CaDAnCe-101

R/R CLL/SLL

BGB-16673 in Patients With Relapsed or Refractory B-Cell Malignancies

BGB-16673-101 – CADANCE-101 (R/R CLL/SLL)

Phase 1

Study Identifier:
BGB-16673-101, CaDAnCe-101, NCT05006716

Primary Endpoint: Safety[a] and tolerability, define MTD and RP2D
Key Secondary Endpoints: Characterize PK, pharmacodynamics, and preliminary antitumor activity[b]

Key eligibility criteria (CLL/SLL)

- Meets iwCLL 2018 criteria for treatment
- ≥2 prior therapies, including covalent BTK inhibitor if approved for disease
- ECOG PS 0-2
- Adequate end-organ function

Part 1: Monotherapy Dose Finding

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

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

Part 2: Dose Expansion

Determination of BGB-16673 RP2D

- **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]Safety was assessed according to CTCAE v5.0 in all patients and iwCLL hematologic toxicity criteria in patients with CLL. [b]Response was assessed per iwCLL 2018 criteria after 12 weeks in patients with CLL. [c]Treatment was administered until progression, intolerance, or other criteria were met for treatment discontinuation.
BTK=Bruton tyrosine kinase, cBTKi=covalent Bruton tyrosine kinase inhibitor, CLL=chronic lymphocytic leukemia, DLCBL=diffuse large B-cell lymphoma, ECOG PS=Eastern Cooperative Oncology Group performance status, FL=follicular lymphoma, GCB=germinal center B-cell type, IGHV=immunoglobulin heavy chain variable region, MCL=mantle cell lymphoma, MTD=maximum tolerated dose, MZL=marginal zone lymphoma, PK=pharmacokinetics, QD=once daily, RP2D=recommended phase 2 dose, R/R=relapsed/refractory, RT=Richter transformation, SLL=small lymphocytic leukemia, TP53=tumor protein 53, WM=Waldenström macroglobulinemia.
1. Scarfò L, et al. Oral Presentation at EHA 2025; S158. 2. https://clinicaltrials.gov/study/NCT05006716?term=NCT05006716&rank=1. Accessed October 9, 2025.

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Baseline Patient Characteristics

CaDAnCe-101: CLL/SLL

- Heavily pretreated, with high-risk CLL features

	Total (N=68)
Age, median (range), years	70 (47-91)
Male, n (%)	47 (69.1)
ECOG PS, n (%)	
0	38 (55.9)
1	29 (42.6)
2	1 (1.5)
CLL/SLL risk characteristics at study entry, n/N with known status (%)	
Binet stage C	29/64 (45.3)
Unmutated IGHV	38/49 (77.6)
del(17p) and/or *TP53* mutation	46/68 (67.6)
Complex karyotype (≥3 abnormalities)	22/44 (50.0)

	Total (N=66)
Mutation status, n/N (%)	
BTK mutation present	26/66 (39.4)
PLCG2 mutation present	10/66 (15.2)
BTK and *PLCG2* mutation present	5/66 (7.6)
No. of prior lines of therapy, median (range)	4 (2-10)
Prior therapy, n (%)	
Chemotherapy	49 (71.2)
cBTK inhibitor	64 (94.1)
ncBTK inhibitor	14 (20.6)
BCL2 inhibitor	56 (82.4)
cBTK + BCL2 inhibitors	44 (64.7)
cBTK + ncBTK + BCL2 inhibitors	12 (17.6)
Discontinued prior BTK inhibitor due to PD, n/N (%)[a]	57/64 (89.1)

Data cutoff: August 22, 2025.
[a]The remaining 7 patients discontinued prior BTK inhibitor due to toxicity (n=4), and other (n=3).
BCL2, B-cell lymphoma 2; BTK, Bruton tyrosine kinase; cBTK, covalent Bruton tyrosine kinase; CLL, chronic lymphocytic leukemia; ECOG PS, Eastern Cooperative Oncology Group performance status; IGHV, immunoglobulin heavy chain variable region; ncBTK, noncovalent Bruton tyrosine kinase; PD, progressive disease; SLL, small lymphocytic lymphoma.
Ahn IE, et al. Oral Presentation at ASH 2025;8349.

