

ADITYA MAMTORA, JESSICA OSANYINPEJU, and Noah C. Federman

**A Randomized, Double-Blind, Placebo-Controlled, Phase 3 Trial (NCT03785964) of Nirogacestat Versus Placebo In Adult Patients With Progressing Desmoid Tumors/Aggressive Fibromatosis (DT/AF)**

Background: Desmoid tumors/aggressive fibromatosis (DT/AF), are locally aggressive tumors with no known potential for metastasis. Local surgery and radiation have been the mainstay of therapies for DT/AF; however, they have a high rate of recurrence after complete resection. Nirogacestat is a potent, oral noncompetitive inhibitor of gamma secretase and is being investigated as a treatment for DT/AF. The Phase 1 study supported long-term durable responses and safety of nirogacestat in DT/AF participants. Phase 2 resulted in a 29% response of significant tumor shrinkage with no progress while on therapy, warranting the further study of nirogacestat in this population. Methods: This is a phase 3, multicenter, randomized, double-blind, placebo-controlled study to compare the efficacy, safety, and tolerability of nirogacestat in progressing DT/AF participants ages 18 years and older. This study consists of 2 phases, a double-blind and an optional open-label extension (OLE) phase. The primary outcome measure is progression free survival (PFS) by Response Evaluation Criteria in Solid Tumors. Secondary outcome measures include incidence of adverse events, overall response rate, duration of response and patient reported outcomes. This trial is currently active and recruiting subjects at UCLA.