BG-68501

CDK2 Inhibitor

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BG-68501-101 Trial Design

Phase 1

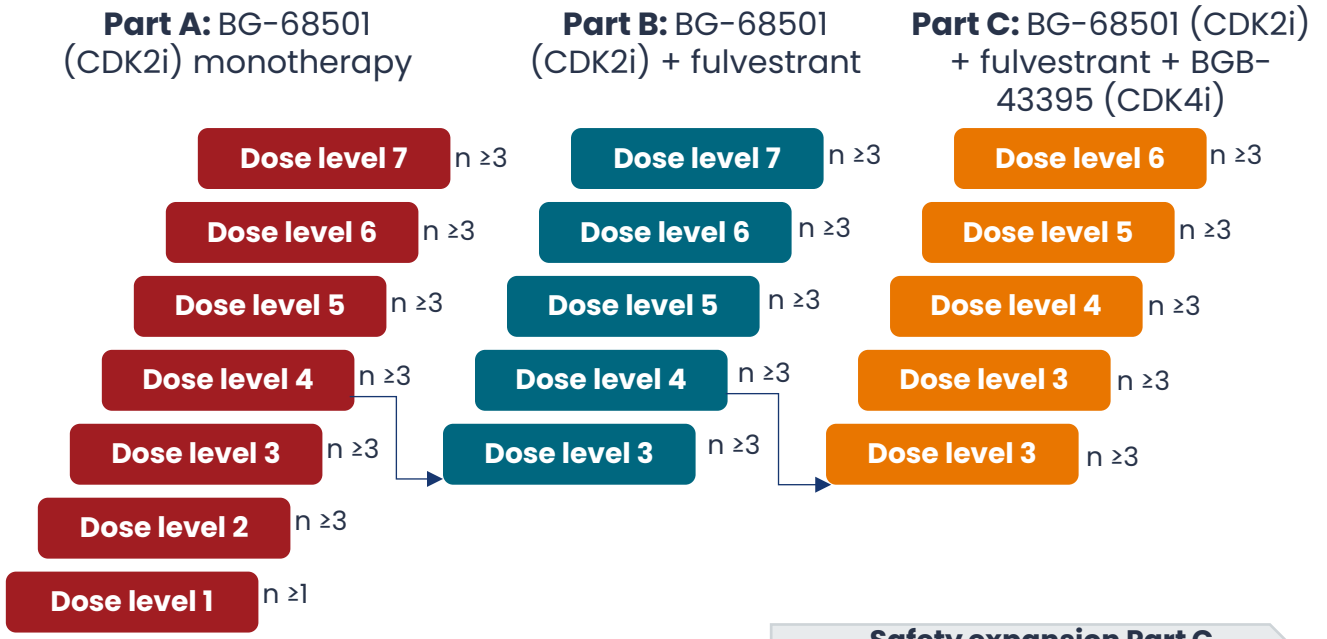
Study Identifier:
BG-68501-101, NCT06257264

Primary Endpoints: Phase 1a: Safety, MTD and MAD, RDFE; Phase 1b: ORR
Secondary Endpoints: Phase 1a: ORR, DoR, TTR, DCR, CBR, PK; Phase 1b: DoR, TTR, DCR, CBR, PK, safety

Key eligibility criteria

- ≥18 years
- Advanced or metastatic solid tumors potentially associated with CDK2 dependency
- Prior available SOC systemic therapies
- GnRH agonists for ovarian function suppression (unless menopausal)
- GnRH agonists for males treated with fulvestrant
- ECOG PS ≤1
- Measurable disease per RECIST v1.1
- No uncontrolled/untreated brain metastases
- No prior therapy selectively targeting CDK2

Part 1 (Phase 1a): Dose escalation + safety expansion



Safety expansion Part A
SE PROC[a]: BG-68501 (CDK2i) mono
(2-3 dose levels)

Safety expansion Part C
SE BC: BG-68501 (CDK2i) + BGB-43395 (CDK4i) + fulvestrant for 2L+ HR+/HER2-
(2-3 dose levels)

Part 2 (Phase 1b): Dose expansion

Cohort A:
CDK4/6i progressed HR+/HER2– metastatic BC
BG-68501 (CDK2i) + fulvestrant + BGB-43395 (CDK4i)

