P1-19-17

DOSE ESCALATION AND EXPANSION STUDY OF LEROCICLIB (G1T38), AN ORAL CDK4/6 INHIBITOR, DOSED WITH NO DRUG HOLIDAY IN COMBINATION WITH FULVESTRANT IN PATIENTS WITH HR+/HER2- ADVANCED BREAST CANCER

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BACKGROUND

- Endocrine therapy is the preferred treatment for patients with hormone receptor-positive (HR+) human epidermal growth factor receptor 2-negative (HER2-) advanced or metastatic breast cancer; endocrine resistance remains a serious challenge in the clinic[1,2]
- Cyclin-dependent kinase 4/6 (CDK4/6) inhibitors in combination with fulvestrant represent an established treatment for HR+/HER2- advanced or metastatic breast cancer and have demonstrated significant improvements in progression-free survival (PFS) and overall survival (OS)[3-5]
  - Two of three approved CDK4/6 inhibitors induce dose-limiting neutropenia requiring a drug holiday, potentially limiting efficacy[6]
  - The third approved CDK4/6 inhibitor is administered continuously but is limited by gastrointestinal toxicity[6]
  - There is a significant clinical need for a well-tolerated, continuously dosed oral CDK4/6 inhibitor
- Lerociclib (G1T38) is a potent and selective oral CDK4/6 inhibitor that has consistently demonstrated efficacy in several preclinical models of HR+ breast cancer[7]
- Preliminary results of this phase 1b/2 study demonstrated that continuous dosing of lerociclib with fulvestrant was generally well tolerated and showed early evidence of antitumor activity[8]
- Here, we present updated data as of October 7, 2019, from this ongoing phase 1b/2 study of continuous lerociclib dosing with fulvestrant; results are presented by dose group combined from part 1 and part 2

STUDY OBJECTIVES

Primary Objectives:

- Evaluate the safety, tolerability, and dose-limiting toxicities (DLTs) of lerociclib administered with fulvestrant
- Determine the recommended phase 2 dose (RP2D) and schedule (once daily [QD] or twice daily [BID]) of lerociclib administered continuously with fulvestrant

Secondary Objectives:

- Determine the pharmacokinetic (PK) parameters of lerociclib when administered with fulvestrant
- Assess fulvestrant and goserelin day 15 plasma concentrations when administered with lerociclib
- Assess response rate, clinical benefit rate, PFS, and OS

Key Exploratory Objectives:

- Assess archival tumor tissue for predictors of response/resistance to lerociclib
- Assess correlation between changes in cell-free DNA (cfDNA) with efficacy measures
- Assess the relationships between PK parameters and efficacy parameters

METHODS

Study Design

- Part 1: open-label, 3 + 3, parallel-dose escalation of lerociclib 200 mg–850 mg QD and 100 mg–425 mg BID administered continuously (NCT02983071; EudraCT number 2016-001485-29)
- Part 2: open-label expansion at lerociclib doses of 400 mg QD, 500 mg QD, 150 mg BID, and 200 mg BID administered continuously
- Fulvestrant 500 mg on days 1, 15, and 29, then once monthly as per standard of care
- Pre or perimenopausal patients also received goserelin as per local standard of care for the duration of study treatment. A luteinizing hormone-releasing hormone agonist must have started ≥ 28 days before the first dose of lerociclib

Key Inclusion Criteria

- Locally advanced or metastatic HR+/HER2- breast cancer
- Women of any menopausal status ≥ 18 years old
- Progressed during or within 12 months after adjuvant therapy or progressed during or within 2 months after endocrine therapy for advanced or metastatic disease
- Part 1: ≤ 2 chemotherapy regimens in the advanced/metastatic setting
- Part 2: ≤ 1 chemotherapy regimen in the advanced/metastatic setting
- Eastern Cooperative Oncology Group performance status 0–1

Key Exclusion Criteria

- Parts 1 and 2: prior treatment with fulvestrant
- Part 2: prior treatment with a CDK4/6 inhibitor
- Known active uncontrolled or symptomatic central nervous system metastases

