11564 **Poster Session**

Impact of nirogacestat on pain, a key symptom in patients with desmoid tumors (DT): Results from the phase 3 DeFi study.

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Background: Pain reduction is a key treatment goal in DT (aggressive fibromatosis): 60% of patients (pts) experience chronic pain. In the phase 3 DeFi trial, nirogacestat (NIRO; n = 70) significantly improved progression-free survival compared with placebo (PBO; n = 72) in pts with progressing DT (HR: 0.29 [95% CI, 0.15–0.55]; $P < 0.001$). Also as previously reported, NIRO significantly reduced pain severity by 1.50 points (on a 10-point scale) compared with PBO at cycle 10 (28-day cycles; $P < 0.001$) per the prespecified secondary endpoint of "worst pain" from the Brief Pain Inventory Short Form (BPI-SF). Additional aspects of pain were collected in DeFi to further characterize treatment impact and consistency across multiple pain assessment tools. **Methods:** In DeFi, pts completed 3 prespecified pain assessment tools through end of treatment: BPI-SF (worst pain), GOunder/Desmoid Tumor Research Foundation DEsmoid Symptom Scale (GODDESS-DTSS pain scale: worst pain, dull pain, shooting pain), European Organisation for Research and Treatment of Cancer Core Quality of Life Questionnaire (QLQ-C30 pain scale: pain, pain interference with daily activities). Change from baseline (BL) in pain scores was compared between arms; analyses included mixed models for repeated measures to compare change from BL and stratified Cochran-Mantel-Haenszel to compare proportions of pts with clinically meaningful pain reduction (defined using prespecified thresholds) at cycle 10. Cycle 10 was preselected to allow adequate time for a treatment effect to be observed. **Results:** Statistically significant and clinically meaningful pain reductions were observed with NIRO compared with PBO at cycle 10 across all assessment tools; statistically significant differences between arms occurred as early as cycle 2 and were sustained throughout treatment. At cycle 10, NIRO reduced mean BL pain per GODDESS-DTSS (0–10 range) by 1.78 points (SE = 0.26) and PBO increased pain by 0.32 points (SE = 0.27; $P < 0.001$). At cycle 10, NIRO reduced mean BL pain per QLQ-C30 (0–100 range) by 22.05 points (SE = 3.38) and PBO increased pain by 7.19 points (SE = 3.64; $P < 0.001$). Clinically meaningful pain reduction (by $\geq$2.0 points) per BPI-SF worst pain (0–10 range) was achieved by 72% of pts with NIRO vs 29% of pts with PBO at cycle 10 ($P < 0.001$). Per GODDESS-DTSS, clinically meaningful pain reduction (by $\geq$1.9 points) was achieved by 62% of pts with NIRO vs 19% of pts with PBO at cycle 10 ($P = 0.002$). **Conclusions:** Rapid, sustained, and consistent reductions in different aspects of pain were observed with NIRO compared with PBO across multiple assessment tools in pts with DT. Furthermore, a significantly greater proportion of pts achieved clinically meaningful reductions in pain with NIRO than with PBO. As pain is the most commonly reported symptom, pain reduction should be a key clinical trial endpoint and a key treatment goal in DT. Clinical trial information: NCT03785964. Research Sponsor: SpringWorks Therapeutics, Inc.