A021602

Randomized, Double-Blinded Phase III Study of CABozantinib Versus Placebo IN Patients With Advanced NEuroendocrine Tumors After Progression on Prior Therapy (CABINET)

ClinicalTrials.gov Identifier: NCT03375320

Study Background

Trial Description

This phase III trial studies cabozantinib to see how well it works compared with placebo in treating patients with neuroendocrine or carcinoid tumors that may have spread from where it first started to nearby tissue, lymph nodes, or distant parts of the body (advanced). Cabozantinib is a chemotherapy drug known as a tyrosine kinase inhibitor, and it targets specific tyrosine kinase receptors, that when blocked, may slow tumor growth.

Arms:

Arm I (cabozantinib S-malate): (Experimental): Patients receive cabozantinib Smalate PO QD on days 1-28 of each cycle. Cycles repeat every 28 days in the absence of disease progression or unacceptable toxicity. Patients also undergo CT, MRI, and/or x-ray imaging during screening and on study.

Arm II (placebo): (Placebo Comparator): Patients receive placebo PO QD on days 128 of each cycle. Cycles repeat every 28 days in the absence of disease progression or unacceptable toxicity. Patients also undergo CT, MRI, and/or x-ray imaging during screening and on study. A protocol amendment activated in November 2020 permitted patients who were receiving placebo to cross over to open-label cabozantinib after real-time central confirmation of progressive disease.

Objectives:

PRIMARY OBJECTIVES:

I. To determine whether cabozantinib S-malate (cabozantinib) can significantly improve progression-free survival (PFS) compared to placebo in patients with advanced pancreatic neuroendocrine tumors (NET) whose disease has progressed after prior therapy.

II. To determine whether cabozantinib can significantly improve progression-free survival (PFS) compared to placebo in patients with advanced carcinoid tumors whose disease has progressed after prior therapy. SECONDARY OBJECTIVES: I. To determine whether cabozantinib can significantly improve overall survival (OS) compared to placebo in patients with advanced pancreatic NET whose disease has progressed after prior therapy.

III. To determine whether cabozantinib can significantly improve overall survival (OS) compared to placebo in patients with advanced carcinoid tumors whose disease has progressed after prior therapy.

IV. To evaluate safety and tolerability of cabozantinib versus placebo in patients with advanced pancreatic NET using Common Terminology Criteria for Adverse Events (CTCAE) and Patient-Reported Outcomes Version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE).

V. To evaluate safety and tolerability of cabozantinib versus placebo in patients with advanced carcinoid tumors using CTCAE and PRO-CTCAE. V. To evaluate the overall radiographic response rate of cabozantinib versus placebo in patients with advanced pancreatic NET whose disease has progressed after prior therapy.

VI. To evaluate the overall radiographic response rate of cabozantinib versus placebo in patients with advanced carcinoid tumors whose disease has progressed after prior therapy.

OTHER OBJECTIVE:
I. Results of the primary analysis will be examined for consistency, while taking into account the stratification factors and/or covariates of baseline quality of life (QOL) and fatigue.

QUALITY OF LIFE SUBSTUDY OBJECTIVE:
I. To compare overall quality of life, disease-related symptoms, and other domains between the two treatment groups (cabozantinib versus [vs.] placebo) within each cohort of patients (pancreatic NET vs. carcinoid tumor). (Quality of Life Substudy Objective - A021602-HO1)

POPULATION PHARMACOKINETICS SUBSTUDY OBJECTIVE:
I. To describe the population pharmacokinetic and exposure-response relationships of cabozantinib in patients with advanced neuroendocrine tumors. (Population Pharmacokinetics Substudy Objective - A021602-PP1)

OUTLINE: Patients are randomized to 1 of 2 arms.

ARM I: Patients receive cabozantinib S-malate orally (PO) once daily (QD) on days 128 of each cycle. Cycles repeat every 28 days in the absence of disease progression or unacceptable toxicity. Patients also undergo computed tomography (CT), magnetic resonance imaging (MRI), and/or x-ray imaging during screening and on study.

ARM II: Patients receive placebo PO QD on days 1-28 of each cycle.
Cycles repeat every 28 days in the absence of disease progression or unacceptable toxicity. Patients also undergo CT, MRI, and/or x-ray imaging during screening and on study. A protocol amendment activated in November 2020 permitted patients who were receiving placebo to cross over to open-label cabozantinib after real-time central confirmation of progressive disease. After completion of study treatment, patients are followed up every 12 weeks until disease progression or start of new anticancer therapy, and then every 6 months until 8 years after registration.

Study Milestones:

Start date: October 26, 2018

Primary Completion Date: August 23, 2023

Publication Information:

Analysis Type: Primary

PubMed ID: 39282913

Citation: Chan, Jennifer A et al. Phase 3 Trial of Cabozantinib to Treat Advanced Neuroendocrine Tumors. The New England journal of medicine, 10.1056/NEJMoa2403991. 16 Sep. 2024, doi:10.1056/NEJMoa2403991

Associated Datasets: NCT03375320-D1-Dataset.csv (pt_chars), NCT03375320-D2-Dataset.csv (txct), NCT03375320-D3-Dataset.csv (hrql), NCT03375320-D4-Dataset.csv (pfs_interim)

Dataset Information:

Dataset Name: NCT03375320-D2-Dataset.csv (txct)

Description: Dataset NCT03375320-D2-Dataset.csv (txct) is one of 4 datasets associated with PubMed ID 39282913. This dataset contains data presented in the adverse event tables.

Data can be used to approximate published study findings, but exact reproduction of previous manuscripts may not be possible in some cases (e.g., when data must be modified for de-identification purposes or have undergone further data cleaning).

Blank values indicate data not applicable or missing, except where otherwise noted.

NCT03375320-D2-Dataset.csv (txct) Data Dictionary:

LABEL	NAME	ELEMENTS	COMMENTS
Data Center ID	SUBJECT		
Cycle	CYCLE		
AE Attribution (Relatedness)	REL_SMED	1=Unrelated | 2=Unlikely | 3=Possible | 4=Probable | 5=Definite	
Adverse Event (AE)	toxicity		
AE Grade	grade	1 | 2 | 3 | 4 | 5	
AE Occurred in SFU & Within 30 Days of Treatment	sfu_ae	0=No | 1=Yes	
Adverse Event Identifier	AE_ID		This variable is intended to provide a unique row key for this dataset