Pharmacokinetics Analysis

- Part 1: Blood samples for lerociclib analysis were collected predose and 1, 2, 3, 4, 6, 8, 10, 12, and 24 hours postdose
- PK parameters (including time to maximum concentration [T_{max}], maximum concentration [C_{max}], and area under the curve over 24 hours [AUC_{0-24h}]) were determined by noncompartmental analysis (Phoenix® software)

Pharmacodynamic Analysis

- To evaluate mutational changes in cfDNA, peripheral blood samples were drawn at baseline, week 3 day 1 (cycle 1 day 15), and each time point when tumor assessments were performed during the treatment period. If a scan was obtained at the posttreatment follow-up visit, a blood sample for cfDNA was requested. Samples were processed and analyzed at Guardant Health, Inc. and Fios Genomics

RESULTS

Patient Demographics, Baseline Characteristics, Disposition, and Lerociclib Exposure

- As of October 7, 2019, 110 patients have been treated (46 in part 1 and 64 in part 2); 59 (53.6%) remain on lerociclib treatment
- 48 patients (43.6%) discontinued lerociclib treatment due to progressive disease, 2 (1.8%) withdrew by choice, and 1 (0.9%) due to an adverse event (AE)
- Median (range) duration of lerociclib exposure was 6.0 (1.0–31.0) months
- Patient demographics and baseline characteristics are summarized in **Table 1**

