**INTRODUCTION**

- Desmoid tumors (aggressive fibromatoses) are rare, locally invasive, soft-tissue tumors that can result in severe pain, functional impairment, and other complications.
- Pain is the most debilitating symptom reported by patients with desmoid tumors, and the potential for dependence on narcotics is a substantial concern.
- As many as 80% of patients with desmoid tumors experience chronic pain, and pain may indicate tumor progression.

**METHODS**

- DeFi was a phase 3, global, double-blind, randomized, placebo-controlled study evaluating the efficacy and safety of nirogacestat in patients aged 18 years or older with a histologically confirmed diagnosis of progressing desmoid tumors.
- Patients received oral nirogacestat (150 mg) or placebo daily, taken continuously in 28-day cycles until the time of disease progression, death, or trial discontinuation due to other reasons.
- During the DeFi study, patients completed three assessment tools (including pain measurements).

**OBJECTIVE**

- To evaluate the impact of nirogacestat on desmoid tumor pain (secondary and exploratory study endpoints) in the phase 3 DeFi study.

**RESULTS**

**BASELINE CHARACTERISTICS**

- From May 2019 through August 2020, a total of 142 patients were randomized 70 to the nirogacestat group and 72 to the placebo group across 37 sites in the United States, Canada, and Europe.
- Baseline characteristics were similar between groups and representative of the general patient population for desmoid tumors.

**PAIN ASSESSMENTS**

- In DeFi, nirogacestat (n=70) significantly improved progression-free survival (the primary endpoint) compared with placebo (n=72) in patients with progressing desmoid tumors (hazard ratio: 0.38; 99% CI: 0.21–0.68; two-sided P=0.0017).

**CONCLUSIONS**

- In the phase 3 DeFi study, patients with progressing desmoid tumors who received nirogacestat achieved a rapid, sustained, and consistent reduction in pain from baseline with a low risk of dependency on narcotics.
- Significantly greater proportions of patients achieved clinically meaningful pain reduction in nirogacestat compared with placebo.
- The benefit of nirogacestat versus placebo in reducing pain was consistent across multiple patient-reported assessment tools, which included pain measurements.
- Analyses of the most commonly reported symptom by patients with desmoid tumors, pain reduction should be a key clinical study endpoint and treatment goal.

**REFERENCES:**