ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: January 19, 2017

ClinicalTrials.gov ID: NCT01355302

Study Identification

Unique Protocol ID:	E7050-703
Brief Title:	E7050 in Combination With Cisplatin and Capecitabine Versus Cisplatin and Capecitabine Alone in Patients With Advanced or Metastatic Solid Tumors and Previously Untreated Gastric Cancer
Official Title:	An Open-Label, Multicenter, Randomized, Phase Ib/II Study of E7050 in Combination With Cisplatin and Capecitabine Versus Cisplatin and Capecitabine Alone in Patients With Advanced or Metastatic Solid Tumors and Previously Untreated Gastric Cancer
Secondary IDs:	2011-000774-58 [EudraCT Number]

Study Status

Record Verification:	January 2017
Overall Status:	Terminated [Sites not recruiting]
Study Start:	November 2011 []
Primary Completion:	April 2013 [Actual]
Study Completion:	July 2013 [Actual]

Sponsor/Collaborators

Sponsor:	Eisai Inc.
Responsible Party:	Sponsor
Collaborators:	Quintiles, Inc.

Oversight

U.S. FDA-regulated Drug:	
U.S. FDA-regulated Device:	
Unapproved/Uncleared Device:	No
IND/IDE Protocol:	Yes
IND/IDE Information:	FDA Center: CDER IND/IDE Number: 109062 Serial Number: Has Expanded Access No
Human Subjects Review:	Board Status: Approved Approval Number: QUI1-11-367 Board Name: Copernicus Group IRB Board Affiliation: Copernicus Group Independent Review Board Phone: 888-303-2224 Email: irb@cgirb.com
Data Monitoring:	No
Plan to Share IPD:	
FDA Regulated Intervention:	Yes
Section 801 Clinical Trial:	Yes

Study Description

Brief Summary:	The purpose of this study is to determine the following: 1. Find the maximum tolerated dose of E7050 when given in combination with cisplatin and capecitabine in patients with advance or metastatic solid tumors, and 2) Whether E7050 in combination with cisplatin and capecitabine is more effective in patients with previously untreated gastric cancer versus cisplatin and capecitabine alone.
Detailed Description:	This open-label, multicenter, randomized study will consist of 2 phases: Phase Ib: a safety run-in period with 3 ascending doses of E7050 in combination with fixed doses of Cisplatin and Capecitabine. This phase will enroll approximately 10 to 15 patients. • Phase II: a randomized 2-arm design which will enroll 80 patients. In the phase II portion, Patients will receive study treatment , E7050 in combination with Cisplatin and Capecitabine versus Cisplatin and Capecitabine Alone) for approximately six 21-day cycles (18 weeks). Beyond 18 weeks, patients who are experiencing clinical benefit may continue E7050, with or without Capecitabine (Arm 1), or may continue Capecitabine alone (Arm 2), depending on the original randomization treatment arm. Patients will continue treatment for as long as clinical benefit is

sustained and the treatment is well tolerated, until the occurrence of progressive disease (PD), unacceptable toxicity, withdrawal of consent, or withdrawal by investigator, whichever occurs first. Patients will participate in either phase Ib or phase II.

Conditions

Conditions: Advanced or Metastatic Solid Tumors
Previously Untreated Gastric Cancer

Keywords: Cancer
Solid Tumors
Gastric
Phase I
Phase II

Study Design

Study Type: Interventional

Primary Purpose: Treatment

Study Phase: Phase 1/Phase 2

Interventional Study Model: Parallel Assignment

Number of Arms: 2

Masking: No masking

Allocation: Randomized

Enrollment: 7 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Phase Ib: Cohort 1 and 2 and 3 Phase Ib: Cohort 1; 200 mg E7050 + 80 mg/m2 cisplatin + 1000 mg/m2 capecitabine Cohort 2; 300 mg E7050 + 80 mg/m2 cisplatin + 2000 mg/m2 capecitabine Cohort 3; 400 mg E7050 + 80 mg/m2 cisplatin + 2000 mg/m2 capecitabine	Drug: E7050 E7050 given orally at either 200, 300, or 400 mg once daily. Drug: cisplatin Cisplatin will be administered at 80 mg/m2 by intravenous infusion over 60 minutes on Day 1 of each 21-day treatment cycle. Drug: capecitabine Capecitabine will be administered at 1000 mg/m2 orally, twice daily (2000 mg/m2 total daily dose) on Days 1 through 14 of each 21-day treatment cycle.
Active Comparator: Phase II: Arm 1; E7050 + cisplatin+ capecitabine	Drug: E7050 E7050 given orally at either 200, 300, or 400 mg once daily.

