Nirogacestat Pediatric Compassionate Use Program: Cross-Sectional Data Review

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INTRODUCTION

- Desmoid tumors (DT) are clinically impactful and rare, with an estimated incidence of 3 to 5 cases per million in the general population, and affect both adults and children[1-3]
- In children, DT often presents as a painless mass, though this can vary depending on tumor location; nearly 50% of pediatric DT develop in the extremities while 10–30% develop in the head/neck[3-5]
- There are no documented incidence estimates, published treatment guidelines, or approved systemic treatments for pediatric DT[1,2]
- Nirogacestat is an oral, targeted gamma secretase inhibitor, and the only US Food and Drug Administration-, European Commission-, and UK Medicines and Healthcare Products Regulatory Agency-approved treatment for adults with progressing DT who require systemic treatment[6-8]
- The efficacy and safety of nirogacestat is under investigation in pediatric patients in an ongoing phase 2 clinical trial (NCT04195399)[9]
- Since 19 February 2019, eligible pediatric patients with DT have obtained access to nirogacestat through the compassionate use program (CUP; NCT05041036) if they cannot be treated satisfactorily with, or have exhausted, available standard treatment options and do not qualify for an ongoing SpringWorks Therapeutics clinical trial in an accessible geographic location
  - Global utilization of the CUP by pediatric patients with DT grew considerably in 2023 and remained steady through the data cutoff (23 April 2025)

OBJECTIVE

- The objective of this analysis was to describe the baseline characteristics, demographics, and treatment experience of pediatric patients with DT who were treated with nirogacestat, outside of the clinical trial setting, as part of the SpringWorks CUP

METHODS

- Patients <18 years old with DT at CUP enrollment between 19 February 2019 through 23 April 2025 were eligible for inclusion in the anonymized analysis
  - Body surface area calculated pediatric dose of nirogacestat was 90 mg/m^2/dose (maximum per dose: 150 mg) twice daily
- Requests for access to nirogacestat through the CUP were made voluntarily by the patient's treating physician, and individual patient requests were reviewed by the SpringWorks medical team for program eligibility
- Patients' baseline characteristics, dosing regimen, verification of continued benefit by physician opinion, and safety events were provided by the treating physician per their institutional parameters and reported to external agencies as required
- Data were extracted from the CUP order system, anonymized, and summarized for this analysis
- Free text was manually reviewed and standardized for this analysis. Standard data dictionaries, Medical Dictionary for Regulatory Activities (MedDRA) v24.0 and WHODrug-Global-B3-202103, were used when possible to classify prior treatments, prior medical history, comorbidities, and functional impairments
- Treatment duration was calculated per the quantity of drug provided
- Safety data were summarized from the SpringWorks pharmacovigilance database

RESULTS

PATIENT CHARACTERISTICS IN THE CUP

- Analysis included 53 pediatric patients (median age [range]: 15 years old [<1–17]) across 11 countries (**Figures 1 and 2**)

