CaDAnCe-101

R/R WM

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

BGB-16673-101 – CADANCE-101 (R/R WM)

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 (WM)

- Met IWWM-7 criteria for treatment
- ≥2 prior therapies, including anti-CD20 monoclonal antibody and covalent BTK inhibitor (US and EU only)
- 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. [b]Responses were assessed per IWWM-6, modified Owen 2013 criteria after 4 weeks. [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. Frustaci AM, et al. Oral Presentation at EHA 2025; S231.; 2. https://clinicaltrials.gov/study/NCT05006716?term=NCT05006716&rank=1. Accessed October 9, 2025.

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Baseline Patient Characteristics

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- Heavily pretreated with high rate of poor risk features

	Total (N=36)
Age, median (range), years	72.0 (49-81)
Male, n (%)	22 (61.1)
ECOG PS, n (%)	
0	17 (47.2)
1	17 (47.2)
2	2 (5.6)
Hemoglobin, median (range), g/L	102 (60-146)
Hemoglobin ≤110 g/L, n/N with known status (%)	25/34 (73.5)
Neutrophils, median (range), 10^9/L	2.6 (0.2-7.4)
Neutrophils ≤1.5×10^9/L, n/N with known status (%)	11/33 (33.3)
Platelets, median (range), 10^9/L	153.5 (14.0-455.0)
IgM, median (range), g/L	35.1 (0.3-92.6)

	Total (N=36)
Mutation status, n/N with known status (%)[a]	
MYD88 mutation present	31/35 (88.6)
CXCR4 mutation present	19/35 (54.3)
BTK mutation present	11/31 (35.5)
TP53 mutation present	16/31 (51.6)
No. of prior lines of therapy, median (range)	3 (1-11)
Prior therapy, n (%)	
cBTK inhibitor	36 (100)
Anti-CD20 antibody	36 (100)
Chemotherapy	34 (94.4)
Proteasome inhibitor	11 (30.6)
BCL2 inhibitor	9 (25.0)
ncBTK inhibitor[b]	7 (19.4)
Discontinued prior BTK inhibitor due to PD, n (%)	30 (83.3)

Data cutoff: March 3, 2025.
[a]Confirmed by central laboratory. [b]All seven patients with ncBTK inhibitor exposure were also exposed to a cBTK inhibitor.
BCL2=B-cell lymphoma 2, BTK=Bruton tyrosine kinase, cBTK=covalent BTK, ECOG PS=Eastern Cooperative Oncology Group performance status, IgM=immunoglobulin M, ncBTK=noncovalent BTK, PD=progressive disease, WM=Waldenström macroglobulinemia.
Frustaci AM, et al. Oral Presentation at EHA 2025; S231.