Table 1. Patient Demographics and Baseline Characteristics

	QD					BID				Total
	200 mg (n = 6)	300 mg (n = 3)	400 mg (n = 15)	500 mg (n = 30)	650 mg (n = 6)	100 mg (n = 6)	150 mg (n = 20)	200 mg (n = 21)	250 mg (n = 3)	All doses (N = 110)
Median age, years (range)	57.5 (44–69)	46.0 (45–72)	56.0 (50–68)	57.0 (25–85)	62.5 (56–65)	60.5 (47–67)	55.0 (33–84)	55.0 (34–78)	54.0 (34–57)	56.0 (25–85)
Race, n (%)										
Black/African American	0	0	0	0	0	1 (16.7)	0	1 (4.8)	0	2 (1.8)
White	6 (100)	3 (100)	14 (93.3)	26 (86.7)	6 (100)	5 (83.3)	20 (100)	20 (95.2)	3 (100)	103 (93.6)
NR	0	0	1 (6.7)	4 (13.3)	0	0	0	0	0	5 (4.5)
ECOG PS, n (%)										
0	4 (66.7)	1 (33.3)	13 (86.7)	21 (70.0)	5 (83.3)	5 (83.3)	17 (85.0)	17 (81.0)	3 (100)	86 (78.2)
1	2 (33.3)	2 (66.7)	2 (13.3)	9 (30.0)	1 (16.7)	1 (16.7)	3 (15.0)	4 (19.0)	0	24 (21.8)
Menopausal status, n (%)										
Postmenopausal	5 (83.3)	3 (100)	13 (86.7)	22 (73.3)	6 (100)	5 (83.3)	14 (70.0)	15 (71.4)	3 (100)	86 (78.2)
Pre/perimenopausal	1 (16.7)	0	2 (13.3)	8 (26.6)	0	1 (16.7)	6 (30.0)	6 (28.6)	0	24 (21.8)
Median (range) number of prior lines of therapy for advanced disease	2 (0–2)	1 (0–2)	1 (0–3)	1 (0–4)	3 (0–6)	1 (0–3)	1 (0–5)	1 (0–6)	0 (0–1)	1 (0–6)
Number of prior lines of therapy for advanced disease, n (%)										
0	1 (16.7)	1 (33.3)	5 (33.3)	6 (20.0)	1 (16.7)	3 (50.0)	7 (35.0)	9 (42.9)	2 (66.7)	35 (31.8)
1	1 (16.7)	1 (33.3)	3 (20.0)	12 (40.0)	0	0	5 (25.0)	2 (9.5)	1 (33.3)	25 (22.7)
2	4 (66.7)	1 (33.3)	4 (26.7)	7 (23.3)	0	2 (33.3)	4 (20.0)	7 (33.3)	0	29 (26.4)
3	0	0	3 (20.0)	4 (13.3)	3 (50.0)	1 (16.7)	2 (10.0)	2 (9.5)	0	15 (13.6)
≥4	0	0	0	1 (3.3)	2 (33.3)	0	2 (10.0)	1 (4.8)	0	6 (5.5)
Prior anticancer therapy for advanced disease, n (%)	5 (83.3)	2 (66.7)	10 (66.7)	24 (80.0)	5 (83.3)	3 (50.0)	13 (65.0)	12 (57.1)	1 (33.3)	75 (68.2)
Chemotherapy	2 (33.3)	1 (33.3)	4 (26.7)	13 (43.3)	5 (83.3)	3 (50.0)	10 (50.0)	6 (28.6)	1 (33.3)	45 (40.9)
Endocrine therapy	5 (83.3)	2 (66.7)	9 (60.0)	22 (73.3)	5 (83.3)	3 (50.0)	11 (55.5)	12 (57.1)	1 (33.3)	70 (63.6)
AI (steroidal)	2 (33.3)	0	3 (20.0)	2 (6.7)	1 (16.7)	0	2 (10.0)	6 (28.6)	0	16 (14.5)
AI (nonsteroidal)	4 (66.7)	1 (33.3)	7 (46.7)	18 (60.0)	4 (66.7)	2 (33.3)	6 (30.0)	10 (47.6)	1 (33.3)	53 (48.2)
Oral SERD	0	0	0	1 (3.3)	0	0	0	0	0	1 (0.9)
SERM[a]	1 (16.7)	1 (33.3)	4 (26.7)	6 (20.0)	4 (66.7)	2 (33.3)	5 (25.0)	4 (19.0)	0	27 (24.5)
Targeted therapy	0	0	3 (20.0)	1 (3.3)	1 (16.7)	0	1 (5.0)	2 (9.5)	0	8 (7.3)
mTOR inhibitor	0	0	2 (13.3)	1 (3.3)	1 (16.7)	0	1 (5.0)	2 (9.5)	0	7 (6.4)
Bone-only disease, n (%)	1 (16.7)	0	1 (7.1)[b]	0	1 (16.7)	1 (16.7)	2 (10.0)	3 (14.3)	0	9 (8.3)[b]
Visceral metastasis, n (%)	4 (66.7)	3 (100)	12 (80.0)	23 (76.7)	4 (66.7)	5 (83.3)	15 (75.0)	14 (66.7)	3 (100)	83 (75.5)

[a] Includes tamoxifen and toremifene.
[b] One patient had missing bone assessment data and was not included in the denominator.
AI, aromatase inhibitor; BID, twice daily; ECOG PS, Eastern Cooperative Oncology Group performance status; mTOR, mammalian target of rapamycin; NR, not reported; QD, once daily; SERD, selective estrogen receptor degrader; SERM, selective estrogen receptor modulator.