Overall Safety Summary

CaDAnCe-101: CLL/SLL

- Tolerable safety profile, with no treatment-related TEAEs leading to death

Patients, n (%)	Total (N=68)
Any TEAE	65 (95.6)
Any treatment-related	52 (76.5)
Grade ≥3	42 (61.8)
Treatment-related grade ≥3	23 (33.8)
Serious	33 (48.5)
Treatment-related serious	9 (13.2)
Leading to death	5 (7.4)
Treatment-related leading to death	0
Leading to treatment discontinuation	12 (17.6)
Treatment-related leading to treatment discontinuation	3 (4.4)

Data cutoff: August 22, 2025.
Median study follow-up in safety-evaluable patients: 19.8 months (range, 0.3-34.0+ months).
TEAE, treatment-emergent adverse event.
Ahn IE, et al. Oral Presentation at ASH 2025;8349.

Summary of All-Grade TEAEs in ≥10% of All Patients

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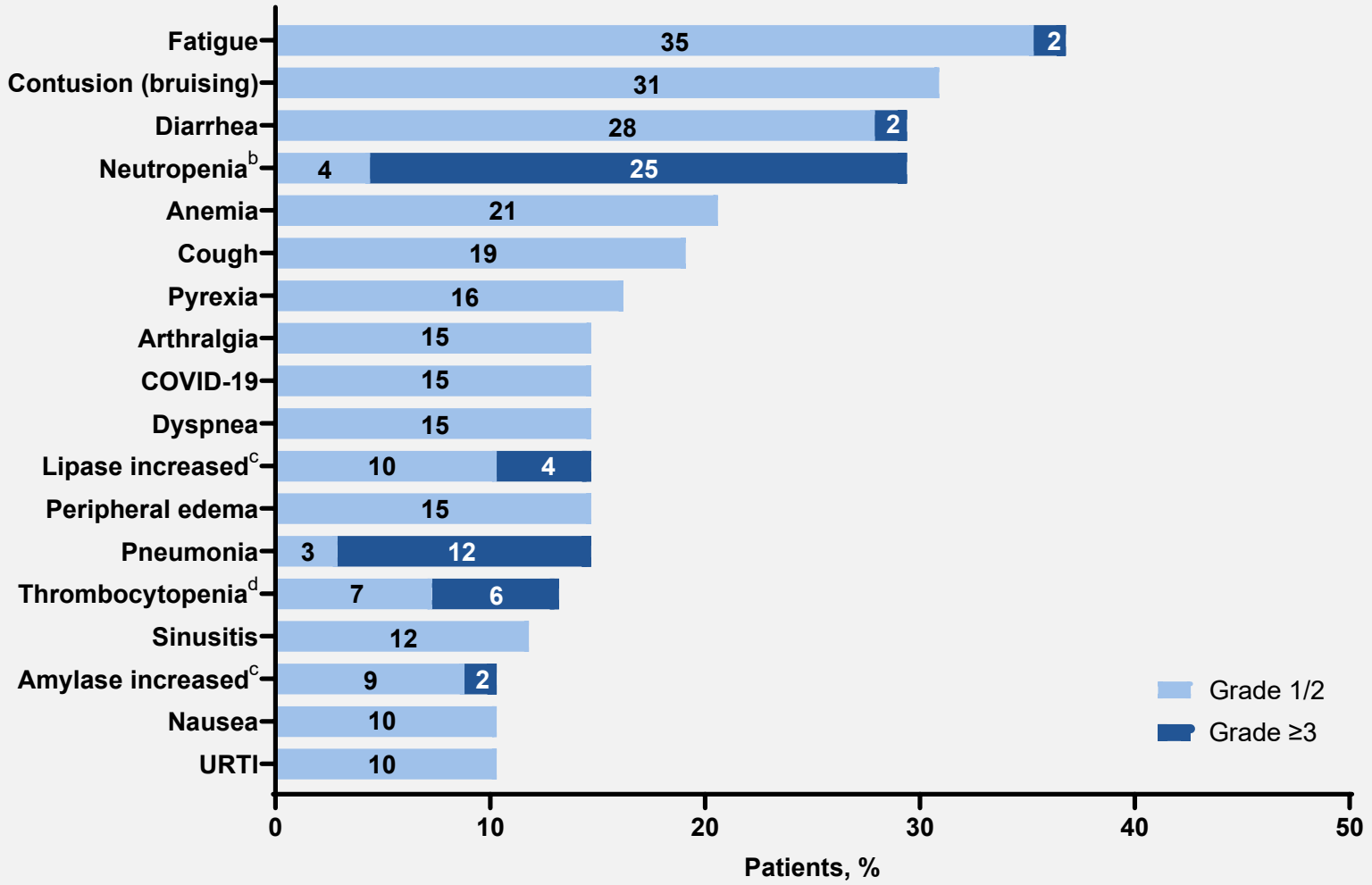
- Most common TEAEs were fatigue (36.8%) and contusion (bruising; 30.9%)
- Grade ≥3 neutropenia: n=17 (25.0%); 16 patients (23.5%) had grade ≥2 neutropenia at baseline
  - Neutropenic fever: n=1
- Atrial fibrillation: n=3 (Grade 1, n=1; Grade 2, n=2, all in the context of infection and PD and were assessed as unrelated to treatment)
- Treatment-related major hemorrhagea: n=2 (one Grade 3 subdural hemorrhage and one Grade 3 post-procedural hematuria)