Arms	Assigned Interventions
Phase II: Arm 1; MTD E7050 + 80 mg/m2 cisplatin + 2000 mg/m2 capecitabine	Drug: cisplatin Cisplatin will be administered at 80 mg/m2 by intravenous infusion over 60 minutes on Day 1 of each 21-day treatment cycle. Drug: capecitabine Capecitabine will be administered at 1000 mg/m2 orally, twice daily (2000 mg/m2 total daily dose) on Days 1 through 14 of each 21-day treatment cycle.

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age:

Sex: All

Gender Based:

Accepts Healthy Volunteers: No

Criteria: Inclusion Criteria

- Histologically confirmed, unresectable, locally advanced or metastatic gastric cancer, including adenocarcinoma of the gastroesophageal junction (Phase II). For the Phase Ib portion, any unresectable, locally advanced or metastatic solid tumor;
- ECOG PS of 0-1;
- Blood pressure must be well-controlled. Patients must have no history of hypertensive crisis or hypertensive encephalopathy; Adequate end organ function

Exclusion Criteria

- Gastric cancer patients who have had a complete gastrectomy;
- Patients with known HER2 over-expressing advanced or metastatic gastric cancer;
- Previously received E7050, its chemical derivatives, anti-cMet, anti-angiogenic therapy, (prior anti-angiogenic therapy is permitted in Phase Ib only).
- For Phase Ib prior systemic therapy is allowed as long as PS and end organ function meet entry criteria;
- For Phase II no prior palliative chemotherapy is permitted. Adjuvant/neoadjuvant chemotherapy is permitted if less than 12 months have elapsed between the end of adjuvant/neoadjuvant therapy and first recurrence;
- Known central nervous system lesions, except for asymptomatic non-progressing, treated brain metastases. Treatment for brain mets, but have been completed at least 4 weeks prior to Day 1
- Palliative radiotherapy is not permitted throughout the study period. Prior palliative radiotherapy within 30 days prior to commencing study treatment;

- Clinically significant hemoptysis;
- Patients with known dihydropyrimidine dehydrogenase deficiency;
- Patients with clinically significant hearing loss that may be further diminished by treatment with cisplatin plus capecitabine (significance of hearing loss to be determined by the Investigator;
- Serious non-healing wound, ulcer, or active bone fracture;
- Major surgical procedure, open biopsy, or significant traumatic injury within the 21 days prior to commencing study treatment;
- Clinically significant gastrointestinal bleeding within 6 months prior to first dose.

Contacts/Locations

Study Officials: Melissa Versola
Study Director
Quintiles

Locations: Russian Federation
FSI "SRC of Oncology n. a. N.N.Petrov of Rosmedtekhnologiy"
St Petersburg, Russian Federation, 197758

GOU VPO St-Petersburg SMA n/a Mechnikov Fed. Agen. of Healthcare and Social Developm.
St Petersburg, Russian Federation, 195067

Chelyabinsk Regional Oncology Dispensary
Chelyabinsk, Russian Federation, 454087

Ukraine
SI Dnipropetrovsk Medical Academy of MOHU ch of Oncology and Medical Radiology
Dnipropetrovsk, Ukraine, 49102

Municipal Clinical Medical and Prophylactic Institution Donetsk Regional Antitumor Centre
Donetsk, Ukraine, 83092

Kyiv City Clinical Oncological Center
Kyiv, Ukraine, 3115

Lviv State Oncol. Reg. Treatment and Diagnostic Center
Lviv, Ukraine, 79031

United States, Michigan
Barbara Ann Karmanos Cancer Institute
Detroit, Michigan, United States, 48084

Henry Ford Medical Center
Detroit, Michigan, United States, 48202

United States, Florida
Boca Raton Clinical Research Associates, Inc
Plantation, Florida, United States, 33324