Safety and Tolerability

- The maximum tolerated dose determined in part 1 was 500 mg QD based on 2/6 patients (33.3%) experiencing a DLT at 650 mg QD (Grade 3 neutropenia with bronchitis; Grade 3 alanine aminotransferase/Grade 2 aspartate aminotransferase elevations)
- Overall, the most common lerociclib-related AEs (≥ 10%) were neutropenia (74.5%), nausea (54.5%), leukopenia (49.1%), diarrhea (45.5%), anemia (30.0%), vomiting (23.6%), thrombocytopenia (22.7%), fatigue (22.7%), and lymphocytopenia (10.0%) (**Table 2**). Additionally, stomatitis and alopecia were 6.4% and 4.5%, respectively
  - Serious AEs considered related to lerociclib were reported in 6 patients (5.5%)
    - 200 mg BID: 1 patient (4.8%) with Grade 1 pyrexia
    - 500 mg QD: 5 patients (16.7%) experienced a total of 9 serious AEs (3 cases of diarrhea, and 1 case each of diverticulitis, dyspnea, large intestine perforation, lung infection, nausea, and vomiting)
  - One patient (0.9%) discontinued treatment due to an AE: Grade 4 neutropenia at 200 mg QD; this event resolved
  - Most common Grade 3/4 laboratory abnormalities were observed in absolute neutrophil (49.1%), leukocyte (35.5%), and lymphocyte (11.8%) counts
  - No cases of QTcF prolongation (≥ 480ms or ≥ 60ms increase), or venous thromboembolism occurred at any dose level
  - Lerociclib dose reduction occurred in 34 patients (30.9%)
- Continuous lerociclib dosing with fulvestrant resulted in a dose-dependent decline and subsequent plateau of neutrophils at the end of cycle 1 (week 4)
  - Per protocol, no lerociclib dose interruptions or reductions were necessary due to Grade 3 neutropenia without associated infection or fever

Table 2. Most Common Lerociclib-Related AEs (≥ 10% of All Patients)

	QD										BID								Total			
Patients, n (%)	200 mg (n = 6)		300 mg (n = 3)		400 mg (n = 15)		500 mg (n = 30)		650 mg (n = 6)		100 mg (n = 6)		150 mg (n = 20)		200 mg (n = 21)		250 mg (n = 3)		Total TRAEs (N = 110)		Total TEAEs (N = 110)	
Grade	All	≥ 3	All	≥ 3	All	≥ 3	All	≥ 3	All	≥ 3	All	≥ 3	All	≥ 3	All	≥ 3	All	≥ 3	All	≥ 3	All	≥ 3
Any AE	4 (66.7)	2 (33.3)	3 (100)	2 (66.7)	15 (100)	5 (33.3)	29 (96.7)	23 (76.7)	6 (100)	6 (100)	5 (83.3)	1 (16.7)	15 (75.0)	7 (35.0)	21 (100)	9 (42.9)	3 (100)	2 (66.7)	101 (91.8)	57 (51.8)	107 (97.3)	64 (58.2)
Neutropenia	4 (66.7)	2 (33.3)	3 (100)	2 (66.7)	15 (100)	5 (33.3)	24 (80.0)	19 (63.3)	6 (100)	4 (66.7)	4 (66.7)	1 (16.7)	11 (55.0)	7 (35.0)	13 (61.9)	9 (42.9)	2 (66.7)	2 (66.7)	82 (74.5)	51 (46.4)	83 (75.5)	51 (46.4)
Nausea	0	0	3 (100)	0	13 (86.7)	0	21 (70.0)	1 (3.3)	5 (83.3)	0	2 (33.3)	0	3 (15.0)	0	10 (47.6)	0	3 (100)	0	60 (54.5)	1 (0.9)	61 (55.5)	1 (0.9)
Leukopenia	4 (66.7)	2 (33.3)	2 (66.7)	0	7 (46.7)	2 (13.3)	12 (40.0)	7 (23.3)	5 (83.3)	4 (66.7)	3 (50.0)	0	8 (40.0)	3 (15.0)	10 (47.6)	6 (28.6)	3 (100)	1 (33.3)	54 (49.1)	25 (22.7)	54 (49.1)	25 (22.7)
Diarrhea	1 (16.7)	0	2 (66.7)	0	8 (53.3)	1 (6.7)	19 (63.3)	3 (10.0)	6 (100)	1 (16.7)	1 (16.7)	0	4 (20.0)	0	8 (38.1)	1 (4.8)	1 (33.3)	0	50 (45.5)	6 (5.5)	55 (50.0)	6 (5.5)
Anemia	3 (50.0)	0	1 (33.3)	0	4 (26.7)	0	11 (36.7)	1 (3.3)	3 (50.0)	0	2 (33.3)	1 (16.7)	4 (20.0)	1 (5.0)	4 (19.0)	0	3 (100)	0	33 (30.0)	3 (2.7)	36 (32.7)	3 (2.7)
Vomiting	0	0	2 (66.7)	0	7 (46.7)	0	9 (30.0)	1 (3.3)	5 (83.3)	0	0	0	2 (10.0)	0	1 (4.8)	0	0	0	26 (23.6)	1 (0.9)	26 (23.6)	1 (0.9)
Thrombocytopenia	0	0	1 (33.3)	0	5 (33.3)	0	9 (30.0)	1 (3.3)	1 (16.7)	1 (16.7)	1 (16.7)	0	2 (10.0)	1 (5.0)	4 (19.0)	1 (4.8)	2 (66.7)	0	25 (22.7)	4 (3.6)	26 (23.6)	4 (3.6)
Fatigue	0	0	2 (66.7)	0	5 (33.3)	0	12 (40.0)	1 (3.3)	2 (33.3)	0	1 (16.7)	0	2 (10.0)	0	1 (4.8)	0	0	0	25 (22.7)	1 (0.9)	29 (26.4)	1 (0.9)
Lymphocytopenia	1 (16.7)	0	0	0	1 (6.7)	1 (6.7)	3 (10.0)	1 (3.3)	1 (16.7)	1 (16.7)	0	0	0	0	4 (19.0)	3 (14.3)	0	0	11 (10.0)	6 (5.5)	12 (10.9)	7 (6.4)