Data cutoff: August 22, 2025.
Median follow-up in safety-evaluable patients: 19.8 months (range, 0.3-34.0+ months).
[a]Grade ≥3, serious, or any central nervous system bleeding. [b]Neutropenia combines preferred terms neutrophil count decreased and neutropenia. [c]All events were laboratory 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.
PD, progressive disease; TEAE, treatment-emergent adverse event; UTRI, upper respiratory tract infection.
Ahn IE, et al. Oral Presentation at ASH 2025;8349.

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Cytopenia Improvement in Patients With Treatment Response

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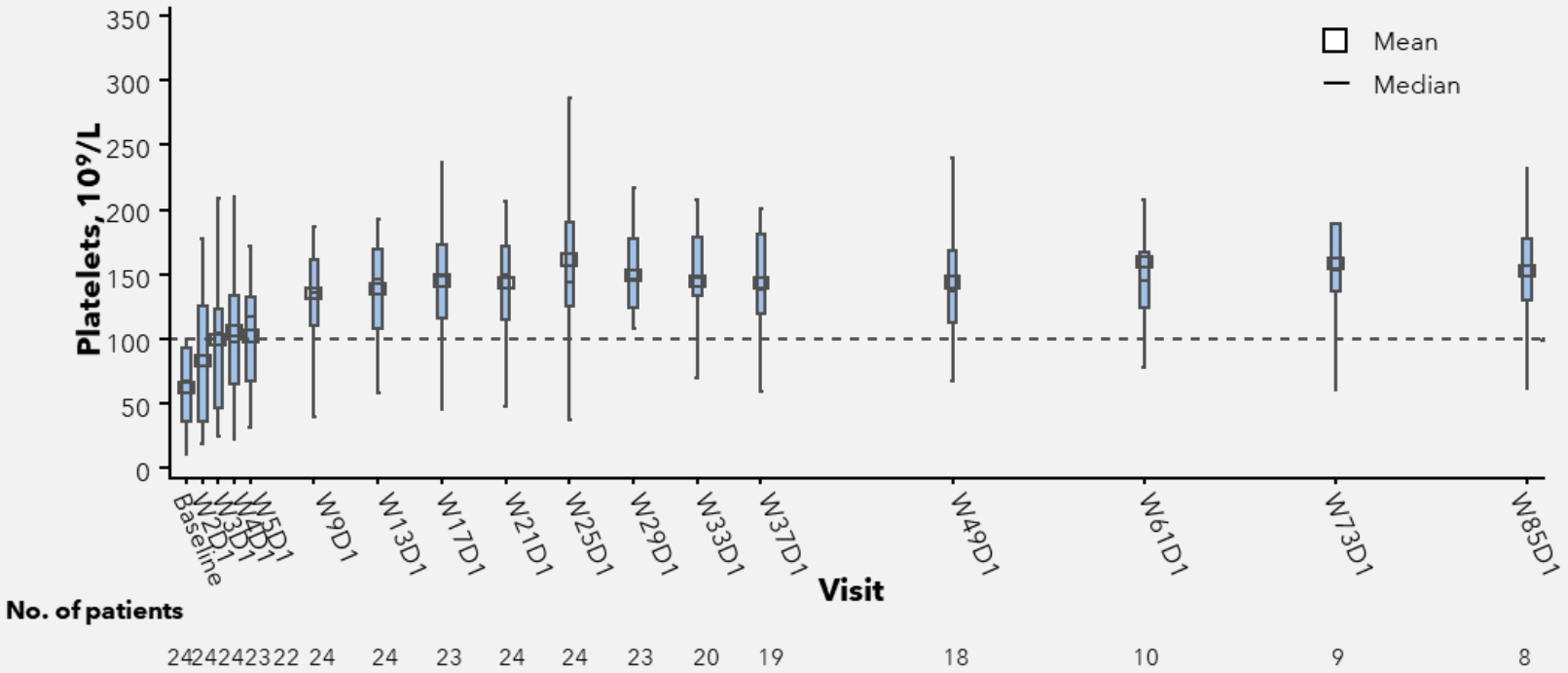
	Baseline	W9D1
Platelet count,[a] median, 10^9/L	67.5	136.0
Neutrophil count,[b] median, 10^9/L	1.1	2.4

