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"An Update on the Phase 3 DeFi Trial Evaluating Nirogacestat in Adult Patients with Progressing Desmoid Tumors"

Nirogacestat is an investigational, oral, selective, small molecule gamma-secretase inhibitor currently in evaluation in the DeFi trial. DeFi is a global, randomized, double-blind, placebo-controlled Phase 3 trial to evaluate the efficacy, safety and tolerability of nirogacestat in adult patients with progressing desmoid tumors. The study was designed to enroll approximately 118 patients across 50 sites in North America and Europe. Patients were randomized 1:1 to receive 150 mg of nirogacestat twice daily or placebo at same schedule. Key eligibility criteria included tumor progression by ≥20% as measured by Response Evaluation Criteria in Solid Tumors (RECIST v1.1) within 12 months prior to the screening visit scan. The primary endpoint is progression-free survival and secondary endpoints include safety and tolerability measures, objective response rate, duration of best response and changes in patient-reported outcomes. The study started patient recruitment in 2019 and completed enrollment in July 2020. The study is expected to have top-line results by the end of this year.

Nirogacestat has received Orphan Drug Designation from the U.S. Food and Drug Administration (FDA) for the treatment of desmoid tumors (June 2018) and from the European Commission for the treatment of soft tissue sarcoma (September 2019). The FDA also granted Fast Track and Breakthrough Therapy Designations for the treatment of adult patients with progressive, unresectable, recurrent or refractory desmoid tumors or deep fibromatosis (November 2018 and August 2019).