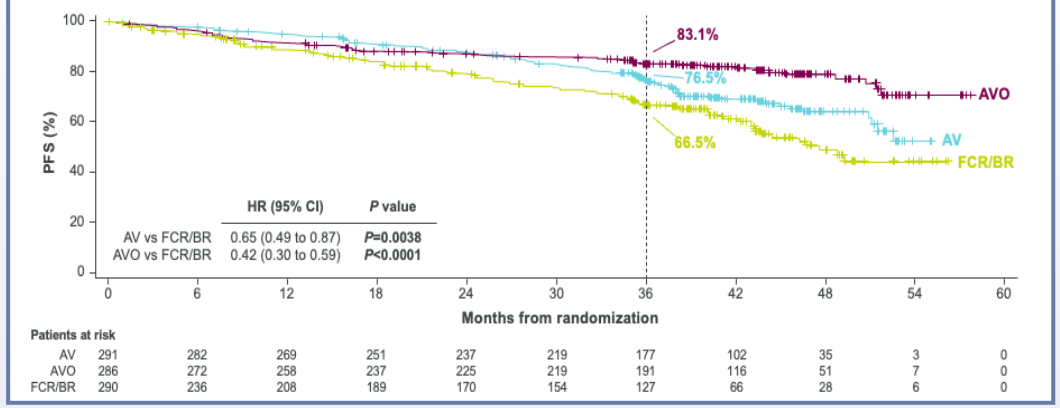


Sequoia 1L unfit CLL, COVID adjusted

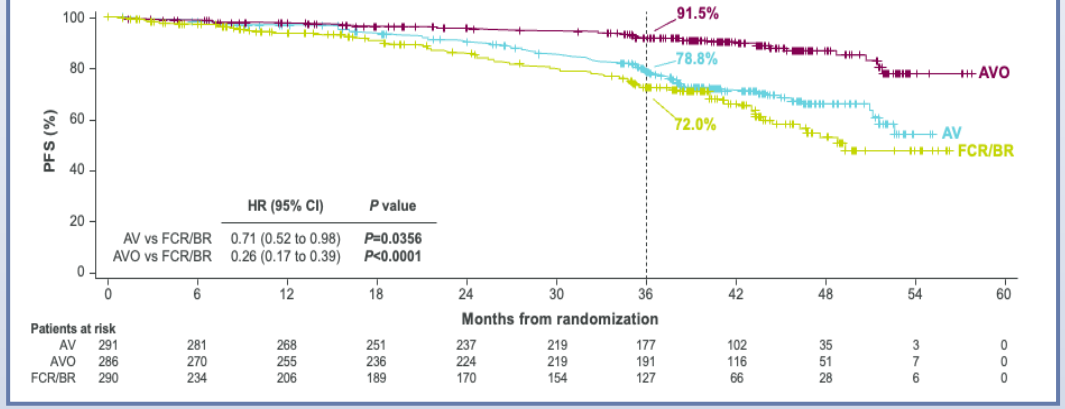


Median age = 61

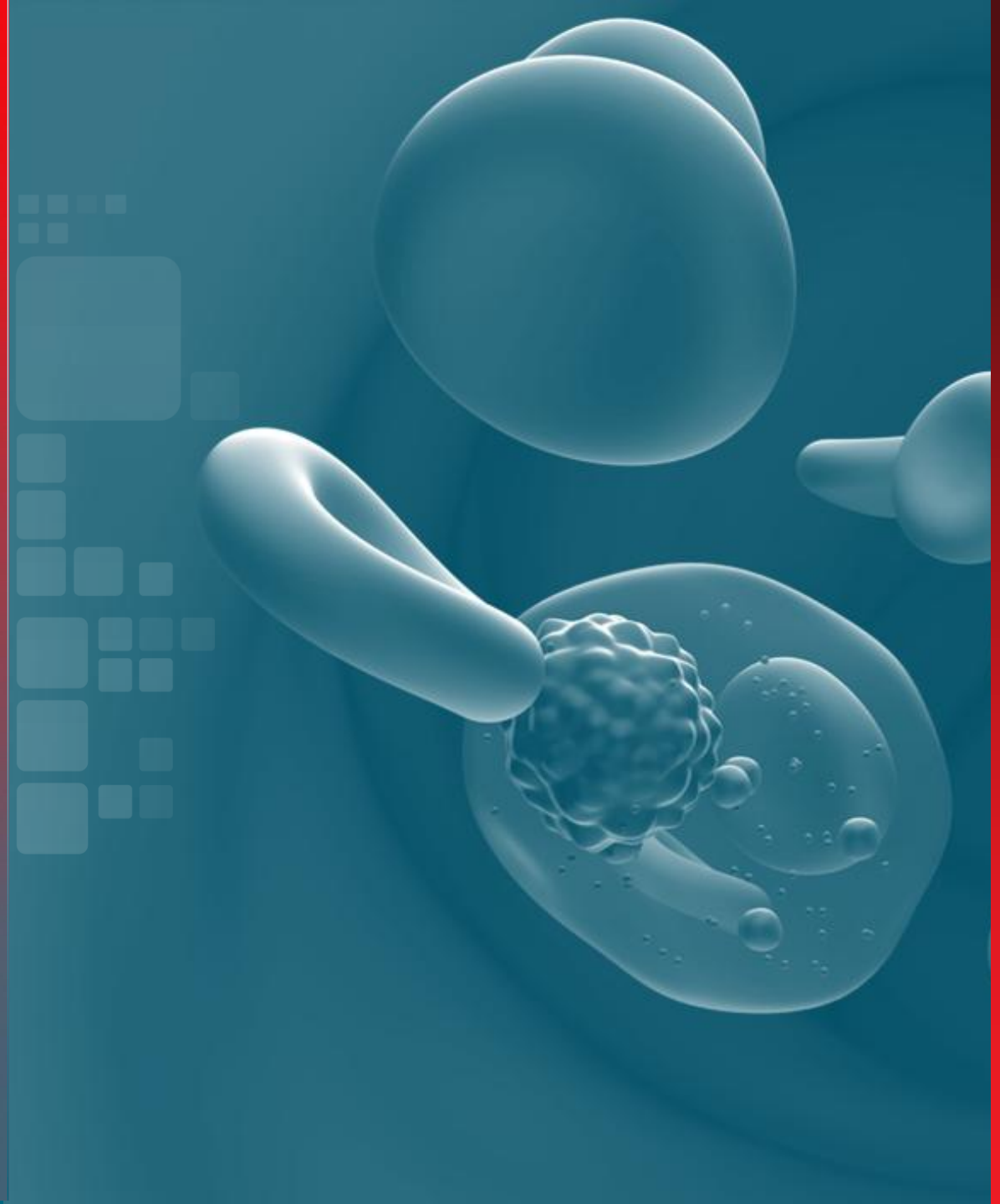
AMPLIFY 1L fit CLL, ITT AV/AVO vs. FCR/BR*



AMPLIFY COVID adjusted AV/AVO vs. FCR/BR*



[1] Brown et al, ASH, 2024



BRUKINSA (zanubrutinib)

Sonrotoclax

BGB-16673 (BTK CDAC)

Sonrotoclax, BCL2 Inhibitor With Best-in-Class Potential

More potent and specific BCL2i; unique PK profile

- **Greater potency** vs. venetoclax in preclinical models; an important feature of a BCL2i
- **Higher selectivity** towards BCL2 believed to translate to **improved safety**
- Shorter **half-life** vs. venetoclax and **no drug accumulation to improve tolerability**

Clinical superiority observed to date

- **1600+ patients** clinical data **reinforces pre-clinical** and best-in-class potential
- **Deep and durable responses** seen in monotherapy and combos including combos with BRUKINSA; **better data than venetoclax combos**
- Improved **safety and feasibility**

Broadest label of any BCL2 inhibitor planned

- **Ph 3 study ongoing in TN CLL** with potential to be best in disease **fixed duration combination and SOC** globally
- **Ph2 studies** with **early registration potential** in CLL, WM and MCL in post-BTKi setting
- **Two Ph3 studies in RR CLL and RR MCL** starting in H1 2025

Remove existing barriers to BCL2i adoption

- **Head-to-Head superiority** against relevant gold standard comparators in all pivotal studies
- **Differentiated ramp up** in current studies could unlock **wide use by all physicians**
- **Further ramp-up optimization ongoing**; **aligned with health authorities** based on no observed TLS

Expands Hematology leadership

- Protects and grows **leadership in CLL** as well as **other B-cell malignancies**
- **Expand into AML**
- **Potentially first approved BCL2i in MM with t(11;14)**, based on dex doublet with potential earlier line studies of triplets with CD38 or proteasome inhibitor possible

TN – Treatment Naïve
CLL - Chronic Lymphocytic Leukemia
SoC – Standard of Care
WM - Waldenström's Macroglobulinemia
MCL - Mantle Cell Lymphoma
R/R – Relapsed Refractory
TLS – Tumor Lysis Syndrome
AML - Acute Myeloid Leukemia
MM - Multiple Myeloma

2024 ASH BeiGene Key Presentations Sonrotoclax

Topic	Title	First author / significance	Status
BGB-11417-101 S+Z TN CLL	Sonrotoclax and zanubrutinib as frontline treatment for CLL demonstrates high MRD clearance rates with good tolerability: Updated data on the ongoing phase 1/1b study BGB-11417-101	**Jacob D. Soumerai** Sonrotoclax + zanubrutinib has the potential for best in disease combination with impressive deep and durable responses. At a longer follow up (18.3mo), all patients responded to therapy and 90% achieved uMRD by week 48 while no clinical or lab TLS or other safety signals were observed. No progressions in 320mg cohort to date.	**Oral 1012**
CELESTIAL-TNCLL Trial in Progress (TiP)	CELESTIAL-TNCLL: An Ongoing, Open-Label, Multiregional, Phase 3 Study of Sonrotoclax (BGB-11417) + Zanubrutinib vs Venetoclax + Obinutuzumab for Treatment-Naive CLL	**Piers E.M. Patten** CELESTIAL-TNCLL (BGB-11417-301; NCT06073821) aims to assess and establish fixed duration sonrotoclax + zanubrutinib in TN CLL; Only ongoing study designed to show superiority vs. venetoclax +obinutuzumab	**Poster 3257**
BGB-11417-203 Trial in Progress (TiP)	BGB-11417-203, an Ongoing, Phase 2 Study of Sonrotoclax (BGB-11417), a Next-Generation BCL2 Inhibitor, in Patients With Waldenström Macroglobulinemia	**Hui-Peng Lee** Based on promising data from Ph1, BGB-11417-203 (NCT05952037) is an potentially registration enabling phase 2 study of sonrotoclax monotherapy, and sonrotoclax in combination with zanubrutinib, in patients with WM	**Poster 1661**

American Society *of* Hematology

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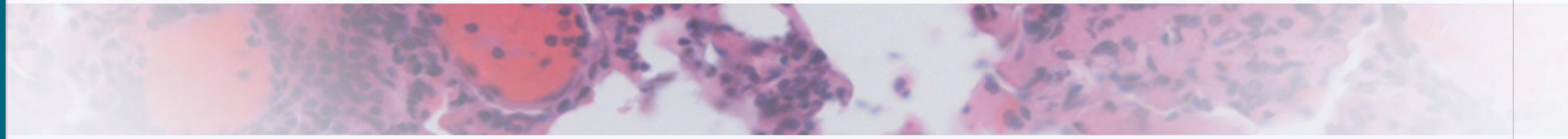


Sonrotoclax and Zanubrutinib as Frontline Treatment for CLL Demonstrates High MRD Clearance Rates with Good Tolerability: Data from an Ongoing Phase 1/1b Study BGB-11417-101