	Baseline	W13D1
Hemoglobin level,[c] median, g/L	99.0	111.0

Platelet Count in Patients Who Had Baseline Thrombocytopenia and Responded to Treatment



Data cutoff: August 22, 2025.
[a]In n=25 patients based on 100×10^9/L cutoff. [b]In n=14 patients based on 1.5×10^9/L cutoff. [c]In n=25 patients based on 11.0 g/dL cutoff.
D, day; W, week.
Ahn IE, et al. Oral Presentation at ASH 2025;8349.

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Overall Response Rate

R/R CLL/SLL

- Significant responses, particularly at 200-mg dose level

	50 mg (n=1)	100 mg (n=22)	200 mg (n=18)	350 mg (n=15)	500 mg (n=12)	Total (N=68)
Best overall response, n (%)						
CR/CRi	0	1 (4.5)	1 (5.6)	0	0	**2 (2.9)**
PR[a]	1 (100)	14 (63.6)	12 (66.7)	11 (73.3)	11 (91.7)	49 (72.1)
PR-L	0	2 (9.1)	4 (22.2)	0	1 (8.3)	7 (10.3)
SD	0	5 (22.7)	0	0	0	5 (7.4)
PD	0	0	1 (5.6)	1 (6.7)	0	2 (2.9)
Discontinued prior to first assessment	0	0	0	3 (20.0)	0	3 (4.4)
ORR, n (%)[b]	1 (100)	17 (77.3)	**17 (94.4)**	11 (73.3)	12 (100)	**58 (85.3)**
Time to first response, median (range), months[c]	2.9 (2.9-2.9)	2.8 (2.0-6.2)	2.9 (2.6-8.3)	2.9 (2.6-19.4)	2.8 (2.7-13.8)	2.8 (2.0-19.4)
Time to best response, median (range), months	2.9 (2.9-2.9)	2.9 (2.0-11.1)	3.0 (2.6-13.8)	5.6 (2.6-19.4)	8.4 (2.7-13.8)	4.2 (2.0-19.4)
Duration of exposure, median (range), months	29.6 (29.6-29.6)	12.3 (3.4-25.4)	14.4 (2.9-30.3)	19.8 (0.2-28.5)	20.4 (6.8-27.1)	13.6 (0.2-30.3)

Data cutoff: August 22, 2025.
[a]Of 49 patients with PRs,16 achieved all nodes normalized. [b]Includes best overall response of PR-L or better. [c]In patients with a best overall response of PR-L or better.
CR=complete response, CRi=complete response with incomplete marrow recovery, ORR=overall response rate, PD=progressive disease, PR=partial response, PR-L=partial response with lymphocytosis, SD=stable disease.
Ahn IE, et al. Oral Presentation at ASH 2025;8349.