AE, adverse event; BID, twice daily; QD, once daily; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.

- The projected RP2D of 150 mg BID or 200 mg BID demonstrated an improved tolerability profile relative to QD dosing, including decreased rates of gastrointestinal AEs as well as lower rates of neutropenia (**Table 2**)
  - One patient at 150 mg BID (5.0%) and 4 patients at 200 mg BID (19.0%) experienced Grade 4 neutropenia; no other Grade 4 AEs were reported at these dose levels

Efficacy

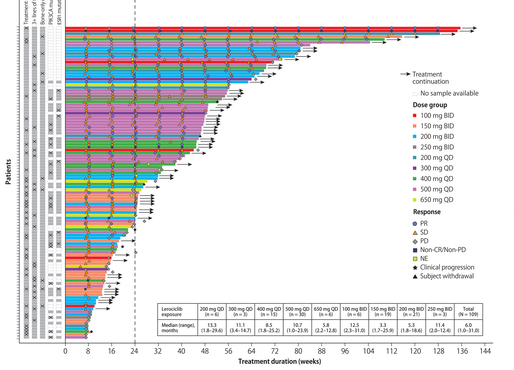
- Confirmed objective response rate was 21.4% across all dose levels (**Table 3; Figure 1**)
- Clinical benefit rate (complete response [CR] + partial response [PR] + stable disease [SD] lasting ≥ 24 weeks) was 65.2% across all dose levels (**Table 3**)
- Median PFS across the entire study was 15.0 months (**Figure 2**)
  - 12.8 months for all QD dose levels combined
  - Not reached for all BID dose levels combined

