ASH 2023 – Data Following BGNE Investor Event

December 11, 2023

ASH 2023 BeiGene Presentations Following Investor Event

Study	Title	First author/significance	Date / time
BGB- 11417-105 R/R MM t(11;14)	**Sonrotoclax (BGB-11417) in Combination With Dexamethasone for the Treatment of Relapsed/Refractory Multiple Myeloma With t(11;14): Safety, Efficacy, and Determination of Recommended Phase 2 Dose**	**Hang Quach, MD** Data demonstrating deep responses and favorable safety for sonrotoclax + dexamethasone cohort at RP2D Given recent failure of venetoclax in MM (CANOVA study), this data positions sonrotoclax as the potential first and only safe and effective BCL2 inhibitor in t(11;14) MM patients	**Oral 12/11/2023 4:30 pm**
16673-101 Dose finding	**First Results from a Phase 1, First-in-Human Study of the Bruton's Tyrosine Kinase (BTK) Degrader BGB-16673 in Patients (Pts) with Relapsed or Refractory (R/R) B-Cell Malignancies**	**John Seymour, MD** First scientific presentation of BGB-16673 demonstrating compelling safety and efficacy in dose escalation cohorts of patients including those with prior BTKi and BCL2i treatment	**Poster 4401 12/11/2023 6:00 pm**

Sonrotoclax

BCL2 inhibitor

Sonrotoclax (BGB-11417) Acknowledgments

Sonrotoclax (BGB-11417) in Combination With Dexamethasone for the Treatment of Relapsed/Refractory Multiple Myeloma With t(11;14): Safety, Efficacy, and Determination of Recommended Phase 2 Dose

- **Hang Quach**,[1] Doug Sborov,[2] Dickran Kazandijan,[3] Andrew Spencer,[4] Michael Low,[5] Susan Bal,[6] Natalie Callander,[7] Huan Cheng,[8] Sheel Patel,[8] Rocco Crescenzo,[8] Amit Agarwal,[8] Binod Dhakal[9]

- [1]St. Vincent's Hospital Melbourne, University of Melbourne, Melbourne, VIC, Australia; [2]Huntsman Cancer Institute, University of Utah, Salt Lake City, UT, USA; [3]University of Miami, Coral Gables, FL, USA; [4]Alfred Health - Monash University, Melbourne, VIC, Australia; [5]Monash Health, Melbourne, VIC, Australia; [6]University of Alabama at Birmingham Medicine, Birmingham, AL, USA; [7]UW Health University Hospital, Madison, WI, USA; [8]BeiGene USA, Inc, San Mateo, CA, USA; [9]Medical College of Wisconsin, Milwaukee, WI, USA

Background

- Venetoclax, a first-generation BCL2 inhibitor, has demonstrated antimyeloma activity as monotherapy or combination treatment but has no regulatory approvals for MM[1,2]
- Sonrotoclax (BGB-11417), a next-generation BCL2 inhibitor, has shown more potent and selective BCL2 inhibition and better activity against BCL2-dependent hematological tumors than venetoclax in vitro[3]

	IC_{50}	Relative IC_{50} for various proteins in the BCL2 family				$T_{1/2}$
	BCL2	BCL-XL	BCL-W	MCL1	A1	
Venetoclax	0.20 nM	1:325	1:13,700	1:<50,000	1:<50,000	26 h
Sonrotoclax	0.014 nM	1:2000	1:129,000	1:714,000	1:714,000	4.5 h

- Here, preliminary data from the sonrotoclax + dexamethasone dose-escalation cohorts of an ongoing phase 1b/2 study in patients with R/R MM harboring the t(11;14) translocation are presented

h, hours; IC_{50}, half maximal inhibitory concentration; $t_{1/2}$, half-life.

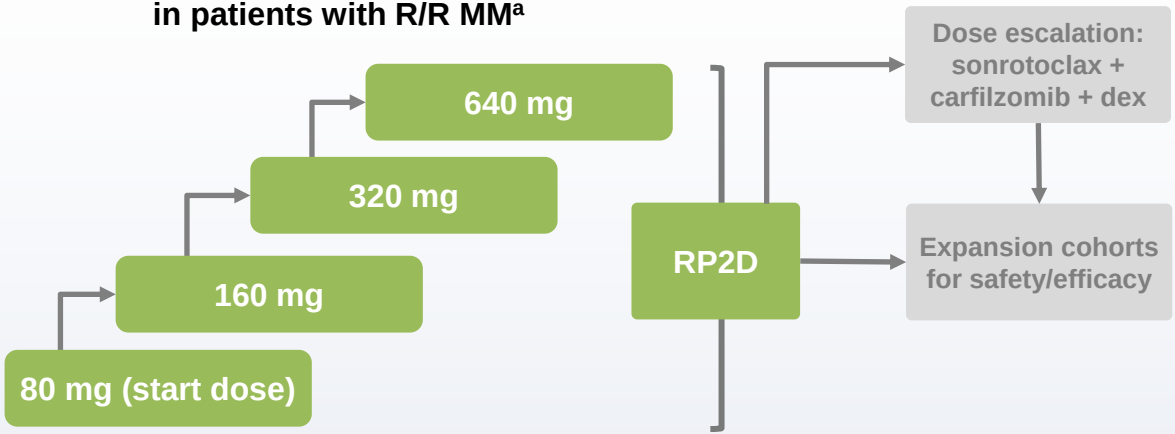
1. Kumar S, et al. *Blood*. 2017;130(22):2401-2409; 2. Mateos MV, et al. IMS 2023. Abstract OA-52; 3. Hu N, et al. AACR 2020. Abstract 3077.

