Assessment of Pain Diagnosis and Pain Medication Use in Adults Treated With Nirogacestat: A United States Real-World Analysis

Shengfan Zhou, MS[1]; Eileen Farrelly, MPH[2]; Shahla Amin, MS[2]; Brad Tumminello, PharmD[1]*; Timothy Bell, MHA[1]

[1]SpringWorks Therapeutics, Inc., Stamford, CT, USA; [2]Cencora, Inc., Conshohocken, PA, USA

*At time of analysis

INTRODUCTION

- Desmoid tumors (DT) are rare, locally aggressive, and invasive soft-tissue tumors, often associated with debilitating symptom burden[1,2]
- Pain is among the most debilitating symptoms of DT, which can exert additional negative effects on function in the daily lives of patients, including sleep, physical function, and emotions[1,2]
- Nirogacestat is an oral, targeted gamma secretase inhibitor, and the only US FDA- and European Commission-approved treatment for adults with progressing DT who require systemic treatment[3,4]
- In the global, multicenter, phase 3 DeFi trial (NCT03785964), nirogacestat demonstrated statistically significant and clinically meaningful early and sustained improvement in pain versus placebo in patients with progressing DT[5]
- Improved awareness of the real-world evidence for the benefits of nirogacestat may help reduce symptom burden or utilization of pain medications and enhance clinical outcomes for patients with DT

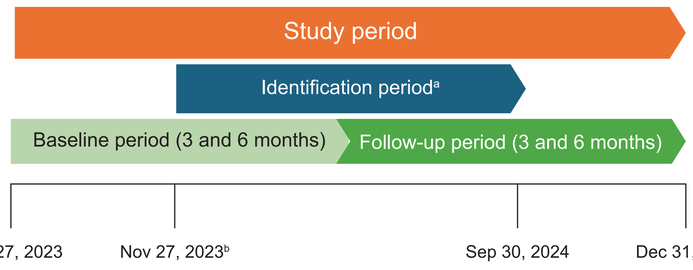
OBJECTIVE

- To assess pain diagnoses (dx) and pain medication use (PMU), including use of opioids, as primary endpoints in adult patients before and after initiating a nirogacestat prescription

METHODS

- A US claims database (May 27, 2023–December 31, 2024) was used to identify patients who initiated treatment with nirogacestat, using the date of first prescription fill as the index date. The assessment window spans 3- and 6-month observation periods with a balanced baseline (BL) and follow-up (FU; **Figure 1**)
  - Given the recent implementation of DT-specific dx codes and approval of nirogacestat for DT, it was assumed that patients with a filled nirogacestat prescription during this period were being treated for DT and took nirogacestat as instructed
- Eligibility criteria included age ≥18 years at index date, ≥2 prescription fills of nirogacestat, and ≥3 months of continuous enrollment for 3-month assessment or ≥6 months for 6-month assessment in the BL and FU
- Separate cohorts for pain dx and PMU were constructed for both 3- and 6-month observation periods; these cohorts were not mutually exclusive
  - In recognition that the maximum prescription supply for PMU was 90 days and based on expert opinion that frequent pain assessment is recommended (at every visit) for patients on active treatment, the 3-month period was selected as the initial assessment period; the 6-month period was evaluated for consistency in findings

Figure 1. Description of study period



[a]Defined as the time window in which investigators identified patients and the date of their first use of nirogacestat. Identification period began on November 27, 2023 and ran to September 30, 2024, to allow for a minimum of 3 months follow-up before the end of the study.
[b]November 27, 2023 was the date nirogacestat received FDA approval and thus, was the earliest possible date of nirogacestat treatment.

- Change in the prevalence of pain dx in the FU was assessed among patients with a pain dx identified in the BL using pain-specific ICD-10 dx codes; change in the prevalence of PMU in the FU was assessed among patients with a PMU identified in the BL
  - PMU was identified by patients filling a prescription for opioids or nonsteroidal anti-inflammatory drugs (NSAIDs)
  - Opioid dose reduction in FU relative to BL was calculated as a decrease in total morphine milligram equivalent (MME) dose
- Proportions and frequencies for patients with pain dx and PMU were assessed using descriptive statistics. Subgroups included sex and age (≤30 y versus >30 y); patients with unknown sex or age were excluded from subgroup analyses

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REFERENCES: 1. Bektas M, et al. *Adv Ther.* 2023;40(9):3697-3722. **2.** Kasper B, et al. *Ann Oncol.* 2017;28(10):2399-2408. **3.** US Food and Drug Administration. FDA approves nirogacestat for desmoid tumors. 2023. Accessed August 27, 2025. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-nirogacestat-desmoid-tumors **4.** European Commission. Union Register of medicinal products for human use - Ogsiveo. 2025. Accessed September 22, 2025. https://ec.europa.eu/health/documents/community-register/html/h1932.htm. **5.** Gounder M, et al. *N Engl J Med.* 2023;388(10):898-912. **6.** Ratan R, et al. *J Clin Oncol.* 2025;JCO2500582.

