ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 09/24/2015

ClinicalTrials.gov ID: NCT00437073

Study Identification

Unique Protocol ID:	107671
Brief Title:	Brain Metastases In ErbB2-Positive Breast Cancer
Official Title:	Study EGF107671 - a Phase II Study of Lapatinib Plus Topotecan or Lapatinib Plus Capecitabine in the Treatment of Recurrent Brain Metastases From ErbB2-Positive Breast Cancer Following Cranial Radiotherapy
Secondary IDs:	

Study Status

Record Verification:	October 2012
Overall Status:	Terminated
Study Start:	May 2007
Primary Completion:	January 2009 [Actual]
Study Completion:	February 2010 [Actual]

Sponsor/Collaborators

Sponsor:	GlaxoSmithKline
Responsible Party:	Sponsor
Collaborators:	

Oversight

FDA Regulated?:	Yes
Applicable Trial?:	Section 801 Clinical Trial? Yes

	Delayed Posting? No
IND/IDE Protocol?:	Yes
IND/IDE Information:	Grantor: CDER IND/IDE Number: 61362 Serial Number: TBD Has Expanded Access? No
Review Board:	Approval Status: Board Name: Board Affiliation: Phone: Email:
Data Monitoring?:	
Plan to Share Data?:	
Oversight Authorities:	United States: Food and Drug Administration

Study Description

Brief Summary:	This study is for patients with ErbB2 overexpressing breast cancer that has spread to the brain and is still progressing there even after radiation treatment using WBRT (whole brain radiotherapy) or SRS (stereotactic radiosurgery) to the brain. The study will determine how safe and effective lapatinib is when given in combination with capecitabine to treat patients with ErbB2 overexpressing breast cancer that has spread to the brain. Lapatinib is an oral drug that will be taken every day. Tests for safety and efficacy will be performed regularly during the course of the study.
Detailed Description:	

Conditions

Conditions:	Neoplasms, Breast
Keywords:	brain metastases ErbB2 lapatinib Breast Cancer HYCAMTIN topotecan capecitabine metastatic breast cancer TYKERB XELODA

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 2
Intervention Model:	Parallel Assignment
Number of Arms:	2
Masking:	Open Label
Allocation:	Non-Randomized
Endpoint Classification:	Safety/Efficacy Study
Enrollment:	22 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: lapatinib plus capecitabine A total of 55 isubjects will be enrolled into this arm. Subjects with progression of CNS and/or non-CNS disease will be considered progressors. At the time of radiographically-documented CNS and/or non-CNS disease progression, a subject randomized to this arm will be allowed to cross over to the alternative arm.	Drug: capecitabine capecitabine 2000mg/m2/day orally, Days 1-14, every 21 days Other Names: • Xeloda Drug: lapatinib lapatinib administered 1250mg once daily orally Other Names: • Tykerb/Tyverb
Experimental: lapatinib + topotecan A total of 55 isubjects will be enrolled into this arm. Subjects with progression of CNS and/or non-CNS disease will be considered progressors. At the time of radiographically-documented CNS and/or non-CNS disease progression, a subject randomized to this arm will be allowed to cross over to the alternative arm.	Drug: topotecan topotecan intravenous (IV, in the vien) 3.2mg/m2 Days 1, 8 and 15; every 28 days Other Names: • Hycamtin Drug: lapatinib lapatinib administered 1250mg once daily orally Other Names: • Tykerb/Tyverb

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age:

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion criteria:

Subjects eligible for enrollment in the study must meet all of the following criteria:

- Signed written informed consent;
- Females or males age ≥ 18 years old;
- Eastern Cooperative Oncology Group (ECOG) Performance Status 0-1;
- Life expectancy of at least 12 weeks;
- Subjects must have histologically or cytologically confirmed invasive breast cancer, with Stage IV disease;
- ErbB2 overexpressing breast cancer, defined as 3+ staining by immunohistochemistry (IHC), or 2+ staining by IHC in conjunction with ErbB 2 gene amplification by FISH, or ErbB 2 gene amplification by FISH alone (in subjects whose tumor blocks were not assessed by IHC). Subjects with tumors that are 2+ by IHC but negative or borderline by FISH assay are ineligible. For subjects with a history of more than one primary breast cancer, each breast cancer must be ErbB2 overexpressing to be eligible;
- ErbB2 overexpressing breast cancer, defined as 3+ staining by immunohistochemistry (IHC), or 2+ staining by IHC in conjunction with ErbB2 gene amplification by FISH, or ErbB2 gene amplification by FISH alone (in subjects whose tumor blocks were not assessed by IHC). ErbB2 gene amplification is defined by: > 6 ErbB2 gene copies/nucleus for test systems without an internal control probe or an ErbB2/CEP 17 ratio of more than 2.2. Subjects with tumors that are 2+ by IHC but negative or borderline by FISH assay are ineligible. For subjects with a history of more than one primary breast cancer, each breast cancer must be ErbB2 overexpressing to be eligible;
- Prior treatment of brain metastases with WBRT and/or SRS;
- Unequivocal evidence of new and / or progressive lesions in the brain on an imaging study; Note: Subjects with progressive brain lesions are not required to meet RECIST criteria for CNS progression in order to be eligible for this study.
- Prior treatment with trastuzumab, either alone or in combination with chemotherapy is required. Trastuzumab will be discontinued at least 2 weeks prior to enrollment on study;
- Cardiac ejection fraction within institutional range of normal as measured by echocardiogram. Subjects who require cardiac medications (e.g. positive inotropic agents or afterload reducers) for normal ejection fraction are ineligible. MUGA scans will be accepted in cases where an echocardiogram cannot be performed or is inconclusive;
- At least 2 weeks since prior radiotherapy, last chemotherapy, immunotherapy, biologic therapy, or hormonal therapy for cancer, and sufficiently recovered or stabilized from side effects associated with prior therapy. Concurrent treatment with bisphosphonates is permitted;
- At least 3 weeks since major surgical procedures;
- Able to swallow and retain oral medications;