United Kingdom
Sarah Cannon Research UK
London, Greater London, United Kingdom, W1G 6AD

The Christie NHS Foundation Trust
Manchester, Greater Manchester, United Kingdom, M20 4BX

United States, Arizona
Arizona Oncology Associates, PC - CASA
Tucson, Arizona, United States, 85715

United States, Illinois
Robert H. Lurie Comprenhensive Cancer Center of Northwestern University
Chicago, Illinois, United States, 60611

United Kingdom
Barts and the London NHS Trust
London, Greater London, United Kingdom, EC1A 7BE

United States, North Carolina
University of North Carolina at Chapel Hill
Chapell Hill, North Carolina, United States, 27599

Duke University Medical Center
Durham, North Carolina, United States, 27710

United States, Michigan
University of Michigan Comprehensive Cancer Center
Ann Arbor, Michigan, United States, 48109

United States, Ohio
Mercy Cancer Centerr at St. Anne
Toledo, Ohio, United States, 43623

References

Citations:

Links:

Study Data/Documents:

Delayed Results

Delay Type	Certify Initial Approval
Intervention Name(s)	E7050

Study Results

Participant Flow

Pre-Assignment Details	Subjects were to only participate in either the Phase 1b or Phase 2 portion of the study.

Reporting Groups

	Description
Phase 1b: Golvatinib+Capecitabine +Cisplatin	Oral golvatinib (200 mg) was taken at about the same time each day of every 21-day treatment cycle, with or without food. Oral capecitabine (1000 mg/m2 tablet) was taken twice a day (2000 mg/m2 total daily) with food at about the same time (after golvatinib), on Days 1 through 14 of each 21-day cycle. At least 2 hours after capecitabine was taken, cisplatin (80 mg/m2) was administered by intravenous (IV) infusion over 60 minutes (after appropriate hydration or according to the institutional guidelines), on Day 1 of each 21-day cycle. Pretreatment hydration included 1 liter of normal saline by IV infusion over 120 minutes. Posttreatment hydration included 500 mL normal saline over 60 minutes. The dose level of golvatinib was to be escalated (to 300 and 400 mg) for additional cohorts after 3 participants enrolled into a given cohort unless there was a dose-limiting toxicity (DLT) in the first 3 participants.
Phase 2: Golvatinib+Capecitabine +Cisplatin	The dose of golvatinib was to be the maximum tolerated dose (MTD) as determined during the Phase 1b portion of the study in combination with capecitabine and cisplatin as described for Phase 1b. The study was terminated prior to Phase 2.
Phase 2: Capecitabine + Cisplatin	Oral capecitabine (1000 mg/m2 tablet) was taken twice a day (2000 mg/m2 total daily) with food at about the same time (after golvatinib), on Days 1 through 14 of each 21-day cycle. At least 2 hours after capecitabine was taken, cisplatin (80 mg/m2) was administered by intravenous (IV) infusion over 60 minutes (after appropriate hydration or according to the institutional guidelines), on Day 1 of each 21-day cycle. Pretreatment hydration included 1 liter of normal saline by IV infusion over 120 minutes. Posttreatment hydration included 500 mL normal saline over 60 minutes.

Phase 1b

	Phase 1b: Golvatinib +Capecitabine+Cisplatin	Phase 2: Golvatinib +Capecitabine+Cisplatin	Phase 2: Capecitabine + Cisplatin
Started	7 [1]	0	0
Completed	1 [2]	0	0
Not Completed	6	0	0
Death	4	0	0
Study terminated by sponsor	2	0	0

[1] Replaced 1 subject; who discontinued study drug in first cycle
[2] The subject who completed 6 cycles was withdrawn by sponsor request.