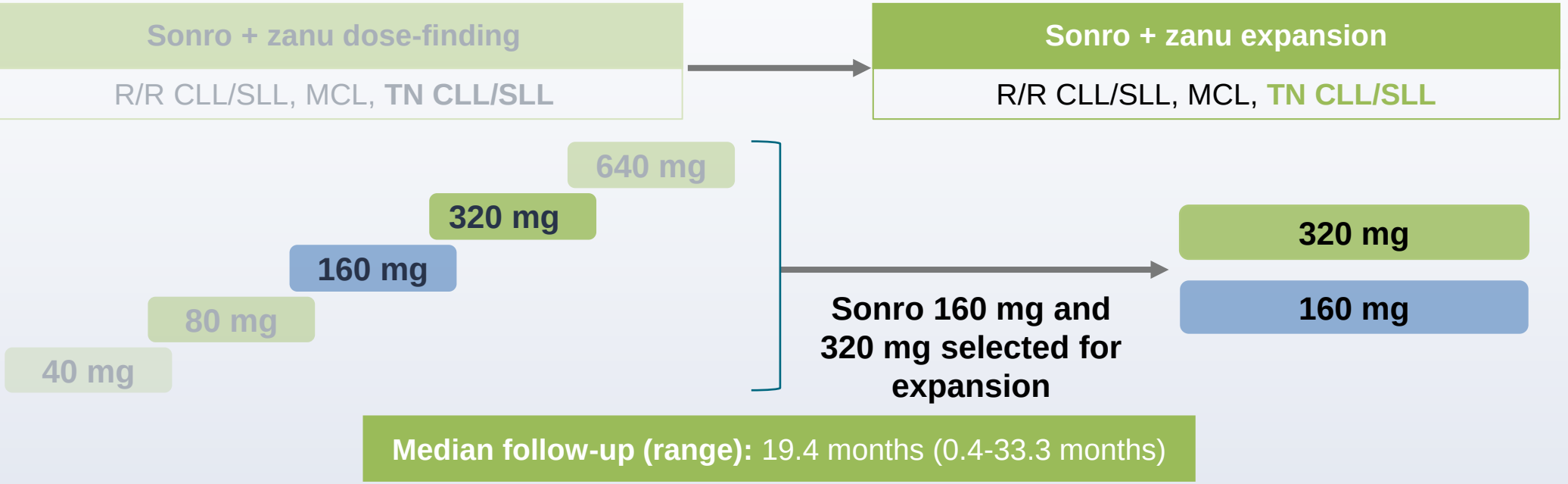
Jacob D. Soumerai,[1] Chan Y. Cheah,[2-4] Mary Ann Anderson,[5,6] Masa Lasica,[7] Emma Verner,[8,9] Stephen S. Opat,[10] Shuo Ma,[11] Robert Weinkove,[12,13] Raul Cordoba,[14] Paolo Ghia,[15,16] Sophie Leitch,[17] David Westerman,[18,19] Sheel Patel,[20] Yiqian Fang,[21] Wei Ding,[20] Haiyi Guo,[21] Constantine S. Tam[22]

[1]Massachusetts General Hospital Cancer Center and Harvard Medical School, Boston, MA, USA; [2]Sir Charles Gairdner Hospital, Nedlands, WA, Australia; [3]Medical School, University of Western Australia, Crawley, WA, Australia; [4]Linear Clinical Research, Nedlands, WA, Australia; [5]Royal Melbourne Hospital and Peter MacCallum Cancer Centre, Melbourne, VIC, Australia; [6]The Walter and Eliza Hall Institute, Melbourne, VIC, Australia; [7]St Vincent's Hospital Melbourne, Fitzroy, VIC, Australia; [8]Concord Repatriation General Hospital, Concord, NSW, Australia; [9]University of Sydney, Sydney, NSW, Australia; [10]Lymphoma Research Group, School of Clinical Sciences at Monash Health, Monash University, Clayton, VIC, Australia; [11]Robert H. Lurie Comprehensive Cancer Center, Northwestern University Feinberg School of Medicine, Chicago, IL, USA; [12]Te Rerenga Ora Blood and Cancer Centre, Te Whatu Ora Health New Zealand Capital Coast & Hutt Valley, Wellington, New Zealand; [13]Cancer Immunotherapy Programme, Malaghan Institute of Medical Research, Wellington, New Zealand; [14]Hospital Universitario Fundación Jiménez Díaz, Madrid, Spain; [15]Università Vita-Salute San Raffaele, Milano, Italy; [16]IRCCS Ospedale San Raffaele, Milano, Italy; [17]Te Whatu Ora Health New Zealand-Waitemata, Auckland, New Zealand; [18]Peter MacCallum Cancer Centre, Melbourne, VIC, Australia; [19]University of Melbourne, Melbourne, VIC, Australia; [20]BeiGene USA, Inc, San Mateo, CA, USA; [21]BeiGene (Shanghai) Co, Ltd, Shanghai, China; [22]Alfred Hospital and Monash University, Melbourne, VIC, Australia

BeiGene

BGB-11417-101 - Sonrotoclax (NCT04277637) Study Design

- BGB-11417-101 is a global phase 1/1b study evaluating sonrotoclax as monotherapy, or in combination with zanubrutinib and/or obinutuzumab in patients with B-cell malignancies
- The study endpoints included safety per CTCAE v5.0, RP2D and efficacy
- Treatment consisted of 8-12 weeks of zanubrutinib lead-in (320 mg QD or 160 mg BID), then zanubrutinib + sonrotoclax until disease progression or intolerance



Presented at the 2024 66th ASH Annual Meeting and Exposition

CTCAE – Common Terminology Criteria for Adverse Events
RP2D – Recommended Phase 2 Dose
TN – Treatment Naïve
CLL/SLL - Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma
MCL - Mantle Cell Lymphoma

TN CLL - Sonrotoclax + Zanubrutinib Baseline Characteristics

Characteristics	Sonro 160 mg + zanu (n=51)	Sonro 320 mg + zanu (n=86)	All Patients (N=137)
Study follow-up, median (range), months	19.5 (12.6-33.3)	19.3 (0.4-29.7)	19.4 (0.4-33.3)
Age, median (range), years	63 (38-82)	61 (32-84)	62 (32-84)
≥65 years, n (%)	20 (39.2)	35 (40.7)	55 (40.1)
Male sex, n (%)	37 (72.5)	61 (70.9)	98 (71.5)
Disease type, n (%)			
CLL	48 (94.1)	82 (95.3)	130 (94.9)
SLL	3 (5.9)	4 (4.7)	7 (5.1)
Risk status, n/tested (%)			
del(17p)	5/45 (11.1)	6/77 (7.8)	11/122 (9.0)
TP53 muta	11/47 (23.4)	13/62 (21.0)	24/109 (22.0)
del(11q)	10/45 (22.2)	11/77 (14.3)	21/122 (17.2)
IGHV status, n/tested (%)			
Unmutated IGHV	32/47 (68.1)	32/60 (53.3)	64/107 (59.8)
High tumor bulk[b] at baseline, n/tested (%)	22/51 (43.1)	17/82 (20.7)	39/133 (29.3)

Data cutoff: August 23, 2024.
[a] *TP53* mutations defined as >0.1% VAF. [b] Nodes ≥10 cm or nodes >5 cm and ALC >25×10⁹/L.

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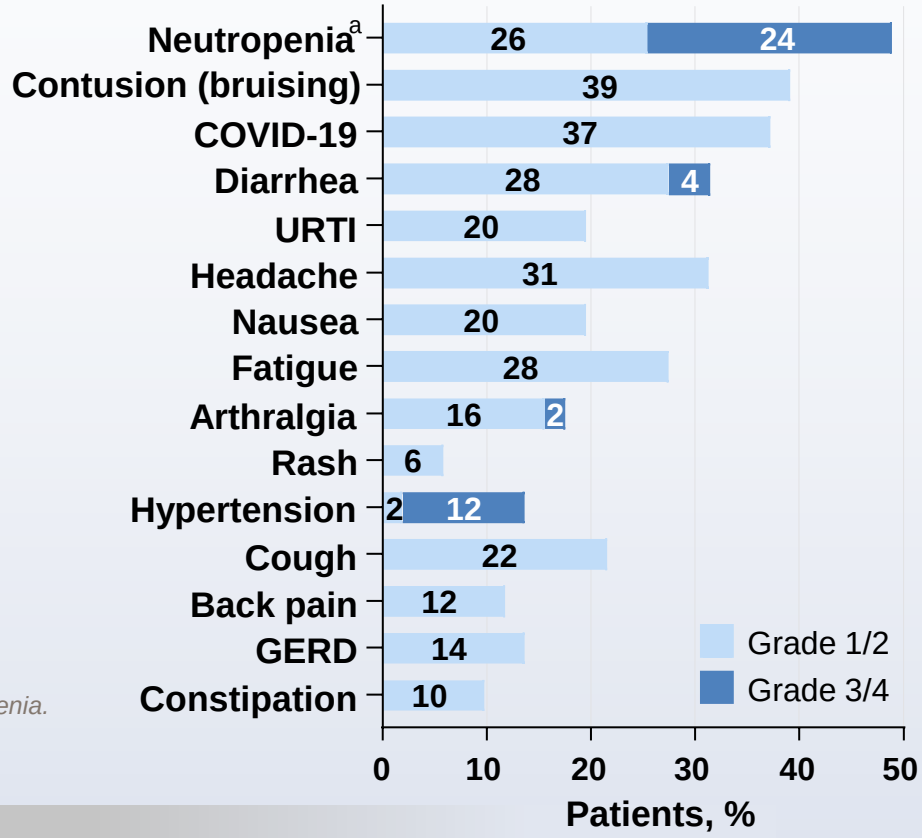
TN CLL - TEAEs Observed with Sonrotoclax+Zanubrutinib Were Mostly Low Grade and Transient

- No TLS
- Neutropenia was transient and did not lead to higher rates of grade ≥3 infections

TEAEs in ≥10% of all patients

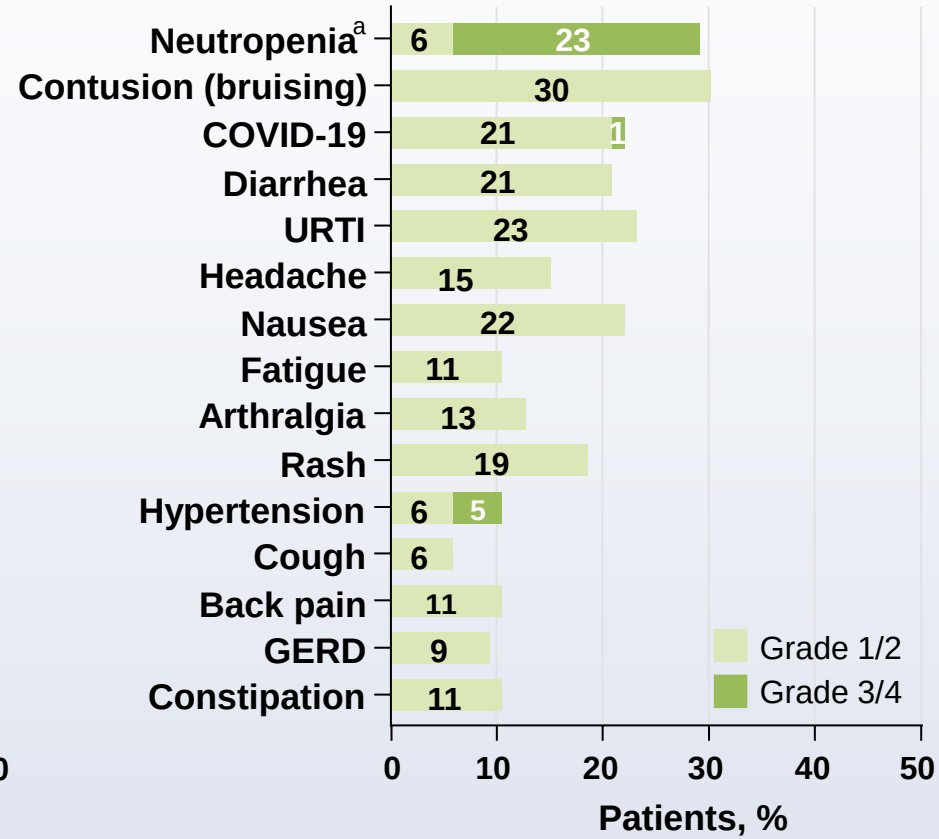
Sonro 160 mg + zanu (n=51)

Median follow-up: 19.5 mo (range, 12.6-33.3 mo)