- Women of childbearing potential must have a negative serum pregnancy test at screening and must use an approved contraceptive method, if appropriate (for example, intrauterine device [IUD], birth control pills, or barrier device) beginning 2 weeks before the first dose of investigational product and for 28 days after the final dose of investigational product. Males able to father a child must practice adequate methods of birth control or practice complete abstinence from intercourse from the first dose of investigational treatment until one week after the final dose of investigational treatment.
- Subjects must complete all screening assessments as outlined in the protocol;
- Normal organ and marrow function as defined by these LABORATORY VALUES : ANC (absolute neutrophil count) ≥ 1.5 x 10^9/L; Hemoglobin ≥ 10 g/dL (after transfusion if needed); Platelets ≥ 100 x 10^9/L; Albumin ≥ 2.5 g/dL; Serum bilirubin ≤ 1.5x ULN unless due to Gilbert's syndrome; AST and ALT ≤ 5x ULN if documented liver metastases ≤ 3x ULN without liver metastases; Serum Creatinine ≤ 1.2 mg/dL or Calculated Creatinine Clearance1 ≥ 50 mL/min

Exclusion Criteria:

Subjects meeting any of the following criteria must not be enrolled in the study:

- Subjects who have had chemotherapy or radiotherapy within 2 weeks prior to entering the study or who have unresolved or unstable, serious toxicity from prior administration of another investigational drug and/or of prior cancer treatment;
- Concurrent treatment with an investigational agent or participation in another treatment clinical trial;
- Prior therapy with a topoisomerase 1 inhibitor;
- Prior lapatinib therapy;
- Prior therapy with capecitabine;
- Known dihydropyrimidine dehydrogenase (DPD) deficiency;
- ECOG Performance Status 2 or greater;
- Subjects receiving concurrent chemotherapy, radiation therapy, immunotherapy, biologic therapy (including an ErbB1 and/or ErbB2 inhibitor), or hormonal therapy for treatment of their cancer. Hormone therapy for ovarian suppression which has been used for > 6 months, during which time there has been disease progression in the brain, is allowed. Concurrent treatment with bisphosphonates is allowed;
- Subjects with evidence of leptomeningeal carcinomatosis at screening;
- History of allergic reactions attributed to compounds of similar chemical composition (quinazolines) to lapatinib;
- History of allergic reactions attributed to compounds chemically related to capecitabine, fluorouracil or any excipients;
- Concurrent treatment with medications listed as Prohibited Medications;
- Malabsorption syndrome, disease significantly affecting gastrointestinal function, or resection of the stomach or small bowel. Subjects with active, uncontrolled ulcerative colitis are also excluded;
- History of immediate or delayed hypersensitivity reaction to gadolinium contrast agents, or other contraindication to gadolinium contrast;
- Other known contraindication to MRI, such as a cardiac pacemaker, implanted cardiac defibrillator, brain aneurysm clips, cochlear implant, ocular foreign body, or shrapnel;
- Concurrent disease or condition that would make the subject inappropriate for study participation or any serious medical or psychiatric disorder that would interfere with the subject's safety;
- Anticoagulant therapy (other than coumadin or aspirin as catheter prophylaxis) at study entry;
- Dementia, altered mental status, or any psychiatric condition that would prohibit the understanding or rendering of informed consent, unless a legally acceptable representative could provide informed consent (if in accord with the policies of the local Ethics Committee);
- Pre-existing severe cerebral vascular disease, such as stroke involving a major vessel, CNS vasculitis, or malignant hypertension;
- Active cardiac disease, defined as one or more of the following:

- History of uncontrolled or symptomatic angina
- History of arrhythmias requiring medications, or clinically significant
- Myocardial infarction < 6 months from study entry
- Uncontrolled or symptomatic congestive heart failure
- Ejection fraction below the institutional normal limit
- Any other cardiac condition, which in the opinion of the treating physician, would make this protocol unreasonably hazardous for the patient;
- Uncontrolled infection;
- Pregnant or lactating females;
- History of other malignancy, except for curatively treated basal cell carcinoma or squamous cell carcinoma of the skin, or carcinoma in situ of the cervix. Subjects with other malignancies who have been disease-free for at least 5 years are eligible.
- Have current active hepatic or biliary disease (with exception of subjects with Gilbert's syndrome, asymptomatic gallstones, liver metastases or stable chronic liver disease per investigator assessment).

Contacts/Locations

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References

Citations: Lin N, Doering, Eierman, Greil, Campone, Kaufman, Lane S, Zembryki D, Rubin S, Winer E. Randomized Phase II Study of Lapatinib plus Capecitabine or Lapatinib plus Topotecan for Patients with HER2-Positive Breast Cancer Brain Metastases. [J Neurooncol]. 2011;

Links:

Study Data/Documents:

Study Results

Participant Flow

Reporting Groups

	Description
Lapatinib Plus Capecitabine	Participants received a daily dose of 5 tablets of lapatinib (1250 milligrams [mg]) at approximately the same time every day, either 1 hour (or more) before breakfast or 1 hour (or more) after breakfast. Participants also received capecitabine 2000 mg per meters squared (mg/m^2) per day, divided and administered orally twice daily, 12 hours apart, for 14 days, every 21 days. Capecitabine was taken with food or within 30 minutes after a breakfast meal with approximately 200 milliliters (ml) of water.
Lapatinib Plus Topotecan	Participants received a daily dose of 5 tablets of lapatinib (1250 milligrams [mg]) at approximately the same time every day, either 1 hour (or more) before breakfast or 1 hour (or more) after breakfast. Participants also received an intravenous (IV) infusion of topotecan 3.2 mg/m^2 over the course of at least 30 minutes on Days 1, 8, and 15 (+/- 2 days) of a 28-day treatment cycle.

Overall Study

	Lapatinib Plus Capecitabine	Lapatinib Plus Topotecan
Started	13	9
Completed	12	8
Not Completed	1	1
Sponsor Terminated Study	1	0
Physician Decision	0	1

Baseline Characteristics

Reporting Groups

	Description
Lapatinib Plus Capecitabine	Participants received a daily dose of 5 tablets of lapatinib (1250 milligrams [mg]) at approximately the same time every day, either 1 hour (or more) before breakfast or 1 hour (or more) after breakfast. Participants also received capecitabine 2000 mg per meters squared (mg/m^2) per day, divided and administered orally twice daily, 12 hours apart, for 14 days, every 21 days. Capecitabine was taken with food or within 30 minutes after a breakfast meal with approximately 200 milliliters (ml) of water.
Lapatinib Plus Topotecan	Participants received a daily dose of 5 tablets of lapatinib (1250 milligrams [mg]) at approximately the same time every day, either 1 hour (or more) before breakfast or 1 hour (or more) after breakfast. Participants also received an intravenous (IV) infusion of topotecan 3.2 mg/m^2 over the course of at least 30 minutes on Days 1, 8, and 15 (+/- 2 days) of a 28-day treatment cycle.