Phase 2

	Phase 1b: Golvatinib +Capecitabine+Cisplatin	Phase 2: Golvatinib +Capecitabine+Cisplatin	Phase 2: Capecitabine + Cisplatin
Started	0 [1]	0 [2]	0 [2]
Completed	0	0	0
Not Completed	0	0	0

[1] Treatment arm not designated for phase 2.
[2] The study was terminated prior to enrollment

Baseline Characteristics

Reporting Groups

	Description
Phase 1b: Golvatinib+Capecitabine +Cisplatin	Oral golvatinib (200 mg) was taken at about the same time each day of every 21-day treatment cycle, with or without food. Oral capecitabine (1000 mg/m2 tablet) was taken twice a day (2000 mg/m2 total daily) with food at about the same time (after golvatinib), on Days 1 through 14 of each 21-day cycle. At least 2 hours after capecitabine was taken, cisplatin (80 mg/m2) was administered by intravenous (IV) infusion over 60 minutes (after appropriate hydration or according to the institutional guidelines), on Day 1 of each 21-day cycle. Pretreatment hydration included 1 liter of normal saline by IV infusion over 120 minutes. Posttreatment hydration included 500 mL normal saline over 60 minutes. The dose level of golvatinib was to be escalated (to 300 and 400 mg) for additional cohorts after 3 participants enrolled into a given cohort unless there was a dose-limiting toxicity (DLT) in the first 3 participants.

Baseline Measures

		Phase 1b: Golvatinib+Capecitabine+Cisplatin
Overall Number of Participants		7
Age, Customized Measure Type: Number Unit of measure: Participants	Number Analyzed	7 participants
Age range 47 to 80 years		7
Sex: Female, Male Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	7 participants
	Female	4 57.14%
	Male	3 42.86%

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Area Under The Concentration-Time Curve (AUC) From 0 to 24 Hours of Golvatinib

Measure Description	On days when pharmacokinetic (PK) samples were to be drawn, a predose blood sample was obtained prior to administration of golvatinib and capecitabine. After administration of study drugs, a second postdose blood sample was taken. The amount of golvatinib in the participant's blood was analyzed and the AUC was calculated. The AUC reflects the actual body exposure to drug after administration of a dose of the drug and is dependent on the rate of elimination of the drug from the body and the dose administered. Predose samples that were below the limit of quantitation (BLQ) or missing were assigned a numerical value of zero for the calculation of AUC. Any other BLQ concentrations were assigned a value of zero.
Time Frame	Cycle 1/Day -2 and Cycle 2/Day 1

Analysis Population Description

Pharmacokinetic (PK) population: All participants in the Safety Population who had sufficient concentration data to derive one or more of the PK parameters. Participants with partial data were evaluated on a case-by-case basis to determine if sufficient data were available for meaningful PK analysis.

Reporting Groups

	Description
Phase 1b: Golvatinib+Capecitabine +Cisplatin	Oral golvatinib (200 mg) was taken at about the same time each day of every 21-day treatment cycle, with or without food. Oral capecitabine (1000 mg/m2 tablet) was taken twice a day (2000 mg/m2 total daily) with food at about the same time (after golvatinib), on Days 1 through 14 of each 21-day cycle. At least 2 hours after capecitabine was taken, cisplatin (80 mg/m2) was administered by intravenous (IV) infusion over 60 minutes (after appropriate hydration or according to the institutional guidelines), on Day 1 of each 21-day cycle. Pretreatment hydration included 1 liter of normal saline by IV infusion over 120 minutes. Posttreatment hydration included 500 mL normal saline over 60 minutes. The dose level of golvatinib was to be escalated (to 300 and 400 mg) for additional cohorts after 3 participants enrolled into a given cohort unless there was a dose-limiting toxicity (DLT) in the first 3 participants.

Measured Values

	Phase 1b: Golvatinib+Capecitabine+Cisplatin
Overall Number of Participants Analyzed	7
Area Under The Concentration-Time Curve (AUC) From 0 to 24 Hours of Golvatinib Median (Full Range) Unit of measure: ng h/mL	
Cycle 1, Day -2	23400 (5000 to 56100)
Cycle 2, Day 1	26300 (17400 to 62400)

2. Primary Outcome Measure:

Measure Title	Maximum Concentration (Cmax) of Golvatinib

Measure Description	Blood samples were drawn to analyze the amount of golvatinib in the participant's serum. Maximum concentration refers to the maximum (or peak) serum concentration of study drug in the participant's system after administration of the study drug and prior to the administration of a second dose of the study drug.
Time Frame	Cycle 1/Day -2 and Cycle 2/Day 1

Analysis Population Description

Pharmacokinetic (PK) population: All participants in the Safety Population who had sufficient concentration data to derive one or more of the PK parameters. Participants with partial data were evaluated on a case-by-case basis to determine if sufficient data were available for meaningful PK analysis.