CaDAnCe-101

High Overall Response Rates in High-Risk Subgroups

R/R CLL/SLL

Characteristic, n/N with known status (%)	ORR
Prior cBTKi + BCL2i	41/44 (93.2)
Prior cBTKi + ncBTKi + BCL2i	9/12 (75.0)
6 or more prior lines of therapy	13/16 (81.3)
del(17p) and/or *TP53* mutation	37/46 (80.4)
Complex karyotype (≥3 abnormalities)	16/22 (72.7)
***BTK* mutations**	20/26 (76.9)
***PLCG2* mutations**	9/10 (90.0)

Data cutoff: August 22, 2025.
BCL2i=B-cell lymphoma 2 inhibitor, cBTKi=covalent Bruton tyrosine kinase inhibitor, ncBTKi=noncovalent Bruton tyrosine kinase inhibitor, ORR=overall response rate.
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Progression-Free Survival

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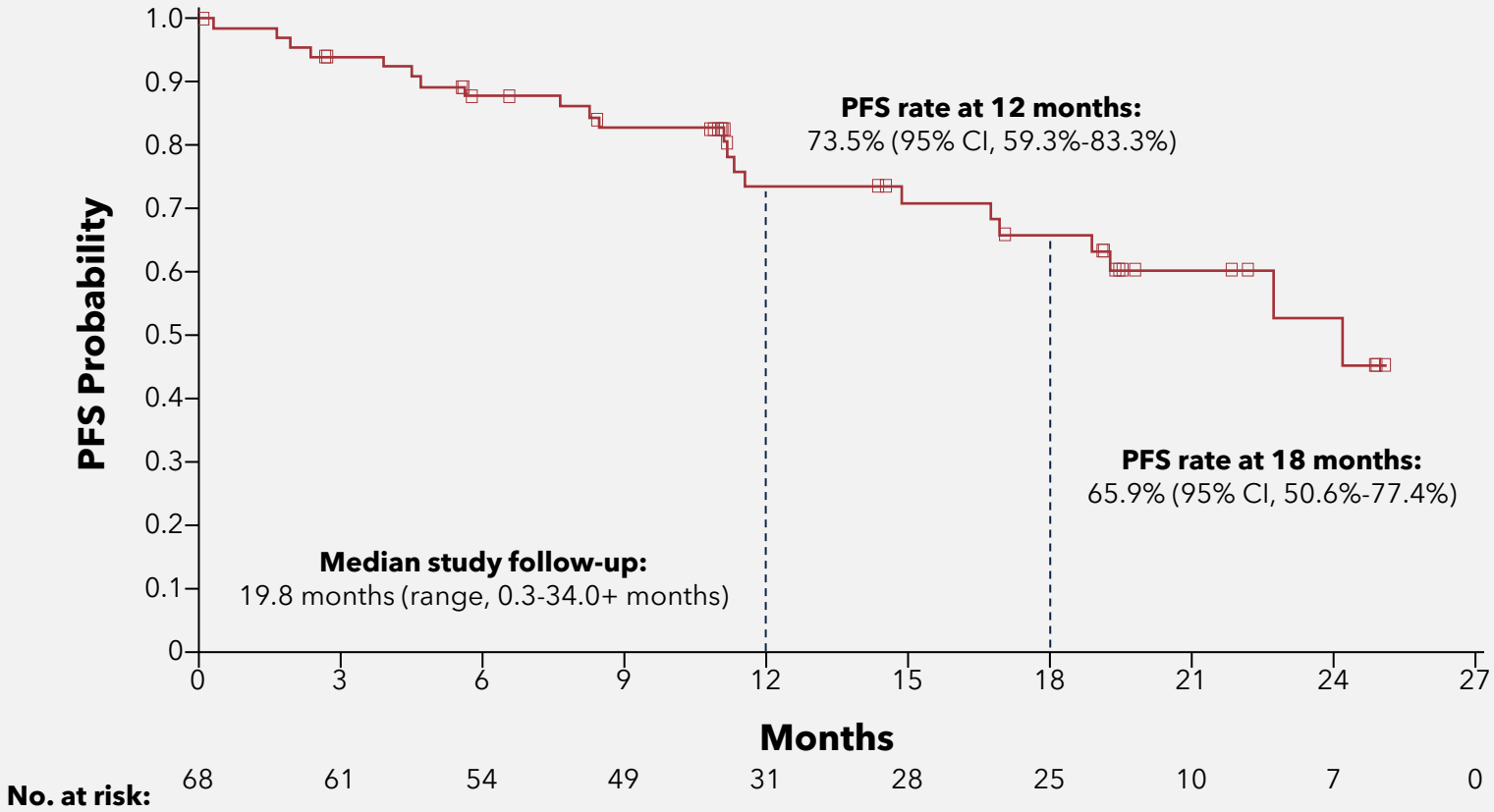