Baseline Measures

	Lapatinib Plus Capecitabine	Lapatinib Plus Topotecan	Total
Number of Participants	13	9	22
Age, Continuous [units: Years] Mean (Standard Deviation)	49.4 (9.29)	54.6 (10.54)	51.5 (9.92)
Gender, Male/Female [units: Participants]			
Female	13	9	22
Male	0	0	0

	Lapatinib Plus Capecitabine	Lapatinib Plus Topotecan	Total
Race/Ethnicity, Customized White [units: participants]	13	9	22

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Number of Participants With the Indicated Central Nervous System (CNS) Objective Response (OR)
Measure Description	CNS OR is defined as the number of participants with either a complete response (CR) or partial response (PR) as assessed by volumetric analysis of brain magnetic resonance imaging (MRI) and Response Evaluation Criteria In Solid Tumors (RECIST). CR: complete resolution of all evaluable and non-evaluable brain metastases; PR: =>50% reduction in the volumetric sum of all evaluable brain metastases compared to baseline.
Time Frame	From the start of treatment until disease progression, death, or discontinuation from the study, up to a maximum of Week 88
Safety Issue?	No

Analysis Population Description

Modified Intent-to-Treat (mITT) Population: all participants who had at least one evaluable CNS target lesion at baseline and who had received at least two doses of lapatinib medication

Reporting Groups

	Description
Lapatinib Plus Capecitabine	Participants received a daily dose of 5 tablets of lapatinib (1250 milligrams [mg]) at approximately the same time every day, either 1 hour (or more) before breakfast or 1 hour (or more) after breakfast. Participants also received capecitabine 2000 mg per meters squared (mg/m^2) per day, divided and administered orally twice daily, 12 hours apart, for 14 days, every 21 days. Capecitabine was taken with food or within 30 minutes after a breakfast meal with approximately 200 milliliters (ml) of water.
Lapatinib Plus Topotecan	Participants received a daily dose of 5 tablets of lapatinib (1250 milligrams [mg]) at approximately the same time every day, either 1 hour (or more) before breakfast or 1 hour (or more) after breakfast. Participants also received an intravenous (IV) infusion of topotecan 3.2 mg/m^2 over the course of at least 30 minutes on Days 1, 8, and 15 (+/- 2 days) of a 28-day treatment cycle.

Measured Values

	Lapatinib Plus Capecitabine	Lapatinib Plus Topotecan
Number of Participants Analyzed	13	9
Number of Participants With the Indicated Central Nervous System (CNS) Objective Response (OR) [units: participants]	5	0

Statistical Analysis 1 for Number of Participants With the Indicated Central Nervous System (CNS) Objective Response (OR)

Statistical Analysis Overview	Comparison Groups	Lapatinib Plus Capecitabine
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [percentage of participants]
	Estimated Value	38
	Confidence Interval	(2-Sided) 95% 13.9 to 68.4
	Estimation Comments	The estimated value indicates the percentage of participants with CNS OR in the Lapatinib plus Capecitabine treatment arm.

2. Primary Outcome Measure:

Measure Title	Number of Participants With the Indicated CNS Responses
Measure Description	CNS responses were assessed by volumetric (V) analysis of brain MRI and RECIST. CR: complete resolution of all evaluable and non-evaluable brain metastases (BMs). PR: =>50% reduction in the V sum of all evaluable BMs compared to baseline. A response of "Other" was used for participants who discontinued the study prior to the first efficacy assessment. Stable Disease (SD): disease that does not meet CR, PR, or CNS progression criteria. Progressive disease (PD): a requirement for a new steroid or an increasing steroid dose for the treatment of worsening neurological signs/symptoms due to BMs.
Time Frame	From the start of treatment until disease progression, death, or discontinuation from the study, up to a maximum of Week 88
Safety Issue?	No

Analysis Population Description

mITT Population

Reporting Groups

	Description
Lapatinib Plus Capecitabine	Participants received a daily dose of 5 tablets of lapatinib (1250 milligrams [mg]) at approximately the same time every day, either 1 hour (or more) before breakfast or 1 hour (or more) after breakfast. Participants also received capecitabine 2000 mg per meters squared (mg/m^2) per day, divided and administered orally twice daily, 12 hours apart, for 14 days, every 21 days. Capecitabine was taken with food or within 30 minutes after a breakfast meal with approximately 200 milliliters (ml) of water.
Lapatinib Plus Topotecan	Participants received a daily dose of 5 tablets of lapatinib (1250 milligrams [mg]) at approximately the same time every day, either 1 hour (or more) before breakfast or 1 hour (or more) after breakfast. Participants also received an intravenous (IV) infusion of topotecan 3.2 mg/m^2 over the course of at least 30 minutes on Days 1, 8, and 15 (+/- 2 days) of a 28-day treatment cycle.

Measured Values

	Lapatinib Plus Capecitabine	Lapatinib Plus Topotecan
Number of Participants Analyzed	13	9
Number of Participants With the Indicated CNS Responses [units: participants]		
Complete response	0	0
Partial response	5	0
Stable Disease	6	3
Progressive Disease	2	1
Unknown	0	3
Other	0	2

3. Secondary Outcome Measure:

Measure Title	Duration of CNS Objective Response (Defined as the Time From the First Documented Evidence of CNS PR or CR Until the First Documented Sign of Disease Progression or Death, if Sooner)
Measure Description	CNS OR is defined as the number of participants with either a CR or PR as assessed by volumetric analysis of brain MRI and RECIST. CR: complete resolution of all evaluable and non-evaluable brain metastases; PR: =>50% reduction in the volumetric sum of all evaluable brain metastases compared to baseline. This study was closed before full enrollment was achieved; thus, predefined secondary efficacy endpoints were not assessed because there were not enough participants enrolled in the study to provide statistically valid analyses.