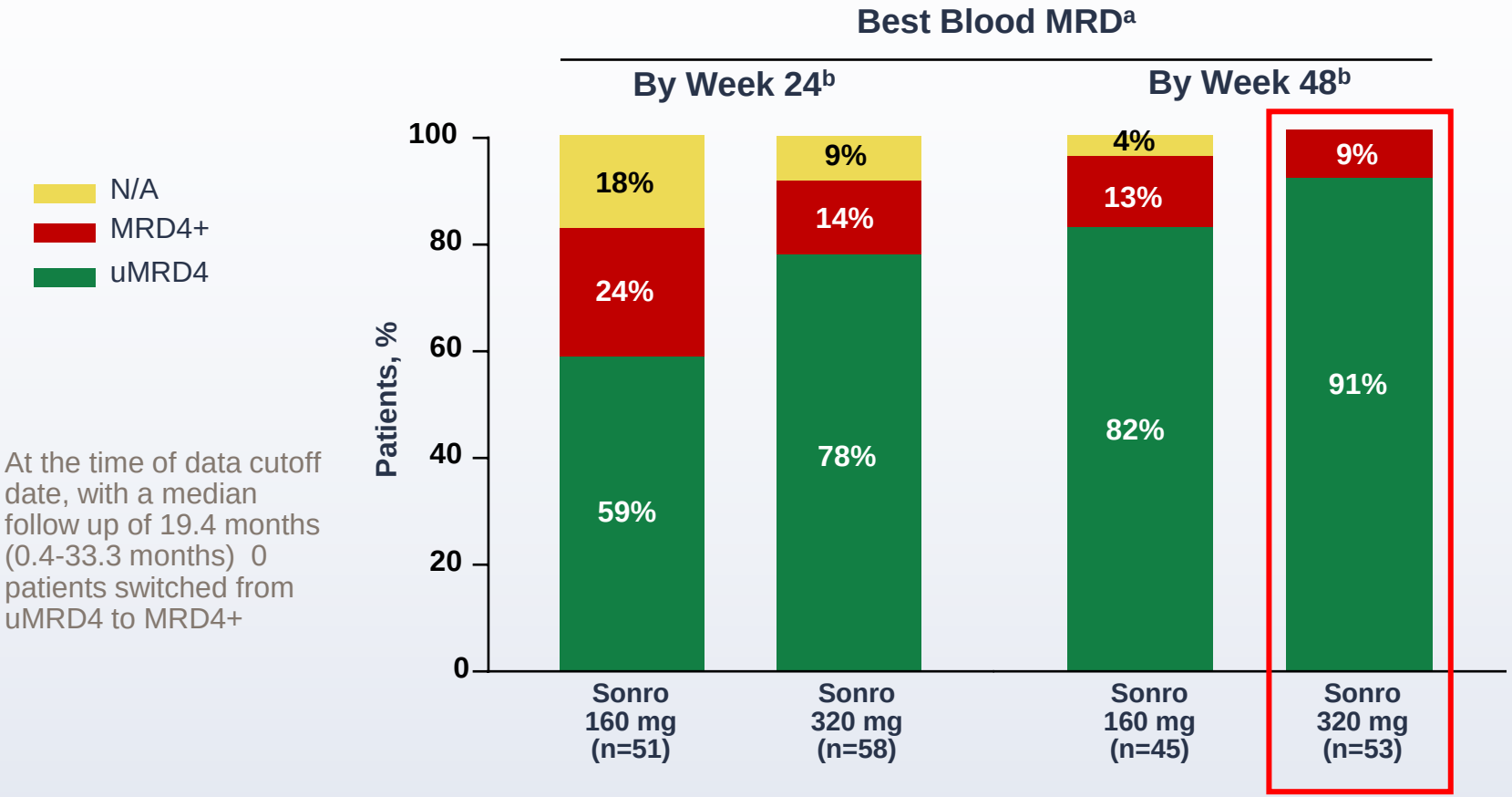
Sonro 320 mg + zanu (n=86)

Median follow-up: 19.3 mo (range, 0.4-29.7 mo)



[a] Includes the combined preferred terms *neutrophil count decreased* and *neutropenia*.

TN CLL - High and Early Blood uMRD4 with Sonrotoclax+Zanubrutinib Deepening Responses to Week 48 Across Risk Factor Groups



At the time of data cutoff date, with a median follow up of 19.4 months (0.4-33.3 months) 0 patients switched from uMRD4 to MRD4+

AMPLIFY

AMPLIFY Study Arms	PB uMRD4 Rate (%)	
	Key secondary Endpoint*	EOT
AV	26.8	34.4
AVO	66.4	67.1
FCR/BR	51.0	45.5

*Key secondary at Cycle 9 (AV), Cycle 10 (AVO), Cycle 6 + 12 weeks (FCR/BR). uMRD by flow.

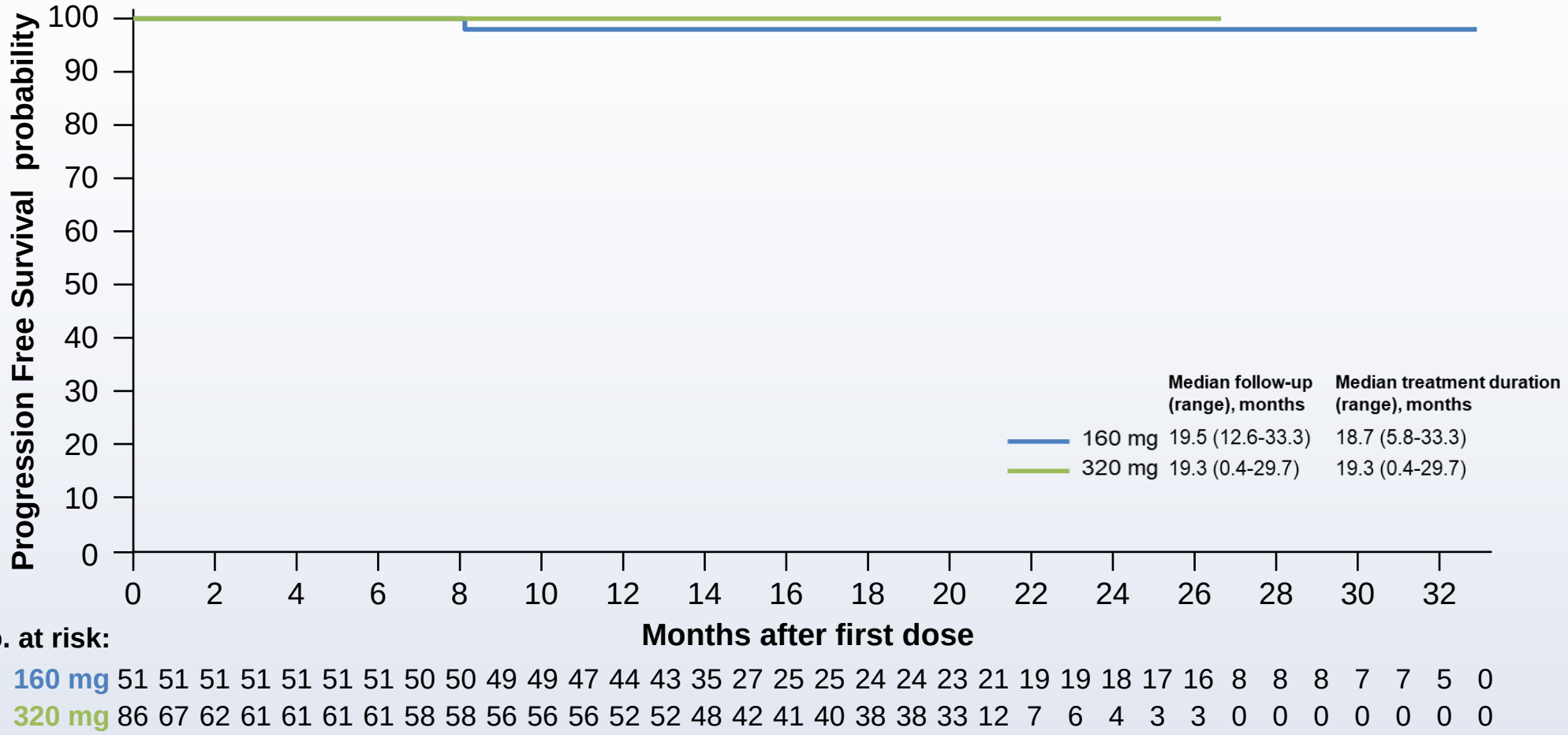
ZS uMRD4 compares favorably to AV/AVO/chemo, at similar timepoints[1]

[1] Brown et al, ASH, 2024

uMRD – Undetectable Minimal Residual Disease
AV – Acalabrutinib/ Venetoclax
AVO- – Acalabrutinib/ Venetoclax/. Obinutuzumab
a As measured by ERIC flow cytometry panel uMRD4 is defined as less than 1 CLL cell per 10,000 leukocytes ($<10^{-4}$);
b Number of weeks at target dose, following zanu monotherapy and sonro ramp-up to target dose

TN CLL - at Median Study Follow-Up of 19.4 Months
No Progression Observed with Sonrotoclax 320 mg + Zanubrutinib

1 PFS event in sonrotoclax 160-mg cohort (Richter transformation)



TN CLL - Sonrotoclax Authors' Conclusion:

With longer follow-up, S+Z continued to demonstrate encouraging safety and efficacy in TN CLL

- Sonrotoclax 160 or 320 mg in combination with zanubrutinib (320 mg) was **generally safe and well tolerated**, with a median relative dose intensity of 99%
  - No laboratory or clinical TLS occurred
  - Majority of TEAEs were low grade; low rates of GI TEAEs, predominantly grade 1, were observed
  - The most common grade ≥3 TEAE was neutropenia, which was mostly transitory
  - No fatal TEAEs, no complicated COVID-19 case or death

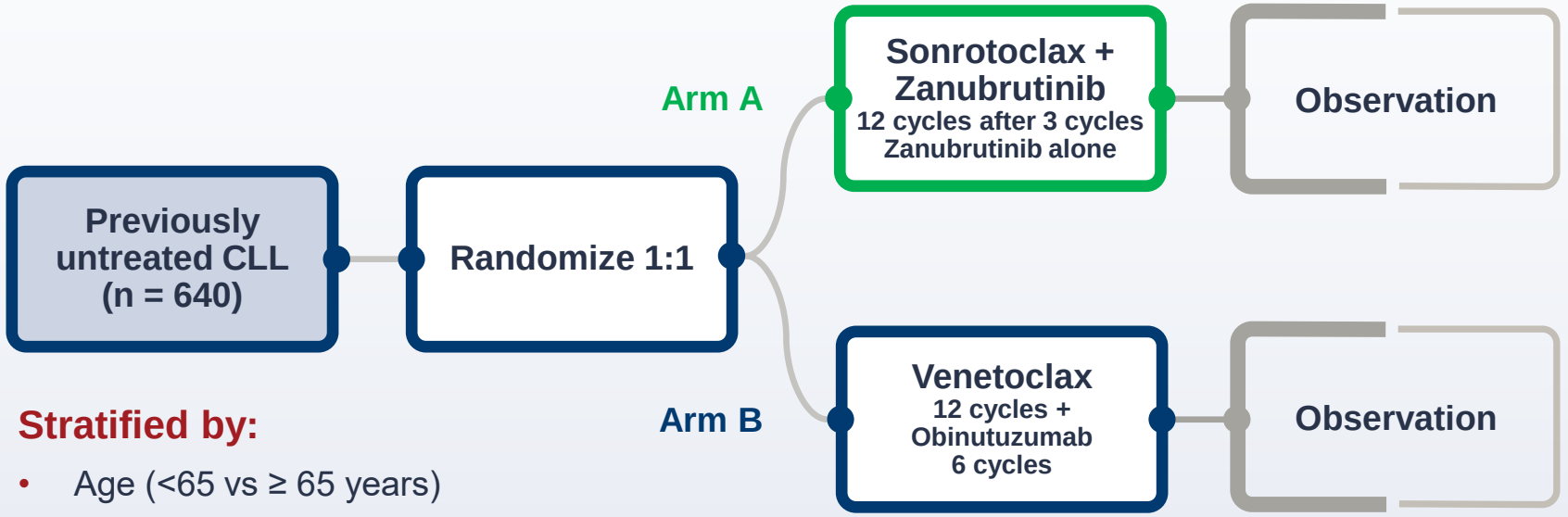
- **Substantial efficacy was observed in this all-comer TN CLL/SLL population**, including in patients with high-risk features
  - The sonrotoclax + zanubrutinib combination demonstrated a high response rate, including 100% ORR in the 320-mg cohort
  - High and early blood uMRD4 was seen by week 24 of combination therapy in both dose cohorts, with higher rates in the 320-mg cohort and further deepening by week 48 in both cohorts. No patient has progressed from uMRD4 to MRD4+
  - With median follow-up of 19.4 months, only 1 primary progression occurred in the 160-mg cohort that was an RT