BGB-11417-105 (NCT04973605) Study Design: Sonrotoclax + Dex Only

Eligible patients

- Relapsed or refractory to most recent therapy line
- t(11;14) positive by FISH
- Failed ≥3 prior lines of therapy including a proteasome inhibitor, IMiD, and an anti-CD38 monoclonal antibody

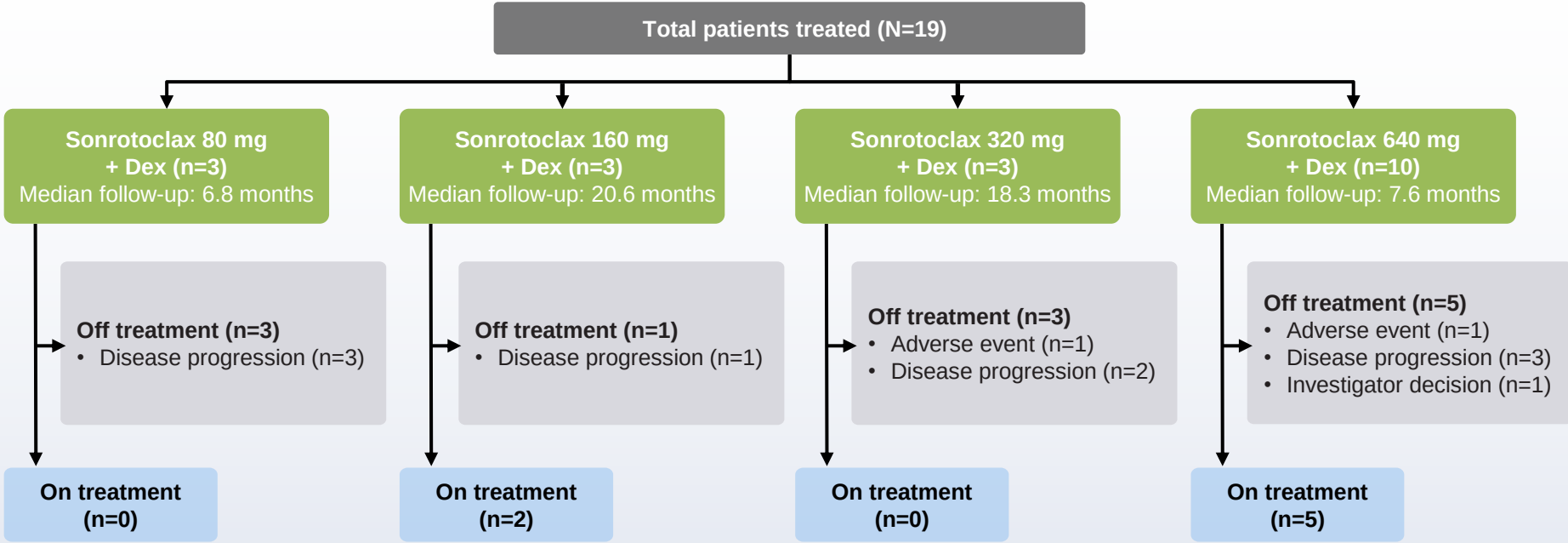
Dose escalation for sonrotoclax + dex in patients with R/R MM[a]



Primary endpoints: Safety and tolerability, MTD/MAD, RP2D
Key secondary/exploratory endpoints: PK, biomarkers, disease response per IMWG 2016 criteria

[a]Daily doses administered orally in 21-day cycles.

Patient Disposition



Data cutoff date: September 18, 2023.

Baseline Demographics and Disease Characteristics

Characteristics	Sonrotoclax 640 mg + Dex (n=10)	All (N=19)
Age, median (range), years	68.5 (56-74)	68.0 (52-81)
Sex, n (%)		
Female	6 (60)	12 (63)
Male	4 (40)	7 (37)
Race, n (%)		
White	9 (90)	18 (95)
Black	1 (10)	1 (5)
ECOG PS, n (%)		
0	4 (40)	10 (53)
1	6 (60)	9 (47)
R-ISS stage at initial diagnosis, n (%)		
Stage I	2 (20)	4 (21)
Stage II	5 (50)	9 (47)
Stage III	1 (10)	4 (21)
Unknown	2 (20)	2 (11)

Characteristics	Sonrotoclax 640 mg + Dex (n=10)	All (N=19)
Time from most recent R/R episode to first dose, median (range), months	2.86 (0.4-17.9)	2.43 (0.4-17.9)
Cytogenic risk, n (%)		
High[a]	2 (20)	3 (16)
Not high risk	8 (80)	12 (63)
Unknown	0	4 (21)
Number of prior lines, median (range)	**4 (3-12)**	**4 (1-12)**
Anti-CD38 antibody	9 (90)[b]	13 (68)[c]
Immunomodulatory agent	10 (100)	19 (100)
Proteasome inhibitor	10 (100)	19 (100)

[a]High-risk group consisted of patients with genetic subtype t(4;14), 1p deletion, del(17p13), and 1q21 amplification. [b]One patient in 640 mg group was incorrectly enrolled by study investigator and did not have prior anti-CD38 exposure. [c]Some patients in 160 mg (n=3) and 320 mg (n=2) group enrolled prior to protocol amendment requiring prior anti-CD38 treatment.

Overall Safety Summary and DLTs

	Sonrotoclax 80 mg + Dex (n=3)	Sonrotoclax 160 mg + Dex (n=3)	Sonrotoclax 320 mg + Dex (n=3)	Sonrotoclax 640 mg + Dex (n=10)	All (N=19)
Treatment cycles, median (range), n	3.0 (2-4)	28.0 (11-30)	6.0 (4-6)	8.0 (4-22)	7.0 (2-30)
Serious TEAE, n (%)	0	0	1 (33)	1 (10)	2 (11)
TEAE leading to death, n (%)	0	0	1 (33)	0	1 (5)
TEAE leading to discontinuation, n (%)					
Sonrotoclax	0	0	1 (33)	2 (20)[a]	3 (16)
Dexamethasone	0	0	1 (33)	2 (20)	3 (16)
TEAE leading to dose interruption, n (%)					
Sonrotoclax	0	2 (67)	1 (33)	2 (20)	5 (26)
Dexamethasone	0	2 (67)	0	1 (10)	3 (16)
TEAE leading to dose reduction, n (%)					
Sonrotoclax	0	0	0	0	0
Dexamethasone	2 (67)	2 (67)	1 (33)	4 (40)	9 (47)

- Serious TEAEs were COVID-19 and cancer pain (n=1 each)
- Three patients[a] discontinued sonrotoclax due to TEAEs (COVID-19, hematuria, cancer pain; n=1 each)
- No DLTs occurred
- Four patients (21%) died on study; no deaths were related to study treatment
  - One patient died while receiving study therapy (COVID-19)
  - Three patients died ≥50 days after treatment discontinuation (COVID-19, PD, unknown, n=1 each)[b]

[a]One patient originally reporting a TEAE (cancer pain) leading to discontinuation was subsequently found to have PD. [b]All AEs and serious AEs, regardless of relationship to the study drug(s), were reported until 30 days after the last dose of study drug or until initiation of new anticancer therapy; 3 of 4 patients got subsequent treatment.

