Real-World Data from a Single Institution on Nirogacestat for Refractory, Symptomatic Desmoid Tumor: Dosing, Adverse Event Management and Symptom Improvement from Medical Record Review

Background:

Nirogacestat is a promising treatment for desmoid tumors. It was FDA-approved in November 2023. This study aims to provide real-world data from a single institution on the initial dosing strategy, first-month management of adverse events (AEs), and patient-reported outcome.

Methods:

We retrospectively reviewed all patients with symptomatic, refractory desmoid tumors treated with nirogacestat at Northwestern University between January 2024 and March 2025. Key variables evaluated included tumor location, size, sex, age, previous therapies, history of familial adenomatous polyposis (FAP), initial dosing, adverse events (AE) during the first month, and patient-reported symptom improvement from electronic medical records review.

Results:

Cohort consisted of 16 patients. It included intrabdominal (n=7, 44%), neck (n=3, 19%), extremities (n=3, 19%), paraspinal (n=3, 19%). The median largest diameter was 8.9 cm (3.7–20.3 cm), with n=5, 38% with multifocal disease at evaluation. Median age was 41 years (range: 26–67). n=3, 19% had history of FAP. Previous treatments included surgery (n=6, 38%), chemotherapy (n=4, 25%), and tyrosine kinase inhibitors (TKI) (n=5, 31%). Median follow-up was 42 weeks (15–65 weeks). All patients were started on 150 mg BID, except for one, started on 50 mg BID and titrated up. Nine patients (56%) experienced dose interruptions, and 3 (19%) dose reductions; One patient discontinued therapy due to personal preference after experiencing radiographic response. At first month of follow-up, n=7, 44% experienced rash (e.g. acneiform rash, drug rash, and milliaria); n=8, 50% diarrhea; n=3, 19% required phosphate supplement. Noticeable delayed adverse events included hidradenitis, n=1. Among the 6 female patients of reproductive age, 4 (67%) experienced any signals of ovarian toxicity, (hot flashes, delayed menstrual periods, laboratorial changes). No patients reported new-onset sexual dysfunction. One patient's regular menstrual cycles spontaneously returned after 2 months. The 3 patients who underwent dose reductions did so due to rash; diarrhea and fatigue; and diarrhea, respectively. All tolerated 100 mg BID post-reduction. One patient titrated back to 150 mg BID. At the most recent follow-up, 10 patients (62%) had reported improved pain or physical function from baseline.

Conclusion:

Nirogacestat was well tolerated, with management of adverse events at first month associated with dose interruptions but infrequent dose reductions. These findings support the recommended starting dose of 150 mg twice daily (BID) in real-world experience, provided patients have adverse events management support. Treatment was generally well tolerated and dose reductions and discontinuations were infrequent.