A Study of ARQ 197 Versus Investigator's Choice of Second-Line Chemotherapy in Patients With Locally Advanced or Metastatic Gastric Cancer Who Have Progressive Neoplastic Disease Following Treatment With One Prior Chemotherapy Regimen

ClinicalTrials.gov Identifier: NCT01070290

Recruitment Status : Withdrawn
First Posted : February 18, 2010
Last Update Posted : January 7, 2014

Sponsor:
ArQule

Information provided by (Responsible Party):
ArQule

Tracking Information	
First Submitted Date ICMJE	February 16, 2010
First Posted Date ICMJE	February 18, 2010
Last Update Posted Date	January 7, 2014
Study Start Date ICMJE	*Not Provided*
Primary Completion Date	*Not Provided*
Current Primary Outcome Measures ICMJE **(submitted: February 17, 2010)**	Compare the progression-free survival (PFS) of ARQ 197 versus investigator's choice of second-line chemotherapy in patients with advanced gastric cancer who have failed first-line treatment.
	Same as current

Original Primary Outcome Measures ICMJE	
Change History	Complete list of historical versions of study NCT01070290 on ClinicalTrials.gov Archive Site
Current Secondary Outcome Measures ICMJE **(submitted: February 17, 2010)**	• Compare overall response rate (ORR) of ARQ 197 versus investigator's choice of second-line chemotherapy • Compare 6-month and 1-year overall survival (OS) rates of ARQ 197 versus investigator's choice of second-line chemotherapy • Further characterize the safety profile of ARQ 197
Original Secondary Outcome Measures ICMJE	*Same as current*
Current Other Pre-specified Outcome Measures	*Not Provided*
Original Other Pre-specified Outcome Measures	*Not Provided*

Descriptive Information

Brief Title ICMJE	A Study of ARQ 197 Versus Investigator's Choice of Second-Line Chemotherapy in Patients With Locally Advanced or Metastatic Gastric Cancer Who Have Progressive Neoplastic Disease Following Treatment With One Prior Chemotherapy Regimen
Official Title ICMJE	A Randomized Phase 2 Study of ARQ 197 Versus Investigator's Choice of Second-Line Chemotherapy in Patients With Locally Advanced or Metastatic Gastric Cancer Who Have Progressive Neoplastic Disease Following Treatment With One Prior Chemotherapy Regimen

Brief Summary	This will be a multi-center, open-label randomized phase 2 study designed to evaluate the progression free survival (PFS) of patients with advanced gastric cancer following treatment with either ARQ 197 or one of three standard regimens (investigator's choice). Patients with unresectable (locally advanced or metastatic) gastric carcinoma who have progressive neoplastic disease following treatment with a prior regimen consisting of at least two of the drugs 5-FU, cisplatin and docetaxel. The study will also evaluate other efficacy and safety parameters including overall response rate, overall survival and adverse events in the two treatment arms.
Detailed Description	This will be a multi-center, open-label randomized phase 2 study designed to evaluate the PFS of ARQ 197 versus investigator's choice of second-line chemotherapy in patients with unresectable (locally advanced or metastatic) gastric carcinoma who have progressive neoplastic disease following treatment with a prior regimen consisting of at least two of the drugs 5-FU, cisplatin and docetaxel. Patients will be randomized to ARQ 197 arm or investigator's choice arm in a 1:1 ratio. The study will also evaluate other efficacy and safety parameters including ORR, OS and adverse events in the two treatment arms. Patients assigned to the investigator's choice arm may receive any one of the following: • Oxaliplatin 85 mg/m2 i.v. every two weeks (each cycle = 4 weeks) • Capecitabine 1250 mg/m2 p.o. twice daily for 14 days followed by 7 days of no therapy every 3 weeks (each cycle = 3 weeks) • Irinotecan 125 mg/m2 i.v. weekly for 4 weeks followed by 2 weeks of no therapy every 6 weeks (each cycle = 6 weeks) Treatment will continue unless one of the treatment discontinuation criteria is met. Dose reductions should occur based on the current labels for each of the investigator choice agents. Patients randomly assigned to the ARQ arm will receive 120 mg of ARQ 197 twice daily (240 mg/day) throughout the treatment period. The treatment of ARQ 197 can be continued until unacceptable toxicity, documented progression of disease, or another discontinuation criterion is

met. A cycle of ARQ 197 treatment will be defined as 21 days and cycles may be repeated every 3 weeks (21 days) based on toxicity and response.

The assigned treatment should continue until unacceptable toxicity, disease progression (clinical or radiological) or another discontinuation criterion is met.

Tumor evaluations: Tumor evaluations will be performed at 6-week or 8-week intervals. Tumor response will be evaluated using Response Evaluation Criteria in Solid Tumors (RECIST).

Progression-free survival: The time of disease progression-free will be calculated from date of randomization until disease progression per RECIST or death due to any cause. Patients who are alive and progression free will be censored at the date of their last tumor evaluation.

Overall response rate: The ORR will be calculated for the intent to treat patient population as the number of patients with a confirmed complete response or partial response divided by the number of randomized patients.

Overall survival: Overall survival time will be calculated from the date of randomization until death due to any cause.

Safety assessments: Data on vital signs, physical examination, adverse events, serum chemistry, hematological laboratory tests, and electrocardiograms will be collected.