Most Common TEAEs (≥10% of All Patients)

Patients, n (%)	Sonrotoclax 640 mg + Dex (n=10)		All (N=19)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
≥1 TEAE	10 (100)	3 (30)	19 (100)	5 (26)
Insomnia	4 (40)	0	10 (53)	0
Fatigue	3 (30)	1 (10)	7 (37)	1 (5)
Nausea	4 (40)	0	7 (37)	0
Arthralgia	2 (20)	0	5 (26)	0
COVID-19	2 (20)	0	4 (21)	1 (5)[a]
Alopecia	2 (20)	0	3 (16)	0
Diarrhea	2 (20)	0	3 (16)	1 (5)
Dyspnea	1 (10)	0	3 (16)	0
Rash	1 (10)	0	3 (16)	0
Vomiting	1 (10)	0	3 (16)	0
Back pain	0	0	2 (11)	0
GERD	1 (10)	0	2 (11)	0
Headache	2 (20)	0	2 (11)	0
Toothache	1 (10)	0	2 (11)	0
UTI	0	0	2 (11)	0

Only 1 Grade ≥3 TEAE (diarrhea) was assessed as sonrotoclax-related

[a]One fatal case of COVID-19 in the 320 mg group.

Hematologic and Infection TEAEs

Patients, n (%)	Sonrotoclax 640 mg + Dex (n=10)	All (N=19)
Hematologic toxicities	3 (30)	4 (21)
Anemia	1 (10)	1 (5)
Decreased lymphocyte count	1 (10)	1 (5)
Neutropenia/decreased neutrophil count	1 (10)	2 (11)[a]
Decreased platelet count	1 (10)	1 (5)

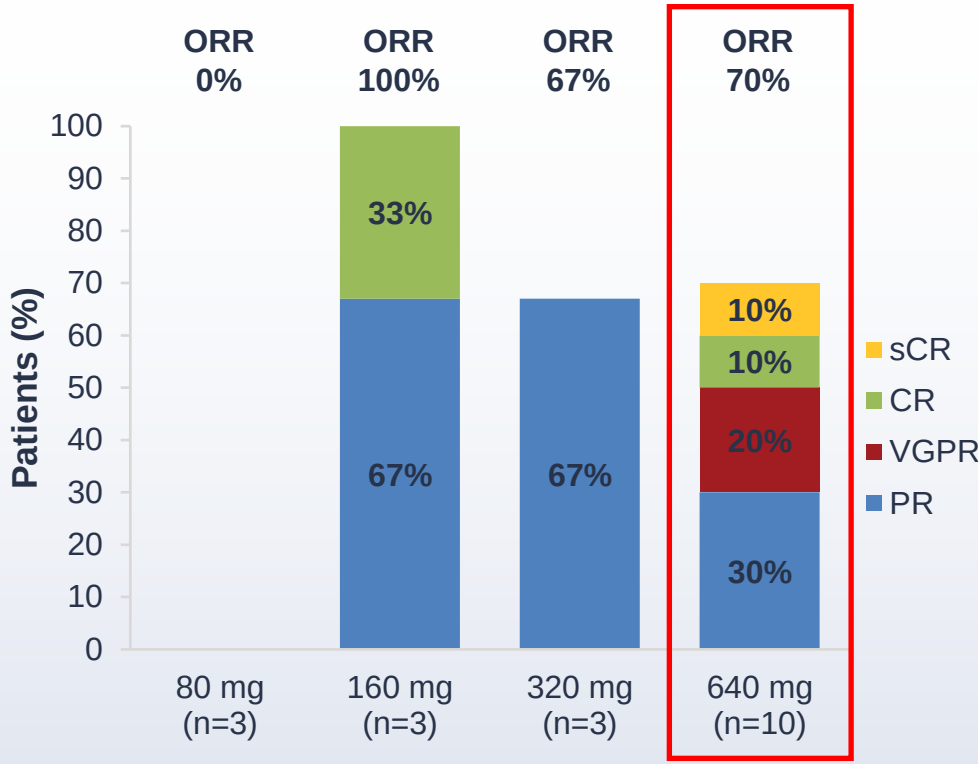
Patients, n (%)	Sonrotoclax 640 mg + Dex (n=10)	All (N=19)
Infections and infestations	2 (20)	6 (32)
COVID-19	2 (20)	4 (21)
UTI	0	2 (11)
Conjunctivitis	0	1 (5)
Respiratory syncytial virus infection	0	1 (5)
Rhinovirus infection	0	1 (5)
URI	1 (10)	1 (5)

- Of the hematologic TEAEs, decreased lymphocyte count and decreased platelet count were Grade 3
- All infections were Grade 1-2 except for 1 case of COVID-19

[a]Neutropenia occurred in 1 patient at a dose <640 mg.

Investigator-Assessed Response Rates

- Median treatment duration:
  All patients: 5.1 months (range, 1.2-21.1 months)
  640 mg: 5.5 months (range, 2.4-15.1 months)
- Rate of VGPR or better was 40% in a heavily pretreated patient population (median of 4 prior lines of therapy)
- The longest DoR was 18.9 months, which was still ongoing at data cutoff
  - This patient is a 70-year-old woman with high cytogenic risk. She received 160 mg sonrotoclax + dex and achieved PR at 1.4 months, VGPR at 4.1 months, and CR at 7.8 months. She was still in CR at her most recent assessment at 20.2 months



Conclusions

- Sonrotoclax + dexamethasone combination treatment was well tolerated in a heavily pretreated population (median of 4 prior lines of therapy), with no DLTs observed at any tested dose level and the majority (74%) of patients only experienced Grade 1 or 2 AEs
  - No significant hematologic toxicity was seen at any dose
  - Diarrhea was low grade and manageable with dose interruption
  - Only 1 infection was Grade ≥3 (COVID-19)
- Sonrotoclax + dexamethasone 640 mg is being evaluated in the expansion cohort based on the totality of safety and efficacy data
  - The majority of patients (70%) receiving 640 mg achieved a clinical response including ≥VGPRs of 40%
- Recruitment is ongoing for the sonrotoclax + dexamethasone expansion cohort and the sonrotoclax + dexamethasone + carfilzomib dose-finding arms
- Later cohorts in this study will investigate other combinations

Acknowledgments

- The authors thank the patients and their families, investigators, co-investigators, and the study teams at each of the participating centers
- We would also like to thank Adam Idoine (BeiGene) for assistance in development of this presentation
- This study was sponsored by BeiGene, Ltd
- Medical writing support was provided by Brittany Gifford, PharmD, of Nucleus Global, an Inizio Company, and was funded by BeiGene