Reporting Groups

	Description
Phase 1b: Golvatinib+Capecitabine +Cisplatin	Oral golvatinib (200 mg) was taken at about the same time each day of every 21-day treatment cycle, with or without food. Oral capecitabine (1000 mg/m2 tablet) was taken twice a day (2000 mg/m2 total daily) with food at about the same time (after golvatinib), on Days 1 through 14 of each 21-day cycle. At least 2 hours after capecitabine was taken, cisplatin (80 mg/m2) was administered by intravenous (IV) infusion over 60 minutes (after appropriate hydration or according to the institutional guidelines), on Day 1 of each 21-day cycle. Pretreatment hydration included 1 liter of normal saline by IV infusion over 120 minutes. Posttreatment hydration included 500 mL normal saline over 60 minutes. The dose level of golvatinib was to be escalated (to 300 and 400 mg) for additional cohorts after 3 participants enrolled into a given cohort unless there was a dose-limiting toxicity (DLT) in the first 3 participants.

Measured Values

	Phase 1b: Golvatinib+Capecitabine+Cisplatin
Overall Number of Participants Analyzed	7
Maximum Concentration (Cmax) of Golvatinib Median (Full Range) Unit of measure: ng/mL	
Cycle 1, Day -2	1680 (268 to 3890)
Cycle 2, Day 1	1620 (834 to 3430)

3. Primary Outcome Measure:

Measure Title	Number of Participants With a Treatment-Emergent Adverse Event (TEAE)
Measure Description	A TEAE was defined as an adverse event (AE) that had an onset date, or a worsening in severity from Baseline (pretreatment), on or after the first dose of study drug up to 30 days after the date of last study treatment.
Time Frame	Baseline to End of Study

Analysis Population Description

Safety Population included all participants who received at least one dose of study drug and who had at least one safety assessment after the first dose of study drug.

Reporting Groups

	Description
Phase 1b: Golvatinib+Capecitabine +Cisplatin	Oral golvatinib (200 mg) was taken at about the same time each day of every 21-day treatment cycle, with or without food. Oral capecitabine (1000 mg/m2 tablet) was taken twice a day (2000 mg/m2 total daily) with food at about the same time (after golvatinib), on Days 1 through 14 of each 21-day cycle. At least 2 hours after capecitabine was taken, cisplatin (80 mg/m2) was administered by intravenous (IV) infusion over 60 minutes (after appropriate hydration or according to the institutional guidelines), on Day 1 of each 21-day cycle. Pretreatment hydration included 1 liter of normal saline by IV infusion over 120 minutes. Posttreatment hydration included 500 mL normal saline over 60 minutes. The dose level of golvatinib was to be escalated (to 300 and 400 mg) for additional cohorts after 3 participants enrolled into a given cohort unless there was a dose-limiting toxicity (DLT) in the first 3 participants.

Measured Values

	Phase 1b: Golvatinib+Capecitabine+Cisplatin
Overall Number of Participants Analyzed	7
Number of Participants With a Treatment-Emergent Adverse Event (TEAE) Measure Type: Number Unit of measure: Participants	7

4. Primary Outcome Measure:

Measure Title	Time to Maximum Concentration (Tmax) of Golvatinib
Measure Description	Tmax was defined as the time at which Cmax was observed for golvatinib in combination with cisplatin and capecitabine.
Time Frame	Cycle 1/Day -2 and Cycle 2/Day 1

Analysis Population Description

Pharmacokinetic (PK) population: All participants in the Safety Population who had sufficient concentration data to derive one or more of the PK parameters. Participants with partial data were evaluated on a case-by-case basis to determine if sufficient data were available for meaningful PK analysis.