Time Frame	From the start of treatment until disease progression, death, or discontinuation from the study, up to a maximum of Week 88
Safety Issue?	No

Analysis Population Description
mITT Population

Reporting Groups

	Description
Lapatinib Plus Capecitabine	Participants received a daily dose of 5 tablets of lapatinib (1250 milligrams [mg]) at approximately the same time every day, either 1 hour (or more) before breakfast or 1 hour (or more) after breakfast. Participants also received capecitabine 2000 mg per meters squared (mg/m^2) per day, divided and administered orally twice daily, 12 hours apart, for 14 days, every 21 days. Capecitabine was taken with food or within 30 minutes after a breakfast meal with approximately 200 milliliters (ml) of water.
Lapatinib Plus Topotecan	Participants received a daily dose of 5 tablets of lapatinib (1250 milligrams [mg]) at approximately the same time every day, either 1 hour (or more) before breakfast or 1 hour (or more) after breakfast. Participants also received an intravenous (IV) infusion of topotecan 3.2 mg/m^2 over the course of at least 30 minutes on Days 1, 8, and 15 (+/- 2 days) of a 28-day treatment cycle.

Measured Values

	Lapatinib Plus Capecitabine	Lapatinib Plus Topotecan
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

4. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Clinical Benefit
Measure Description	Clinical benefit is defined as CR (complete resolution of all evaluable and non-evaluable brain metastases), PR (=>50% reduction in the volumetric sum of all evaluable brain metastases compared to baseline), or stable disease (disease that does not meet CR, PR, or CNS progression criteria) for at least 6 months. This study was closed before full enrollment was achieved; thus, predefined secondary efficacy endpoints were not assessed because there were not enough participants enrolled in the study to provide statistically valid analyses.
Time Frame	From the start of treatment until disease progression, death, or discontinuation from the study, up to a maximum of Week 88
Safety Issue?	No

Analysis Population Description
mITT Population

Reporting Groups

	Description
Lapatinib Plus Capecitabine	Participants received a daily dose of 5 tablets of lapatinib (1250 milligrams [mg]) at approximately the same time every day, either 1 hour (or more) before breakfast or 1 hour (or more) after breakfast. Participants also received capecitabine 2000 mg per meters squared (mg/m^2) per day, divided and administered orally twice daily, 12 hours apart, for 14 days, every 21 days. Capecitabine was taken with food or within 30 minutes after a breakfast meal with approximately 200 milliliters (ml) of water.
Lapatinib Plus Topotecan	Participants received a daily dose of 5 tablets of lapatinib (1250 milligrams [mg]) at approximately the same time every day, either 1 hour (or more) before breakfast or 1 hour (or more) after breakfast. Participants also received an intravenous (IV) infusion of topotecan 3.2 mg/m^2 over the course of at least 30 minutes on Days 1, 8, and 15 (+/- 2 days) of a 28-day treatment cycle.

Measured Values

	Lapatinib Plus Capecitabine	Lapatinib Plus Topotecan
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

5. Secondary Outcome Measure:

Measure Title	Percentage of Participants (Par.) With Objective Response by RECIST in Non-CNS Disease
Measure Description	Non-CNS disease (for par. with measurable baseline non-CNS disease) OR is defined as the number of par. with either a CR or PR as assessed by computed tomography (CT) or MRI scan and RECIST. CR: disappearance of all target lesions; PR: at least a 30% decrease in the sum of the longest diameter (LD) of target lesions taking as reference the baseline sum LD. This study was closed before full enrollment was achieved; thus, predefined secondary efficacy endpoints were not assessed because there were not enough par. enrolled in the study to provide statistically valid analyses.
Time Frame	From the start of treatment until disease progression, death, or discontinuation from the study, up to a maximum of Week 88
Safety Issue?	No

Analysis Population Description

mITT Population

Reporting Groups

	Description
Lapatinib Plus Capecitabine	Participants received a daily dose of 5 tablets of lapatinib (1250 milligrams [mg]) at approximately the same time every day, either 1 hour (or more) before breakfast or 1 hour (or more) after breakfast. Participants also received capecitabine 2000 mg per meters squared (mg/m^2) per day, divided and administered orally twice daily, 12 hours apart, for 14 days, every 21 days. Capecitabine was taken with food or within 30 minutes after a breakfast meal with approximately 200 milliliters (ml) of water.
Lapatinib Plus Topotecan	Participants received a daily dose of 5 tablets of lapatinib (1250 milligrams [mg]) at approximately the same time every day, either 1 hour (or more) before breakfast or 1 hour (or more) after breakfast. Participants also received an intravenous (IV) infusion of topotecan 3.2 mg/m^2 over the course of at least 30 minutes on Days 1, 8, and 15 (+/- 2 days) of a 28-day treatment cycle.

Measured Values

	Lapatinib Plus Capecitabine	Lapatinib Plus Topotecan
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

6. Secondary Outcome Measure:

Measure Title	Time to CNS Objective Response (Defined as the Time From the Start of Treatment Until the First Documented Evidence of Partial or Complete Tumor Response [Whichever Status is Recorded First])
Measure Description	CNS OR is defined as the number of participants with either a CR or PR as assessed by volumetric analysis of brain MRI and RECIST. CR: complete resolution of all evaluable and non-evaluable brain metastases; PR: =>50% reduction in the volumetric sum of all evaluable brain metastases compared to baseline. This study was closed before full enrollment was achieved; thus, predefined secondary efficacy endpoints were not assessed because there were not enough participants enrolled in the study to provide statistically valid analyses.
Time Frame	From the start of treatment until disease progression, death, or discontinuation from the study, up to a maximum of Week 88
Safety Issue?	No

Analysis Population Description

mITT Population

Reporting Groups

	Description
Lapatinib Plus Capecitabine	Participants received a daily dose of 5 tablets of lapatinib (1250 milligrams [mg]) at approximately the same time every day, either 1 hour (or more) before breakfast or 1 hour (or more) after breakfast. Participants also received capecitabine 2000 mg per meters squared (mg/m^2) per day, divided and administered orally twice daily, 12 hours apart, for 14 days, every 21 days. Capecitabine was taken with food or within 30 minutes after a breakfast meal with approximately 200 milliliters (ml) of water.
Lapatinib Plus Topotecan	Participants received a daily dose of 5 tablets of lapatinib (1250 milligrams [mg]) at approximately the same time every day, either 1 hour (or more) before breakfast or 1 hour (or more) after breakfast. Participants also received an intravenous (IV) infusion of topotecan 3.2 mg/m^2 over the course of at least 30 minutes on Days 1, 8, and 15 (+/- 2 days) of a 28-day treatment cycle.