BGB-16673

BTK CDAC

BGB-16673 (BTK CDAC) Acknowledgments

First Results From a Phase 1, First-in-Human Study of the Bruton Tyrosine Kinase Degrader BGB-16673 in Patients With Relapsed or Refractory B-Cell Malignancies

John F. Seymour,[1] Chan Y. Cheah,[2-4] Ricardo Parrondo,[5] Meghan C. Thompson,[6] Don Stevens,[7] Masa Lasica,[8] Michael Wang,[9] Abhijeet Kumar,[10] Judith Trotman,[11] Maan Alwan,[12] Wei Ding,[13] Kunthel By,[14] Bilal Tariq,[14] Xiangmei Chen,[14] Shannon Fabre,[14] Jason Paik,[14] Amit Agarwal,[14] Constantine S. Tam[15,16]

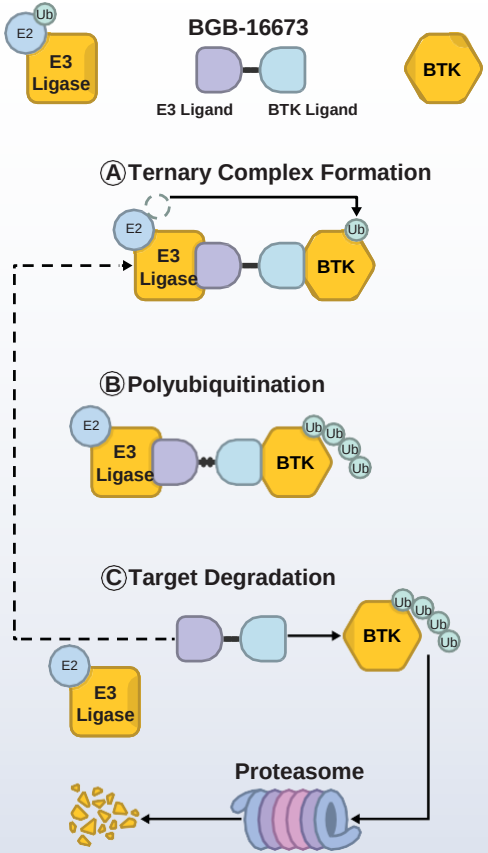
[1]Peter MacCallum Cancer Centre, Royal Melbourne Hospital, and University of Melbourne, Melbourne, VIC, Australia; [2]Department of Haematology, Sir Charles Gairdner Hospital and Pathwest Laboratory Medicine, Nedlands, WA, Australia; [3]Medical School, University of Western Australia, Crawley, WA, Australia; [4]Linear Clinical Research, Nedlands, WA, Australia; [5]Mayo Clinic-Jacksonville, Jacksonville, FL, USA; [6]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [7]Norton Healthcare, Louisville, KY, USA; [8]St Vincent's Hospital Melbourne, Fitzroy, VIC, Australia; [9]MD Anderson Cancer Center, Houston, TX, USA; [10]University of Arizona College of Medicine – Tucson, Tucson, AZ, USA; [11]Concord Repatriation General Hospital, University of Sydney, Concord, NSW, Australia; [12]Perth Blood Institute, West Perth, WA, Australia; [13]Mayo Clinic-Rochester, Rochester, MN, USA; [14]BeiGene (Shanghai) Co, Ltd, Shanghai, China, and BeiGene USA, Inc, San Mateo, CA, USA; [15]Alfred Hospital, Melbourne, VIC, Australia; [16]Monash University, Clayton, VIC, Australia

Introduction

- BTK inhibitors have become a standard of care treatment for patients with CLL, Waldenström macroglobulinemia, MCL, and marginal zone lymphoma
- However, many patients experience disease progression in part due to resistance mutations within BTK that arise during treatment with both covalent or non-covalent BTK inhibitors[1,2]
- BGB-16673, a CDAC, is a bivalent molecule comprising a BTK-binding moiety + linker + E3 ligase binder (**Figure 1**); engagement of the drug with BTK activates the ubiquitination pathway, resulting in degradation of BTK
- In preclinical models, BGB-16673 degraded both wild-type BTK and known covalent and noncovalent BTK inhibitor–resistant mutant proteins such as V416L, M437R, T474I, C481S, C481F, C481Y, and L528W, leading to tumor suppression[3,4]
- Here, we report the preliminary safety and efficacy results of the BGB-16673-101 study (NCT05006716) in patients with relapsed or refractory B-cell malignancies

BTK, Bruton tyrosine kinase; CDAC, chimeric degradation activating compound; CLL, chronic lymphocytic leukemia; MCL, mantle cell lymphoma.

Figure 1. BGB-16673: A BTK-Targeted CDAC



Attributes and Potential Advantages of BGB-16673

- Catalytic pharmacology that does not require sustained target binding
- Can interrupt formation of oncogenic protein complexes (“scaffolding”)
- Potential to overcome resistance mutations eg, BTK C481S
- Has substantially reduced immunomodulatory drug activity; Aiolos and Ikaros are not significantly degraded

BTK, Bruton tyrosine kinase; CDAC, chimeric degradation activating compound.

Figure 2. BGB-16673-101 Study Design[a]

Key eligibility criteria

- Received ≥2 prior therapies (≥1 prior therapy for RT)
- Received a cBTKi if approved for their disease
- ECOG PS 0-2
- Adequate end-organ function
- No current or history of central nervous system involvement by B-cell malignancy

Key study objectives

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

Part 1: Monotherapy dose finding (concurrent enrollment)

Part 1a: Dose escalation[b]

Selected R/R B-cell malignancies
(MZL, FL, MCL, CLL/SLL, WM, DLBCL, RT)
n≤72

600 mg QD
500 mg QD
350 mg QD
200 mg QD
100 mg QD
50 mg QD

Oral dosing

Part 1b: Safety expansion

Selected R/R B-cell malignancies
(MZL, MCL, CLL/SLL, WM)
n≤120

Up to 20 patients enrolled at doses that are cleared in part 1a: dose escalation and recommended for additional evaluation by the safety monitoring committee

Part 1c: Additional safety expansion

Selected R/R B-cell malignancies
(MZL, WM, RT, DLBCL, FL)
n≤40

After part 2 is opened, up to 40 patients enrolled in up to 3 dose levels as recommended by the safety monitoring committee