- Sonrotoclax 320 mg in combination with zanubrutinib is being evaluated in patients with TN CLL in the phase 3 study, **CELESTIAL-TNCLL (NCT06073821); enrollment is currently ongoing**

Presented at the 2024 66th ASH Annual Meeting and Exposition

Sonrotoclax CELESTIAL - TN CLL Is the ONLY Phase 3 Trial Designed to Show PFS Superiority of FD S+Z Over V+O Standard of Care

Sonrotoclax +Zanubrutinib has the potential for best-in-disease fixed duration therapy and expressed high interest for investigators and patients



Stratified by:

- Age (<65 vs ≥ 65 years)
- IGHV (mutated vs unmutated)
- del(17p)/*TP53* (no abnormality versus any abnormality)

Primary Endpoint

PFS Superiority of SZ versus VO by IRC

Key Secondary Endpoints

- **uMRD4 rate**
- Complete response rate
- Overall survival

Presented at the 2024 66th ASH Annual Meeting and Exposition

PFS – Progression Free Survival
uMRD – Undetectable Minimal Residual Disease
IGHV – Immunoglobulin Heavy Chain Variable Region

Delivering the potentially broadest label of any BCL2 inhibitor

Pivotal aim to demonstrate clinical superiority and differentiated profile removing barriers to use

Sonrotoclax BGB-11417 (BCL2 inhibitor)

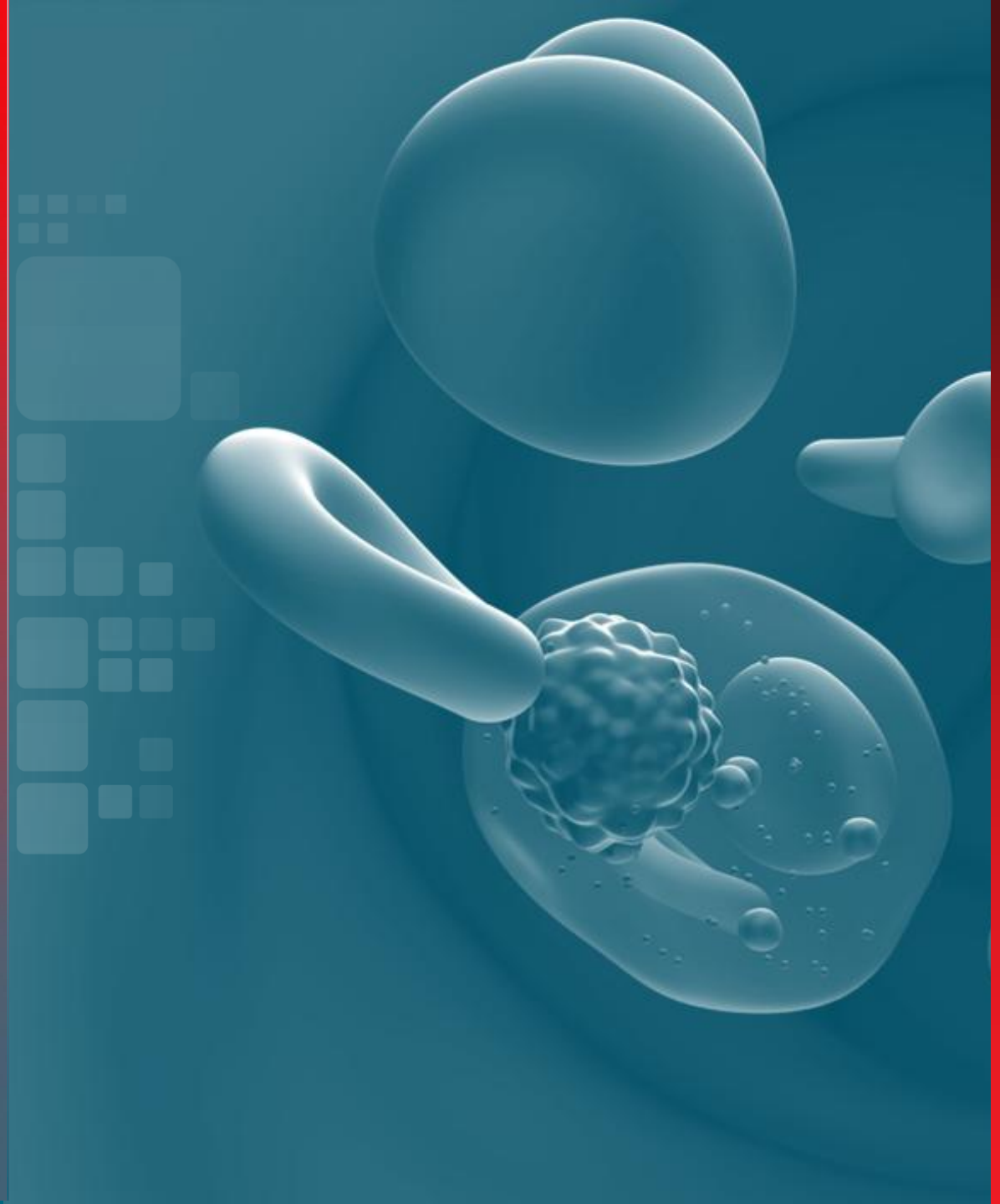
R/R MCL	Phase 2	**Potentially pivotal.** Monotherapy in patients with **R/R MCL post-BTKi** in the BGB-11417-201 trial
R/R CLL/SLL	Phase 2	**Potentially pivotal.** Monotherapy in patients with **R/R CLL/SLL post- BTKi** in the BGB-11417-202 trial in China
R/R WM	Phase 2	**Potentially pivotal.** Monotherapy in patients with **R/R WM post-BTKi** and post-chemoimmunotherapy in the BGB-11417-203 global trial
TN CLL/SLL	Phase 2	**Supporting registration** Fixed duration combination with BRUKINSA in **TN CLL/SLL** patients vs. Brukinsa in the BGB-11417-204 global trial
TN CLL/SLL	Phase 1/2	**Ramp up optimization-** Open label basket trial to explore additional ramp-ups for sonrotoclax in various indications BGB-11417-108
TN CLL/SLL	Phase 3	**Pivotal.** Fixed duration combination with BRUKINSA in **TN CLL/SLL** patients in the BGB-11417-301 global pivotal trial
R/R MCL	Phase 3	***Confirmatory Option.*** Combination with BRUKINSA in **MCL** patients

Planned

R/R CLL/SLL	Phase 3	***Pivotal Option.*** Combination with CD20 in **R/R CLL/SLL** patients
TN WM	Phase 3	***Confirmatory Option.*** Combination with BRUKINSA in **TN WM** patients
1L AML	Phase 3	***Pivotal Option.*** Combination with HMA in **1L Unfit AML** patients
R/R MM	Phase 3	***Pivotal Option.*** Combination with SOC agents in **R/R MM** patients

R/R – Relapsed Refractory
MCL - Mantle Cell Lymphoma
CLL/SLL - Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma
WM - Waldenström's Macroglobulinemia
TN – Treatment Naive
AML - Acute Myeloid Leukemia
MM - Multiple Myeloma

Presented at the 2024 66th ASH Annual Meeting and Exposition



BRUKINSA (zanubrutinib)

Sonrotoclax

BGB-16673 (BTK CDAC)

BTK CDAC (BGB-16673) is the Most Advanced Hematology Degrader in the Clinic with Potential to Become Both First and Best-in-class

Demonstrable potency of BeiGene's degrader platform

- Novel MOA leads to degradation of target proteins
- Degradation of protein could be **more potent than inhibitors**
- Can **overcome** and/or **obviate emergent resistance mutations**
- CDAC platform **optimized for safety and efficacy** before candidate entered clinic

Differentiated BTK degrader

- Preclinical data confirms:
  - **degradation of wild-type and mutant BTK**[1,2]
  - **blood brain barrier penetration**
- **Lack of IMiD activity**; a safety advantage vs. other degraders
- Potential to **displace** BTKis with monotherapy or combinations

Striking Clinical Data

- With **400+ patients** treated in **14 countries**, resounding clinical **efficacy** in **variety of B cell malignancies** including in BTKi-resistant **CLL** patients
- **Rapid improvement** of disease status; **deep (CRs in CLL, RT, iNHL and VGPRs in WM) and durable responses** observed in heavily pretreated patients **including those with BTK mutations**
- **Safety** profile appears comparable to 2nd gen BTKis and **supports earlier line use**

Robust clinical development plan

- **R/R CLL**; **Phase 2 expansion with pivotal intent**
  - Strong data where significant unmet need exists. Fast-track designation
  - **Starting ph3 confirmatory in 2025**
- **Other expansions planned**
- **Initiated a platform study; allows different novel combinations** including with BeiGene's assets in **multiple B-cell malignancies**
- **Aggressive development plan** for earlier lines including in CLL (1L, 2L)

BeiGene's Leadership

- **Testament to BeiGene's strong expertise** to develop and execute the optimal clinical development plan
- **Further enhance leadership** in **CLL** and improving patients' outcomes
- Launch opportunities in other B-cell malignancies with monotherapy and combinations:
  - WM
  - 1L FL
  - MZL
  - Aggressive NHL (DLBCL, MCL and RT)

IMiD – Immune Mediated Inflammatory Disease
CLL - Chronic Lymphocytic Leukemia
RT – Richter Transformation
iNHL – Indolent Non-Hodgkin Lymphoma
WM - Waldenström's Macroglobulinemia
RR – Relapsed Refractory
FL – Follicular Lymphoma
MZL – Marginal Zone Lymphoma
DLBCL – Diffuse Large B-cell Lymphoma
MCL – Mantle Cell Lymphoma

1. Feng X, et al. EHA 2023. Abstract P1239
2. Wang H, et al. EHA 2023. Abstract P1219

2024 ASH BeiGene Heme Presentations
BTK CDAC (Clinical)

Topic	Title	First author / significance	Status
CaDAnCe-101 CLL	Preliminary efficacy and safety of the Bruton tyrosine kinase degrader BGB-16673 in patients with relapsed or refractory chronic lymphocytic leukemia/small lymphocytic lymphoma: Results from the phase 1 CaDAnCe-101 study	**Meghan C. Thompson** Promising efficacy with a manageable safety profile in heavily pretreated RR CLL patients, many of whom have high risk features. Response rates higher and deeper than NX-5948: ORR-94% at 200 mg including 2 CR/CRis as well as CR in RT	Oral 885
CaDAnCe-101-WM	Preliminary efficacy and safety of the Bruton tyrosine kinase degrader BGB-16673 in patients with relapsed or refractory Waldenström macroglobulinemia: Results from the phase 1 CaDAnCe-101 study	**John F. Seymour** Rapid responses with 26% of patients achieving VGPR, responses observed in traditionally high-risk patients Rapid decline in IgM (a PD marker) has a favorable slope to that of NX-5948	Oral 860
CaDAnCe-101 NHL	Preliminary efficacy and safety of the Bruton tyrosine kinase degrader BGB-16673 in patients with relapsed or refractory (R/R) indolent NHL: Results from the phase 1 CaDAnCe-101 study	**Constantine S. Tam** Early data showing meaningful efficacy in FL and MZL patients including 1 CR each BTK-CDAC might be more potent in some diseases compared to BTKis	Poster 1649

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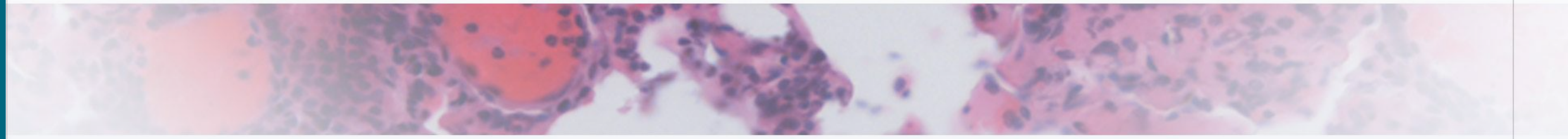

Preliminary Efficacy and Safety of the Bruton Tyrosine Kinase Degrader BGB-16673 in Patients With Relapsed or Refractory Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma: Results From the Phase 1 CaDAnCe-101 Study