Based on the data for irinotecan, it is estimated that the median PFS in the second-line chemotherapy arm will be 4 months. In order to demonstrate an improvement in median PFS to 5.5 months (37.5% improvement, hazard ratio of 0.73) based on a two-sided log rang test, 338 patients (169 per arm) will be required, assuming an 18 month enrollment and a 12 month follow-up, an alpha of 0.05 and 90% power. The sample size assumes a 10% loss to follow-up rate.

A futility analysis will be performed when 33% of the events required for the final analysis have occurred by an Independent Data Monitoring Committee. The futility boundary will be described in the full statistical analysis plan for the study.

Study Type ICMJE	Interventional
Study Phase ICMJE	Phase 2
Study Design ICMJE	Allocation: Randomized Intervention Model: Parallel Assignment Masking: None (Open Label) Primary Purpose: Treatment
Condition ICMJE	Gastric Cancer
Intervention ICMJE	• Drug: ARQ 197 120 mg capsule administered twice daily • Drug: Oxaliplatin, capecitabine or irinotecan Investigator's choice or oxaliplatin, capecitabine or irinotecan
Study Arms ICMJE	• Experimental: 1 ARQ 197 Intervention: Drug: ARQ 197 • Active Comparator: 2 Investigator's choice of oxaliplatin, capecitabine or irinotecan Intervention: Drug: Oxaliplatin, capecitabine or irinotecan
Publications *	*Not Provided*

*** Includes publications given by the data provider as well as publications identified by ClinicalTrials.gov Identifier (NCT Number) in Medline.**

Recruitment Information

Recruitment Status ICMJE	Withdrawn
Actual Enrollment ICMJE **(submitted: January 6, 2014)**	0
Original Estimated Enrollment ICMJE **(submitted: February 17, 2010)**	338
Study Completion Date ICMJE	*Not Provided*
Primary Completion Date	*Not Provided*
Eligibility Criteria ICMJE	Inclusion Criteria: 1. Provide signed and dated informed consent prior to study-specific screening procedures 2. ≥ 18 years old 3. Histologically or cytologically confirmed locally advanced or metastatic unresectable gastric carcinoma 4. Progressive neoplastic disease despite treatment with a regimen consisting of at least two of the following agents given concurrently: 5-FU, cisplatin and docetaxel OR intolerance to such a regimen 5. Measurable disease as defined by Response Evaluation Criteria in Solid Tumors (RECIST) 6. Eastern Cooperative Oncology Group performance status 0 to 2

7. Male or female patients of child-producing potential must agree to use double barrier contraception, oral contraceptives or avoidance of pregnancy measures during the study and for 90 days after the last day of treatment
8. Females of childbearing potential must have a negative serum pregnancy test
9. Aspartate transaminase (AST) and alanine transaminase (ALT) ≤ 2.5 × upper limit of normal (ULN) or ≤ 5 × ULN with known metastatic liver disease
10. Total bilirubin ≤ 1.5 × ULN
11. Serum creatinine ≤ 1.5 x ULN
12. Absolute neutrophil count (ANC) ≥ 1.5 x 10^9/L
13. Platelets ≥ 100 x 10^9/L

Exclusion Criteria:

1. Received more than one prior systemic regimen for the treatment of gastric cancer (including chemotherapy, immunotherapy, vaccines, monoclonal antibodies)
2. Known or suspected central nervous system metastases
3. Pregnant or lactating
4. Significant gastrointestinal disorder that, in the opinion of Investigator, could interfere with the absorption of ARQ 197 (e.g. Crohn's disease, ulcerative colitis, extensive gastric resection)
5. Unable or unwilling to swallow ARQ 197 capsules twice daily
6. Any contraindication to treatment with ARQ 197, capecitabine, oxaliplatin or irinotecan
7. Prior treatment with capecitabine, oxaliplatin or irinotecan
8. Any known hypersensitivity to any of the components of ARQ 197, capecitabine, oxaliplatin or irinotecan

	9. Treatment with an investigational agent within 30 days of first dose of protocol defined treatments 10. Other malignancies within the last five years, with the exception of adequately treated intraepithelial carcinoma of the cervix uteri, prostate carcinoma with a PSA value < 0.2 ng/ml or basal or squamous cell carcinoma of the skin 11. Any other significant co-morbid conditions that in the opinion of the Investigator would impair study participation or cooperation 12. Known human immunodeficiency virus (HIV), hepatitis B virus (HBV) or hepatitis C virus (HCV) infection
Sex/Gender ICMJE	Sexes Eligible for Study: All
Ages ICMJE	18 Years and older (Adult, Older Adult)
Accepts Healthy Volunteers ICMJE	No
Contacts ICMJE	*Contact information is only displayed when the study is recruiting subjects*
Listed Location Countries ICMJE	*Not Provided*
Removed Location Countries	
Administrative Information	
NCT Number ICMJE	NCT01070290
Other Study ID Numbers ICMJE	ARQ 197-206

Has Data Monitoring Committee	Yes
U.S. FDA-regulated Product	*Not Provided*
IPD Sharing Statement ICMJE	*Not Provided*
Responsible Party	ArQule
Study Sponsor ICMJE	ArQule
Collaborators ICMJE	*Not Provided*
Investigators ICMJE	*Not Provided*
PRS Account	ArQule
Verification Date	January 2014

ICMJE **Data element required by the International Committee of Medical Journal Editors and the World Health Organization ICTRP**

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No Study Results Posted on ClinicalTrials.gov for this Study

Study was withdrawn before participants were enrolled.

About Study Results Reporting on ClinicalTrials.gov

Recruitment Status :	Withdrawn
Primary Completion Date :	*No date given*
Study Completion Date :	*No date given*