Measured Values

	Lapatinib Plus Capecitabine	Lapatinib Plus Topotecan
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

7. Secondary Outcome Measure:

Measure Title	Number of Participants With the Indicated Site of Initial Disease Progression
Measure Description	The site of initial disease will be determined by taking the earliest date of known progression and assigning the appropriate category (CNS or non-CNS) based on the source of the earliest date. This study was closed before full enrollment was achieved; thus, predefined secondary efficacy endpoints were not assessed because there were not enough participants enrolled in the study to provide statistically valid analyses.
Time Frame	From the start of treatment until disease progression, death, or discontinuation from the study, up to a maximum of Week 88
Safety Issue?	No

Analysis Population Description

mITT Population

Reporting Groups

	Description
Lapatinib Plus Capecitabine	Participants received a daily dose of 5 tablets of lapatinib (1250 milligrams [mg]) at approximately the same time every day, either 1 hour (or more) before breakfast or 1 hour (or more) after breakfast. Participants also received capecitabine 2000 mg per meters squared (mg/m^2) per day, divided and administered orally twice daily, 12 hours apart, for 14 days, every 21 days. Capecitabine was taken with food or within 30 minutes after a breakfast meal with approximately 200 milliliters (ml) of water.

	Description
Lapatinib Plus Topotecan	Participants received a daily dose of 5 tablets of lapatinib (1250 milligrams [mg]) at approximately the same time every day, either 1 hour (or more) before breakfast or 1 hour (or more) after breakfast. Participants also received an intravenous (IV) infusion of topotecan 3.2 mg/m^2 over the course of at least 30 minutes on Days 1, 8, and 15 (+/- 2 days) of a 28-day treatment cycle.

Measured Values

	Lapatinib Plus Capecitabine	Lapatinib Plus Topotecan
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

8. Secondary Outcome Measure:

Measure Title	Progression-free Survival
Measure Description	Progression-free survival is defined as the time from the start of treatment until the first documented sign of disease progression at any site or death due to any cause, if sooner. This study was closed before full enrollment was achieved; thus, predefined secondary efficacy endpoints were not assessed because there were not enough participants enrolled in the study to provide statistically valid analyses.
Time Frame	From the start of treatment until disease progression, death, or discontinuation from the study, up to a maximum of Week 88
Safety Issue?	No

Analysis Population Description

mITT Population

Reporting Groups

	Description
Lapatinib Plus Capecitabine	Participants received a daily dose of 5 tablets of lapatinib (1250 milligrams [mg]) at approximately the same time every day, either 1 hour (or more) before breakfast or 1 hour (or more) after breakfast. Participants also received capecitabine 2000 mg per meters squared (mg/m^2) per day, divided and administered orally twice daily, 12 hours apart, for 14 days, every 21 days. Capecitabine was taken with food or within 30 minutes after a breakfast meal with approximately 200 milliliters (ml) of water.
Lapatinib Plus Topotecan	Participants received a daily dose of 5 tablets of lapatinib (1250 milligrams [mg]) at approximately the same time every day, either 1 hour (or more) before breakfast or 1 hour (or more) after breakfast. Participants also received an intravenous (IV) infusion of topotecan 3.2 mg/m^2 over the course of at least 30 minutes on Days 1, 8, and 15 (+/- 2 days) of a 28-day treatment cycle.

Measured Values

	Lapatinib Plus Capecitabine	Lapatinib Plus Topotecan
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

9. Secondary Outcome Measure:

Measure Title	Overall Survival
Measure Description	Overall survival is defined as the time from the start of treatment until death due to any cause. This study was closed before full enrollment was achieved; thus, predefined secondary efficacy endpoints were not assessed because there were not enough participants enrolled in the study to provide statistically valid analyses.
Time Frame	From the start of treatment until disease progression, death, or discontinuation from the study, up to a maximum of Week 88
Safety Issue?	No

Analysis Population Description

mITT Population

Reporting Groups

	Description
Lapatinib Plus Capecitabine	Participants received a daily dose of 5 tablets of lapatinib (1250 milligrams [mg]) at approximately the same time every day, either 1 hour (or more) before breakfast or 1 hour (or more) after breakfast. Participants also received capecitabine 2000 mg per meters squared (mg/m^2) per day, divided and administered orally twice daily, 12 hours apart, for 14 days, every 21 days. Capecitabine was taken with food or within 30 minutes after a breakfast meal with approximately 200 milliliters (ml) of water.
Lapatinib Plus Topotecan	Participants received a daily dose of 5 tablets of lapatinib (1250 milligrams [mg]) at approximately the same time every day, either 1 hour (or more) before breakfast or 1 hour (or more) after breakfast. Participants also received an intravenous (IV) infusion of topotecan 3.2 mg/m^2 over the course of at least 30 minutes on Days 1, 8, and 15 (+/- 2 days) of a 28-day treatment cycle.

Measured Values

	Lapatinib Plus Capecitabine	Lapatinib Plus Topotecan
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

10. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Baseline Tumor-related (TR) Neurological Signs and Symptoms (NSS), Who Experienced Improvement in NSS as Measured by the Neurological Examination Worksheet (NEW)
Measure Description	TR NSS was to be recorded by the Investigator on the NEW, using the National Cancer Institute Common Terminology Criteria for Adverse Events Version 3.0 (CTCAE V3.0). Improvement was to be defined as a decrease of 1 or more CTCAE grades from baseline of any TR NSS. This study was closed before full enrollment was achieved; thus, predefined secondary efficacy endpoints were not assessed because there were not enough participants enrolled in the study to provide statistically valid analyses.
Time Frame	From the start of treatment until disease progression, death, or discontinuation from the study, up to a maximum of Week 88
Safety Issue?	No

Analysis Population Description

mITT Population

Reporting Groups

	Description
Lapatinib Plus Capecitabine	Participants received a daily dose of 5 tablets of lapatinib (1250 milligrams [mg]) at approximately the same time every day, either 1 hour (or more) before breakfast or 1 hour (or more) after breakfast. Participants also received capecitabine 2000 mg per meters squared (mg/m^2) per day, divided and administered orally twice daily, 12 hours apart, for 14 days, every 21 days. Capecitabine was taken with food or within 30 minutes after a breakfast meal with approximately 200 milliliters (ml) of water.
Lapatinib Plus Topotecan	Participants received a daily dose of 5 tablets of lapatinib (1250 milligrams [mg]) at approximately the same time every day, either 1 hour (or more) before breakfast or 1 hour (or more) after breakfast. Participants also received an intravenous (IV) infusion of topotecan 3.2 mg/m^2 over the course of at least 30 minutes on Days 1, 8, and 15 (+/- 2 days) of a 28-day treatment cycle.