Determination of BGB-16673 RP2D

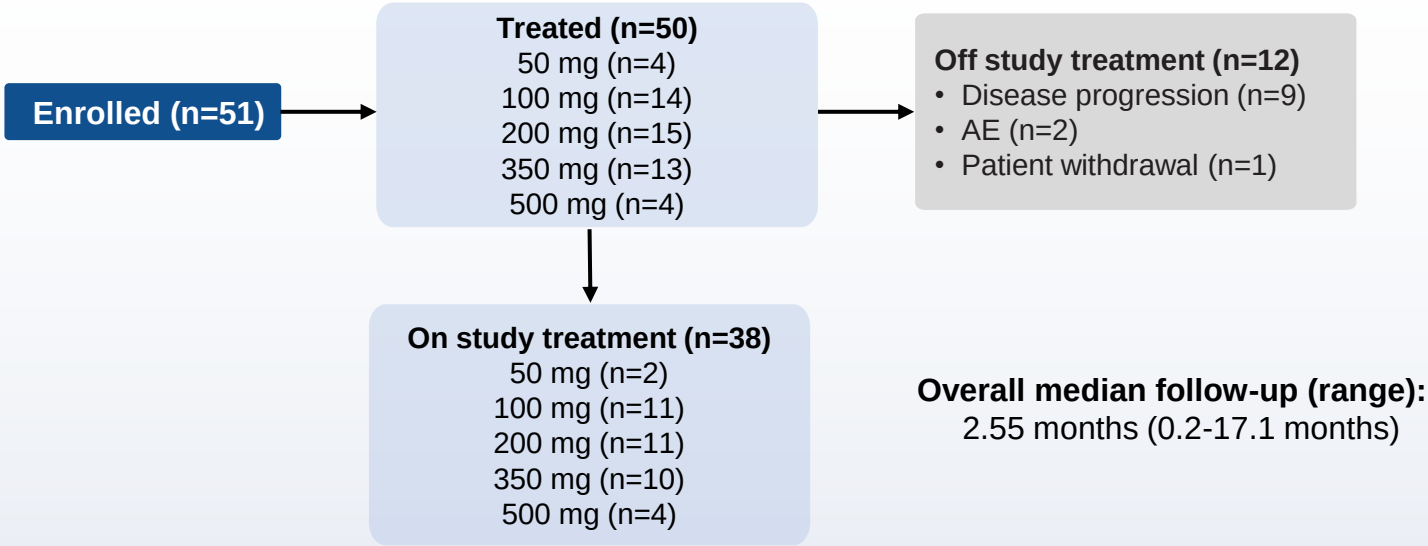
Part 2: Dose Expansion

Cohort 1: Post-BTK inhibitor, R/R CLL/SLL

Cohort 2: Post-BTK inhibitor, R/R MCL

[a] Gray portions of the diagram are intended trial elements that have not yet commenced. [b] Bayesian optimal interval design with 6 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.
[d] Response was assessed per Lugano criteria for all patients except those with CLL (per iwCLL 2018 criteria) and WM (per IWWM-6 criteria)[5-7]
cBTKi, covalent Bruton tyrosine kinase inhibitor; RT, Richter transformation.

Figure 3. Patient Disposition[a]



Overall median follow-up (range):
2.55 months (0.2-17.1 months)

[a] Data for parts 1a and 1b were pooled for each dose level and histology. One patient was enrolled but had not yet received study treatment at the September 1, 2023 data cutoff date.

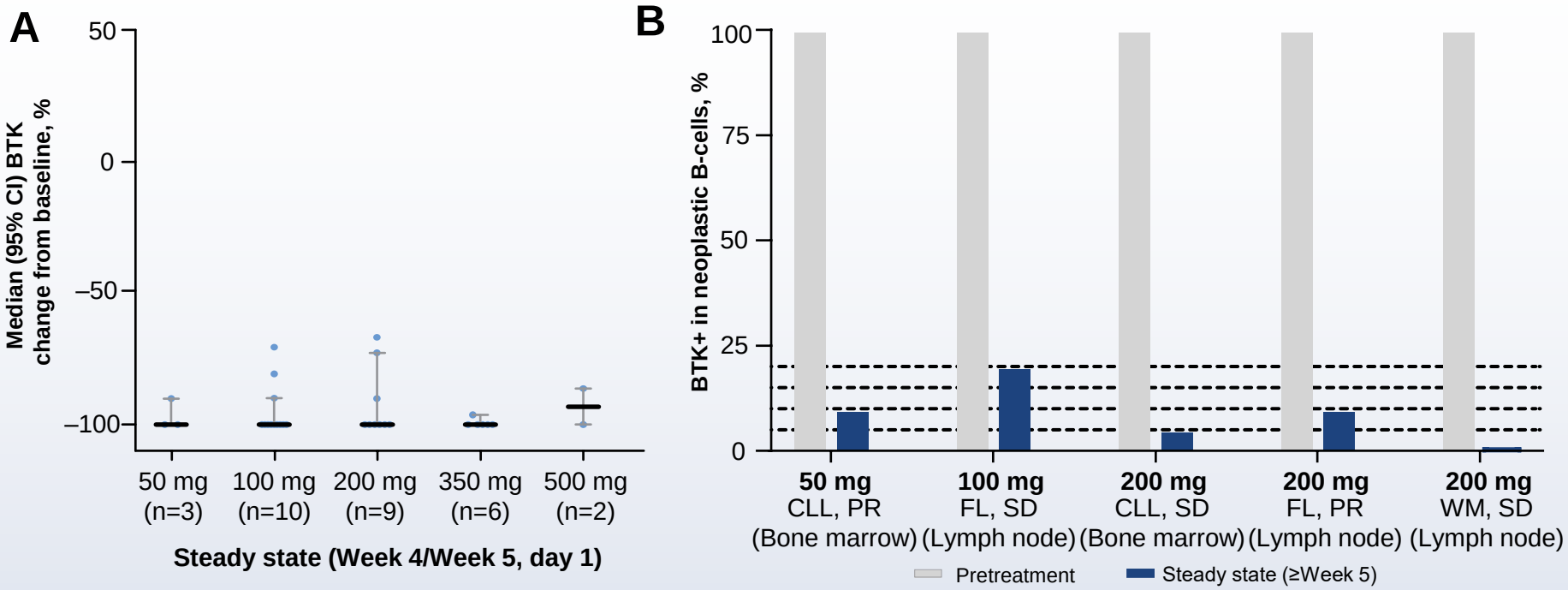
Table 1. Demographic and Baseline Characteristics