Table 3. Best Overall Response (Confirmed) in Patients With Measurable Disease

	QD					BID				Total	
Patients, n (%)	200 mg (n = 6)	300 mg (n = 3)	400 mg (n = 13)	500 mg (n = 30)	650 mg (n = 6)	100 mg (n = 5)	150 mg (n = 18)	200 mg (n = 19)	250 mg (n = 3)	All QD doses (n = 58)	All BID doses (n = 45)	All doses (N = 103)[a]
CR	0	0	0	0	0	0	0	0	0	0	0	0
PR	1 (16.7)	1 (33.3)	4 (30.8)	9 (30.0)	0	1 (20.0)	2 (11.1)	4 (21.1)	0	15 (25.9)	7 (15.6)	22 (21.4)
SD	4 (66.7)	1 (33.3)	9 (69.2)	19 (63.3)	5 (83.3)	2 (40.0)	12 (66.7)	12 (62.3)	2 (66.7)	38 (65.5)	28 (62.2)	66 (64.1)
SD ≥ 24 weeks	4 (66.7)	1 (33.3)	6 (46.2)	13 (43.3)	2 (33.3)	2 (40.0)	2 (22.2)[b]	4 (28.6)[b]	2 (66.7)	26 (44.8)	10 (32.3)[b]	36 (40.4)[b]
PD	1 (16.7)	1 (33.3)	0	2 (6.7)	1 (16.7)	2 (40.0)	4 (22.2)	2 (10.5)	1 (33.3)	5 (8.6)	9 (20.0)	14 (13.6)
NE	0	0	0	0	0	0	0	1 (5.3)	0	0	1 (2.2)	1 (1.0)
Clinical benefit[a]	5 (83.3)	2 (66.7)	10 (76.9)	22 (73.3)	2 (33.3)	3 (60.0)	4 (44.4)[c]	8 (57.1)[d]	2 (66.7)	41 (70.7)	17 (54.8)[e]	58 (65.2)[f]

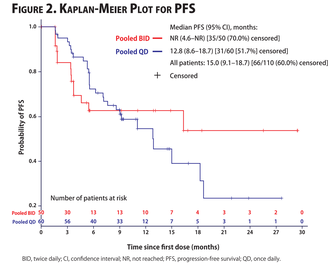
Based on Response Criteria in Solid Tumors (RECIST), Version 1.1.
[a] Seven patients (6.4%) did not have measurable disease or had measurable disease but no postbaseline tumor scans.
[b] Clinical benefit = CR + PR + SD lasting ≥ 24 weeks. Percentages were calculated by excluding those on treatment who did not have a confirmed objective response and have not made it to the week 24 assessment.
[c] n = 9. [d] n = 14. [e] n = 31. [f] n = 89.
BID, twice daily; CR, complete response; NE, not evaluable; PD, progressive disease; PR, partial response; SD, stable disease; QD, once daily.

Figure 1. Treatment Duration and Response by Dose Group: (A) All Patients and (B) Patients Receiving 150 mg BID or 200 mg BID



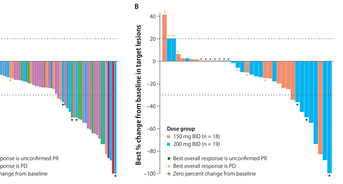
*In advanced/metastatic setting.
BID, twice daily; CR, complete response; ESR1, estrogen receptor 1; NE, not evaluable; PD, progressive disease; PIK3CA, phosphatidylinositol 4,5-bisphosphate 3-kinase catalytic subunit alpha; PR, partial response; QD, once daily; SD, stable disease.

Figure 2. Kaplan-Meier Plot for PFS



BID, twice daily; CI, confidence interval; NR, not reached; PFS, progression-free survival; QD, once daily.

Figure 3. Best Relative Change From Baseline in Tumor Size for Target Lesions by Dose Level: (A) All Patients and (B) Patients Receiving 150 mg BID or 200 mg BID



A (All patients): 26/103 patients (25.2%) experienced ≥ 30% reduction in target lesions.
B (150 mg BID and 200 mg BID): 9/37 patients (24.3%) experienced ≥ 30% reduction in target lesions.
Includes all patients who received ≥ 1 dose of study drug, have measurable target lesions at baseline and ≥ 1 postbaseline target lesion assessment.
BID, twice daily; PD, progressive disease; PR, partial response; QD, once daily.