Measured Values

	Lapatinib Plus Capecitabine	Lapatinib Plus Topotecan
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

11. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Disease Stabilization for 6 Months or More

Measure Description	The percentage participants with disease stabiliztion for 6 months or more were defined as those treated participants with a best CNS objective response of SD whose disease stabilization lasted 6 months or more from the start of treatment. This study was closed before full enrollment was achieved; thus, predefined secondary efficacy endpoints were not assessed because there were not enough participants enrolled in the study to provide statistically valid analyses.
Time Frame	From the start of treatment until disease progression, death, or discontinuation from the study, up to a maximum of Week 88
Safety Issue?	No

Analysis Population Description
mITT Population

Reporting Groups

	Description
Lapatinib Plus Capecitabine	Participants received a daily dose of 5 tablets of lapatinib (1250 milligrams [mg]) at approximately the same time every day, either 1 hour (or more) before breakfast or 1 hour (or more) after breakfast. Participants also received capecitabine 2000 mg per meters squared (mg/m^2) per day, divided and administered orally twice daily, 12 hours apart, for 14 days, every 21 days. Capecitabine was taken with food or within 30 minutes after a breakfast meal with approximately 200 milliliters (ml) of water.
Lapatinib Plus Topotecan	Participants received a daily dose of 5 tablets of lapatinib (1250 milligrams [mg]) at approximately the same time every day, either 1 hour (or more) before breakfast or 1 hour (or more) after breakfast. Participants also received an intravenous (IV) infusion of topotecan 3.2 mg/m^2 over the course of at least 30 minutes on Days 1, 8, and 15 (+/- 2 days) of a 28-day treatment cycle.

Measured Values

	Lapatinib Plus Capecitabine	Lapatinib Plus Topotecan
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

12. Secondary Outcome Measure:

Measure Title	Percentage of Participants With a >=20% Volumetric Reduction in CNS Lesions
Measure Description	The percentage of participants with a >=20% volumetric reduction in CNS lesions was defined as the percentage of treated participants achieving at least a 20% volumetric reduction in CNS lesions relative to baseline. This study was closed before full enrollment was achieved; thus, predefined secondary efficacy endpoints were not assessed because there were not enough participants enrolled in the study to provide statistically valid analyses.
Time Frame	Baseline; from the start of treatment until disease progression, death, or discontinuation from the study, up to a maximum of Week 88

Safety Issue?	No

Analysis Population Description
mITT Population

Reporting Groups

	Description
Lapatinib Plus Capecitabine	Participants received a daily dose of 5 tablets of lapatinib (1250 milligrams [mg]) at approximately the same time every day, either 1 hour (or more) before breakfast or 1 hour (or more) after breakfast. Participants also received capecitabine 2000 mg per meters squared (mg/m^2) per day, divided and administered orally twice daily, 12 hours apart, for 14 days, every 21 days. Capecitabine was taken with food or within 30 minutes after a breakfast meal with approximately 200 milliliters (ml) of water.
Lapatinib Plus Topotecan	Participants received a daily dose of 5 tablets of lapatinib (1250 milligrams [mg]) at approximately the same time every day, either 1 hour (or more) before breakfast or 1 hour (or more) after breakfast. Participants also received an intravenous (IV) infusion of topotecan 3.2 mg/m^2 over the course of at least 30 minutes on Days 1, 8, and 15 (+/- 2 days) of a 28-day treatment cycle.

Measured Values

	Lapatinib Plus Capecitabine	Lapatinib Plus Topotecan
Number of Participants Analyzed	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

Reported Adverse Events

Time Frame	All serious and non-serious on-therapy adverse events, defined as occurring from the first dose of investigational product until five days after the last dose (up to Week 37) were recorded, regardless of whether or not they were considered drug related.
Additional Description	Serious and non-serious adverse events were collected in members of the ITT Population, comprised of all participants who received at least one dose of study medication.

Reporting Groups

	Description
Lapatinib Plus Capecitabine	Participants received a daily dose of 5 tablets of lapatinib (1250 milligrams [mg]) at approximately the same time every day, either 1 hour (or more) before breakfast or 1 hour (or more) after breakfast. Participants also received capecitabine 2000 mg per meters squared (mg/m^2) per day, divided and administered orally twice daily, 12 hours apart, for 14 days, every 21 days. Capecitabine was taken with food or within 30 minutes after a breakfast meal with approximately 200 milliliters (ml) of water.
Lapatinib Plus Topotecan	Participants received a daily dose of 5 tablets of lapatinib (1250 milligrams [mg]) at approximately the same time every day, either 1 hour (or more) before breakfast or 1 hour (or more) after breakfast. Participants also received an intravenous (IV) infusion of topotecan 3.2 mg/m^2 over the course of at least 30 minutes on Days 1, 8, and 15 (+/- 2 days) of a 28-day treatment cycle.

Serious Adverse Events

	Lapatinib Plus Capecitabine	Lapatinib Plus Topotecan
	Affected/At Risk (%)	Affected/At Risk (%)
Total	6/13 (46.15%)	5/9 (55.56%)
Gastrointestinal disorders		
Constipation [A] †	1/13 (7.69%)	0/9 (0%)
Diarrhoea [A] †	2/13 (15.38%)	1/9 (11.11%)
General disorders		
General physical health deterioration [A] †	1/13 (7.69%)	1/9 (11.11%)
Multi-organ failure [A] †	1/13 (7.69%)	0/9 (0%)
Pyrexia [A] †	1/13 (7.69%)	0/9 (0%)
Infections and infestations		
Erysipelas [A] †	1/13 (7.69%)	0/9 (0%)
Sepsis [A] †	0/13 (0%)	2/9 (22.22%)
Urinary tract infection [A] †	0/13 (0%)	1/9 (11.11%)
Investigations		
Hepatic enzyme increased [A] †	1/13 (7.69%)	0/9 (0%)
Metabolism and nutrition disorders		