Cohort B:
BG-68501 (CDK2i) monotherapy in PROC[a,b]

Inclusion criteria for the Safety Expansion Parts A and C matches inclusion criteria for the equivalent Phase 1b dose expansion cohorts. [a]Including fallopian tube or primary peritoneal cancer. [b]Patients may be selected based on cyclin E1 expression; cut-off to be determined.
2L+=second-line or greater, CBR=clinical benefit rate, DCR=disease control rate, DoR=duration of response, ET=endocrine therapy, MAD=maximum administered dose, MTD=maximum tolerated dose, ORR=objective response rate, OS=overall survival, PFS=progression-free survival, PK=pharmacokinetics, PROC=platinum-refractory or resistant serous ovarian cancer, RDFE=recommended dose for expansion, RECIST=response evaluation criteria in solid tumors, SE=safety expansion, TTR=time to response.
Barve M, et al. Poster Presentation at SABCS 2024; P4-08-20.

Baseline Characteristics and Patient Disposition (Safety Analysis Set)

- A total of 57 patients were enrolled
- This was a heavily pretreated cohort of patients with a median (range) of 4.0 (0-15) prior lines of therapy
  - Out of 19 patients with HR+/HER2– BC, all were previously treated with CDK4/6 inhibitors and endocrine therapy, 73.7% with chemotherapy, and 26.3% with antibody-drug conjugates, whereas out of 16 patients with ovarian cancer, 31.3% had received a PARP inhibitor and 43.8% a VEGF inhibitor
- Of the 13 patients with available local CCNE1 amplification status, 8 patients had CCNE1 amplification
- To date, 6 dose levels of BG-68501 monotherapy and 2 dose levels in combination with fulvestrant have been assessed
- The median (range) duration of exposure was 1.7 (0.2-8.3) months
- Median (range) study follow-up was 2.9 (0.3-11.3) months

	Part A BG-68501 monotherapy n=49	Part B BG-68501 + fulvestrant n=8	Total N=57
Median (range) age, years	63.0 (32.0-86.0)	60.0 (54.0-73.0)	62.0 (32.0-86.0)
Sex, n (%)			
Female	40 (81.6)	8 (100.0)	48 (84.2)
Male	9 (18.4)	0	9 (15.8)
Race, n (%)			
Asian	17 (34.7)	0	17 (29.8)
White	30 (61.2)	8 (100.0)	38 (66.7)
Other	2 (4.1)	0	2 (3.5)
Ethnicity, n (%)			
Hispanic or Latino	1 (2.0)	1 (12.5)	2 (3.5)
Not Hispanic or Latino	48 (98.0)	7 (87.5)	55 (96.5)
ECOG PS, n (%)			
0	18 (36.7)	5 (62.5)	23 (40.4)
1	31 (63.3)	3 (37.5)	34 (59.6)
Tumor type, n (%)			
HR+/HER2- BC	11 (22.4)	8 (100.0)	19 (33.3)
Endometrial	8 (16.3)	0	8 (14.0)
Ovarian[a]	16 (32.7)	0	16 (28.1)
Other[b]	14 (28.6)	0	14 (24.5)
Median (range) prior lines of therapy	4.0 (0-15)	3.0 (1-8)	4.0 (0-15)

Data cut-off: March 27, 2025.
[a]Ovarian cancer includes fallopian tube high-grade serous carcinoma (n=1), ovarian cancer besides PROC (n=3), and PROC (n=12). [b]Includes esophageal cancer (n=1), gastric cancer (n=1), small cell gallbladder cancer (n=2), prostate cancer (n=1), small cell lung cancer (n=4), triple-negative BC (n=5).
ECOG PS=Eastern Cooperative Oncology Group Performance Status, PROC=platinum refractory or resistant ovarian cancer.
Joshi R, et al. Poster Presentation at ASCO 2025;poster 430.