Parameter	Total (N=50)
Age, median (range), years	70.5 (26-91)
Sex, n (%)	
Male	33 (66)
Female	17 (34)
ECOG performance status, n (%)	
0-1	47 (94)
2	3 (6)
Disease type, n (%)	
CLL/SLL	24 (48)
MCL	7 (14)
MZL	3 (6)
WM	6 (12)
DLBCL	2 (4)
FL	6 (12)
RT	2 (4)
Number of prior lines, median (range)	4 (2-10)
Prior covalent BTK inhibitor	40 (80)
Prior noncovalent BTK inhibitor	7 (14)
Discontinued BTK inhibitor due to PD	28 (56)
BCL2 inhibitor	28 (56)

Parameter	Total (N=50)
Mutation status, n/N (%)	
BTK mutation present	7/24 (29)
PLCG2 mutation present	2/24 (8)
BCL2 mutation present	12/27 (44)
CLL/SLL risk characteristics at study entry, n/N (%)	
Binet stage 3 at study entry	12/23 (52)
Unmutated IGHV locus	16/19 (84)[a]
del(17p)	8/24 (33)
TP53 mutation	10/23 (42)[b]
del(17p) or *TP53* mutation	11/23 (46)[b]
del(11q)	2/24 (8)
Complex karyotype (≥3 abnormalities)	8/20 (40)[c]

[a] Results missing for 5 patients. [b] Results missing for 1 patient. [c] Results missing for 4 patients.
BCL2, B-cell lymphoma 2; BTK, Bruton tyrosine kinase; IGHV, immunoglobulin heavy chain variable region; *TP53*, tumor protein 53.

Figure 4. Reduction of BTK Protein Levels in A) Peripheral Blood and B) Tumor Tissue



[a] BTK protein levels were measured in whole blood lysates by ELISA. [b] Percentage of BTK-positive neoplastic B-cells were measured by immunohistochemistry in paired pretreatment and steady state tumor tissue collected from lymph nodes or bone marrow. Week 13 response data are shown.
BTK, Bruton tyrosine kinase; ELISA, enzyme-linked immunosorbent assay.

Table 2. Overall Safety Summary

Patients, n (%)	50 mg (n=4)	100 mg (n=14)	200 mg (n=15)	350 mg (n=13)	500 mg (n=4)	All (N=50)
Any TEAE	4 (100)	13 (93)	13 (87)	12 (92)	4 (100)	46 (92)
Any treatment-related	3 (75)	11 (79)	8 (53)	8 (62)	2 (50)	32 (64)
Grade 3 or higher	3 (75)	4 (29)	6 (40)	5 (38)	1 (25)	19 (38)
Treatment-related Grade 3 or higher	2 (50)	4 (29)	2 (13)	3 (23)	0	11 (22)
Serious	1 (25)	4 (29)	5 (33)	4 (31)	0	14 (28)
Treatment-related serious	0	2 (14)	2 (13)	1 (8)	0	5 (10)
Leading to death[a]	0	0	2 (13)	0	0	2 (4)
Treatment-related leading to death	0	0	0	0	0	0
Leading to treatment discontinuation	0	0	1 (7)	2 (15)	0	3 (6)
Treatment-related leading to treatment discontinuation[b]	0	0	0	1 (8)	0	1 (2)
Leading to treatment modification	1 (25)	4 (29)	4 (27)	2 (15)	0	11 (22)
Dose interruption	1 (25)	4 (29)	4 (27)	2 (15)	0	11 (22)
Dose reduction[c]	1 (25)	1 (7)	0	0	0	2 (4)
DLT[d]	0	0	1 (7)	0	0	1 (2)

[a] 1) Septic shock (200 mg) in the context of progressive disease; 2) pneumonia (200 mg) in the context of progressive disease. [b] 1) Pneumonia (200 mg) in the context of progressive disease; 2) bronchopulmonary aspergillosis (350 mg) retrospectively identified as being present before treatment; 3) subdural hemorrhage (350 mg), resolving (related). [c] 1) Hematuria (50 mg) in the context of subsequently identified recurrent urothelial carcinoma; 2) arthralgia (100 mg) in the context of a previous history of BTK inhibitor–associated arthralgia. [d] Grade 3 maculopapular rash of face and legs (200 mg) at end of DLT reporting period. After 5-day dose hold and following improvement of rash, treatment was restarted and patient remains on the assigned dose.
BTK, Bruton tyrosine kinase.

Table 3. TEAEs in ≥10% of All Patients or ≥3% for Grade 3 or Higher

	50 mg (n=4)		100 mg (n=14)		200 mg (n=15)		350 mg (n=13)		500 mg (n=4)		All (N=50)	
Patients, n (%)	**All Gr**	**Gr ≥3**	**All Gr**	**Gr ≥3**	**All Gr**	**Gr ≥3**	**All Gr**	**Gr ≥3**	**All Gr**	**Gr ≥3**	**All Gr**	**Gr ≥3**
Contusion	0	0	6 (43)	0	5 (33)	0	2 (15)	0	2 (50)	0	15 (30)	0
Diarrhea	2 (50)	0	2 (14)	0	2 (13)	0	4 (31)	0	2 (50)	0	12 (24)	0
Fatigue	0	0	3 (21)	0	4 (27)	0	1 (8)	0	2 (50)	0	10 (20)	0
Amylase increased[a]	1 (25)	0	3 (21)	0	2 (13)	0	2 (15)	0	0	0	8 (16)	0
Neutropenia/ neutrophil count decreased	1 (25)	1 (25)	3 (21)	2 (14)	2 (13)	1 (7)	1 (8)	1 (8)	1 (25)	1 (25)	8 (16)	6 (12)
Lipase increased[a]	1 (25)	0	2 (14)	1 (7)	2 (13)	0	2 (15)	1 (8)	0	0	7 (14)	2 (4)
Pyrexia	1 (25)	0	4 (29)	0	1 (7)	0	1 (8)	0	0	0	7 (14)	0
Cough	2 (50)	0	2 (14)	0	1 (7)	0	1 (8)	0	0	0	6 (12)	0
Headache	0	0	1 (7)	0	1 (7)	0	1 (8)	0	2 (50)	0	5 (10)	0
Thrombocytopenia/ platelet count decreased	1 (25)	1 (25)	2 (14)	1 (7)	2 (13)	0	0	0	0	0	5 (10)	2 (4)
Pneumonia	1 (25)	1 (25)	0	0	1 (7)	1 (7)	1 (8)	1 (8)	0	0	3 (6)	3 (6)
COVID-19 pneumonia	0	0	0	0	1 (7)	1 (7)	1 (8)	1 (8)	0	0	2 (4)	2 (4)
Grouped TEAEs of interest												
Any bleeding	2 (50)	1 (25)	7 (50)	0	6 (40)	0	4 (31)	1 (8)	2 (50)	0	21 (42)	2 (4)[b]
Any infection[c]	2 (50)	1 (25)	6 (43)	2 (14)	7 (47)	3 (20)	4 (31)	2 (15)	1 (25)	0	20 (40)	8 (16)
Atrial fibrillation/flutter	0	0	0	0	0	0	0	0	0	0	0	0
Hypertension	0	0	0	0	0	0	0	0	0	0	0	0