RESULTS

PATIENT DEMOGRAPHICS (TABLE 1)

- Among patients eligible for the 3-month BL and FU, 52% (80/155) had a pain dx and 40% (125/314) had a PMU during the BL
- Among patients eligible for the 6-month BL and FU, 67% (68/102) had a pain dx and 49% (107/219) had a PMU during the BL
- Patient demographics were similar across cohorts where most patients were >30 years old and female, which is representative of the general DT population

Table 1. Patient demographics at index date

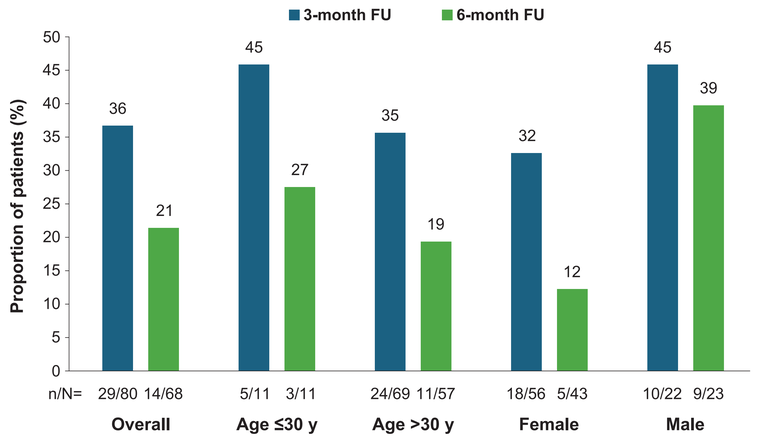
	3-Month Observation Period		6-Month Observation Period	
	Nirogacestat initiation with prior pain dx (n = 80)	Nirogacestat initiation with prior PMU (n=125)	Nirogacestat initiation with prior pain dx (n=68)	Nirogacestat initiation with prior PMU (n=107)
Age, median (min, max), y	43 (18, 77)	42 (18, 88)	41 (18, 77)	39 (18, 88)
Age group, n (%)				
≤30 y	11 (13.8)	25 (20.0)	11 (16.2)	20 (18.7)
>30 y	69 (86.3)	100 (80.0)	57 (83.8)	87 (81.3)
Sex, n (%)				
Female	56 (70)	83 (66.4)	43 (63.2)	67 (62.6)
Male	22 (27.5)	40 (32.0)	23 (33.8)	38 (35.5)
Unknown	2 (2.5)	2 (1.6)	2 (2.9)	2 (1.9)

dx, diagnosis; PMU, pain medication use.

PAIN DX FOR PATIENTS TREATED WITH NIROGACESTAT (FIGURE 2)

- Among 80 patients with a pain dx in the 3-month BL, 36% (29/80) no longer had a pain dx in the 3-month FU
- Among 68 patients with a pain dx in the 6-month BL, 21% (14/68) no longer had a pain dx in the 6-month FU
- The cessation of pain dx was consistently observed across age and sex subgroups for the 3- and 6-month FU periods

Figure 2. Proportion of patients treated with nirogacestat who no longer had a pain dx in the 3- and 6-month FU



n = patients who no longer had a pain dx in FU; N = patients with a pain dx in BL.
BL, baseline; dx, diagnosis; FU, follow-up.