Meghan C. Thompson,[1] Ricardo D. Parrondo,[2] Anna Maria Frustaci,[3] John N. Allan,[4] Paolo Ghia,[5,6] Irina Mocanu,[7] Constantine S. Tam,[8] Judith Trotman,[9] Inhye E. Ahn,[10] Stephan Stilgenbauer,[11] Lydia Scarfò,[5,6] Xiangmei Chen,[12] Kunthel By,[13] Shannon Fabre,[13] Daniel Persky,[13] Amit Agarwal,[13] John F. Seymour[14]

[1]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [2]Mayo Clinic - Jacksonville, Jacksonville, FL, USA; [3]ASST Grande Ospedale Metropolitano Niguarda, Milano, Italy; [4]Weill Cornell Medicine, New York, NY, USA; [5]Università Vita-Salute San Raffaele, Milano, Italy; [6]IRCCS Ospedale San Raffaele, Milano, Italy; [7]Institute of Oncology, ARENSIA Exploratory Medicine, Düsseldorf, Germany; [8]Alfred Hospital and Monash University, Melbourne, VIC, Australia; [9]Concord Repatriation General Hospital, University of Sydney, Concord, NSW, Australia; [10]Dana-Farber Cancer Institute, Boston, MA, USA; [11]Ulm University, Ulm, Germany; [12]BeiGene (Shanghai) Co, Ltd, Shanghai, China; [13]BeiGene USA, Inc, San Mateo, CA, USA; [14]Peter MacCallum Cancer Centre, Royal Melbourne Hospital, and University of Melbourne, Melbourne, VIC, Australia

CaDAnCe-101 BeiGene

BTK CDAC (BGB-16673) CaDAnCe-101: Phase 1/2, Open-Label, Dose-Escalation/ Expansion Study in R/R B-Cell Malignancies

CaDAnCe-101 (BGB-16673-101, NCT05006716)

Key eligibility criteria for CLL/SLL

- Meets iwCLL 2018 criteria for treatment
- ≥2 prior therapies, including cBTKi if approved for disease
- ECOG PS 0-2 & adequate end-organ function

Key study objectives for part 1

- **Primary:** safety[c] and tolerability, MTD, and RP2D
- **Secondary:** PK, PD, and preliminary antitumor activity[d]

Part 1: Monotherapy dose finding[a]

Part 1a: Dose escalation[b]
Selected R/R B-cell malignancies
(MZL, FL, MCL, **CLL/SLL**, WM, DLBCL, RT)
n≤72
Oral, QD, 28-day cycle
Doses: 50 mg, 100 mg, 200 mg, 350 mg, 500 mg, 600 mg

Part 1b: Safety expansion
Selected R/R B-cell malignancies
(MZL, MCL, **CLL/SLL**, WM)
n≤120

Part 1c: Additional safety expansion
Selected R/R B-cell malignancies
(MZL, WM, RT, DLBCL, FL)
n≤100

Part 1d: Additional safety expansion
R/R CLL/SLL
n≤30

Part 1e: Additional safety expansion
Selected R/R B-cell malignancies (Japan only)
(MZL, FL, MCL, CLL/SLL, WM)
n=6-9

Part 1f: Monotherapy safety expansion
Selected BTK inhibitor-naive B-cell malignancies
(MZL, MCL, CLL/SLL, WM, RT)
n≤40

Determination of BGB-16673 RDFE

Phase 2

- **Cohort 1**: Post-BTK inhibitor, R/R CLL/SLL
- **Cohort 2**: Post-BTK inhibitor, R/R MCL
- **Cohort 3**: Post-BTK inhibitor, R/R WM
- **Cohort 4**: Post-BTK inhibitor, R/R MZL
- **Cohort 5**: R/R FL
- **Cohort 6**: R/R non-GCB DLBCL
- **Cohort 7**: Post-BTK inhibitor, R/R RT

[a] Data from gray portions of figure are not included in this presentation. [b] Six dose levels (50-600 mg orally QD). [c] Safety was assessed according to CTCAE v5.0 in all patients and iwCLL hematologic toxicity criteria in patients with CLL; DLTs were assessed during the first 4 weeks of part 1a. [d] Response was assessed per iwCLL 2018 criteria after 12 weeks for patients with CLL.
GCB, germinal center B-cell; RT, Richter transformation.

CLL/SLL - Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma
RP2D – Recommended Phase 2 Dose
MZL – Marginal Zone Lymphoma
FL – Follicular Lymphoma
MCL – Mantle Cell Lymphoma
WM - Waldenström's Macroglobulinemia
RT – Richter Transformation
DLBCL – Diffuse Large B-cell Lymphoma
RR – Relapsed Refractory

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R/R CLL - BTK CDAC (BGB-16673) Baseline Patient Characteristics

Heavily pre-treated, with high-risk R/R CLL features BTK

	Total (N=60)
Age, median (range), years	70 (50-91)
Male, n (%)	39 (65.0)
ECOG PS, n (%)	
0	34 (56.7)
1	25 (41.7)
2	1 (1.7)
CLL/SLL risk characteristics at study entry, n/N (%)	
Binet stage C	27/56 (48.2)
Unmutated IGHV	38/46 (82.6)
del(17p) or *TP53* mutation	40/60 (66.7)
Complex karyotype (≥3 abnormalities)	19/38 (50.0)

	Total (N=60)
Mutation status, n/N (%)	
BTK mutation present	18/54 (33.3)
PLCG2 mutation present	8/54 (14.8)
No. of prior lines of therapy, median (range)	4 (2-10)
Prior therapy, n (%)	
Chemotherapy	43 (71.7)
cBTK inhibitor	56 (93.3)
ncBTK inhibitor	13 (21.7)
BCL2 inhibitor	50 (83.3)
cBTK + BCL2 inhibitors	38 (63.3)
cBTK + ncBTK + BCL2 inhibitors	12 (20.0)
Discontinued prior BTK inhibitor due to PD, n/N (%)	50/56 (89.3)

Data cutoff: September 2, 2024.
cBTK, covalent BTK; ncBTK, noncovalent BTK.

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R/R CLL - BTK CDAC (BGB-16673) Safety Summary and All-Grade TEAEs ≥10% for All Patients

- No atrial fibrillation
- Amylase/lipase elevations were lab findings and transient, mostly occurring during the first 1-3 cycles of treatment, with no clinical pancreatitis
- Major hemorrhage[a]: 3.3% (n=2; grade 1 subarachnoid hemorrhage [n=1] and grade 3 subdural hemorrhage [n=1])
- Febrile neutropenia: 1.7% (n=1; in the context of COVID-19 pneumonia and norovirus diarrhea)

	Total (N=60)	
Patients, n (%)	All Grade	Grade ≥3
Fatigue	18 (30.0)	1 (1.7)
Contusion (bruising)	17 (28.3)	0
Neutropenia[b]	15 (25.0)	13 (21.7)
Diarrhea	14 (23.3)	1 (1.7)
Anemia	11 (18.3)	0
Lipase increased[c]	10 (16.7)	2 (3.3)
Cough	9 (15.0)	0
Pneumonia	8 (13.3)	5 (8.3)
Pyrexia	8 (13.3)	0
Arthralgia	7 (11.7)	0
COVID-19	7 (11.7)	0
Dyspnea	7 (11.7)	0
Peripheral edema	7 (11.7)	0
Thrombocytopenia[d]	7 (11.7)	2 (3.3)
Amylase increased[c]	6 (10.0)	0
Nausea	6 (10.0)	0
Sinusitis	6 (10.0)	0

[a] Grade ≥3, serious, or any central nervous system bleeding. [b] Neutropenia combines preferred terms *neutrophil count decreased* and *neutropenia*. [c] All events were lab findings and were transient, mostly occurring during the first 1-3 cycles of treatment, with no clinical pancreatitis. [d] Thrombocytopenia combines preferred terms *platelet count decreased* and *thrombocytopenia*.

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R/R CLL - BTK CDAC (BGB-16673) High Overall Response Rates and CRs; Including Patients with High-Risk Features

High risk features

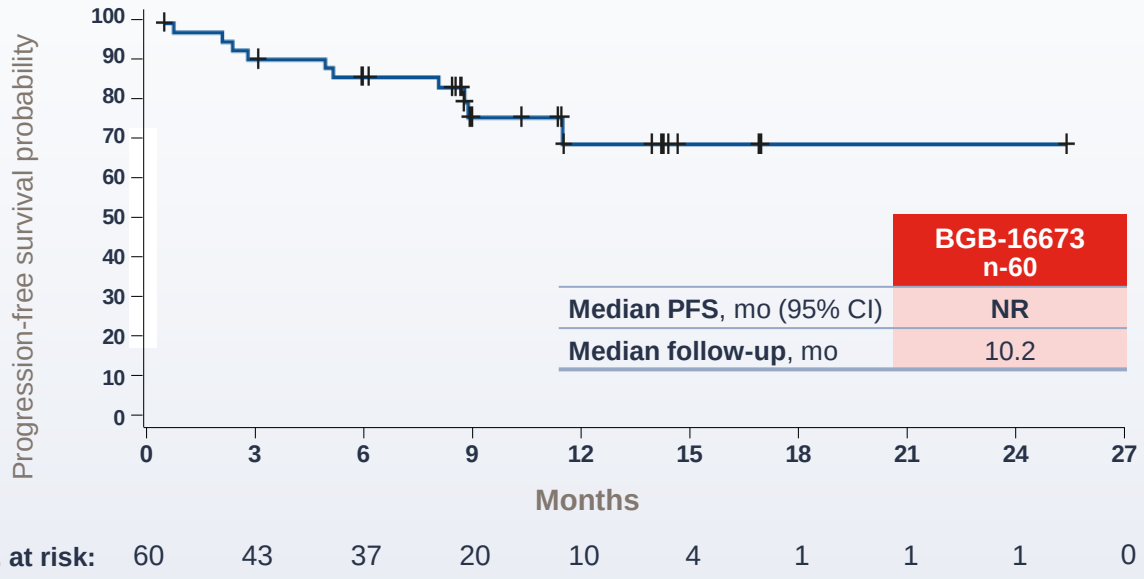
- Double exposure (previously received cBTKi + BCL2 inhibitors): 78.6% (33/42)
- Triple exposure (previously received cBTKi, ncBTKi, + BCL2 inhibitors): 58.3% (7/12)
- del(17p) or *TP53* mutation: 74.2% (23/31)
- Complex karyotype: 73.3% (11/15)
- BTK mutations: 62.5% (10/16)
- PLCG2 mutations: 66.7% (4/6)

	50 mg (n=1)	100 mg (n=5)	200 mg (n=16)	350 mg (n=15)	500 mg (n=12)	Total[a] (N=49)
Best overall response, n (%)						
CR/CRi	0	1 (20.0)	1 (6.3)	0	0	2 (4.1)
PR	1 (100)	3 (60.0)	12 (75.0)	10 (66.7)	7 (58.3)	33 (67.3)
PR-L	0	0	2 (12.5)	0	1 (8.3)	3 (6.1)
SD	0	1 (20.0)	0	1 (6.7)	4 (33.3)	6 (12.2)
PD	0	0	1 (6.3)	1 (6.7)	0	2 (4.1)
Discontinued prior to first assessment	0	0	0	3 (20.0)	0	3 (6.1)
ORR, n (%)[b]	1 (100)	4 (80.0)	15 (93.8)	10 (66.7)	8 (66.7)	38 (77.6)
Disease control rate, n (%)[c]	1 (100)	5 (100)	15 (93.8)	11 (73.3)	12 (100)	44 (89.8)
Time to first response, median (range), months[d]	2.9 (2.9-2.9)	4.2 (2.8-6.2)	2.9 (2.6-8.3)	2.8 (2.6-8.3)	2.8 (2.6-8.3)	2.8 (2.6-8.3)
Duration of exposure, median (range), months	26.4 (26.4-26.4)	13.8 (13.6-18.6)	10.6 (2.9-18.9)	10.3 (0.2-16.8)	9.3 (6.8-15.4)	10.4 (0.2-26.4)