	Lapatinib Plus Capecitabine	Lapatinib Plus Topotecan
	Affected/At Risk (%)	Affected/At Risk (%)
Dehydration [A] †	0/13 (0%)	1/9 (11.11%)
Hypocalcaemia [A] †	1/13 (7.69%)	0/9 (0%)
Hypokalaemia [A] †	1/13 (7.69%)	1/9 (11.11%)
Nervous system disorders		
Loss of consciousness [A] †	1/13 (7.69%)	0/9 (0%)
Memory impairment [A] †	1/13 (7.69%)	0/9 (0%)
Syncope [A] †	0/13 (0%)	1/9 (11.11%)
Psychiatric disorders		
Confusional state [A] †	1/13 (7.69%)	0/9 (0%)
Respiratory, thoracic and mediastinal disorders		
Pulmonary embolism [A] †	1/13 (7.69%)	0/9 (0%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 0%

	Lapatinib Plus Capecitabine	Lapatinib Plus Topotecan
	Affected/At Risk (%)	Affected/At Risk (%)
Total	13/13 (100%)	9/9 (100%)
Blood and lymphatic system disorders		
Anaemia [A] †	1/13 (7.69%)	3/9 (33.33%)
Leukocytosis [A] †	1/13 (7.69%)	0/9 (0%)
Leukopenia [A] †	0/13 (0%)	1/9 (11.11%)
Lymphopenia [A] †	0/13 (0%)	1/9 (11.11%)
Neutropenia [A] †	1/13 (7.69%)	3/9 (33.33%)

	Lapatinib Plus Capecitabine	Lapatinib Plus Topotecan
	Affected/At Risk (%)	Affected/At Risk (%)
Thrombocytopenia [A] †	1/13 (7.69%)	5/9 (55.56%)
White blood cell count decreased [A] †	0/13 (0%)	1/9 (11.11%)
Cardiac disorders		
Left ventricular dysfunction [A] †	0/13 (0%)	1/9 (11.11%)
Palpitations [A] †	1/13 (7.69%)	0/9 (0%)
Pericardial effusion [A] †	1/13 (7.69%)	0/9 (0%)
Ear and labyrinth disorders		
Deafness [A] †	0/13 (0%)	1/9 (11.11%)
Eye disorders		
Dry eyes [A] †	1/13 (7.69%)	0/9 (0%)
Lacrimation increased [A] †	1/13 (7.69%)	0/9 (0%)
Vision blurred [A] †	1/13 (7.69%)	0/9 (0%)
Visual impairment [A] †	0/13 (0%)	1/9 (11.11%)
Gastrointestinal disorders		
Abdominal discomfort [A] †	0/13 (0%)	1/9 (11.11%)
Abdominal pain [A] †	1/13 (7.69%)	1/9 (11.11%)
Abdominal pain upper [A] †	1/13 (7.69%)	0/9 (0%)
Cheilitis [A] †	1/13 (7.69%)	0/9 (0%)
Constipation [A] †	2/13 (15.38%)	2/9 (22.22%)
Diarrhoea [A] †	11/13 (84.62%)	8/9 (88.89%)
Dyspepsia [A] †	2/13 (15.38%)	0/9 (0%)
Gastrooesophageal reflux disease [A] †	1/13 (7.69%)	0/9 (0%)
Nausea [A] †	3/13 (23.08%)	5/9 (55.56%)

	Lapatinib Plus Capecitabine	Lapatinib Plus Topotecan
	Affected/At Risk (%)	Affected/At Risk (%)
Oesophagitis [A] †	1/13 (7.69%)	0/9 (0%)
Stomatitis [A] †	3/13 (23.08%)	0/9 (0%)
Vomiting [A] †	4/13 (30.77%)	2/9 (22.22%)
General disorders		
Asthenia [A] †	1/13 (7.69%)	1/9 (11.11%)
Chills [A] †	0/13 (0%)	1/9 (11.11%)
Facial pain [A] †	1/13 (7.69%)	0/9 (0%)
Fatigue [A] †	8/13 (61.54%)	5/9 (55.56%)
Influenza like illness [A] †	1/13 (7.69%)	0/9 (0%)
Mucosal inflammation [A] †	4/13 (30.77%)	0/9 (0%)
Oedema [A] †	1/13 (7.69%)	1/9 (11.11%)
Oedema peripheral [A] †	5/13 (38.46%)	0/9 (0%)
Pyrexia [A] †	1/13 (7.69%)	1/9 (11.11%)
Hepatobiliary disorders		
Hyperbilirubinaemia [A] †	1/13 (7.69%)	0/9 (0%)
Infections and infestations		
Abscess [A] †	1/13 (7.69%)	0/9 (0%)
Cellulitis [A] †	1/13 (7.69%)	0/9 (0%)
Fungal infection [A] †	0/13 (0%)	1/9 (11.11%)
Infection [A] †	1/13 (7.69%)	1/9 (11.11%)
Nasopharyngitis [A] †	1/13 (7.69%)	0/9 (0%)
Oral fungal infection [A] †	1/13 (7.69%)	0/9 (0%)

	Lapatinib Plus Capecitabine	Lapatinib Plus Topotecan
	Affected/At Risk (%)	Affected/At Risk (%)
Oral infection [A] †	1/13 (7.69%)	0/9 (0%)
Otitis media [A] †	1/13 (7.69%)	0/9 (0%)
Paronychia [A] †	1/13 (7.69%)	0/9 (0%)
Upper respiratory tract infection [A] †	1/13 (7.69%)	0/9 (0%)
Urinary tract infection [A] †	1/13 (7.69%)	0/9 (0%)
Injury, poisoning and procedural complications		
Contusion [A] †	1/13 (7.69%)	0/9 (0%)
Lumbar vertebral fracture [A] †	1/13 (7.69%)	0/9 (0%)
Investigations		
Activated partial thromboplastin time shortened [A] †	0/13 (0%)	1/9 (11.11%)
Alanine aminotransferase [A] †	0/13 (0%)	1/9 (11.11%)
Blood alkaline phosphatase increased [A] †	1/13 (7.69%)	0/9 (0%)
Blood bilirubin [A] †	0/13 (0%)	1/9 (11.11%)
Blood glucose abnormal [A] †	1/13 (7.69%)	0/9 (0%)
Blood glucose increased [A] †	0/13 (0%)	1/9 (11.11%)
Blood phosphorus decreased [A] †	1/13 (7.69%)	0/9 (0%)
Haemoglobin decreased [A] †	2/13 (15.38%)	2/9 (22.22%)
Protein total abnormal [A] †	1/13 (7.69%)	0/9 (0%)
Prothrombin time abnormal [A] †	1/13 (7.69%)	0/9 (0%)
Weight decreased [A] †	1/13 (7.69%)	1/9 (11.11%)
Weight increased [A] †	1/13 (7.69%)	0/9 (0%)
Metabolism and nutrition disorders		