Figure 1. Patient Demographics

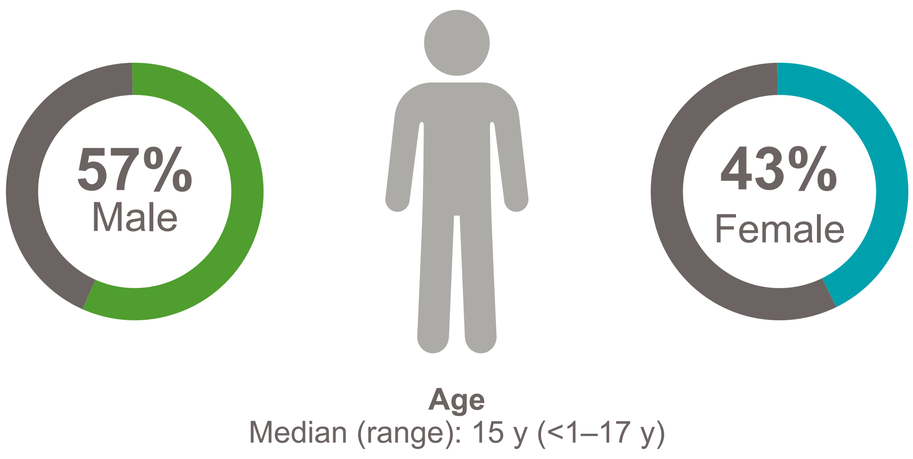
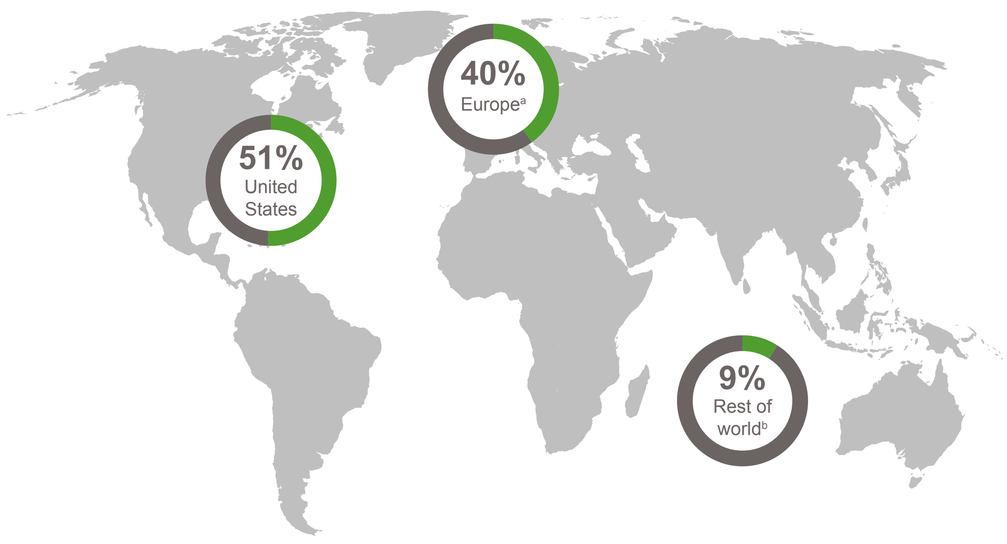


Figure 2. Patient Location



[a]Europe includes Belgium, Finland, France, Italy, the Netherlands, Spain, and the United Kingdom.
[b]Rest of world includes Australia, Canada, and New Zealand.

- Tumor location in the pediatric CUP population was varied (**Table 1**)
  - The most common tumor locations were in the extremities and head/neck

Table 1. CUP Patients by DT Location

Tumor location, n (%)	CUP patients (N=53)
Extremities	22 (42)
Head/neck	11 (21)
Mesentery, pelvis, or abdominal wall	10 (19)
Chest wall	6 (11)
Paraspinal	5 (9)
Other[a]	7 (13)
Not provided[b]	4 (8)