[a] Transient laboratory-only findings; no associated gastrointestinal symptoms or dose modifications. [b] 1) Hematuria (50 mg) in the context of subsequently identified recurrent urothelial carcinoma; 2) subdural hemorrhage (350 mg), resolving (related). [c] Includes 4 upper respiratory tract infection, 3 pneumonia, 3 urinary tract infection, 2 COVID-19 or COVID-19 pneumonia, 2 cellulitis, and 2 hordeolum (stye).
Gr, grade.

Table 4. Responses by Dose in Evaluable Patients

	50 mg (n=4)	100 mg (n=10)	200 mg (n=9)	350 mg (n=4)	500 mg (n=1)	All Doses (N=28)
Best overall response, n (%)						
CR	1 (25)	0	0	0	0	1 (4)
PR	1 (25)	4 (40)	7 (78)	0	1 (100)	13 (46)
PR-L	0	0	1 (11)	0	0	1 (4)
MR	0	1 (10)	0	0	0	1 (4)
SD	0	3 (30)	1 (11)	1 (25)	0	5 (18)
PD	2 (50)	2 (20)	0	1 (25)	0	5 (18)
Discontinued prior to first assessment	0	0	0	2 (50)	0	2 (7)
Disease control rate, n (%)[a]	**2 (50)**	**8 (80)**	**9 (100)**	**1 (25)**	**1 (100)**	**21 (75)**
ORR, n (%)[b]	**2 (50)**	**5 (50)**	**8 (89)**	**0**	**1 (100)**	**16 (57)**
Median time to first response, months[c]	2.60	0.95	2.81	–	2.83	2.76

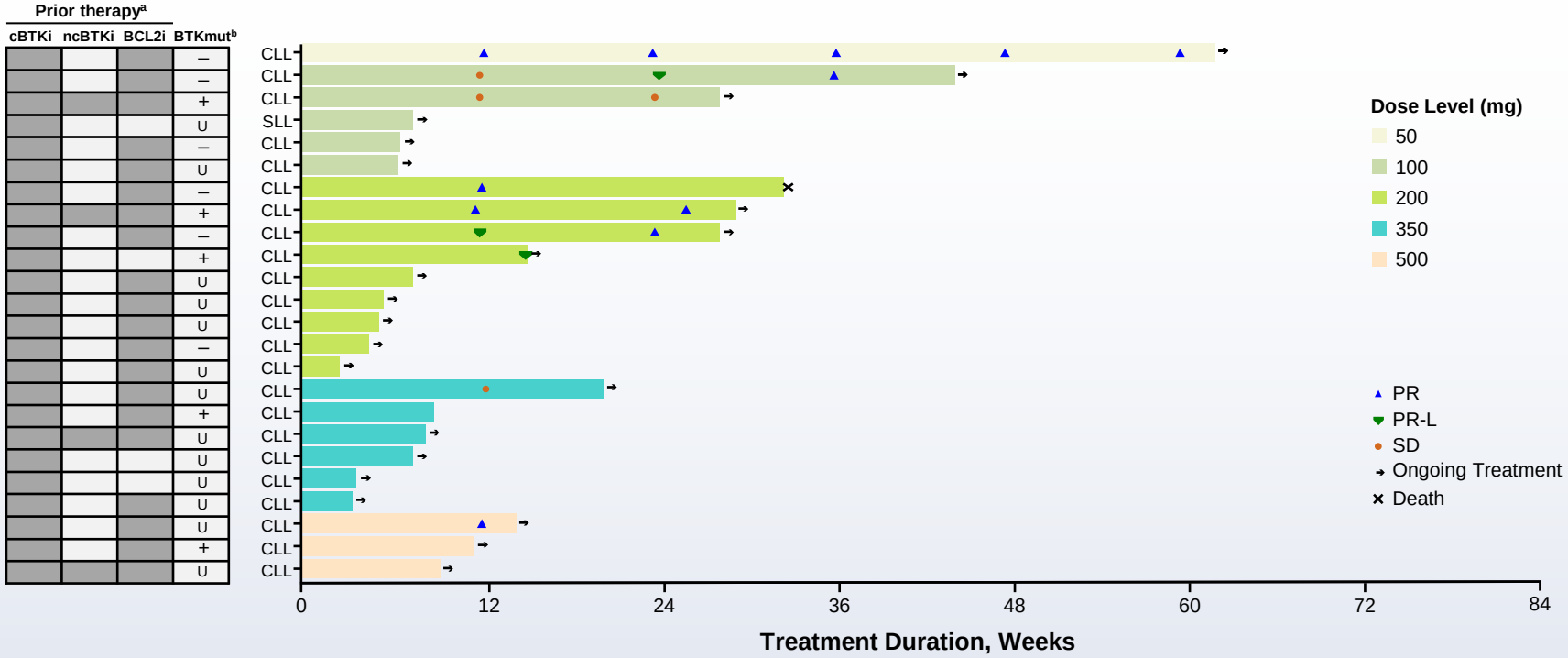
[a] Proportion of patients with a best overall response of SD or higher. [b] Proportion of patients who achieved a best overall response better than SD. [c] Time to first qualifying response in patients with a best overall response better than SD.