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

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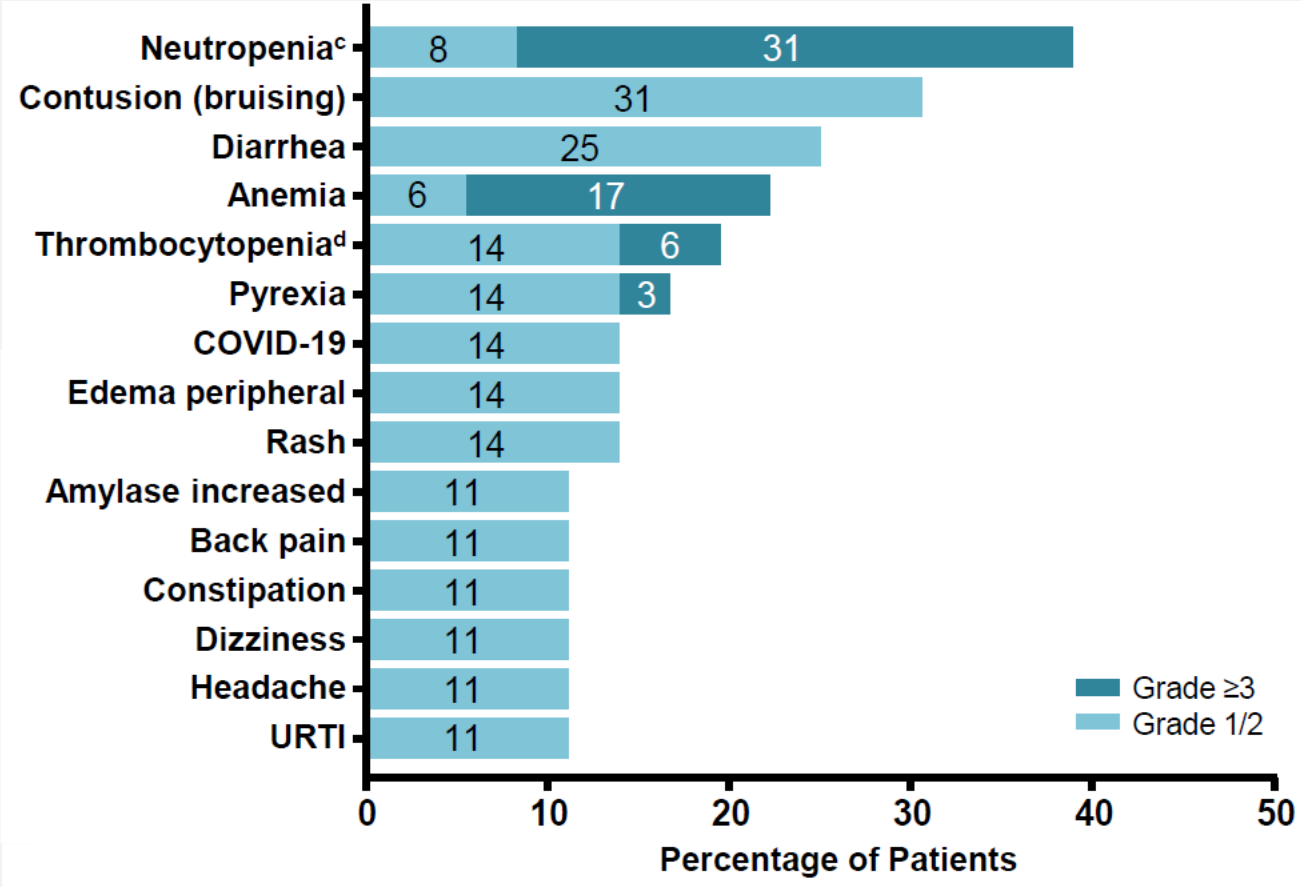
- Most common TEAEs were neutropenia in 39% and contusion (bruising) in 31% of patients
- No atrial fibrillation, major hemorrhage[a], febrile neutropenia, or pancreatitis

Patients, n (%)	Total (N=36)
Any TEAE	32 (88.9)
Any treatment-related	25 (69.4)
Grade ≥3	22 (61.1)
Treatment-related grade ≥3	14 (38.9)
Serious	12 (33.3)
Treatment-related serious	4 (11.1)
Leading to death[b]	1 (2.8)
Treatment-related leading to death	0
Leading to treatment discontinuation	2 (5.6)



Data cutoff: March 3, 2025. Median follow-up: 8.2 months (range, 0.6-30.6 months).
[a]Grade ≥3, serious, or any central nervous system bleeding. [b]Septic shock (200-mg dose level), note in the context of PD. [c]Neutropenia combines preferred terms neutrophil count decreased and neutropenia. [d]Thrombocytopenia combines preferred terms platelet count decreased and thrombocytopenia.
IgM=immunoglobulin M, PD=progressive disease, PR=partial response, TEAE=treatment-emergent adverse event, URTI=upper respiratory tract infection, WM=Waldenström macroglobulinemia.
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Overall Response Rate

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- High response rates across all risk groups
- Responses were observed at all dose levels and in patients with prior chemoimmunotherapy (25/30), cBTK inhibitor (27/32), or ncBTK inhibitor (4/4)

	Total (N=32)[a]
Best overall response, n (%)	
VGPR	10 (31.3)
PR	14 (43.8)
MR	3 (9.4)
SD	3 (9.4)
PD	1 (3.1)
Discontinued prior to first assessment	1 (3.1)
ORR, n (%)[b]	27 (84.4)
Major response rate, n (%)[c]	24 (75.0)
Time to first response, median (range), months[d]	1.0 (0.9-3.7)

Mutation status, n/N tested (%)	ORR (N=32)[a]
BTK	
Mutated	11/11 (100)
Unmutated	15/19 (78.9)
Unknown	1/2 (50.0)
MYD88	
Mutated	25/28 (89.3)
Unmutated	2/3 (66.7)
Unknown	0/1 (0)
CXCR4	
Mutated	16/17 (94.1)
Unmutated	11/14 (78.6)
Unknown	0/1 (0)
TP53	
Mutated	15/15 (100)
Unmutated	11/15 (73.3)
Unknown	1/2 (50.0)