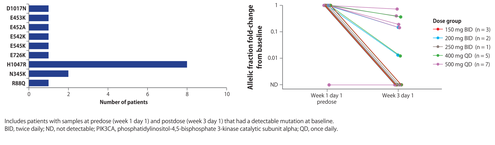
Pharmacokinetics

- PK analyses included 46 patients
- Exposure increased with dose (C_{max} and AUC_{0-24}) and was generally dose proportional for both QD (200 mg–650 mg) and BID (100 mg–250 mg) dosing
- There was minimal lerociclib accumulation between the first dose at week 1 and the steady-state dose at week 5 for QD dosing; however, accumulation was ~2-fold for BID dosing, as would be expected given the shorter dosing interval
- The apparent half-life for lerociclib is 13.8–17.2 hours, which allows for both QD and BID dosing regimens
- There was no indication of a time-dependent change in PK for lerociclib
- Lerociclib active metabolite G1T30 C_{max} and AUC values were much lower than those of lerociclib (~10%) and increased proportionally to the lerociclib dose

Pharmacodynamics

- At the data cutoff, 60/110 patients (54.5%) had a baseline sample analyzed, all of which had detectable cfDNA
  - 17/60 patients (28.3%) with detectable cfDNA had ≥ 1 phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha (PIK3CA) mutation at baseline; most common PIK3CA mutation was H1047R
  - 7/60 patients (12%) with detectable cfDNA had ≥ 1 estrogen receptor 1 (ESR1) mutation at baseline; most common ESR1 mutation was D538G
- Lerociclib treatment demonstrated a consistent decrease in PIK3CA mutant allelic fraction (**Figure 4**)

Figure 4. PIK3CA Mutation Frequency at Baseline and Changes in Mutant Allele Fraction



Includes patients with samples at predose (week 1 day 1) and postdose (week 3 day 1) that had a detectable mutation at baseline.
BID, twice daily; NO, not detectable; PIK3CA, phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha; QD, once daily.

CONCLUSIONS

- Continuous lerociclib dosing with fulvestrant was well tolerated, with BID dosing having a differentiated safety profile
  - Low rates of Grade 4 neutropenia support continuous lerociclib dosing without a drug holiday
  - BID dosing demonstrated an improved safety and tolerability profile compared with QD dosing, with lower rates of gastrointestinal AEs
  - Low rates of lerociclib-related stomatitis and alopecia were observed across all dose levels in both dosing schedules
- Coadministration of fulvestrant had minimal impact on the PK of lerociclib
- The efficacy data are consistent with those from other CDK4/6 inhibitors used in combination with fulvestrant[3-5]
  - The combination of lerociclib and fulvestrant was active, with a 65.2% clinical benefit rate and a median PFS of 15.0 months observed across the entire study; median PFS was 12.8 months for all QD dose levels combined and not reached for all BID dose levels combined
  - The study is currently ongoing; longer duration of follow-up is required to define 150 mg BID or 200 mg BID as the phase 3 dose

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Acknowledgments

- We thank all the investigators and site staff, with special thanks to the patients and their families
- We acknowledge support from the Cancer Research UK Cambridge Centre, NIHR Biomedical Research Centre, Cambridge Clinical Research Centre and Experimental Cancer Medicine Centre, UK; and NIHR Manchester Clinical Research Facility at The Christie NHS Foundation Trust, Manchester, UK
- Study sponsored by G1 Therapeutics, Inc. Medical writing assistance was provided by Alligent Europe (Envision Pharma Group), funded by G1 Therapeutics, Inc.
- We thank Ying Lu and Julio Ruiz for statistical and programming support

References

1. Murphy CG, Dickler MN. *Endocr Relat Cancer*. 2016;23(8):R337–52.
2. Cardoso F, et al. *Ann Oncol*. 2012;23(7):vii11–9.
3. Gnant M, et al. *Lancet Oncol*. 2019;(7):580–592.
4. Sledge GW, et al. *JAMA Oncol* [published online Sep 26, 2019]. doi: 10.1001/jamaoncol.2019.4782.
5. Slamon DJ, et al. *Ann Oncol*. 2019;30:ma2394.
6. Thrill M, Schwick, M. *Ther Adv Med Oncol*. 2018;(10):1758835918783326.
7. Bisi JE, et al. *Oncotarget*. 2017;8(26):42343–58.
8. Bulat I, et al. ASCO poster presentation. 2018;abstract#1061.