Reporting Groups

	Description
Phase 1b: Golvatinib+Capecitabine +Cisplatin	Oral golvatinib (200 mg) was taken at about the same time each day of every 21-day treatment cycle, with or without food. Oral capecitabine (1000 mg/m2 tablet) was taken twice a day (2000 mg/m2 total daily) with food at about the same time (after golvatinib), on Days 1 through 14 of each 21-day cycle. At least 2 hours after capecitabine was taken, cisplatin (80 mg/m2) was administered by intravenous (IV) infusion over 60 minutes (after appropriate hydration or according to the institutional guidelines), on Day 1 of each 21-day cycle. Pretreatment hydration included 1 liter of normal saline by IV infusion over 120 minutes. Posttreatment hydration included 500 mL normal saline over 60 minutes. The dose level of golvatinib was to be escalated (to 300 and 400 mg) for additional cohorts after 3 participants enrolled into a given cohort unless there was a dose-limiting toxicity (DLT) in the first 3 participants.

Measured Values

	Phase 1b: Golvatinib+Capecitabine+Cisplatin
Overall Number of Participants Analyzed	7
Time to Maximum Concentration (Tmax) of Golvatinib Median (Full Range) Unit of measure: Hours	
Cycle 1, Day -2	3.00 (1.00 to 7.78)
Cycle 2, Day 1	6.07 (3.00 to 12.82)

5. Secondary Outcome Measure:

Measure Title	Overall Response Rate (ORR)
Measure Description	The study was terminated prior to enrollment in Phase 2 so this outcome measure was not conducted.
Time Frame	Until disease progression or death for 3 years

Outcome Measure Data Not Reported

6. Secondary Outcome Measure:

Measure Title	Time to Progression (TTP)
Measure Description	The study was terminated prior to enrollment in Phase 2 so this outcome measure was not conducted.
Time Frame	Until disease progression or death for 3 years

Outcome Measure Data Not Reported

Reported Adverse Events

Time Frame	All adverse events (AEs) were collected beginning from the time of informed consent signing through the 30-day follow-up period. Serious AEs were followed for 30 days after last dose of study drug. AEs were collected for approximately 1 year.
Adverse Event Reporting Description	Safety population included all participants enrolled in Phase 1b of this study, except for those who (a) dropped out prior to receiving study drug, or (b) were without any safety assessments after the first dose of study drug. Treatment-emergent AEs, (onset date or worsening in severity from baseline after first dose of study drug), were reported.

Reporting Groups

	Description
Phase 1b: Golvatinib+Capecitabine +Cisplatin	Oral golvatinib (200 mg) was taken at about the same time each day of every 21-day treatment cycle, with or without food. Oral capecitabine (1000 mg/m2 tablet) was taken twice a day (2000 mg/m2 total daily) with food at about the same time (after golvatinib), on Days 1 through 14 of each 21-day cycle. At least 2 hours after capecitabine was taken, cisplatin (80 mg/m2) was administered by intravenous (IV) infusion over 60 minutes (after appropriate hydration or according to the institutional guidelines), on Day 1 of each 21-day cycle. Pretreatment hydration included 1 liter of normal saline by IV infusion over 120 minutes. Posttreatment hydration included 500 mL normal saline over 60 minutes. The dose level of golvatinib was to be escalated (to 300 and 400 mg) for additional cohorts after 3 participants enrolled into a given cohort unless there was a dose-limiting toxicity (DLT) in the first 3 participants.

All-Cause Mortality

	Phase 1b: Golvatinib+Capecitabine+Cisplatin
	Affected/At Risk (%)
Total All-Cause Mortality	/

Serious Adverse Events

	Phase 1b: Golvatinib+Capecitabine+Cisplatin
	Affected/At Risk (%)
Total	5/7 (71.43%)
Cardiac disorders	
Supraventricular tachycardia [A] †	1/7 (14.29%)
Gastrointestinal disorders	
Nausea [A] †	1/7 (14.29%)

	Phase 1b: Golvatinib+Capecitabine+Cisplatin
	Affected/At Risk (%)
Stomatitis [A] †	1/7 (14.29%)
Vomiting [A] †	1/7 (14.29%)
Infections and infestations	
Pneumonia [A] †	1/7 (14.29%)
Psoas abscess [A] †	1/7 (14.29%)
Metabolism and nutrition disorders	
Dehydration [A] †	1/7 (14.29%)
Electrolyte imbalance [A] †	1/7 (14.29%)
Musculoskeletal and connective tissue disorders	
Arthralgia [A] †	1/7 (14.29%)
Nervous system disorders	
Convulsion [A] †	1/7 (14.29%)
Vascular disorders	
Pulmonary embolism [A] †	1/7 (14.29%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA Version 15.0