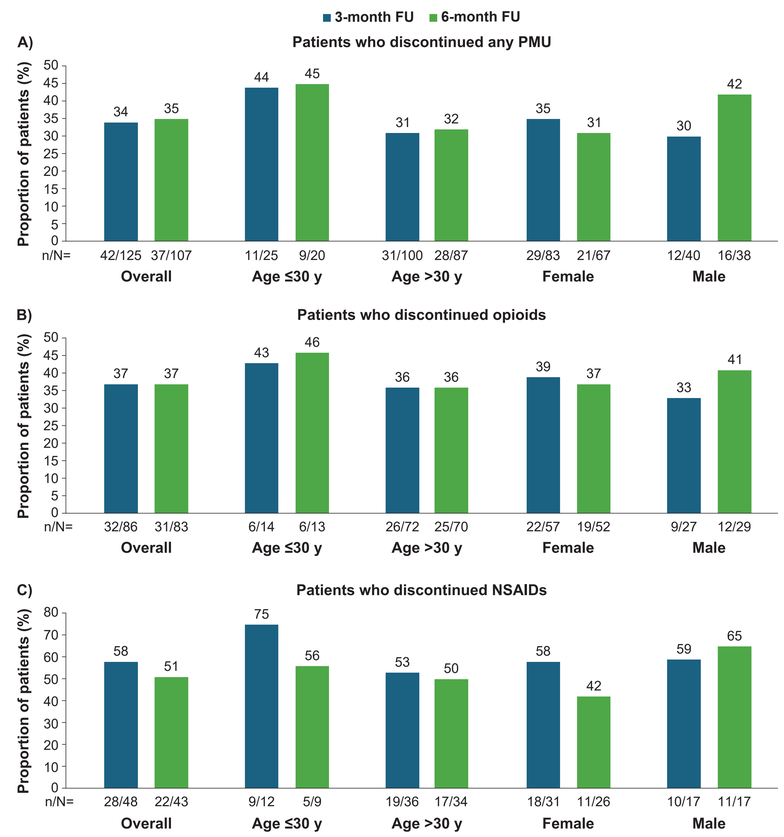
PMU (OPIOIDS OR NSAIDs) FOR PATIENTS TREATED WITH NIROGACESTAT (FIGURE 3)

- In the 3-month FU, 34% (42/125) of patients discontinued any PMU, 37% (32/86) discontinued opioids, and 58% (28/48) discontinued NSAIDs
- In the 6-month FU, 35% (37/107) of patients discontinued any PMU, 37% (31/83) discontinued opioids, and 51% (22/43) discontinued NSAIDs
- The discontinuation of PMU was consistently observed across age and sex subgroups for 3- and 6-month FU

OPIOID DOSE REDUCTION FOR PATIENTS TREATED WITH NIROGACESTAT (FIGURE 4)

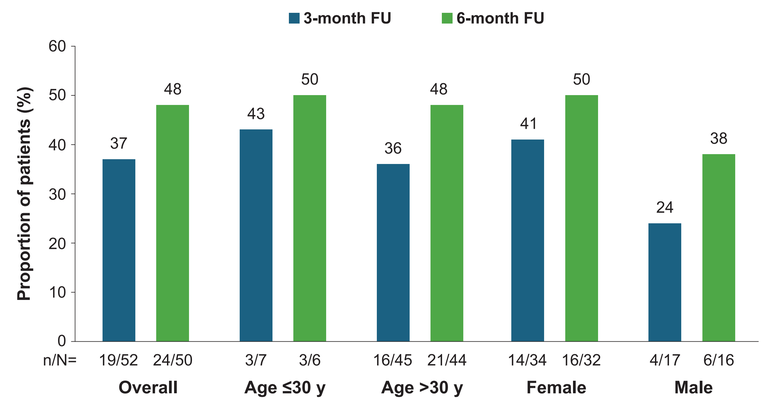
- Among patients taking opioids with available dose information, 37% (19/52) and 48% (24/50) had an opioid dose reduction in the 3- and 6-month FU, respectively
- An opioid dose reduction was consistently observed across age and sex subgroups for 3- and 6-month FU

Figure 3. PMU in patients treated with nirogacestat in the 3- and 6-month FU



n = patients who discontinued pain medication in FU; N = patients who used pain medication BL.
BL, baseline; FU, follow-up; NSAIDs, nonsteroidal anti-inflammatory drugs; PMU, pain medication use.

Figure 4. Proportion of patients treated with nirogacestat who had an opioid dose reduction in the 3- and 6-month FU



n = patients with opioid dose reduction in FU; N = patients who used opioids in BL with available dose information.
Among patients who continued opioid use in FU, the number of patient with missing dose data was 2 for both 3- and 6-month FU.
BL, baseline; FU, follow-up.

CONCLUSIONS

- The analysis showed that a substantial proportion of patients experienced a cessation of a pain dx, a discontinuation of PMU, or an opioid dose reduction, as observed during 3- and 6-month periods following initiation of nirogacestat treatment
- These results are consistent with the clinically meaningful benefit of early and sustained pain reduction associated with nirogacestat, as seen in both the primary DeFi trial and long-term analyses[5,6]
- The cessation of pain dx observed during 3- and 6-month periods following nirogacestat treatment may indicate improved treatment effectiveness and a reduced tumor burden
- The discontinuation of opioid use and opioid dose reduction observed during 3- and 6-month periods following nirogacestat treatment may help reduce symptom burden and further improve patient quality of life

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