Poster QOL-27

Effect of selumetinib treatment on long-term pain medication utilization in pediatric patients: a retrospective study of a US claims database

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STUDY OBJECTIVES

- To assess pain medication utilization (PMU) in pediatric patients aged 2–21 years taking selumetinib over a long-term follow-up period of approximately 3 years
- To quantify dose reductions following selumetinib initiation among patients receiving gabapentin and oxycodone

CONCLUSIONS

- Selumetinib was associated with a consistent and durable reduction in PMU over a follow-up period of approximately 3 years
- A decline in PMU of 20.3% per year of selumetinib treatment was observed, with a significant association between selumetinib treatment duration and PMU reduction (p=0.039)
- Discontinuation of selumetinib was associated with higher PMU, with patients who discontinued selumetinib for any reason receiving pain medications at a rate more than twice as high as those who received selumetinib continuously
- These results support the clinical benefit of selumetinib in pediatric patients with NF1-PN, adding to the existing long-term and real-world data

PLAIN LANGUAGE SUMMARY

Why did we perform this research?
Neurofibromatosis type 1 (NF1) is a condition associated with a variety of signs and symptoms. Up to half of patients with NF1 develop tumors called plexiform neurofibromas (PN), which grow along the nerve. Pain is one of the most common symptoms in patients with NF1-PN, and is experienced by up to 70% of children with this condition. Therefore, patients with NF1-PN often rely on prescription pain medications to manage their pain. At the time of this study, the medication selumetinib was approved in the USA for patients aged at least 2 years with NF1 and PN that cause symptoms and cannot be removed with surgery. In this study, researchers aimed to collect data over a time period of up to 3 years on pain medication use in patients with NF1-PN after they started selumetinib treatment.

How did we perform this research?
This study used a US claims database to collect information on patients based on their health insurance records. Patients aged 2–21 years were included in the study if they had started selumetinib treatment, and had collected at least 3 prescriptions for this medication. These patients were followed for up to 3 years from the date they started selumetinib treatment. A statistical model was used to compare the use of pain medications before and after starting selumetinib treatment.

What were the findings of this research and what are the implications?
Selumetinib treatment was associated with a consistent and long-lasting reduction in pain prescription medication use. Patients who stopped taking selumetinib used twice as much pain medication as those who continued to take selumetinib. These results showed long-term benefits of selumetinib treatment in patients with NF1-PN, adding to the existing information about use in real-world practice.

This study was sponsored by Alexion, AstraZeneca Rare Disease.

Poster | Plain language summary

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https://rarediseaseresource.com/2025/SNO-11-19/Longitudinal_Pediatric_PMU_poster

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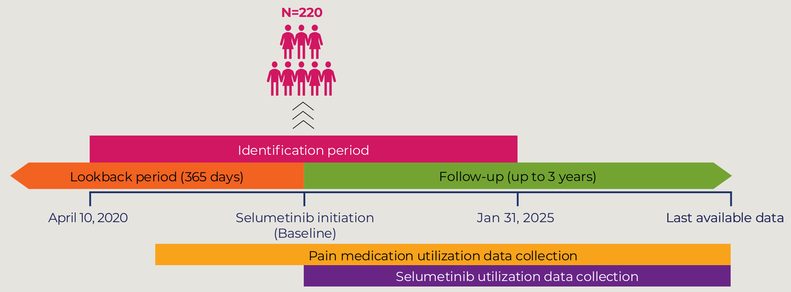
BACKGROUND

- Neurofibromatosis type 1 (NF1) is an autosomal dominant condition caused by pathogenic variants in the *NF1* gene[1]
  - Plexiform neurofibromas (PN) are peripheral nerve sheath tumors that develop in up to 50% of patients with NF1[2,3]
  - PN can be associated with severe morbidities, including pain, neurologic deficits, disfigurement, and functional limitations[2,4]
- NF1-PN can significantly impact patients' quality of life and ability to carry out daily activities[5,6]
  - Pain affects 50–70% of pediatric patients with NF1-PN, and can be debilitating[2,3,5,6]
  - Pediatric patients with NF1-PN may be prescribed medications for pain management[6]
  - A study showed that 93% of pediatric patients rated pain as interfering with functioning to at least some degree, despite taking regular pain medications[7]
- Selumetinib (ARRY-142886, AZD6244) is an oral inhibitor of mitogen-activated protein kinase kinases 1 and 2[8] that reduces PN volume in pediatric patients with NF1 and symptomatic, inoperable PN[2]
  - The selumetinib capsule was first approved by the US Food and Drug Administration (FDA) in April 2020 for the treatment of NF1 and symptomatic, inoperable PN in pediatric patients aged ≥2 years[9]
  - The granule formulation of selumetinib was recently approved by the FDA in September 2025, for the same indication in pediatric patients aged ≥1 years[10]
- A previous real-world analysis showed 6 months of selumetinib treatment led to reduced PMU in pediatric patients[11,12]
  - Building on the previous short-term findings, this study investigated the long-term utilization of pain medications after selumetinib initiation