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	Phase 1b: Golvatinib+Capecitabine+Cisplatin
	Affected/At Risk (%)
Total	7/7 (100%)
Blood and lymphatic system disorders	
Anaemia [A] †	3/7 (42.86%)
Leukocytosis [A] †	1/7 (14.29%)
Leukopenia [A] †	3/7 (42.86%)

	Phase 1b: Golvatinib+Capecitabine+Cisplatin
	Affected/At Risk (%)
Neutropenia [A] †	3/7 (42.86%)
Thrombocytopenia [A] †	2/7 (28.57%)
Cardiac disorders	
Arteriosclerosis coronary artery [A] †	1/7 (14.29%)
Palpitations [A] †	1/7 (14.29%)
Supraventricular tachycardia [A] †	1/7 (14.29%)
Eye disorders	
Eye discharge [A] †	1/7 (14.29%)
Lacrimation increased [A] †	1/7 (14.29%)
Vision blurred [A] †	1/7 (14.29%)
Gastrointestinal disorders	
Abdominal discomfort [A] †	1/7 (14.29%)
Abdominal distension [A] †	1/7 (14.29%)
Abdominal pain [A] †	1/7 (14.29%)
Abdominal pain upper [A] †	1/7 (14.29%)
Abdominal tenderness [A] †	1/7 (14.29%)
Constipation [A] †	3/7 (42.86%)
Diarrhoea [A] †	3/7 (42.86%)
Dry mouth [A] †	1/7 (14.29%)
Dyspepsia [A] †	1/7 (14.29%)
Dysphagia [A] †	1/7 (14.29%)
Enteritis [A] †	1/7 (14.29%)
Glossodynia [A] †	1/7 (14.29%)

	Phase 1b: Golvatinib+Capecitabine+Cisplatin
	Affected/At Risk (%)
Nausea [A] †	7/7 (100%)
Oral pain [A] †	1/7 (14.29%)
Proctalgia [A] †	1/7 (14.29%)
Stomatitis [A] †	1/7 (14.29%)
Vomiting [A] †	5/7 (71.43%)
General disorders	
Asthenia [A] †	2/7 (28.57%)
Chest pain [A] †	2/7 (28.57%)
Chills [A] †	2/7 (28.57%)
Cold sweat [A] †	1/7 (14.29%)
Fatigue [A] †	5/7 (71.43%)
Feeling cold [A] †	1/7 (14.29%)
Feeling hot [A] †	1/7 (14.29%)
Malaise [A] †	1/7 (14.29%)
Mucosal inflammation [A] †	1/7 (14.29%)
Oedema peripheral [A] †	1/7 (14.29%)
Pain [A] †	1/7 (14.29%)
Pallor [A] †	1/7 (14.29%)
Pyrexia [A] †	2/7 (28.57%)
Infections and infestations	
Nasopharyngitis [A] †	1/7 (14.29%)
Oropharyngeal candidiasis [A] †	1/7 (14.29%)
Pneumonia [A] †	1/7 (14.29%)

	Phase 1b: Golvatinib+Capecitabine+Cisplatin
	Affected/At Risk (%)
Streptococcal bacteraemia [A] †	1/7 (14.29%)
Urinary tract infection [A] †	1/7 (14.29%)
Injury, poisoning and procedural complications	
Contusion [A] †	2/7 (28.57%)
Investigations	
Blood alkaline phosphatase increased [A] †	1/7 (14.29%)
Breath sounds abnormal [A] †	1/7 (14.29%)
Electrocardiogram st segment elevation [A] †	1/7 (14.29%)
Weight decreased [A] †	2/7 (28.57%)
Metabolism and nutrition disorders	
Decreased appetite [A] †	4/7 (57.14%)
Dehydration [A] †	5/7 (71.43%)
Dizziness [A] †	2/7 (28.57%)
Electrolyte imbalance [A] †	1/7 (14.29%)
Hyperglycaemia [A] †	1/7 (14.29%)
Hypoalbuminaemia [A] †	2/7 (28.57%)
Hypocalcaemia [A] †	3/7 (42.86%)
Hypoglycaemia [A] †	1/7 (14.29%)
Hypokalaemia [A] †	2/7 (28.57%)
Hypomagnesaemia [A] †	2/7 (28.57%)
Hyponatraemia [A] †	2/7 (28.57%)
Hypophosphataemia [A] †	1/7 (14.29%)
Musculoskeletal and connective tissue disorders	

