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-D6-Dataset.csv (pro_qol)

Description: Dataset NCT02066181-D6-Dataset.csv (pro_qol) is one of 6 datasets associated with PubMed ID 30575484. This dataset contains information that will allow you to recreate the Patient Reported Outcomes (PRO) Quality of Life (QOL) outcomes.

Unless otherwise noted, missing values indicate the patient did not answer or data was not collected.

Data may contain slight discrepancies than those found in the Appendix due to data cleaning efforts subsequent to the publication.

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-D6-Dataset.csv (pro_qol) Data Dictionary:

LABEL	NAME	elements	comments
De-identified patient reference	patref		
Treatment arm assigned at randomization	ARM	Placebo, Sorafenib	
Assessment period	ASSESS_PERIOD	Prior to Randomization (Baseline), Week 4 (Cycle 1), Week 8 (Cycle 2), Week 12 (Cycle 3), Week 16 (Cycle 4), Week 20 (Cycle 5), Week 24 (Cycle 6), Week 28 (Cycle 7), Week 32 (Cycle 8), End of Randomized Treatment	Missing indicates the assessment period did not fall in a pre-specified analysis timepoint.
What was the SEVERITY of your insomnia (including difficulty falling asleep, staying asleep, or	INSOMNIA_SEVERITY	Severe, Moderate, Mild, None, Very Severe	

waking up early) at its WORST?			
How much did insomnia (including difficulty falling asleep, staying asleep, or waking up early) INTERFERE with your usual or daily activities?	INSOMNIA_INTERFERENCE	Somewhat, A little bit, Not at all, Very much, Quite a bit	
What was the SEVERITY of your constipation at its WORST?	CONSTIPATION_SEVERITY	None, Mild, Moderate, Severe, Very Severe	
How OFTEN did you have pain?	PAIN_FREQUENCY	Occasionally, Frequently, Rarely, Never, Almost Constantly	
What was the SEVERITY of your pain at its WORST?	PAIN_SEVERITY	Moderate, Severe, Mild, None, Very Severe	
How much did pain INTERFERE with your usual or daily activities?	PAIN_INTERFERENCE	Somewhat, A little bit, Not at all, Quite a bit, Very much	
What was the SEVERITY of your fatigue, tiredness, or lack of energy at its WORST?	FATIGUE_SEVERITY	Moderate, Mild, Severe, None, Very Severe	
How much did fatigue, tiredness, or lack of energy INTERFERE with your usual or daily activities?	FATIGUE_INTERFERENCE	Somewhat, Quite a bit, A little bit, Not at all, Very much	

How OFTEN did you have nausea?	NAUSEA_FREQUENCY	Never, Rarely, Occasionally, Frequently, Almost Constantly	
What was the SEVERITY of your nausea at its WORST?	NAUSEA_SEVERITY	None, Mild, Moderate, Severe, Very Severe	
How OFTEN did you have vomiting?	VOMITING_FREQUENCY	Never, Occasionally, Rarely, Frequently	
What was the SEVERITY of your vomiting at its WORST?	VOMIT_SEVERITY	None, Severe, Moderate, Mild	
How OFTEN did you have loose or watery stools (diarrhea)?	DIARRHEA_FREQUENCY	Rarely, Never, Occasionally, Frequently, Almost Constantly	
Did you have any rash?	RASH_PRESENCE	No, Yes	
What was the SEVERITY of your hand-foot syndrome (a rash of the hands or feet that can cause cracking, peeling, redness, or pain) at its WORST?	HANDFOOT_SYNDROME_SEVERITY	Mild, None, Moderate, Severe, Very Severe	
How much did hand-foot syndrome (a rash of the hands or feet that can cause cracking, peeling, redness, or pain) INTERFERE with your usual or daily activities?	HANDFOOT_SYNDROME_INTERFERENCE	A little bit, Not at all, Quite a bit, Somewhat, Very much	

What was the SEVERITY of your decreased appetite at its WORST?	DECREASE_APPETITE_SEVERITY	None, Mild, Moderate, Severe, Very Severe	
How much did decreased appetite INTEFERE with your usual or daily activities?	DECREASED_APPETITE_INTERFERENCE	Not at all, A little bit, Somewhat, Very much, Quite a bit	
What was the SEVERITY of your mouth or throat sores at their WORST?	MOUTHTHROAT_SORES_SEVERITY	None, Mild, Moderate, Severe, Very Severe	