Overall Safety Summary (Safety Analysis Set)

- TEAEs occurred in 56 (98.2%) patients overall; Grade ≥3 TEAEs were reported for 16 patients (28.1%)
- Serious TEAEs occurred in 12 patients (21.1%)
  - Dyspnea and intestinal obstruction were the only serious TEAEs to occur in ≥2 patients
- TEAEs leading to treatment discontinuation:
  - At 25 mg BID, 1 patient experienced Grade 1/2 diarrhea, nausea, and vomiting, and the other experienced Grade ≥3 platelet count increased and hypercalcemia. The 200 mg BID patient experienced Grade 1/2 hyperhidrosis, and the 250 mg BID patient experienced Grade 1/2 blood potassium decrease and hyperphosphatemia, and Grade ≥3 cholangitis
- No DLTs were observed
- There were no TEAEs leading to death

	Part A BG-68501 monotherapy							Part B BG-68501 + fulvestrant			
	10 mg BID n=2	25 mg BID n=13	50 mg BID n=10	100 mg BID n=10	200 mg BID n=8	250 mg BID n=6	Subtotal n=49	50 mg BID n=4	100 mg BID n=4	Subtotal n=8	Total N=57
Patients with any TEAE, n (%)	2 (100.0)	13 (100.0)	10 (100.0)	10 (100.0)	8 (100.0)	5 (83.3)	48 (98.0)	4 (100.0)	4 (100.0)	8 (100.0)	56 (98.2)
Grade ≥3	1 (50.0)	6 (46.2)	2 (20.0)	2 (20.0)	2 (25.0)	3 (50.0)	16 (32.7)	0	0	0	16 (28.1)
Serious	1 (50.0)	4 (30.8)	2 (20.0)	2 (20.0)	1 (12.5)	2 (33.3)	12 (24.5)	0	0	0	12 (21.1)
Leading to treatment discontinuation	0	2 (15.4)	0	0	1 (12.5)	1 (16.7)	4 (8.2)	0	0	0	4 (7.0)
Patients with any treatment-related TEAE, n (%)	1 (50.0)	9 (69.2)	6 (60.0)	10 (100.0)	7 (87.5)	5 (83.3)	38 (77.6)	3 (75.0)	3 (75.0)	6 (75.0)	44 (77.2)
Grade ≥3	0	1 (7.7)	0	0	1 (12.5)	0	2 (4.1)[a]	0	0	0	2 (3.5)
Serious	0	0	0	0	0	0	0	0	0	0	
Leading to treatment discontinuation	0	1 (7.7)	0	0	0	0	1 (2.0)	0	0	0	1 (1.8)

Data cut-off: March 27, 2025.
[a]One Grade 3 anemia and one Grade 3 neutropenia. A TEAE is defined as an AE that had onset or increase in severity level date on or after the date of the first dose of study drug and up to 30 days after the last dose of study drug(s) or the initiation of new anti-cancer therapy, whichever is earlier. Treatment-related TEAEs include those events considered by the investigator to be related or with missing assessment of the causal relationship. AEs were classified based on MedDRA and were graded for severity using NCI-CTCAE v5.0.
BID=twice daily, DLT=dose-limiting toxicity, MedDRA=Medical Dictionary for Regulatory Activities, NCI-CTCAE v5.0=National Cancer Institute's Common Terminology Criteria for Adverse Events, version 5.0, TEAE=treatment-emergent adverse event.
Joshi R, et al. Poster Presentation at ASCO 2025;poster 430.

Most Common TEAEs in >10% of Total Patients (Safety Analysis Set)

- The most common TEAEs were vomiting (63.2%), nausea (61.4%), and fatigue (26.3%), none of which were Grade ≥3