Data cutoff: March 3, 2025.
[a]Efficacy-evaluable population; 4 patients were too early in treatment course to be response-evaluable. [b]Includes best overall response of MR or better. [c]Includes best overall response of PR or VGPR. [d]In patients with a best overall response better than SD.
BTK=Bruton tyrosine kinase, cBTK=covalent Bruton tyrosine kinase, MR=minor response, ncBTK=noncovalent Bruton tyrosine kinase, ORR=overall response rate, PD=progressive disease, PR=partial response, SD=stable disease, VGPR=very good partial response, WM=Waldenström macroglobulinemia.
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Cytopenia Improvement in Patients With Treatment Response

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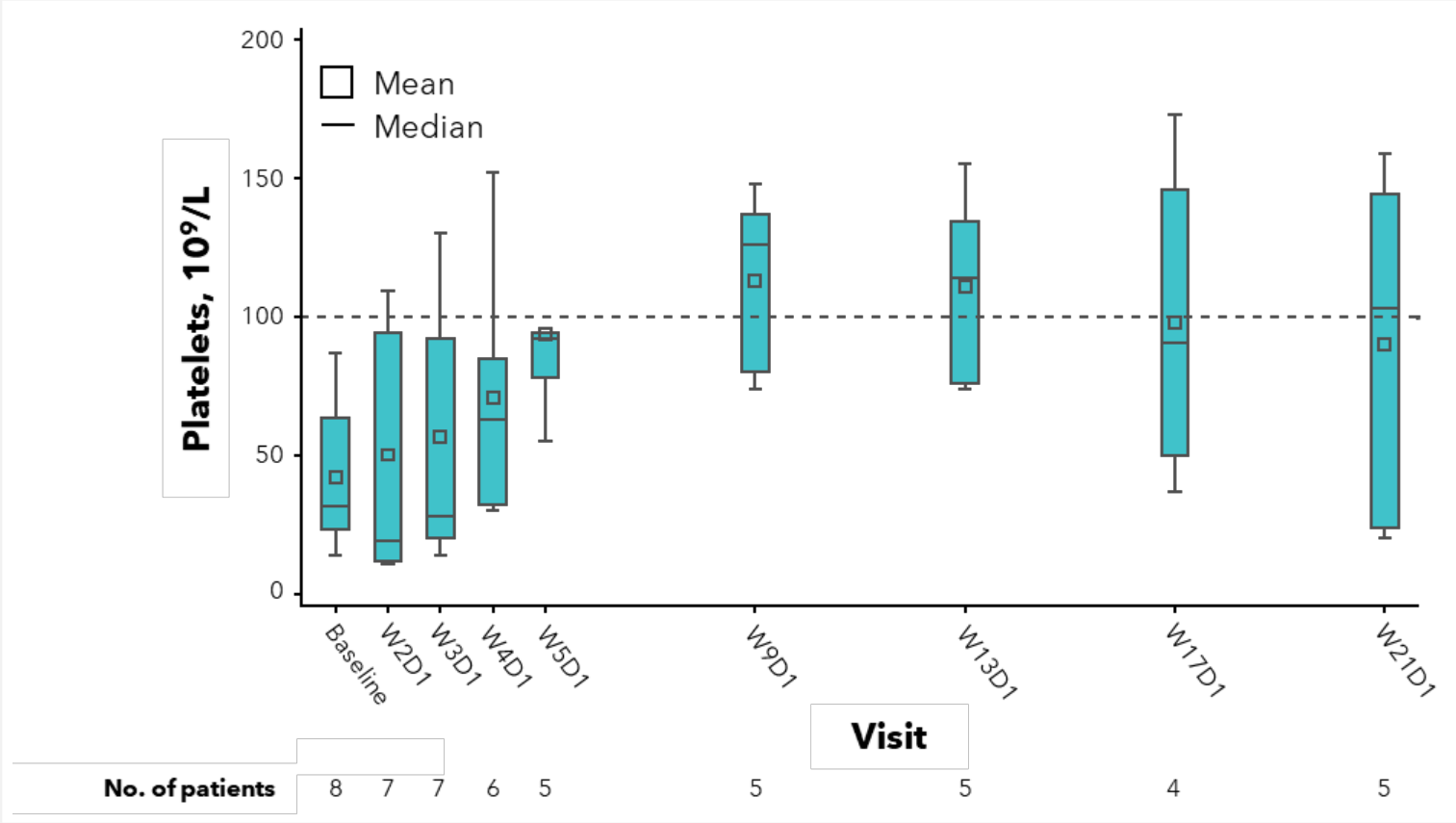
	Baseline	W9D1
Neutrophil count, median, 10^9/L	0.9	1.1
Hemoglobin level, median, g/L	98.0	114.0
Platelet count, median, 10^9/L	39.5	126.0

Platelet Count in Patients With WM Who Had Baseline Thrombocytopenia and Whose Disease Responded to Treatment



Data cutoff: March 3, 2025.
D=day, W=week, WM=Waldenström macroglobulinemia.
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IgM Decreased in All Patients

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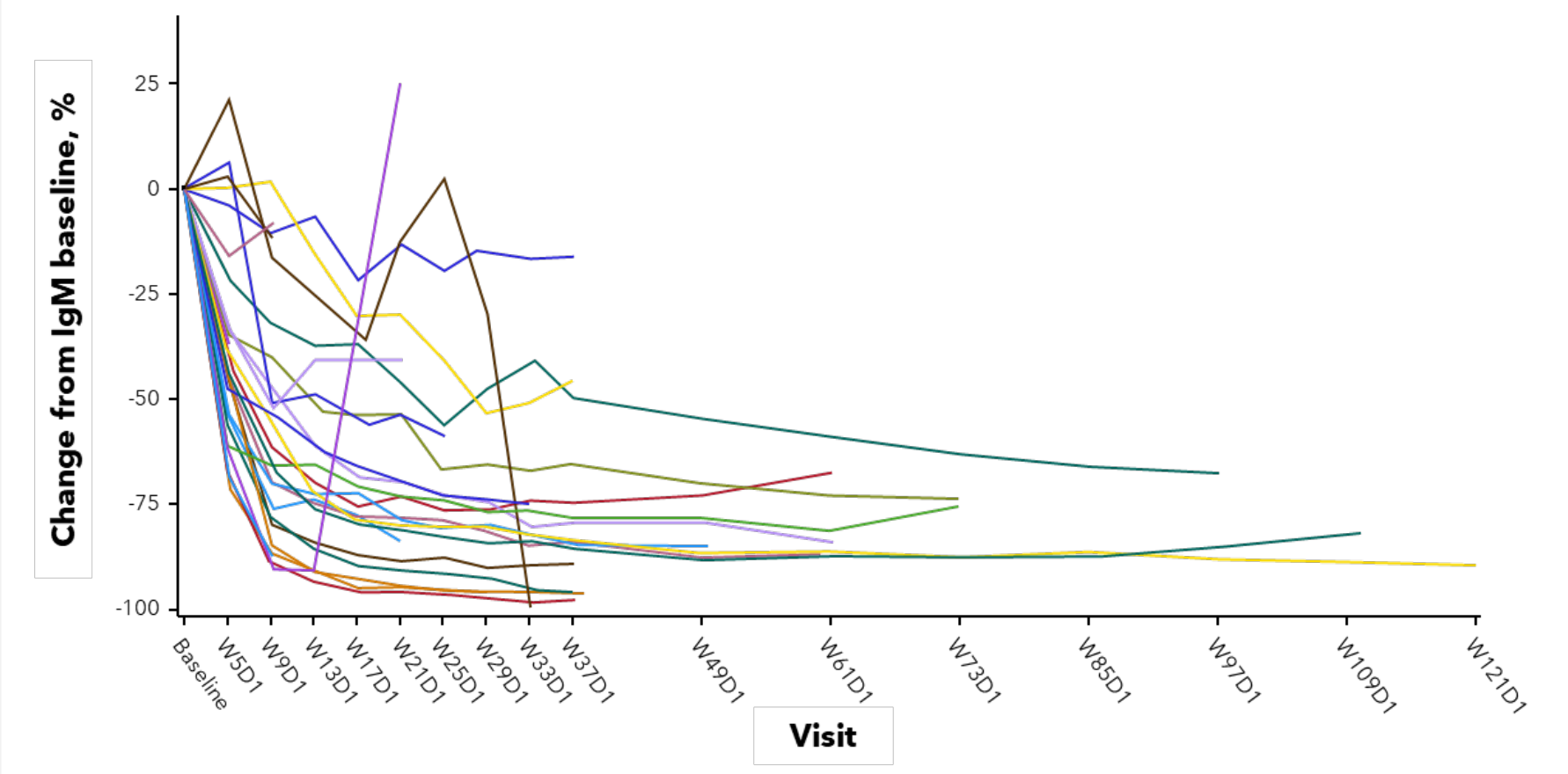
- Rapid and sustained decrease in IgM in most patients



Data cutoff: March 3, 2025.
Patient with rapid IgM increase had BTK, MYD88, CXCR4, and TP53 mutations at baseline, paused treatment for 2-3 weeks due to COVID-19 infection, and developed rapid progression shortly after restarting treatment.
D=day, IgM=immunoglobulin M, W=week, WM=Waldenström macroglobulinemia.
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Median PFS Was Not Reached

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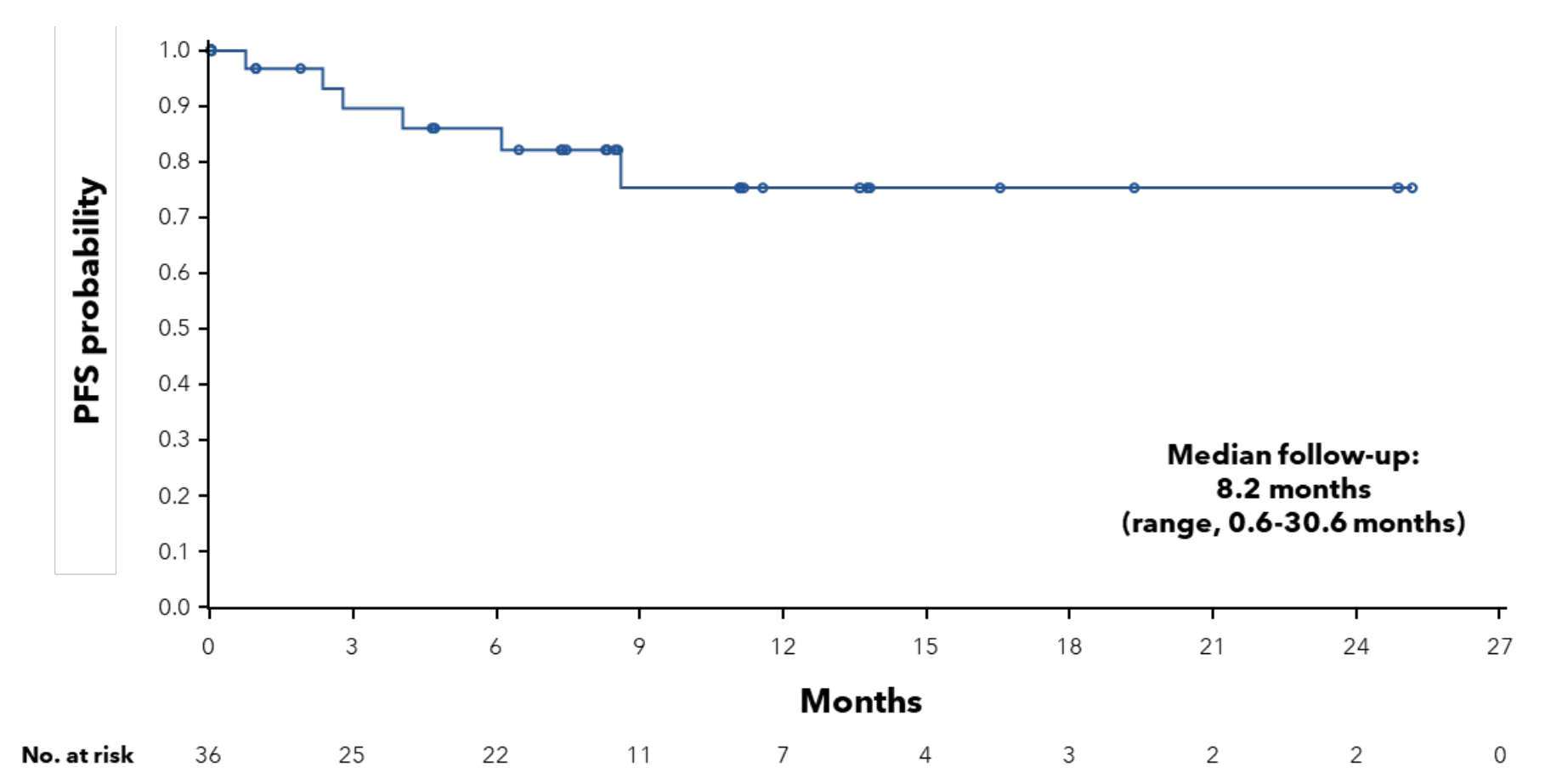

Data cutoff: March 3, 2025.
PFS=progression-free survival, WM=Waldenström macroglobulinemia.
Frustaci AM, et al. Oral Presentation at EHA 2025; S231.

Responses Occurred Regardless of Baseline Mutations
(Best Overall Response vs Baseline Mutation)[a]

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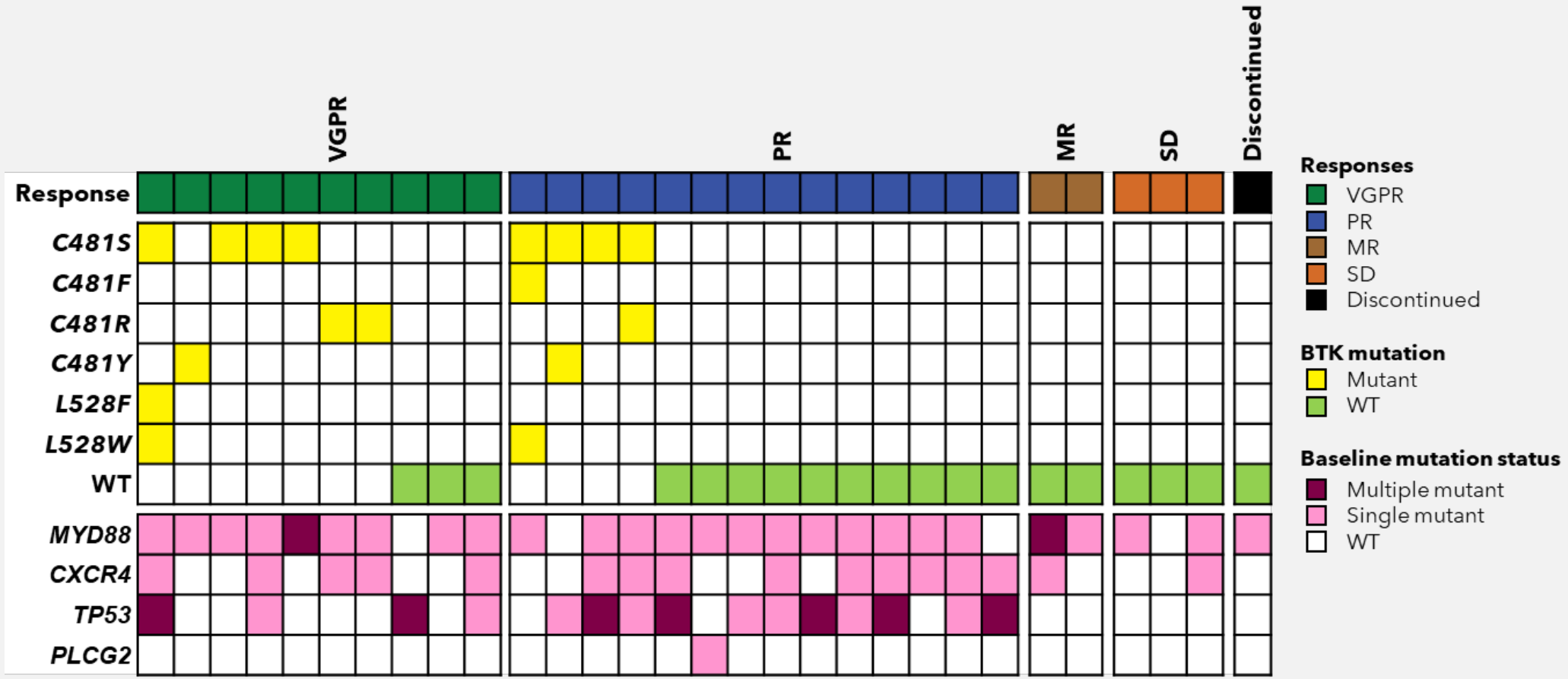

Data cutoff: March 3, 2025.
[a]Genomic mutations were centrally assessed by targeted next-generation sequencing.
BTKi=Bruton tyrosine kinase inhibitor, MR=minor response, NE=not evaluable, PR=partial response, SD=stable disease, VGPR=very good partial response, WM=Waldenström macroglobulinemia, WT=wild type.
Frustaci AM, et al. Oral Presentation at EHA 2025; S231.