METHODS

- This study is a retrospective analysis of patients treated with selumetinib that uses Forian CHRONOS, a hybrid US claims database containing open and closed source claims (**Figure 1**)
- Patients were included if they met the following criteria:
  - Patients who had initiated selumetinib treatment with three or more prescriptions filled between April 10, 2020, and January 31, 2025
  - Aged 2–21 years at the time of selumetinib initiation
  - Continuous enrollment and medical or pharmacy claims activity for ≥12 months
- Patients were followed up for up to 3 years from selumetinib initiation, or through the duration of their available data
- A Generalized Estimating Equation (GEE) statistical model, adjusted for age and sex, was used to compare the utilization of pain medications pre-selumetinib initiation to the longitudinal utilization over 3 years
  - For patients receiving gabapentin or oxycodone, the daily dose was computed for the 12-month periods before and after initiation of selumetinib

Figure 1. Study design



RESULTS

Study population

- Overall, 220 patients were included in the study (**Table 1**), of whom 40% had a pain diagnosis code at baseline
- The most common pain types were **back pain** (14.5%), **abdominal pain** (14.1%), and **limb pain** (11.4%)
- Gabapentin and oxycodone were the most commonly prescribed pain medication and opioid in the population of patients included in this study, respectively

Table 1. Patient demographics and clinical characteristics at selumetinib initiation

Patient characteristics	N=220
Mean age, years (SD)	12.5 (4.6)
Age subgroup, years, n (%)	
2–5	15 (6.8)
6–11	73 (33.2)
12–18	107 (48.6)
19–21	25 (11.4)
Sex, n (%)	
Male	118 (53.6)
Female	102 (46.4)
Payer channel, n (%)	
Commercial	158 (71.8)
Medicaid (State)	29 (13.2)
Managed Medicaid	24 (10.9)
Other/unknown	9 (4.1)
Duration of follow-up, months, n (%)	
≥12	220 (100.0)
≥24	134 (60.9)
≥36	72 (32.7)

SD, standard deviation.

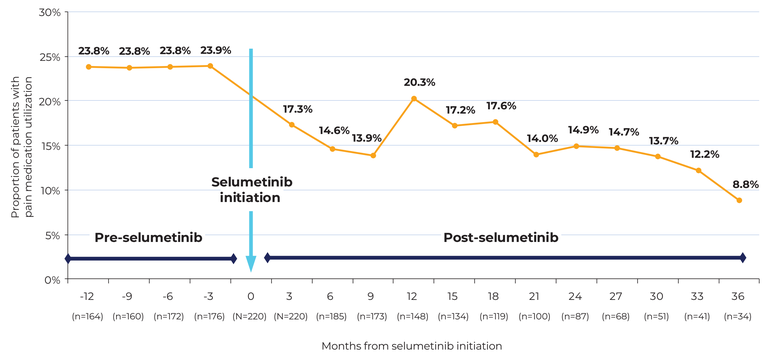
PMU analysis

- PMU steadily decreased over time after initiation of selumetinib (**Figure 2**)
  - At baseline, 24% of patients were receiving prescription pain medications
  - At 6–9 months post-selumetinib initiation, 14% were receiving pain medications
  - There was a temporary increase in PMU at 12 months post-selumetinib initiation (20%), which may be due to a yearly checkup, followed by a consistent and durable decline to 9% at 3 years post-selumetinib initiation

Adjusted statistical analysis uncovered a significant 20.3% reduction in PMU per year for patients treated with selumetinib

- For each 3-month period receiving selumetinib, patients were 5.5% less likely to use pain medication (odds ratios [OR] 0.945; p=0.039)
- Results correspond to a **20.3% reduction in PMU per year** for patients treated with selumetinib (OR 0.797; p=0.039)

Figure 2. Prescription pain medication utilization after initiation of selumetinib



Pain medication dosing analysis

- Of the 11.8% (n=26) patients receiving gabapentin and 7.7% (n=17) patients receiving oxycodone at baseline, 50.0% (n=13) and 82.3% (n=14), respectively, had discontinued use of the respective pain medication over the first year post-selumetinib initiation (**Table 2**)
  - Among those who continued to receive gabapentin, the dose decreased nominally from 802 mg/day to 675 mg/day 1 year post-selumetinib initiation
  - Gabapentin and oxycodone dose reductions were consistent across all age groups

By 1 year post-selumetinib initiation, 50% of patients taking gabapentin at baseline and 82.3% of patients taking oxycodone at baseline discontinued the respective pain medication

Table 2. Doses among patients receiving pain medications pre-selumetinib initiation (n=42)

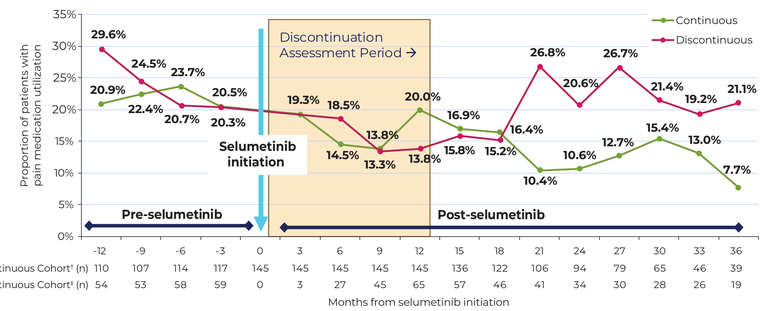
Patients receiving pain medication pre-selumetinib initiation	Gabapentin		Oxycodone	
	Pre-selumetinib initiation (Baseline)	Post-selumetinib initiation (12 months)	Pre-selumetinib initiation (Baseline)	Post-selumetinib initiation (12 months)
Number of patients	26	13 (50.0%)	17	3 (17.6%)
Mean dose, mg/day	802	675*	17.4	NR†

*Nominal p=0.284; †Mean doses for sample sizes n≤3 were NR.
NR, not reported.

PMU among patients who discontinued selumetinib

- Patients were classified into Discontinuous and Continuous Cohorts
- In the Discontinuous Cohort, a steady increase in the proportion of patients with PMU was observed, with PMU more than twice as high versus the Continuous Cohort at 36 months post-selumetinib initiation (21% versus 8%, respectively; **Figure 3**)
- Overall, patients who discontinued selumetinib for any reason experienced an increase in PMU; 26.8% of patients in the Discontinuous Cohort were receiving pain medications at 21 months post-selumetinib initiation versus 10% in the Continuous Cohort

Figure 3. Prescription pain medication* utilization in patients who discontinued versus continuously received selumetinib



*Prescription pain medications included gabapentin, opioids, benzodiazepines, Rx NSAIDs, Rx acetaminophen, and duloxetine; †Patients with continuous use of selumetinib for ≥12 months; ‡Patients who had a gap in receiving selumetinib that was ≥3x the previous prescribed daily supply (i.e., three missed cycles) and within 12 months of initiation, beginning at the end of medication consumption.
NSAID, nonsteroidal anti-inflammatory drug; Rx, prescription.

LIMITATIONS

- The number of patients receiving pain medications may be under-reported, as this study only included prescription pain medications, and US claims data do not capture over-the-counter PMU
- This study assesses pain medication prescription fills, but we could not determine if patients were consuming the pain medications or following their specific dosing schedules
- This study does not assess the reason for PMU; therefore, some pain medications may be used for reasons other than NF1-PN-related pain
- This study did not confirm the indication for selumetinib use as part of the inclusion criteria
- This study was not designed to measure the adherence or persistence to selumetinib, and thus the Discontinuous and Continuous Cohort analysis should be interpreted with caution

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Disclosures
JM received consulting fees and payment from Alexion, AstraZeneca Rare Disease. JM also declares receiving payment for attending meetings and/or travel from the Children's Oncology Group. GL, AB, BG, and TD report employment at Alexion, AstraZeneca Rare Disease, and own stock in Alexion, AstraZeneca Rare Disease. AA, MS, and WvdP declare no conflicts of interest.

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