	Phase 1b: Golvatinib+Capecitabine+Cisplatin
	Affected/At Risk (%)
Arthralgia [A] †	1/7 (14.29%)
Back pain [A] †	1/7 (14.29%)
Muscle spasms [A] †	1/7 (14.29%)
Musculoskeletal pain [A] †	1/7 (14.29%)
Pain in extremity [A] †	2/7 (28.57%)
Psoas abscess [A] †	1/7 (14.29%)
Scoliosis [A] †	1/7 (14.29%)
Spinal osteoarthritis [A] †	1/7 (14.29%)
Nervous system disorders	
Ageusia [A] †	1/7 (14.29%)
Amnesia [A] †	1/7 (14.29%)
Balance disorder [A] †	1/7 (14.29%)
Convulsion [A] †	1/7 (14.29%)
Headache [A] †	3/7 (42.86%)
Hypoaesthesia [A] †	1/7 (14.29%)
Neuralgia [A] †	1/7 (14.29%)
Neuropathy peripheral [A] †	1/7 (14.29%)
Paraesthesia [A] †	1/7 (14.29%)
Peripheral sensory neuropathy [A] †	1/7 (14.29%)
Trigeminal neuralgia [A] †	1/7 (14.29%)
Psychiatric disorders	
Anxiety [A] †	2/7 (28.57%)
Catatonia [A] †	1/7 (14.29%)

	Phase 1b: Golvatinib+Capecitabine+Cisplatin
	Affected/At Risk (%)
Depression [A] †	1/7 (14.29%)
Insomnia [A] †	2/7 (28.57%)
Mood swings [A] †	1/7 (14.29%)
Restlessness [A] †	1/7 (14.29%)
Renal and urinary disorders	
Haematuria [A] †	1/7 (14.29%)
Nocturia [A] †	1/7 (14.29%)
Renal failure acute [A] †	1/7 (14.29%)
Respiratory, thoracic and mediastinal disorders	
Cough [A] †	1/7 (14.29%)
Diaphragmatic paralysis [A] †	1/7 (14.29%)
Dyspnoea [A] †	1/7 (14.29%)
Epistaxis [A] †	1/7 (14.29%)
Hiccups [A] †	1/7 (14.29%)
Hypoxia [A] †	1/7 (14.29%)
Increased upper airway secretion [A] †	1/7 (14.29%)
Nasal dryness [A] †	1/7 (14.29%)
Oropharyngeal pain [A] †	1/7 (14.29%)
Paranasal sinus hypersecretion [A] †	1/7 (14.29%)
Tachypnoea [A] †	1/7 (14.29%)
Wheezing [A] †	1/7 (14.29%)
Skin and subcutaneous tissue disorders	
Decubitus ulcer [A] †	1/7 (14.29%)

	Phase 1b: Golvatinib+Capecitabine+Cisplatin
	Affected/At Risk (%)
Dry skin [A] †	1/7 (14.29%)
Erythema [A] †	1/7 (14.29%)
Palmar-Plantar erythrodysaesthesia Syndrome [A] †	4/7 (57.14%)
Rash [A] †	2/7 (28.57%)
Rash generalised [A] †	1/7 (14.29%)
Scab [A] †	1/7 (14.29%)
Vascular disorders	
Hypotension [A] †	1/7 (14.29%)
Pulmonary embolism [A] †	1/7 (14.29%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA Version 15.0

Limitations and Caveats

The study was terminated prior to enrollment in Phase 2.

More Information

Certain Agreements:

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

There is NOT 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.

Results Point of Contact:

Name/Official Title: Eisai Medical Services
Organization: Eisai Inc.
Phone: 888-422-4743
Email: