A091105

A Phase III, Double Blind, Randomized, Placebo-Controlled Trial of Sorafenib in Desmoid Tumors or Aggressive Fibromatosis (DT/DF)

ClinicalTrial.gov Identifier: NCT02066181

Study Background:

Trial Description:

This randomized phase III trial compares the effects, good and/or bad, of sorafenib tosylate in treating patients with desmoid tumors or aggressive fibromatosis. Sorafenib tosylate may stop the growth of tumor cells by blocking some of the proteins needed for cell growth. [Funding Source - FDA OOPD]

Arms:

Arm I (sorafenib tosylate): (Experimental): Patients receive sorafenib tosylate PO QD on days 1-28.

Arm II (placebo): (Placebo Comparator): Patients receive placebo PO QD on days 1-28. Patients may crossover to Arm I upon disease progression.

Objectives:

PRIMARY OBJECTIVES:

I. To compare the progression-free survival (PFS) rates of patients with desmoid tumors (DT)/deep fibromatosis (DF) who receive either sorafenib (sorafenib tosylate) or placebo using a double-blinded randomized phase III study.

SECONDARY OBJECTIVES:

I. To assess toxicity.

II. To assess time to surgical intervention.

III. To assess tumor response rates and survival.

TERTIARY OBJECTIVES:

I. To evaluate changes in magnetic resonance imaging (MRI) Tesla (T)2 to predict (or correlate) with a biological effect such as tumor growth (by Response Evaluation Criteria in Solid Tumors [RECIST] version [v]1.1), and pain palliation. (Correlative companion study)

II. The mechanism of action of sorafenib in DT/DF remains unknown. In patients consenting to undergo the paired tumor biopsies (A091105-ST1), treatment induced changes will be quantified by histology, gene expression profiling, proteomic changes and selected interrogation of key pathways by western blot and reverse transcription-polymerase chain reaction (RT-PCR). (Correlative companion study)

III. To collect archival tissue, baseline (tumor, blood) and day 8 (tumor, blood) specimens for basic science research (A091105-ST1). (Correlative companion study)

IV. To assess patient-reported adverse events and quality of life (QOL) as measured by the Patient-Reported Outcomes-Common Terminology Criteria for Adverse Events (PRO-CTCAE) and the single-item overall Linear Analogue Self-Assessment (LASA) (A091105-HO1). (Correlative companion study)

V. To assess pain palliation measured by the "worst pain" item of the Brief Pain Inventory Short Form (A091105-HO1). (Correlative companion study)

OUTLINE: Patients are randomized to 1 of 2 treatment arms.

After completion of study treatment, patients are followed up annually for up to 3 years.

Study Milestones:

Start date: March 21, 2014

Primary Completion Date: January 31, 2018

Publication Information:

Analysis Type: Primary

Pubmed ID: 30575484

Citation: N Engl J Med. 2018 Dec 20;379(25):2417-2428. doi: 10.1056/NEJMoa1805052.

Associated Datasets:

NCT02066181-D1-Dataset.csv (consort),

NCT02066181-D2-Dataset.csv (treatment),

NCT02066181-D3-Dataset.csv (bsl_and_endpoints),

NCT02066181-D4-Dataset.csv (adverse_events),

NCT02066181-D5-Dataset.csv (swimmer_waterfall_plots),

NCT02066181-D6-Dataset.csv (pro_qol)

Dataset Information:

Dataset Name: NCT02066181-D3-Dataset.csv (bsl_and_endpoints)

Description: Dataset NCT02066181-D3-Dataset.csv (bsl_and_endpoints) is one of 6 datasets associated with PubMed ID 30575484. This dataset contains information that will allow you to recreate the baseline characteristics table and primary analysis.

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).

NCT02066181-D3-Dataset.csv (bsl_and_endpoints) Data Dictionary:

LABEL	NAME	elements	comments
De-identified patient reference	patref		
Treatment arm assigned at randomization	ARM	Placebo, Sorafenib	
Patient's age at randomization (years)	AGE		
Patient's race	RACE	Black or African American, White, Unknown: Patient unsure, Not reported: patient refused or not available, American Indian or Alaska Native	
Patient's sex	SEX	Male, Female	
Disease status at baseline	DISEASE_STATUS	Newly diagnosed, Recurrent	Missing indicates the data was not collected
Prior radiation therapy for this tumor	PRIOR_RADIATION_THERAPY	No, Yes	
Prior surgical resection of primary tumor	PRIOR_SURGICAL_RESECTION	No, Yes	

site			
Prior systemic (cancer) therapy for this tumor	PRIOR_SYSTEMIC_THERAPY	No, Yes	
Primary tumor site category	PRI_TUMOR_SITE_CAT	Extra-abdominal, Abdominal, Both	Primary tumor sites were categorized by study PI as Extra-abdominal, Abdominal, or Both
Primary tumor site	PRI_TUMOR_SITE	Abdominal wall, Chest wall, Head/Neck NOS (excluding skin and spine), Lower extremities, Mesentery, Multiple, Other, Upper extremities	
Inclusion Criteria 1 - Disease determined to be unresectable or to require surgery with unacceptably high associated morbidity	INCL_PREREG_SURGSTAT	Yes, No	
Inclusion Criteria 2 - Progression detected by radiographic imaging within 6 months before randomization	INCL_PREREG_PROG	No, Yes	
Inclusion Criteria 3 - Symptomatic disease with BPI worst pain score	INCL_PREREG_PAIN	No, Yes	

>= 3 and consideration of pain narcotic introduction or escalation			
ECOG performance-status score	ECOGPS_BSL	0, 1	
Baseline level of pain (stratification factor)	PAIN_BSL	1= Score 0-2, 2= Score 3-6, 3= Score 7-10	
Intra-abdominal disease (stratification factor)	intraabd_strat	1= “Yes”, 2= ”No”	
Overall survival status, Event (death) or censor	OS_stat	0= ”Censored”, 1= ”Event”	
Overall survival, months from registration	OS_mos		
Progression-free survival status, Event (progression or death) or censor	PFS_stat	0= ”Censored”, 1= ”Event”	
Progression-free survival, months from registration	PFS_mos		
Time to progression status, Event (progression) or censor	TTP_Stat	0=”Censored”, 1=”Event”	
Clinical deterioration in the absence of radiographic	CLINICAL_PD_ONLY	Yes	Only for patients that progressed, this flag is to document patients

evidence			that progressed without documented radiographic evidence. This means symptomatic deterioration is the only documented cause of progression
Time to response, months from registration	TTR_mos		Only patients with a response have a value
Overall disease response	disease_response	No Response, Partial Response, Complete Response	
Best percent change in the sum of the target lesions (RECIST)	BEST_PERC_CHG		Missing means a percent change could not be calculated.
Sum of target lesions at randomization (cm)	BSL_SUM_TARGET_LES		