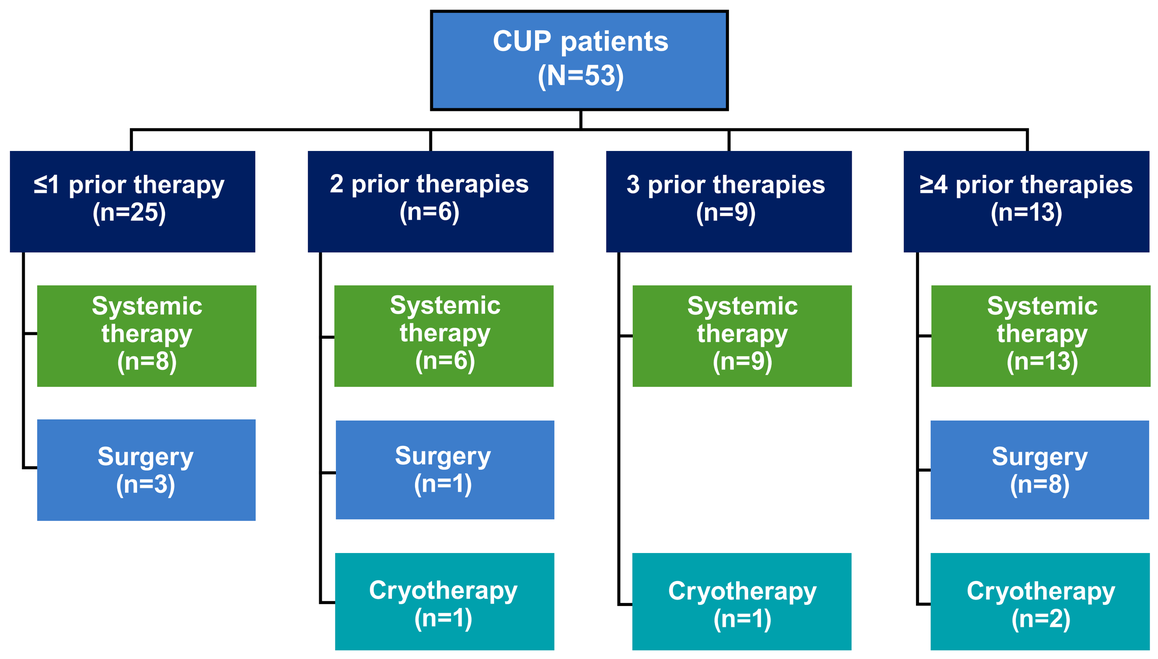
Tumor locations were coded based on Medical Dictionary for Regulatory Activities v24.0 preferred terms.
Patients could have tumors in more than one location.
[a]"Other" tumor locations included intra-thoracic, lungs, mediastinum, multifocal, tissue, and trunk.
[b]In some cases the tumor location was not provided within the data fields on the order form for reporting.
CUP, compassionate use program; DT, desmoid tumor.

RESULTS (CONT.)

PATIENT MEDICAL HISTORY

- *APC* mutations were reported in 7 (13%) patients
- Most patients (38; 72%) reported ≥1 symptom or functional impairment at baseline
  - The most common symptom was pain (18; 34%), followed by decreased mobility (6; 11%), discomfort (5; 9%), and gait disturbances (5; 9%)
- Over half (28; 53%) of patients reported ≥2 therapies prior to CUP enrollment (**Figure 3**)
  - Systemic therapies (36; 68%) and surgery (12; 23%) were the most commonly reported prior treatments
  - Systemic therapies included tyrosine kinase inhibitors (pazopanib, sorafenib, and sunitinib; 28, 53%), vinca alkaloids and analogues (vinblastine, vincristine, and vinorelbine; 21, 40%), and methotrexate (21, 40%)

Figure 3. Cumulative Lines of Prior Therapy in Pediatric Patients With DT in the CUP



Note: Patients who reported having multiple treatments of the same therapy class were counted once.
CUP, compassionate use program; DT, desmoid tumor.

- Concomitant medication use was reported by 43 (81%) patients (**Table 2**)

Table 2. Concomitant Medication Use in ≥15% of CUP Patients

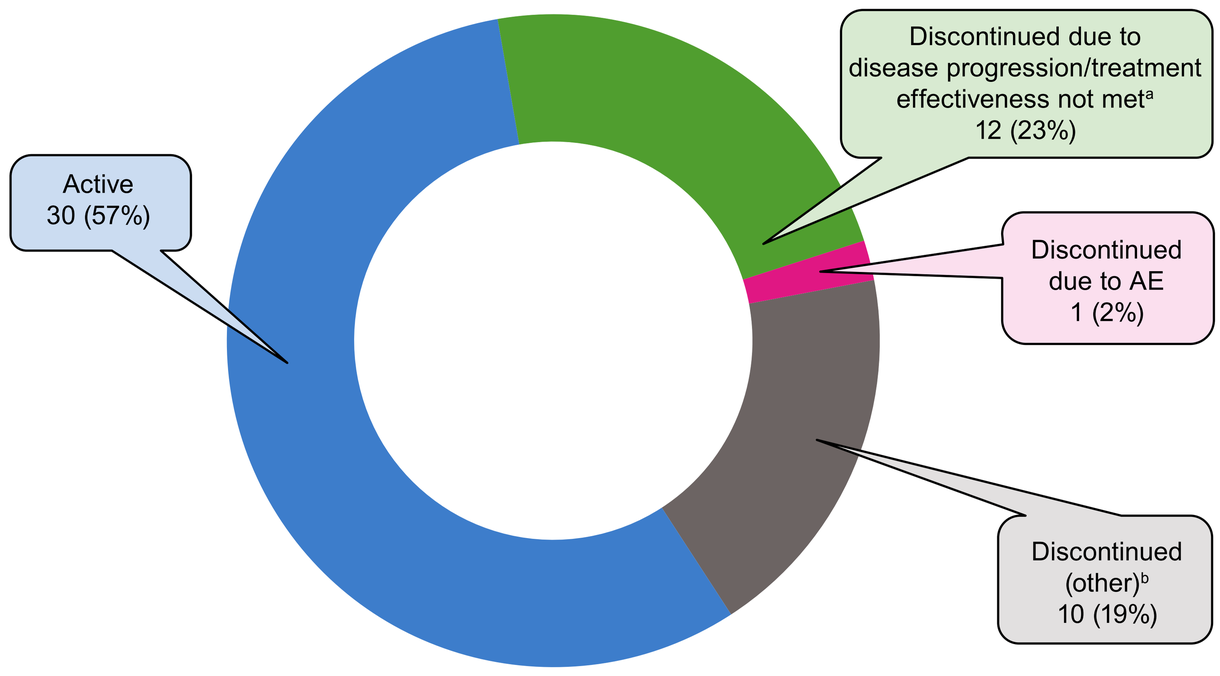
Concomittant medication, n (%)	CUP patients (N=53)
Serotonin antagonists (eg, ondansetron or granisetron hydrochloride)	16 (30)
Opioids (eg, oxycodone or morphine)	15 (28)
Other analgesics (eg, gabapentin or pregabalin)	8 (15)

Patients may have used more than one concomitant medication during the CUP.
CUP, compassionate use program.

PATIENT DISPOSITION

- Estimated median (range) nirogacestat treatment duration was 293 days (24–1347)
- At data cutoff (23 April 2025), 30 (57%) patients with DT were still active in the CUP, 12 (23%) discontinued due to disease progression or treatment effectiveness not met based on physician judgment, 1 (2%) discontinued due to adverse events, and 10 (19%) discontinued for all other reasons (**Figure 4**)

Figure 4. CUP Pediatric Population Disposition at Data Cutoff



Note: Sum of values is greater than 100% due to rounding.
[a]Based on physician judgment.
[b]Of the 10 patients who discontinued for other reasons: 3 transitioned to commercial nirogacestat, 1 completed treatment, 1 was lost to follow-up, 2 discontinued per patient decision, 1 discontinued per sponsor decision, and 2 did not specify a reason.
AE, adverse event; CUP, compassionate use program.

SAFETY

- Of the 26 (49%) patients who reported a treatment emergent adverse event (TEAE), 4 patients reported a dose reduction
- Overall, 17 (32%) pediatric patients reported treatment-related adverse events (TRAEs) and 5 (9%) patients reported serious TRAEs. In total, there were 102 TRAEs reported, including 7 serious TRAEs
  - Due to the nature of data collection method, the same TRAE may have been reported more than once per patient
  - TRAEs were assessed as related by treating physician
- The TRAEs reported in ≥10% of patients were diarrhea and nausea
  - In consideration of the small sample size, TRAEs occurring in <10% are not shown to preserve patient confidentiality; safety outcomes were consistent with the established adult prescribing information
- Grade 3 TRAEs were reported for hypophosphatemia and hidradenitis
  - There were no reported Grade 4 or Grade 5 TRAEs

CONCLUSIONS

- At data cutoff, 53 pediatric patients with DT participated in the CUP with a median treatment duration of 293 days and no new safety signals were identified from these data
- To our knowledge, this is the largest ongoing pediatric CUP in DT, highlighting the unmet need for drug development and approved systemic treatment options in this patient population

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