BGB-43395

CDK4 Inhibitor

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BGB-43395-101 Trial Design

Phase 1

Study Identifier:
BGB-43395-101, NCT06120283

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

Key eligibility criteria

- **Phase 1a:** Histologically or cytologically confirmed advanced, metastatic, or unresectable solid tumor with dependency on CDK4, including HR+ BC, NSCLC, and others
- **Phase 1a:** Received prior therapy (if available), and refractory to or intolerant to SoC
- **Phase 1b:** HR+/HER- BC and others; where CDK4/6 inhibitors are approved and available, must have received ≥1 line of therapy advanced disease including endocrine therapy and a CDK4/6 inhibitor
- ECOG PS ≤1
- Adequate end-organ function
- Females with HR+/HER2- BC must be postmenopausal or receiving ovarian function suppression treatment

Treatment

Phase 1a: Dose Escalation + Safety Expansion

Part A: BGB-43395 monotherapy in advanced solid tumors with CDK4 dependency

Dose Levels 1-8

Initiate combination dosing when Dose 3 is cleared

Part B: BGB-43395 + fulvestrant in 2L+ HR+/HER2- BC, OC, EC

Dose Levels 2-8

Part C: BGB-43395 + letrozole in 2L+ HR+/HER2- BC, OC, EC

Dose Levels 2-8

RDFE(s)

Phase 1b: Dose Expansion

Dose expansion 1:
BGB-43395 + fulvestrant
In 2L+ HR+/HER2- CDK4/6 inhibitor progressed BC

Dose expansion 2:
BGB-43395 + letrozole
In 1L HR+/HER2- CDK4/6 inhibitor naïve BC

Follow-up

Up to 60 months

BC=breast cancer, CBR=clinical benefit rate, CDK4/6=cyclin-dependent kinase 4/6, DCR=disease control rate, DoR=duration of response, ECOG PS=Eastern Cooperative Oncology Group performance status, HER=human epidermal growth factor receptor 2, HR=hormone receptor, IM=intramuscular, MTD=maximum tolerated dose, NSCLC=non-small cell lung cancer, ORR=objective response rate, PFS=progression-free survival, PK=pharmacokinetic, PO=orally, RP2D=recommended phase 2 dose, SoC=standard of care, TTR=time to response.

1. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT06120283. Accessed October 9, 2025. 2. Yap TA, et al. Poster Presentation at SABCS 2024; P4-10-20.

BGB-43395-101

Study Population

Characteristic	Part A All (n=33)	Part A BC[a] (n=6)	Part B (n=17)	Part C (n=15)	Total (N=65)
Median (range) age, years	59.0 (32.0–80.0)	53.0 (32.0–76.0)	60.0 (40.0–75.0)	54.0 (32.0–78.0)	58.0 (32.0–80.0)
Sex, n (%)					
Male	11 (33.3)	0	0	0	11 (16.9)
Female	22 (66.7)	6 (100.0)	17 (100.0)	15 (100.0)	54 (83.1)
Race, n (%)					
White	21 (63.6)	3 (50.0)	11 (64.7)	13 (86.7)	45 (69.2)
Asian	3 (9.1)	1 (16.7)	2 (11.8)	0	5 (7.7)
Tumor types, n (%)					
Breast	7 (21.2)	6 (100.0)	16 (94.1)	15 (100.0)	38 (58.5)
Colorectal	6 (18.2)	0	0	0	6 (9.2)
Liposarcoma	6 (18.2)	0	0	0	6 (9.2)
Ovarian	5 (15.2)	0	1 (5.9)	0	6 (9.2)
Other[b]	9 (27.3)	0	0	0	9 (13.8)
ECOG PS, n (%)					
0	13 (39.4)	4 (66.7)	6 (35.3)	8 (53.3)	27 (41.5)
1	20 (60.6)	2 (33.3)	11 (64.7)	7 (46.7)	38 (58.5)

Characteristic	Part A All (n=33)	Part A BC[a] (n=6)	Part B (n=17)	Part C (n=15)	Total (N=65)
Median (range) prior lines of therapy	4.0 (1–10)	3.5 (2–10)	5.0 (2–11)	6.0 (1–9)	5.0 (1–11)
CDK4/6i	7 (21.2)	6 (100.0)	16 (94.1)	15 (100.0)	38 (58.5)
ET	10 (30.3)	6 (100.0)	16 (94.1)	15 (100.0)	41 (63.1)
CT, including ADC	28 (84.8)	6 (100.0)	16 (94.1)	12 (80.0)	56 (86.2)
Immunotherapy	14 (42.4)	0	0	1 (6.7)	15 (23.1)
Other	21 (63.6)	4 (66.7)	8 (47.1)	10 (66.7)	39 (60.0)
Metastatic disease, n (%)	30 (90.9)	6 (100.0)	17 (100.0)	15 (100.0)	62 (95.4)
Median (range) time from initial diagnosis to first dose, years	4.8 (0.2–25.1)	9.0 (3.2–25.1)	5.4 (0.9–28.7)	9.3 (3.8–32.4)	6.3 (0.2–32.4)
Countries, n (%)					
Australia	9 (27.3)	5 (83.3)	8 (47.1)	4 (26.7)	21 (32.3)
France	5 (15.2)	0	3 (17.6)	5 (33.3)	13 (20.0)
United States	19 (57.6)	1 (16.7)	6 (35.3)	6 (40.0)	31 (47.7)

Data cutoff: September 23, 2024. [a]The BC cohort for Part A includes patients with HR+/HER2- BC only. [b]Includes melanoma (n=1), endometrial cancer (n=3), peritoneal carcinoma (n=1), prostate cancer (n=3) and thymic carcinoma (n=1).
ADC=antibody-drug conjugate, BC=breast cancer, CDK=cyclin-dependent kinase , CT=chemotherapy, ECOG PS= Eastern Cooperative Oncology Group Performance Status, ET=endocrine therapy, HER2=human epidermal growth factor receptor 2, HR=hormone receptor.
Yap TA, et al. Poster Presentation at SABCS 2024; P4-10-20.

Safety Summary

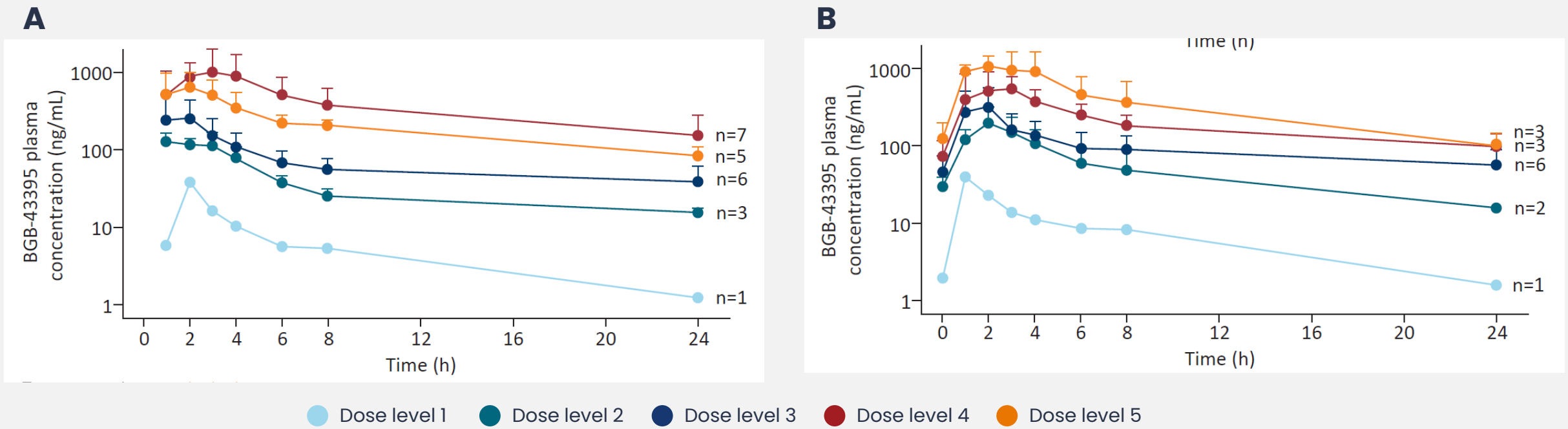
Characteristic, n (%)	Part A All (n=33)	Part A BC (n=6)	Part B (n=17)	Part C (n=15)	Total (N=65)
Any TEAE	33 (100.0)	6 (100.0)	15 (88.2)	13 (86.7)	61 (93.8)
Grade ≥3 TEAEs	10 (30.3)	2 (33.3)	4 (23.5)	1 (6.7)	15 (23.1)
Treatment-related TEAE	31 (93.9)	6 (100.0)	14 (82.4)	12 (80.0)	57 (87.7)
Grade ≥3 treatment-related TEAEs	9 (27.3)	1 (16.7)	1 (5.9)	0	10 (15.4)
Any TESAEs	3 (9.1)	1 (16.7)	2 (11.8)	1 (6.7)	6 (9.2)
Fatal TESAEs	1 (3.0)[a]	0	0	0	1 (1.5)
Leading to study treatment discontinuation	2 (6.1)	2 (6.1)	0	1 (6.7)	3 (4.6)
TEAEs in >10% of patients, n (%)					
Diarrhea	24 (72.7)	2 (33.3)	9 (52.9)	9 (60.0)	42 (64.6)
Grade ≥3	2 (6.1)	0	0	0	2 (3.1)
Nausea	18 (54.5)	3 (50.0)	4 (23.5)	5 (33.3)	27 (41.5)
Grade ≥3	1 (3.0)	0	0	0	1 (1.5)
Vomiting	9 (27.3)	0	2 (11.8)	1 (6.7)	12 (18.5)
Grade ≥3	1 (3.0)	0	0	0	1 (1.5)
Neutrophil count decreased	4 (12.1)	1 (16.7)	5 (29.4)	1 (6.7)	10 (15.4)
Grade ≥3	2 (6.1)	0	0	0	2 (3.1)
Decreased appetite	6 (18.2)	0	1 (5.9)	1 (6.7)	8 (12.3)
Grade ≥3	0	0	0	0	0
Fatigue	4 (12.1)	2 (33.3)	2 (11.8)	2 (13.3)	8 (12.3)
Grade ≥3	0	0	0	0	0

Data cutoff: September 23, 2024.
AEs per NCI-CTCAE v5.0 by type, frequency, severity, timing, seriousness and relationship to drug. [a]One patient had treatment-emergent sepsis (not treatment-related) which led to death.
AE=adverse event, BC=breast cancer, CDK=cyclin-dependent kinase , HER2=human epidermal growth factor receptor 2, HR=hormone receptor, NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events, TEAE=treatment-emergent adverse event, TESAE=treatment-emergent serious adverse event.
Yap TA, et al. Poster Presentation at SABCS 2024; P4-10-20.

Pharmacokinetics

- BGB-43395 was rapidly absorbed after oral administration with median T_{max} occurring ~after 2 hours; limited accumulation was observed with repeated dosing (Figure)
- BGB-43395 exposures increased approximately dose proportionately in the available dose range

Single Dose (A) and Repeated Dose (B) PK of BGB-43395 Monotherapy



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