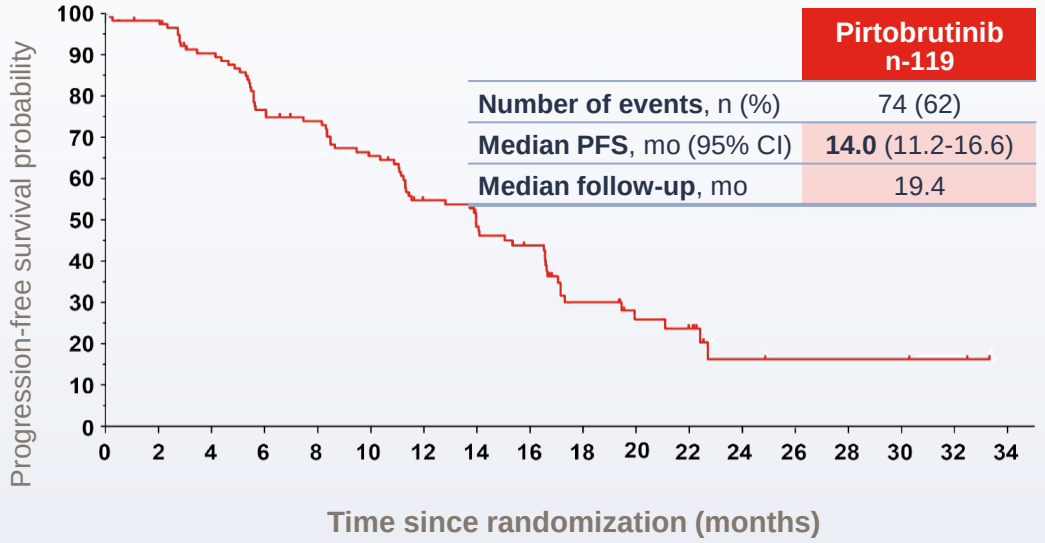
[a] Efficacy-evaluable population
[b] Includes best overall responses of PR-L or better
[c] Includes best overall responses of SD or better
[d] In patients with a best overall response of PR-L or better
CRi, with incomplete marrow recovery; PR-L, partial response with lymphocytosis

R/R CLL - BTK CDAC (BGB-16673) Durable and Sustained Responses; CDAC PFS Estimates Favorable to Pirtobrutinib

BGB-16673: PFS by Investigator



Pirtobrutinib: PFS by IRC[1]



1. Sharnan J. et al ASH 2024

	CaDAnCe-101	BRUIN 321
Median prior lines of therapies	4	3
BTKi+BCL2i exposed	63%	50%
Prior BTKi discontinuation due to PD	89%	71%

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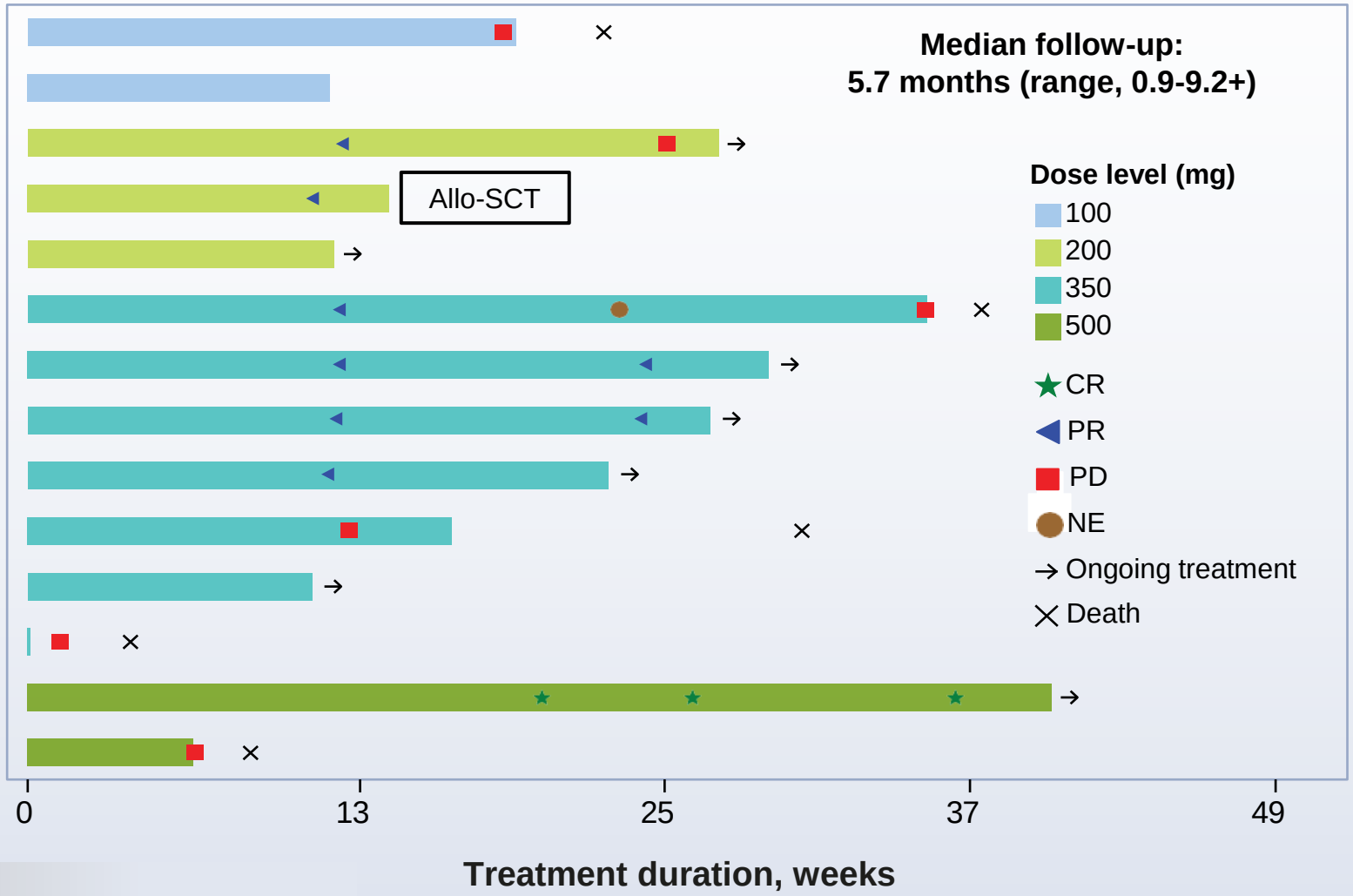
R/R RT- BTK CDAC (BGB-16673) Promising Activity Also Seen in Patients with Richter Transformation

- Safety-evaluable patients, n=14; efficacy-evaluable patients, n=12
- Median age (range): 64 years (47-80 years)
- Median prior number of therapies for RT (range): 2 (1-9)
- All patients previously received a cBTKi; 12/14 had anthracyclines
- ORR: 58.3% (7/12), **CR: 8.3% (1/12)**
- 5 of 7 (71.4%) patients with response on treatment for >6 months



Data cutoff: September 2, 2024
cBTKi, covalent BTK inhibitor; NE, not evaluable

R/R CLL - BTK CDAC (BGB-16673) Authors' Conclusions:

BTK CDAC (BGB-16673) was well tolerated in a Ph1 study in pre-treated R/R CLL/SLL patients

- In phase 1 of CaDAnCe-101, the novel BTK degrader BGB-16673 was **safe and well tolerated** in this heavily pretreated population of patients with R/R CLL/SLL
  - One DLT; MTD not reached
  - No atrial fibrillation
- Significant antitumor activity, including in patients with BTK inhibitor–resistant mutations and those previously exposed to cBTK, ncBTK, and BCL2 inhibitors
  - **ORR 77.6% (38/49) and CR/CRi 4.1% (2/49); ORR 93.8% at 200 mg**
  - Median time to first response: 2.8 months
  - Deepening of response observed over time (median 11.0-month follow-up)
- Promising activity in RT: ORR: 58.3% (7/12), **CR: 8.3% (1/12)**
- A phase 2 cohort of patients with CLL/SLL exposed to both a BTK inhibitor and BCL2 inhibitor is enrolling

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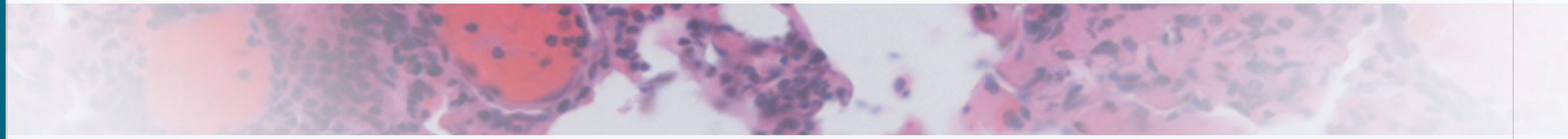

Preliminary Efficacy and Safety of the Bruton Tyrosine Kinase Degrader BGB-16673 in Patients With Relapsed or Refractory Waldenström Macroglobulinemia: Results From the Phase 1 CaDAnCe-101 Study

John F. Seymour,[1] Constantine S. Tam,[2] Chan Y. Cheah,[3-5] Ricardo D. Parrondo,[6] John N. Allan,[7] Judith Trotman,[8] Ranjana Advani,[9] Herbert Eradat,[10] Pier Luigi Zinzani,[11] Masa Lasica,[12] Steven P. Treon,[13] Xiangmei Chen,[14] Kunthel By,[15] Shannon Fabre,[15] Daniel Persky,[15] Amit Agarwal,[15] Anna Maria Frustaci[16]

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CaDAnCe-101 BeiGene

R/R WM BTK CDAC (BGB-16673) Patient Baseline Characteristics

Heavily pre-treated with high rate of WM high risk mutations

	Total (N=27)
Age, median (range), years	73.0 (56-81)
Male, n (%)	15 (55.6)
ECOG PS, n (%)	
0	14 (51.9)
1	12 (44.4)
2	1 (3.7)
Hemoglobin, median (range), g/dL	10.3 (6.0-13.5)
Neutrophils, median (range), 10^9/L	2.71 (0.21-7.43)
Platelets, median (range), 10^9/L	157 (14-455)
Mutation status, n/N (%)[a]	
MYD88 mutation present	24/26 (92.3)
CXCR4 mutation present	12/25 (48.0)
BTK mutation present	11/25 (44.0)
TP53 mutation present	13/25 (52.0)

	Total (N=27)
IgM, median (range), g/L	37.4 (2.8-74.4)
No. of prior lines of therapy, median (range)	3.0 (2-11)
Prior therapy, n (%)	
cBTK inhibitor	27 (100)
Chemotherapy	25 (92.6)
Proteasome inhibitor	9 (33.3)
BCL2 inhibitor	5 (18.5)
ncBTK inhibitor[b]	4 (14.8)
Discontinued prior BTK inhibitor due to PD, n (%)	21 (77.8)

Data cutoff: September 2, 2024
[a] Confirmed by central laboratory
[b] All 4 patients with ncBTK inhibitor exposure were exposed to a cBTK inhibitor
cBTK, covalent BTK; IgM, immunoglobulin M; ncBTK, noncovalent BTK.