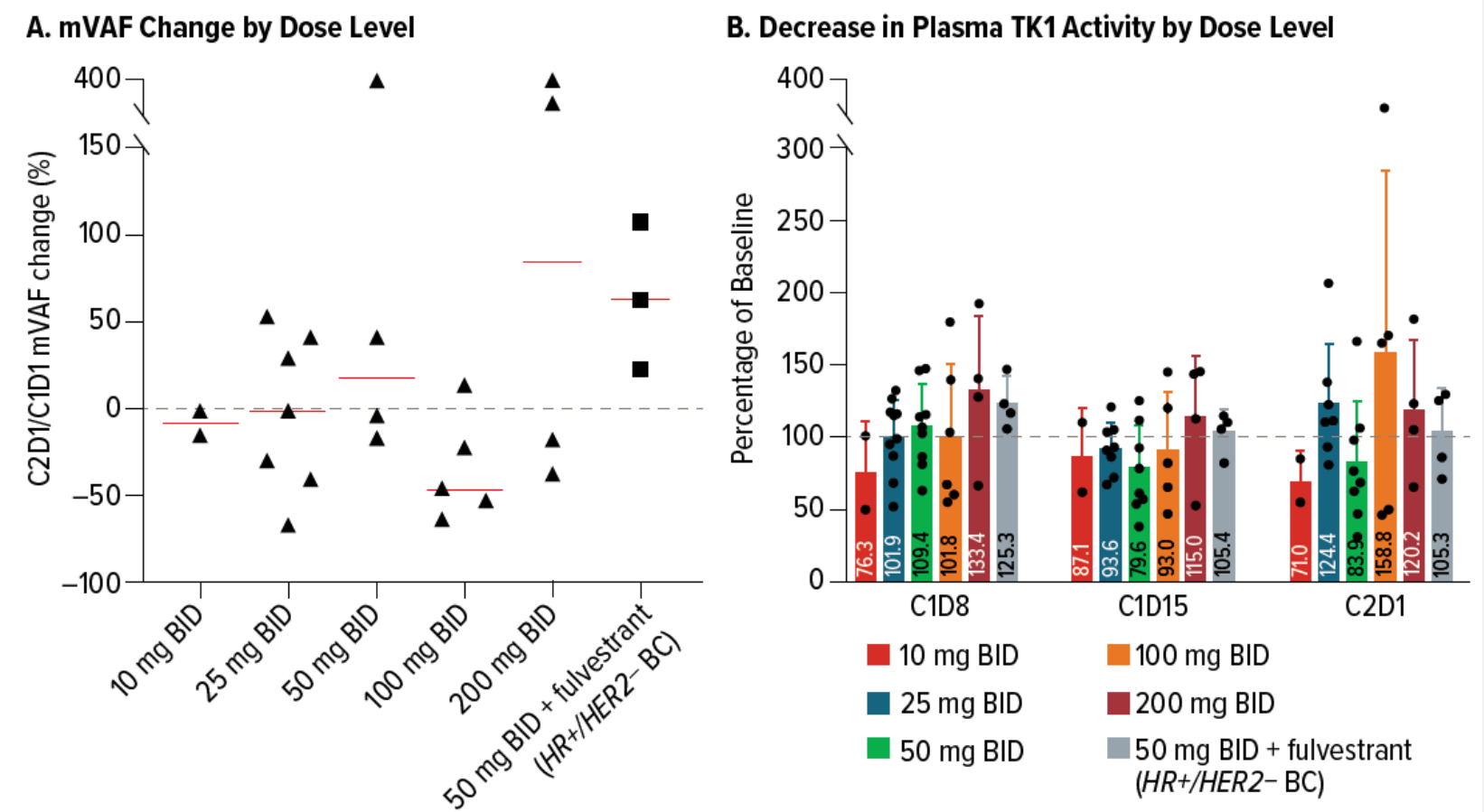
	Part A BG-68501 monotherapy							Part B BG-68501 + fulvestrant			
	10 mg BID n=2	25 mg BID n=13	50 mg BID n=10	100 mg BID n=10	200 mg BID n=8	250 mg BID n=6	Subtotal n=49	50 mg BID n=4	100 mg BID n=4	Subtotal n=8	Total N=57
Vomiting	1 (50.0)	6 (46.2)	3 (30.0)	9 (90.0)	6 (75.0)	5 (83.3)	30 (61.2)	2 (50.0)	4 (100.0)	6 (75.0)	36 (63.2)
Nausea	1 (50.0)	6 (46.2)	6 (60.0)	6 (60.0)	6 (75.0)	5 (83.3)	30 (61.2)	2 (50.0)	3 (75.0)	5 (62.5)	35 (61.4)
Fatigue	1 (50.0)	2 (15.4)	2 (20.0)	4 (40.0)	3 (37.5)	0	12 (24.5)	1 (25.0)	2 (50.0)	3 (37.5)	15 (26.3)
Anemia	0	4 (30.8)	4 (40.0)	0	1 (12.5)	2 (33.3)	11 (22.4)	0	0	0	11 (19.3)
Constipation	0	1 (7.7)	3 (30.0)	0	2 (25.0)	3 (50.0)	9 (18.4)	1 (25.0)	0	1 (12.5)	10 (17.5)
Diarrhea	1 (50.0)	1 (7.7)	1 (10.0)	1 (10.0)	1 (12.5)	0	5 (10.2)	0	2 (50.0)	2 (25.0)	7 (12.3)
Headache	0	1 (7.7)	0	2 (20.0)	2 (25.0)	0	5 (10.2)	0	1 (25.0)	1 (12.5)	6 (10.5)