Data cutoff: August 22, 2025.
CI=confidence interval, PFS=progression-free survival.
Ahn IE, et al. Oral Presentation at ASH 2025;8349.

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Responses Occurred Regardless of Baseline Mutations

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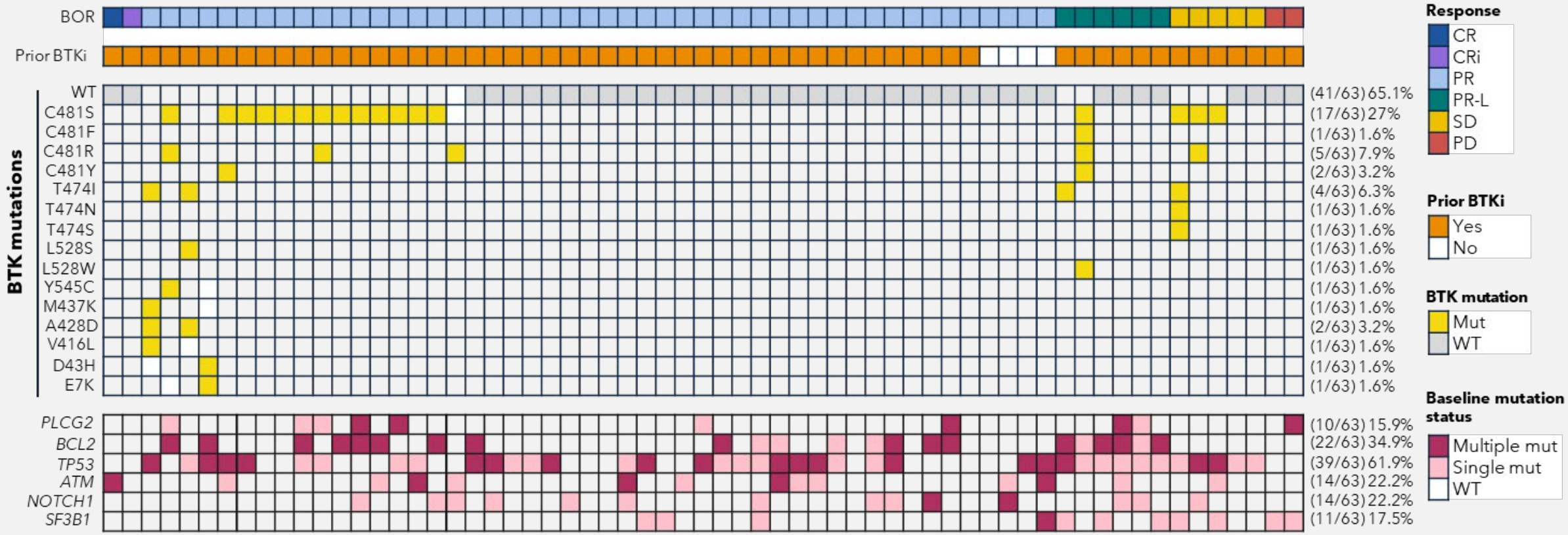
Best overall response vs baseline mutation[a]



Data cutoff: August 22, 2025.
[a]Genomic mutations were centrally assessed by targeted next-generation sequencing.
BTKi=Bruton tyrosine kinase inhibitor, BOR=best overall response, CR=complete response, CRi=complete response with incomplete marrow recovery, mut=mutation, PD=progressive disease, PR=partial response, PR-L=partial response with lymphocytosis, SD=stable disease, WT=wild type.
Ahn IE, et al. Oral Presentation at ASH 2025;8349.