R/R WM - BTK CDAC (BGB-16673) High Overall Response Rates and VGPRs; Including Patients with High-Risk Features

- Responses were observed at the lowest dose (100 mg; 7/9) and in patients with prior cBTK inhibitor (22/27) or ncBTK inhibitor (4/4)
- Responses also occurred in patients with or without mutations in:
  - *BTK* (with, 10/11 [90.9%]; without, 11/14 [78.6%]; unknown, 1/2 [50.0%])
  - *MYD88* (with, 20/24 [83.3%]; without, 1/2 [50.0%]; unknown, 1/1 [100%])
  - *CXCR4* (with, 11/12 [91.7%]; without, 10/13 [76.9%]; unknown, 1/2 [50.0%])
  - *TP53* (with, 12/13 [92.3%]; without 9/12 [75.0%]; unknown 1/2 [50.0%])

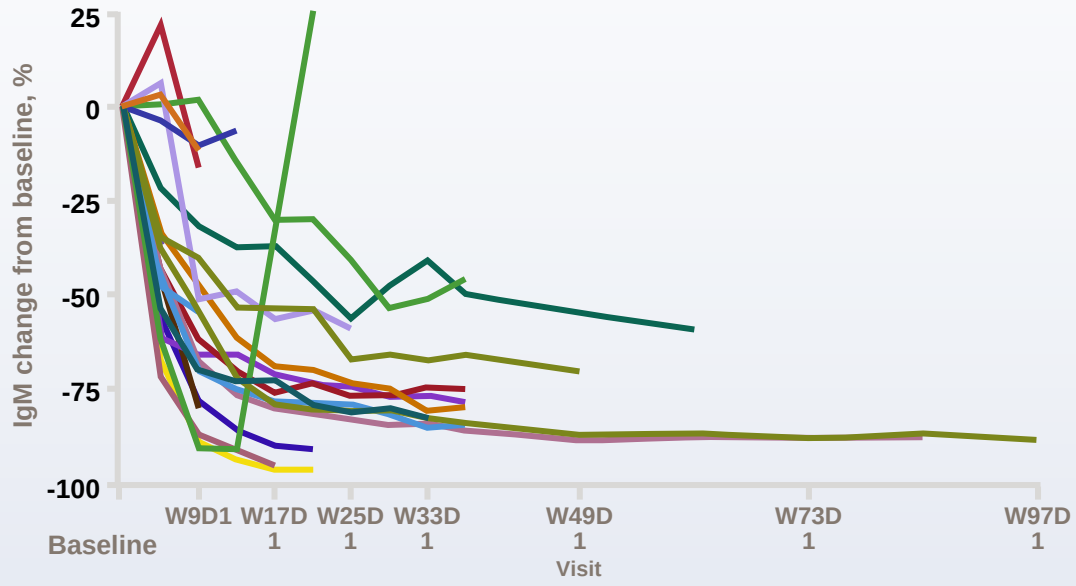
	Total[a] (N=27)
Best overall response, n (%)	
VGPR	7 (25.9)
PR	13 (48.1)
MR	2 (7.4)
SD	3 (11.1)
Not evaluable	1 (3.7)
Discontinued prior to first assessment	1 (3.7)
ORR, n (%)[b]	22 (81.5)
Major response rate, n (%)[c]	20 (74.1)
Disease control rate, n (%)[d]	25 (93.0)
Follow-up time, median (range), months	5.0 (0.8-24.6)
Time to first response, median (range), months[e]	1.0 (0.9-3.7)

[a] Efficacy-evaluable population
[b] Includes best overall responses of MR or better
[c] Includes best overall response of PR or VGPR
[d] Includes best overall responses of SD or better.
[e] In patients with a best overall response better than SD.
cBTK, covalent BTK; IgM, immunoglobulin M; MR, minor response; ncBTK, noncovalent BTK; VGPR, very good partial response.

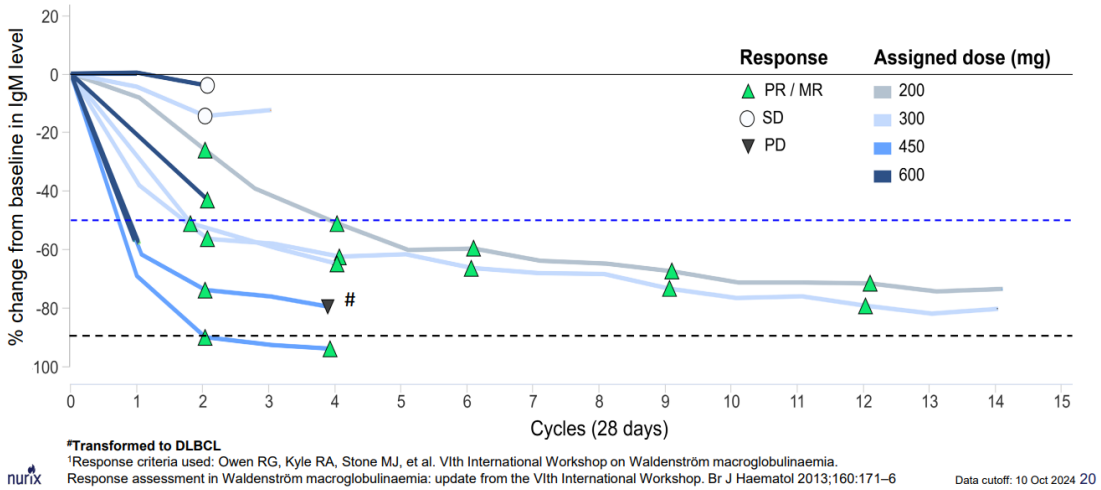
Presented at the 2024 66th ASH Annual Meeting and Exposition

R/R WM – BTK CDAC (BGB-16673) Demonstrated Rapid and Steeper Reductions in IgM in Patients Compared to Nurix's NX-5948

BGB-16673 Reductions in IgM
Rapid deep reduction at all doses



Nurix NX-5948 deepest reductions occurred at highest doses



https://ir.nurixtx.com/node/10496/pdf

IgM, immunoglobulin M.

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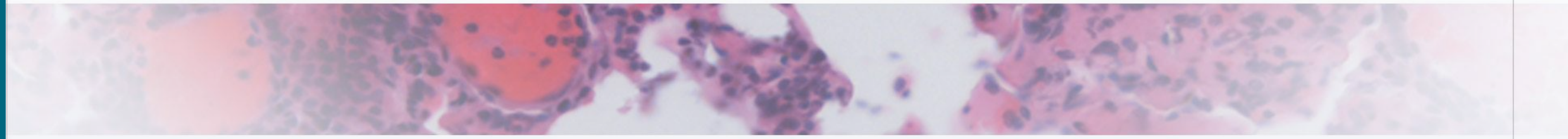


Preliminary Efficacy and Safety of the Bruton Tyrosine Kinase Degrader BGB-16673 in Patients With Relapsed or Refractory Indolent NHL: Results From the Phase 1 CaDAnCe-101 Study

Constantine S. Tam,[1] Anna Maria Frustaci,[2] Fontanet Bijou,[3] Pier Luigi Zinzani,[4] John F. Seymour,[5] Masa Lasica,[6] Herbert Eradat,[7] Victor T.G. Lin,[8] Maan Alwan,[9] Irina Mocanu,[10] Xiangmei Chen,[11] Kunthel By,[12] Shannon Fabre,[12] Daniel Persky,[12] Amit Agarwal,[12] Chan Y. Cheah[13-15]

[1]Alfred Hospital and Monash University, Melbourne, VIC, Australia; [2]ASST Grande Ospedale Metropolitano Niguarda, Milano, Italy; [3]Institut Bergonié, Bordeaux, France; [4]Institute of Hematology "Seràgnoli", University of Bologna, Bologna, Italy; [5]Peter MacCallum Cancer Centre, Royal Melbourne Hospital, and University of Melbourne, Melbourne, VIC, Australia; [6]St Vincent's Hospital Melbourne, Fitzroy, VIC, Australia; [7]David Geffen School of Medicine at UCLA, Los Angeles, CA, USA; [8]Mary Bird Perkins Cancer Center, Baton Rouge, LA, USA; [9]Perth Blood Institute, West Perth, WA, Australia; [10]Institute of Oncology, ARENSIA Exploratory Medicine, Düsseldorf, Germany; [11]BeiGene (Shanghai) Co, Ltd, Shanghai, China; [12]BeiGene USA, Inc, San Mateo, CA, USA; [13]Sir Charles Gairdner Hospital, Nedlands, WA, Australia; [14]Medical School, University of Western Australia, Crawley, WA, Australia; [15]Linear Clinical Research, Nedlands, WA, Australia

BeiGene

R/R FL and MZL - BTK CDAC (BGB-16673) High Rates of Responses Including CRs in Both Histologies

Responses seen in patients with prior covalent BTK inhibitor (7/12 [58%] in MZL) and a noncovalent BTK inhibitor (1/1 in FL)

	FL (n=8)	MZL[a] (n=14)
Best overall response, n (%)		
CR	1 (12.5)	1 (7.1)
PR	3 (37.5)	8 (57.1)
SD	2 (25.0)	2 (14.3)
PD	2 (25.0)	1 (7.1)
ORR, n (%)[b]	4 (50.0)	9 (64.3)
Disease control rate, n (%)[c]	6 (75.0)	11 (78.6)
Follow-up time, median, months[d]	14.4 (3.3-24.0)	4.8 (1.9-19.1)
Time to first response, median (range), months[e]	2.7 (2.6-3.3)	2.8 (2.5-9.9)

[a] Three patients were not yet response evaluable
[b] Includes best overall responses of PR or CR
[c] Includes best overall responses of SD or better
[d] For all enrolled patients: FL, n=8; MZL, n=17
[e] In patients with a best overall response better than SD.

Presented at the 2024 66th ASH Annual Meeting and Exposition

R/R FL and MZL - BTK CDAC Author's Conclusions:

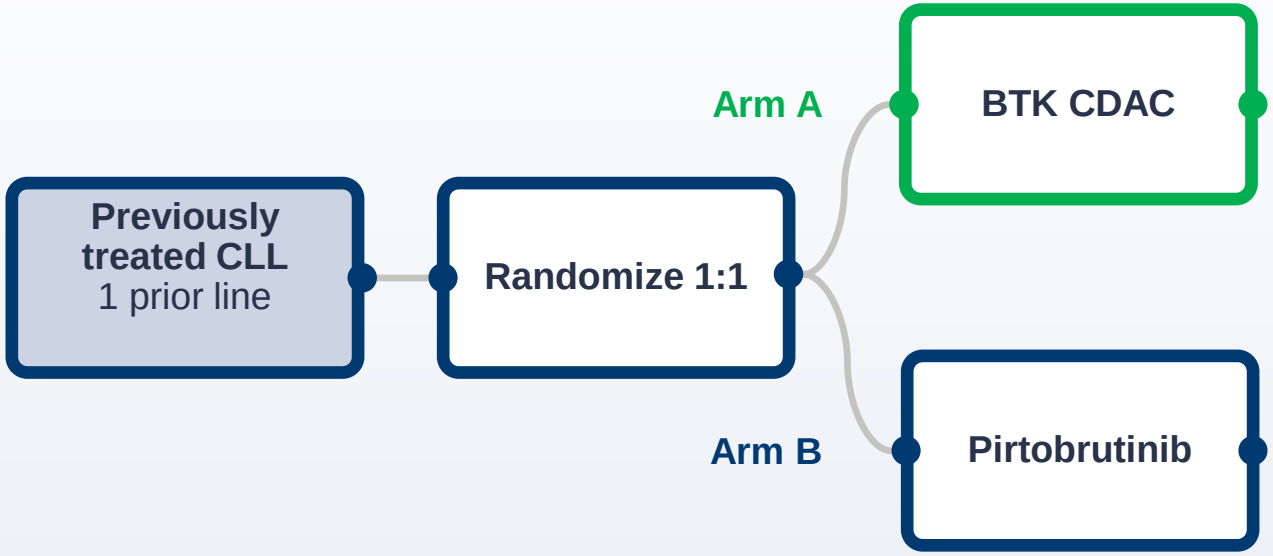
BTK CDAC (BGB-16673) continues to be safe, tolerable with durable activity in FL and MZL patients

- Updated data from this ongoing study show that the novel BTK degrader BGB-16673 was **safe and tolerable in heavily pretreated patients with FL or MZL**; no DLTs occurred and MTD was not reached with dose escalation up to 500 mg
  - Discontinuations due to TEAEs were low; 1 patient discontinued in the context of PD

- BGB-16673 had **durable antitumor activity with a short time to response in heavily pretreated patients** with NHL, including those with BTK inhibitor–exposed disease
  - ORR was 50.0% in FL and 64.3% in MZL
  - Two patients achieved CR (FL, n=1; MZL, n=1)

- These data support further investigation of BGB-16673 clinical activity in patients with NHL; **enrollment in CaDAnCe-101 continues for FL and MZL**

A H2H Study of BTK CDAC (BGB-16673) vs. Pirtobrutinib Is Planned Based on Data From CaDAnCe-101 and BRUIN 321



Primary Endpoint

PFS Superiority of CDAC vs. Pirtobrutinib by IRC

Key Secondary Endpoints

- Complete response rate
- Overall survival

BTK CDAC (BGB-16673) Broadening Development Program

BGB-16673 CDP

CaDAnCe-101	**Phase 1/2**	**Global**	Monotherapy in patients with B-cell malignancies. **BTK naïve cohort for earlier lines. Multiple expansion cohorts including MCL and WM**
CaDAnCe-101 RR CLL	**Phase 2**	**Global**	**Potentially pivotal.** Monotherapy in patients with **R/R CLL/SLL post- BTKi and post-BCL2i**
Platform Study	**Phase 1**	**Global**	**Novel chemo-free combinations** in patients with B-Cell malignancies, including **sonrotoclax, zanubrutinib** and **CD20xCD3 Bispecific**