Data cut-off: March 27, 2025.
Adverse events were classified based on MedDRA and graded for severity using NCI-CTCAE v5.0. Patients with multiple events for a given preferred term were counted once at the preferred term level.
BID=twice daily, MedDRA=Medical Dictionary for Regulatory Activities, NCI-CTCAE v5.0=National Cancer Institute's Common Terminology Criteria for Adverse Events, version 5.0, TEAE=treatment-emergent adverse event.
Joshi R, et al. Poster Presentation at ASCO 2025;poster 430.

Pharmacodynamics

BG-68501-101

- A decrease in circulating tumor DNA mean VAF was observed at 100 mg BID
- Moderate/minimal inhibition of TK1 activity in plasma was detected at all doses



Data cut-off: March 27, 2025.
Red horizontal lines denote the median.
BID=twice daily, C=cycle, D=day, TK1=thymidine kinase 1, VAF=variant allele frequency.
Joshi R, et al. Poster Presentation at ASCO 2025;poster 430.

Antitumor Activity

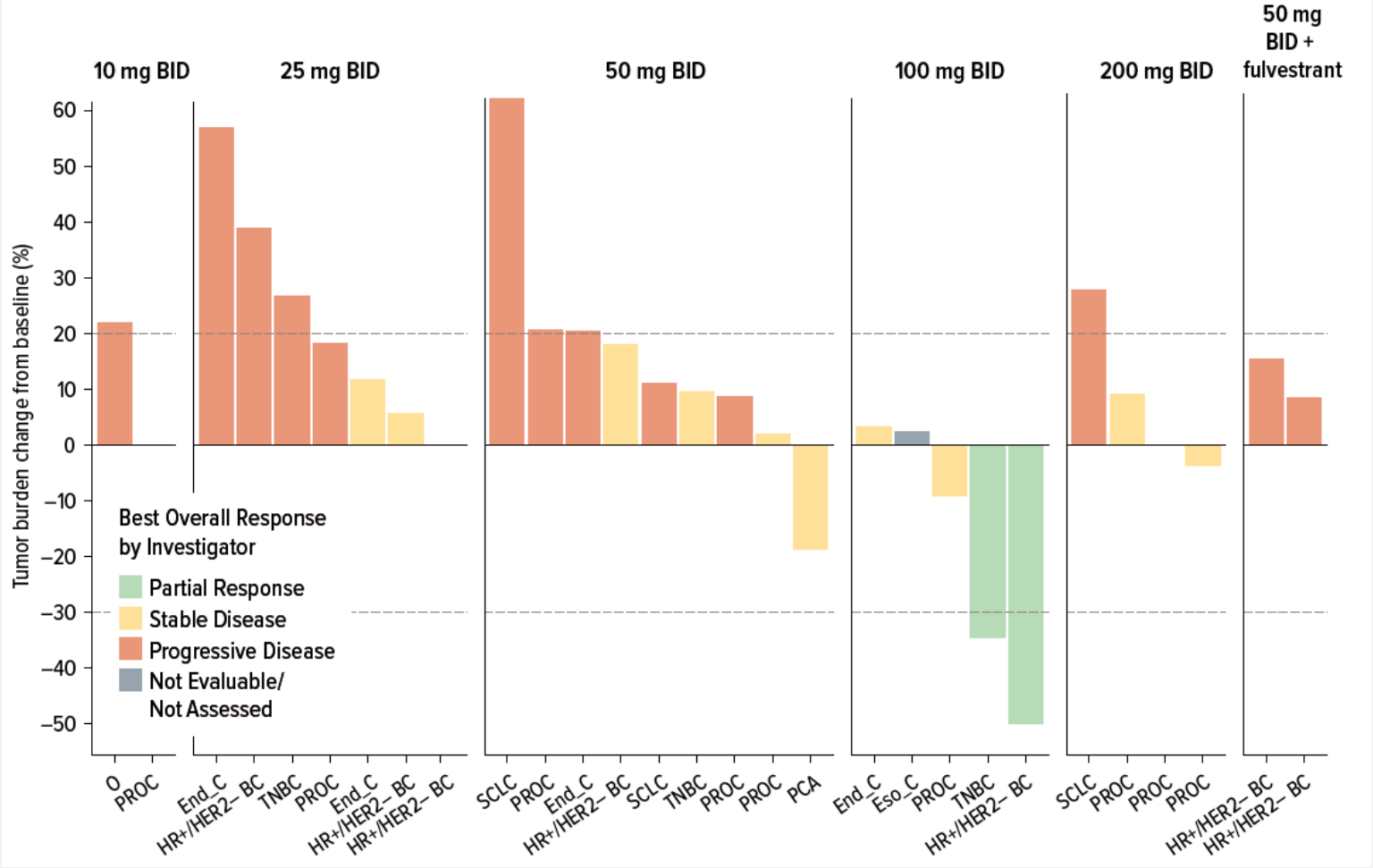
BG-68501-101

- Of the 37 efficacy-evaluable patients (all from Part A), 2 extensively pretreated patients with BC experienced unconfirmed PR, 15 patients had SD, 15 patients had PD, and 5 patients were not evaluable/not assessed