Table 5. Responses by Histology in Evaluable Patients

	CLL/SLL (n=10)	MCL/MZL/WM/ FL (n=16)	DLBCL/RT (n=2)	All (n=28)
Best overall response, n (%)				
CR	0	1 (6)	0	1 (4)
PR	6 (60)	7 (44)	0	13 (46)
PR-L	1 (10)	N/A	0	1 (4)
MR	0	1 (6)	0	1 (4)
SD	2 (20)	3 (19)	0	5 (18)
PD	0	3 (19)	2 (100)	5 (18)
Discontinued prior to first assessment	1 (10)	1 (6)	0	2 (7)
Disease control rate, n (%)[a]	**9 (90)**	**12 (75)**	**0**	**21 (75)**
ORR, n (%)[b]	**7 (70)**	**9 (56)[d]**	**0**	**16 (57)**
Median time to first response, months[c]	2.83	2.33	N/A	2.76

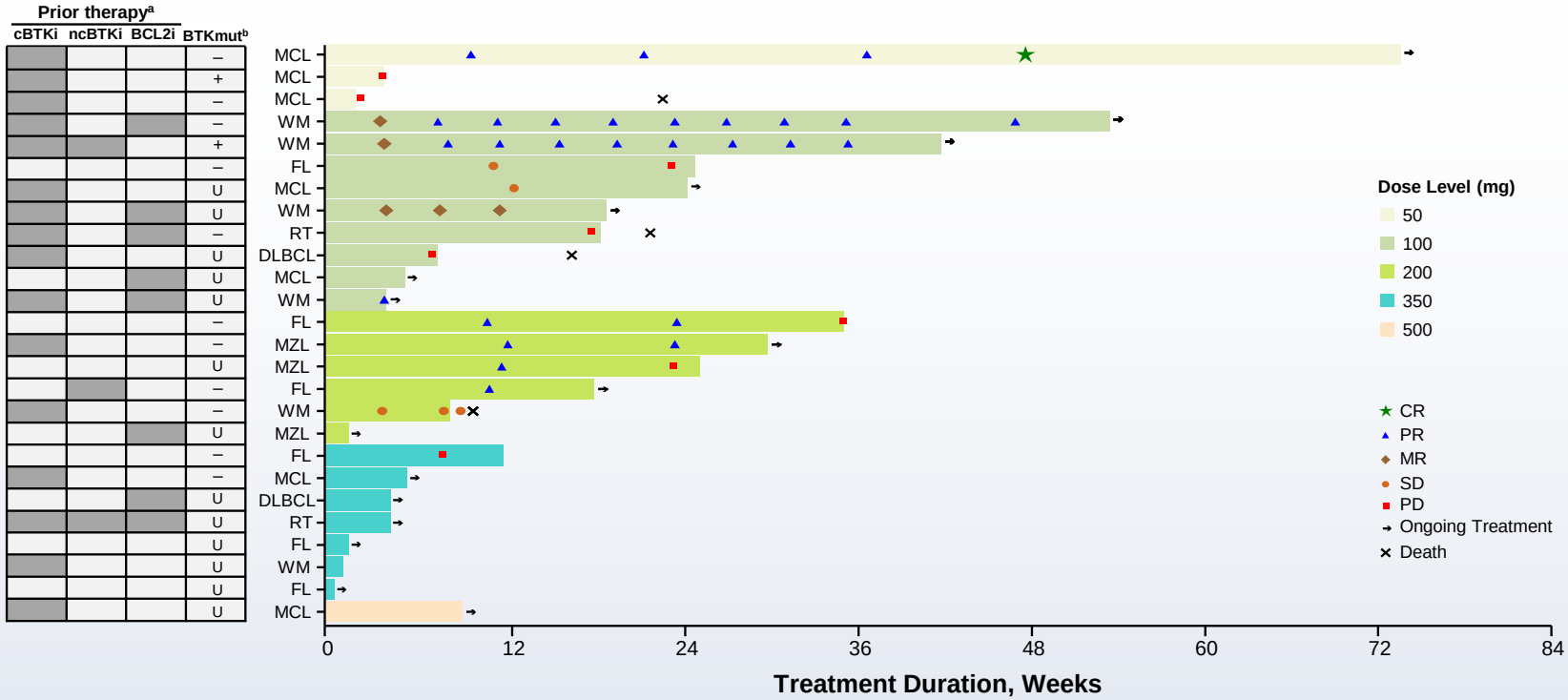
[a] Proportion of patients with a best overall response of SD or higher. [b] Proportion of patients who achieved a best overall response better than SD. [c] Time to first qualifying response in patients with a best overall response better than SD. [d] CR=1 MCL; PR=3 WM, 2 MZL, 2 FL; MR=1 WM.
RT, Richter transformation.

Figure 5. Treatment Duration and Response Assessment in Patients with CLL/SLL



[a] Gray shading = patient had the indicated prior therapy. [b] BTK mutation status was classified as present (+), absent (-), or unknown (U).
BCL2i, B-cell lymphoma 2 inhibitor; BTK, Bruton tyrosine kinase; cBTKi, covalent BTK inhibitor; mut, mutation; ncBTKi, noncovalent BTK inhibitor.

Figure 6. Response Assessment in Patients with Other Indolent B-cell Lymphomas



[a] Gray shading = patient had the indicated prior therapy. [b] BTK mutation status was classified as present (+), absent (-), or unknown (U).
BCL2i, B-cell lymphoma 2 inhibitor; BTK, Bruton tyrosine kinase; cBTKi, covalent BTK inhibitor; mut, mutation; ncBTKi, noncovalent BTK inhibitor.

Conclusions

- Preliminary results from this ongoing, first-in-human study of the novel BTK degrader BGB-16673 demonstrate meaningful clinical responses with a short time to response in heavily pretreated patients with a range of B-cell malignancies
  - In a high-risk, heavily pretreated population of patients with CLL/SLL all treated with cBTK inhibitors, the ORR was 70%
- The safety profile of BGB-16673 appears tolerable to date with a single DLT (rash) reported and the study continues
  - Discontinuations due to TEAEs were low (2 of 50 patients)
  - No atrial fibrillation or hypertension has been reported so far
- Substantial reductions in BTK protein levels in peripheral blood and tumor tissue were also observed, demonstrating proof-of-concept of a strong, on-target effect
- Taken together, these data support further examination of the clinical activity of BGB-16673 across several B-cell malignancies; phase 2 dose expansions are planned within this study for patients with CLL/SLL and MCL

References

1. Woyach JA, et al. *N Engl J Med.* 2014; 370:2286-2294.
2. Wang E, et al. *N Engl J Med.* 2022; 386:735-743.
3. Feng X, et al. EHA 2023. Abstract P1239.
4. Wang H, et al. EHA 2023. Abstract P1219.
5. Cheson BD, et al. *J Clin Oncol.* 2014; 32:3059-3067.
6. Hallek M, et al. *Blood.* 2018; 131:2745-2760.
7. Owen RG, et al. *Br J Haematol.* 2022; 160:171-176.

Thank You

BeiGene