	Lapatinib Plus Capecitabine	Lapatinib Plus Topotecan
	Affected/At Risk (%)	Affected/At Risk (%)
Decreased appetite [A] †	3/13 (23.08%)	2/9 (22.22%)
Dehydration [A] †	1/13 (7.69%)	0/9 (0%)
Hyperkalaemia [A] †	0/13 (0%)	1/9 (11.11%)
Hypoalbuminaemia [A] †	1/13 (7.69%)	0/9 (0%)
Hypocalcaemia [A] †	0/13 (0%)	1/9 (11.11%)
Hypokalaemia [A] †	2/13 (15.38%)	3/9 (33.33%)
Hyponatraemia [A] †	1/13 (7.69%)	1/9 (11.11%)
Hypoproteinaemia [A] †	0/13 (0%)	1/9 (11.11%)
Musculoskeletal and connective tissue disorders		
Arthralgia [A] †	1/13 (7.69%)	1/9 (11.11%)
Back pain [A] †	1/13 (7.69%)	1/9 (11.11%)
Bone pain [A] †	1/13 (7.69%)	0/9 (0%)
Joint swelling [A] †	1/13 (7.69%)	0/9 (0%)
Muscle spasms [A] †	1/13 (7.69%)	0/9 (0%)
Muscular weakness [A] †	0/13 (0%)	2/9 (22.22%)
Myalgia [A] †	2/13 (15.38%)	0/9 (0%)
Neck pain [A] †	1/13 (7.69%)	1/9 (11.11%)
Osteoporosis [A] †	1/13 (7.69%)	0/9 (0%)
Pain in extremity [A] †	0/13 (0%)	2/9 (22.22%)
Nervous system disorders		
Balance disorder [A] †	1/13 (7.69%)	0/9 (0%)
Disorientation [A] †	1/13 (7.69%)	0/9 (0%)

	Lapatinib Plus Capecitabine	Lapatinib Plus Topotecan
	Affected/At Risk (%)	Affected/At Risk (%)
Dizziness [A] †	3/13 (23.08%)	2/9 (22.22%)
Dysgeusia [A] †	2/13 (15.38%)	0/9 (0%)
Headache [A] †	6/13 (46.15%)	3/9 (33.33%)
Hemiparesis [A] †	1/13 (7.69%)	0/9 (0%)
Memory impairment [A] †	0/13 (0%)	1/9 (11.11%)
Muscle contraction involuntary [A] †	0/13 (0%)	1/9 (11.11%)
Neuropathy peripheral [A] †	1/13 (7.69%)	0/9 (0%)
Paraesthesia [A] †	1/13 (7.69%)	0/9 (0%)
Peripheral sensory neuropathy [A] †	1/13 (7.69%)	1/9 (11.11%)
Somnolence [A] †	1/13 (7.69%)	0/9 (0%)
Psychiatric disorders		
Anxiety [A] †	1/13 (7.69%)	0/9 (0%)
Depressed mood [A] †	2/13 (15.38%)	0/9 (0%)
Insomnia [A] †	2/13 (15.38%)	0/9 (0%)
Major depression [A] †	1/13 (7.69%)	0/9 (0%)
Restlessness [A] †	0/13 (0%)	1/9 (11.11%)
Respiratory, thoracic and mediastinal disorders		
Cough [A] †	1/13 (7.69%)	1/9 (11.11%)
Dyspnoea [A] †	2/13 (15.38%)	1/9 (11.11%)
Nasal ulcer [A] †	1/13 (7.69%)	0/9 (0%)
Pleural effusion [A] †	0/13 (0%)	1/9 (11.11%)
Pneumothorax [A] †	0/13 (0%)	1/9 (11.11%)

	Lapatinib Plus Capecitabine	Lapatinib Plus Topotecan
	Affected/At Risk (%)	Affected/At Risk (%)
Sinus congestion [A] †	2/13 (15.38%)	0/9 (0%)
Sinus disorder [A] †	1/13 (7.69%)	0/9 (0%)
Skin and subcutaneous tissue disorders		
Acne [A] †	0/13 (0%)	1/9 (11.11%)
Alopecia [A] †	0/13 (0%)	2/9 (22.22%)
Dermatitis acneiform [A] †	2/13 (15.38%)	0/9 (0%)
Dry skin [A] †	4/13 (30.77%)	2/9 (22.22%)
Erythema [A] †	0/13 (0%)	1/9 (11.11%)
Ingrowing nail [A] †	1/13 (7.69%)	0/9 (0%)
Nail disorder [A] †	1/13 (7.69%)	0/9 (0%)
Palmar-Plantar erythrodysaesthesia syndrome [A] †	8/13 (61.54%)	1/9 (11.11%)
Pruritus [A] †	2/13 (15.38%)	0/9 (0%)
Rash [A] †	5/13 (38.46%)	1/9 (11.11%)
Rash generalised [A] †	0/13 (0%)	1/9 (11.11%)
Skin chapped [A] †	1/13 (7.69%)	0/9 (0%)
Skin fissures [A] †	0/13 (0%)	1/9 (11.11%)
Skin infection [A] †	0/13 (0%)	1/9 (11.11%)
Vascular disorders		
Hot flush [A] †	1/13 (7.69%)	1/9 (11.11%)
Lymphoedema [A] †	0/13 (0%)	1/9 (11.11%)
Thrombophlebitis superficial [A] †	1/13 (7.69%)	0/9 (0%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

GSK agreements may vary with individual investigators, but will not prohibit any investigator from publishing. GSK supports the publication of results from all centers of a multi-center trial but requests that reports based on single-site data not precede the primary publication of the entire clinical trial.

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