Planned

RR CLL	**Phase 3**	**Global**	Pivotal starting in 1H 2025. Monotherapy in patients with R/R CLL/SLL
RR CLL	**Phase 3**	**Global**	Head-to-head study versus pirtobrutinb planned for 2025

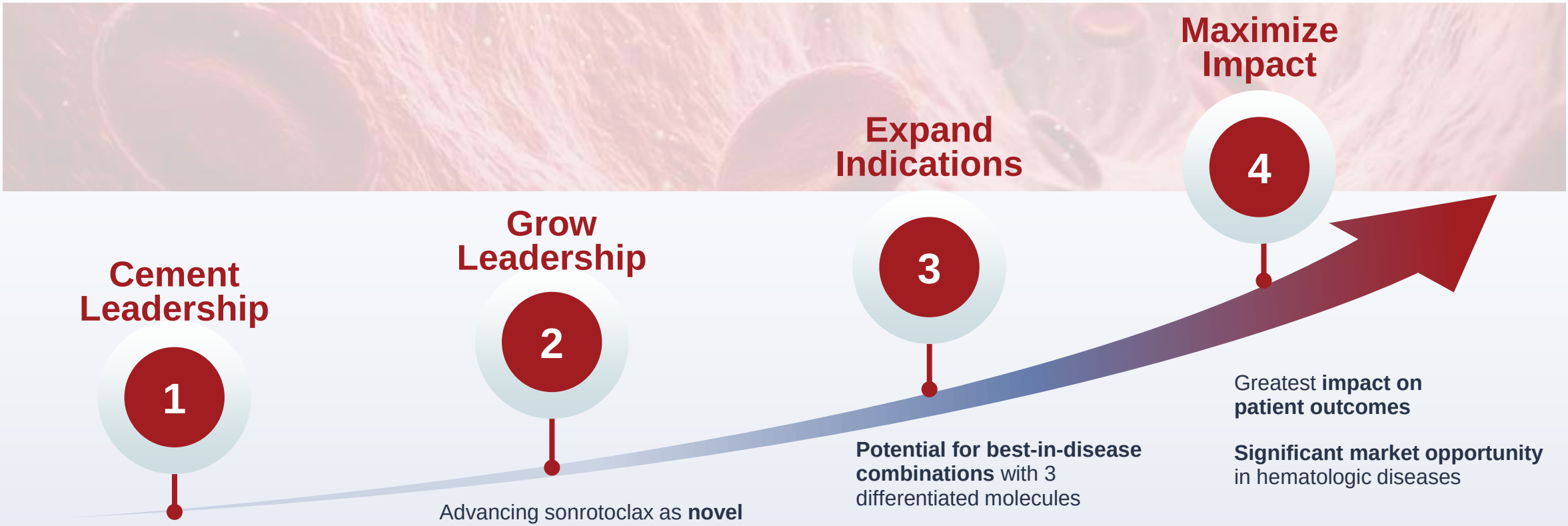
MCL - Mantle Cell Lymphoma
WM - Waldenström's Macroglobulinemia
R/R – Relapsed Refractory
CLL/SLL - Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma

BeiGene Today and in the Future: Our Portfolio will Grow Existing Leadership in CLL, with Options Across Entire Patient Journey

BeiGene wholly owned molecules (approved or in development) will create treatment options available to all Patients and HCPs as monotherapy or best-in-disease combinations with our assets

TN CLL	R/R CLL
Currently approved	
BRUKINSA until progression	BRUKINSA (if not received in TN)
In development	
FD BRUKINSA + sonrotoclax	BTK CDAC mono
BRUKINSA combinations IISs	FD Sonrotoclax + aCD20
BTK CDAC / combos	Sonrotoclax + CDAC

Accelerating Development of Differentiated Assets as a Leader in Broad Range of Hematologic Malignancies



BRUKINSA as the **best-in-class** and **only BTKi for CLL with sustained, superior efficacy** and **favorable safety** vs. ibrutinib

Broadest label globally and exciting lifecycle strategies

Advancing sonrotoclax as **novel BCL2i with best-in-class potential** to registration in CLL and other B cell malignancies

BTK CDAC has a novel MOA and **resounding efficacy and safety** with a defined path to registration; an opportunity to **disrupt the treatment paradigm**

Potential for best-in-disease combinations with 3 differentiated molecules

Ability to **address all lines of therapy**

Expanding into new indications with high unmet medical needs: **AML/MDS, MM, Richter's and LBCL**

Greatest **impact on patient outcomes**

Significant market opportunity in hematologic diseases

CLL - Chronic Lymphocytic Leukemia
AML - Acute Myeloid Leukemia
MDS – Myelodysplastic syndromes
MM - Multiple Myeloma
LBCL – Large B-ell Lymphoma

CLOSING REMARKS

John V. Oyler

Co-Founder, Chairman and CEO

Foundation Set for Hematology Franchise Leadership and Exciting Progress in Early Solid Tumor Portfolio

Sustainable Leadership in CLL & Hematology

Investor Question & Concern		BeiGene's Perspective
1 **How will uptake of fixed duration regimens in the US affect the $12B+ CLL market?** Potential approval of A+V in the US would represent first all oral fixed duration regimen for TN CLL and could erode share from single agent BTKi	»	**a** **AMPLIFY might represent a potential option in the treatment of CLL patients, but is not best solution for patients** ▪ Numerically worse 36-month PFS than SOC ▪ Meaningfully lower uMRD rates than FCR/BR ▪ Early data requiring more follow up, which may deteriorate further **b** **Z+S in Phase 3 for TN CLL has potential to be best in disease combination**
2 **Where will Pirtobrutinib ultimately fall in the CLL treatment paradigm?** Non-covalent BTK inhibitor could displace covalent inhibitors in TN CLL	»	**a** **Pirtobrutinib mPFS deteriorated** **b** **BTK CDAC data impressive: head-to-head trial vs Pirtobrutinib** BTK degradation offers mechanistic advantages over non-covalent BTK inhibition
3 **Even though Sonro and BTK CDAC data is compelling, will IRA or patent expiry for Acala and Ven create pricing pressure for Brukinsa, Sonro, and BTK CDAC?** Imbruvica and Calquence future price deterioration could negatively impact the CLL market and Brukinsa, Sonro and BTK CDAC	»	**a** **Underwhelming AMPLIFY data provides low hurdles to show separation for Brukinsa, Sonro, BTK CDAC from Acala or Ven** **b** **Wholly-owned, unique to BeiGene combinations of Brukinsa, Sonro and BTK CDAC provide additional mitigation**

Early Solid Tumor Portfolio

Major Progress

1 **Compelling early solid tumor pipeline including:**

- CDK4i
- CDK2i
- Pan-KRASi
- EGFR CDAC
- PRMT5i
- MAT2Ai
- B7H4 ADC
- CEA ADC
- FGFR2b ADC

Numerous readouts in the next 12 months

2 **Combination and potential for franchise building in lung, breast and GI cancer**

e.g. **CDK4 inhibitor program**

- Encouraging Phase 1A data showing promising safety and tolerability for CDK4 inhibitor in HR+/HER2- Breast Cancer
- We enrolled 120+ patients in less than a year
- Phase 3 planning underway

QUESTIONS & ANSWERS

BeiGene

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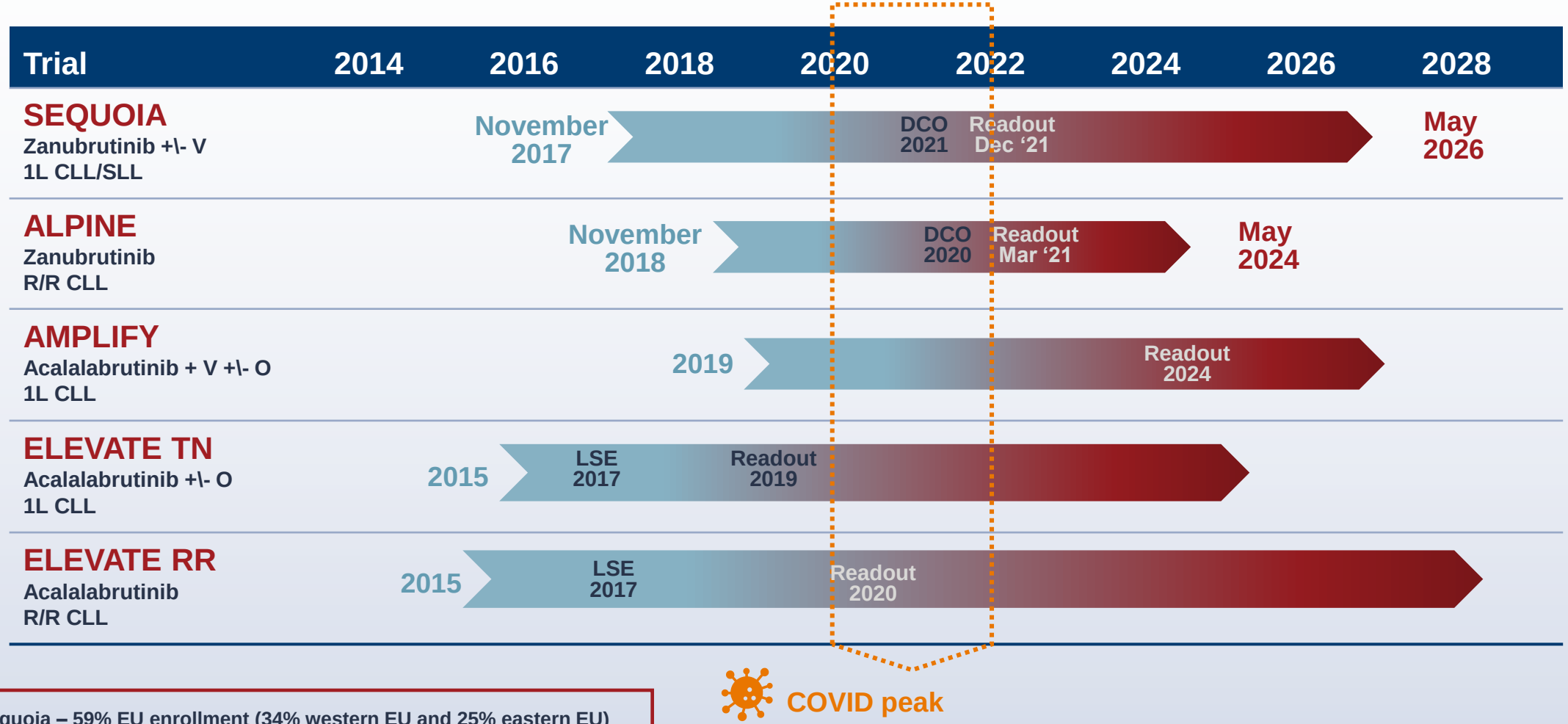
Thank you

Appendix

Timelines of ALPINE, SEQUOIA and AMPLIFY studies



Sequoia – 59% EU enrollment (34% western EU and 25% eastern EU)
Alpine – 61% EU enrollment (18% western EU and 43% eastern EU)

Trial durations from clinicaltrials.gov
BeiGene milestones from internal data
Acalabrutinib milestones from AstraZeneca website

Key Patient Characteristics, mFU, uMRD, PFS, and Death

	AMPLIFY (Phase 3)			CRISTALLO (Phase 3)		CLL13 (Phase 3)	
	A+V N=291	A+V+O N=286	BR/FCR N=290	V+O N=80	BR/FCR N=86	V+O N=229	BR/FCR N=229
Age median (range)	61 (31-84)	61 (29-81)	61 (26-86)	62 (40-83)	61 (36-77)	62 (31-83)	61 (29-84)
del(17p)+ or TP53, n (%)	Excluded			Excluded		Excluded	
IGHV UNmut, n (%)	57.4%	59.1%	59.3%	43.8%	44.2%	57.0%	57.2%
Median Follow Up, mos	41			32		38.8	
uMRD4 at EOT (PB *via flow cytometry*)	34.4%	67.1%	45.5%	81.3%	60.5%	86.5% (mon 15)	52.0% (mon 15)
PFS	36 mo: 76.5% (HR 0.65 vs CIT)	36 mo: 83.1% (HR 0.42 vs CIT)	36 Meng: 66.5%	24 mo: 95.7%	24 mo: 90.4%	36 mo: 87.7%	36 mo: 75.5%
Death, n	18 COVID: 10	37 COVID: 25	40 COVID: 21	NR COVID: 2	NR COVID: 2	11 COVID: 3	12 COVID: 2

NR= Not Reported