- Of the 2 patients with PR, 1 was ongoing at time of data cutoff and the other had discontinued treatment

	Part A BG-68501 monotherapy						Part B BG-68501 + fulvestrant	
	10 mg BID n=2	25 mg BID n=11	50 mg BID n=10	100 mg BID n=5	200 mg BID n=5	Subtotal n=49	50 mg BID n=4	Total N=37
ORR, n (%)	0	0	0	2 (40.0)	0	2 (6.1)	0	2 (5.4)
95% CI	0.0, 84.2	0.0, 28.5	0.0, 30.8	5.3, 85.3	0.0, 52.2	0.7, 20.2	0.0, 60.2	0.7, 18.2
BOR, n (%)								
PR	0	0	0	2 (40.0)	0	2 (6.1)	0	2 (5.4)
SD	1 (50.0)	3 (27.3)	4 (40.0)	2 (40.0)	3 (60.0)	13 (39.4)	2 (50.0)	15 (40.5)
PD	1 (50.0)	5 (45.5)	5 (50.0)	0	2 (40.0)	13 (39.4)	2 (50.0)	15 (40.5)
NE/NA	0	3 (27.3)	1 (10.0)	1 (20.0)	0	5 (15.2)	0	5 (13.5)
CBR, n (%)	1 (50.0)	0	0	2 (40.0)	0	3 (9.1)	0	3 (8.1)
95% CI	1.3, 98.7	0.0, 28.5	0.0, 30.8	5.3, 85.3	0.0, 52.2	1.9, 24.3	0.0, 60.2	1.7, 21.9
DCR, n (%)	1 (50.0)	3 (27.3)	4 (40.0)	4 (80.0)	3 (60.0)	15 (45.5)	2 (50.0)	17 (45.9)
95% CI	1.3, 98.7	6.0, 61.0	12.2, 73.8	28.4, 99.5	14.7, 94.7	28.1, 63.6	6.8, 93.2	29.5, 63.1

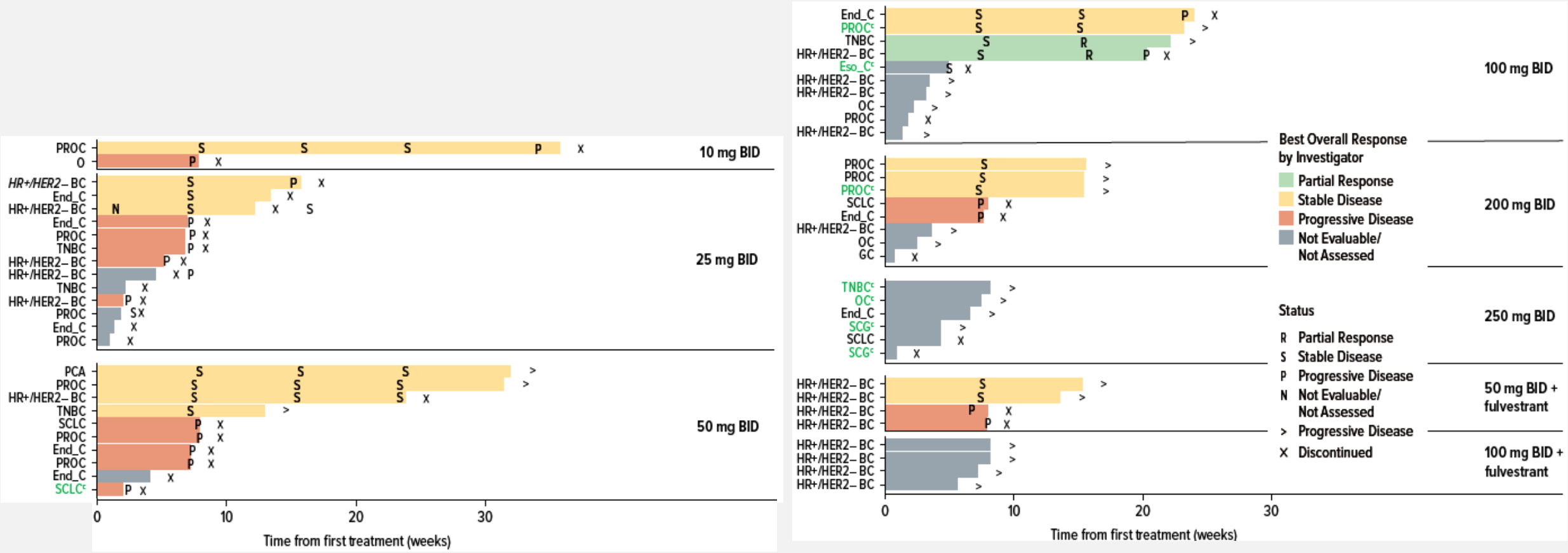
Data cut-off: March 27, 2025.
Responses are unconfirmed. The 95% CI was estimated using the Clopper–Pearson method. CBR was defined as the proportion of patients who have CR, PR, or durable SD of ≥24 weeks in duration. DCR was defined as the proportion of patients who have CR, PR, or SD.
BC=breast cancer, BOR=best overall response, CI=confidence interval, CR=complete response, PD=progressive disease, PR=partial response, SD=stable disease.
Joshi R, et al. Poster Presentation at ASCO 2025;poster 430.

Investigator-Assessed Best Change from Baseline in Target Lesion Sum of Diameters[a]



Data cut-off: March 27, 2025.
Response is unconfirmed. [a]This plot shows post-baseline tumor assessments excluding patients without target lesions up to the initiation of new anti-cancer therapy or the first PD in the efficacy-evaluable population.
BID=twice daily, End_C=endometrial cancer, Eso_C=esophageal cancer, GC=gastric cancer, O=other: fallopian tube high Grade serous, OC=ovarian cancer (besides PROC), PCA=prostate cancer, SCG=small cell gallbladder cancer, SCLC=small cell lung cancer, TNBC=triple-negative breast cancer.
Joshi R, et al. Poster Presentation at ASCO 2025;poster 430.

Duration of Treatment and Response per RECIST 1.1[b]



Data cut-off: March 27, 2025.
Response is unconfirmed. [b]Safety population; [c]Patients with confirmed CCNE1 amplification.
End_C=endometrial cancer, Eso_C=esophageal cancer, GC=gastric cancer, O=other: fallopian tube high Grade serous, OC=ovarian cancer (besides PROC), PCA=prostate cancer, SCG=small cell gallbladder cancer, SCLC=small cell lung cancer, TNBC=triple-negative breast cancer.
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