Poster RWD6

Effect of Selumetinib Treatment on Pain Medication Utilization in Pediatric Patients: A US Claims Database Analysis

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OBJECTIVE

- This closed claims database study aimed to evaluate real-world changes in pain medication utilization (PMU) by pediatric patients before and after they were first prescribed selumetinib

CONCLUSIONS

- This study demonstrated a decrease in pain medication use following the first selumetinib prescription claim in pediatric patients
  - This decrease was mainly driven by a decline in gabapentin and opioid utilization following selumetinib initiation

PLAIN LANGUAGE SUMMARY

Why did we perform this research?

Neurofibromatosis type 1 (NF1) is a genetic disorder that can cause tumors called plexiform neurofibromas (PN) to grow along a person's nerves. PN can affect a person's quality of life. Most children with NF1 and PN experience pain related to their condition, and often use medication to manage this pain. It is not always possible to remove PN completely with surgery. However, selumetinib is a medication that has been approved by regulators in the USA to treat children (2–18 years old) with NF1 and symptomatic, inoperable PN. Selumetinib has also been approved by regulators in multiple other countries and regions (including the EU, China, and Japan) for the treatment of children (3–18 years old) with the same condition.

How did we perform this research?

The aim of this study was to use a research database of medical insurance claims to better understand changes in pain medication utilization by children before and after they were first prescribed selumetinib. Patients eligible for the study were identified between April 10, 2020 (when selumetinib was initially approved for use in the USA) and December 31, 2022 (the time of the latest available data).

What were the findings of this research?

The results from this study showed that pain medication was used less frequently 6 months after selumetinib was first prescribed than it was in the 6 months prior to the first selumetinib prescription.

Poster | Plain language summary | Supplementary material

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https://rarediseaseresource.com/2024/ISPOR-05-05/NF1_Pain_Medication_Utilization_Poster

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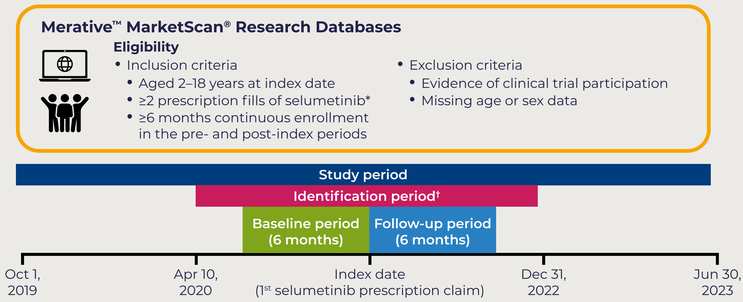
INTRODUCTION

- Selumetinib, an oral mitogen-activated protein kinase kinase (MEK) inhibitor, received U.S. Food and Drug Administration (FDA) approval on April 10, 2020, for pediatric patients (aged ≥2 years) with neurofibromatosis type 1 (NF1) and symptomatic, inoperable plexiform neurofibromas (PN)[1,2]
  - It has also been approved by the regulatory bodies in multiple other regions and countries including in the EU, Japan, and China[3-5]
- PN may develop anywhere in the body, can cause functional limitations, and may be painful[6-8]
  - Most pediatric patients with NF1-PN experience PN-related pain, and the use of pain medication to manage this is common[8]
  - Chronic pain caused by PN affects patient quality of life, even when pain medication is used[9]

METHODS

- An overview of the study design for this descriptive, noninterventional, retrospective cohort study is shown in **Figure 1**

Figure 1: Study design



*Between April 10, 2020 and December 31, 2022; †April 10, 2020 was the date at which the identification period started and is the date selumetinib received FDA approval for pediatric patients with NF1 and symptomatic, inoperable PN. Pain medication utilization was assessed in the baseline and follow-up periods. FDA, US Food and Drug Administration; NF1, neurofibromatosis type 1; PN, plexiform neurofibroma.

- Descriptive statistics were used to describe the patient population, including means and standard deviations (SDs) for continuous variables, and proportions and frequencies for categorical variables
- PMU was assessed in both the baseline (pre-index) and follow-up (post-index) periods, and was defined as the number of patients who filled a prescription for any of the following:
  - Opioids, gabapentin, acetaminophen, non-steroidal anti-inflammatory drugs (NSAIDs), and any pain medication
    - Opioids administered on the same day as a surgical procedure or filled within 1 day following surgery were excluded
- A paired generalized estimating equation (GEE) logistic regression model with an exchangeable correlation structure estimated the odds ratios (ORs) for PMU (binary variable; ≥1 versus 0 prescription fill of pain medication) pre- and post-index
  - GEE was adjusted for sex, age, and Charlson Comorbidity Index
  - In a regression analysis, change in PMU was stratified by patients who were adherent compared with those who were not adherent during the study period
    - Patients with ≥80% proportion of days covered (days covered ÷ days in time frame) were considered adherent

RESULTS

- For the 90 eligible patients (**Table 1**; primary cohort), general baseline indicators of pain included dorsalgia (16.7%), muscle weakness (15.6%), and abdominal pain (13.3%)

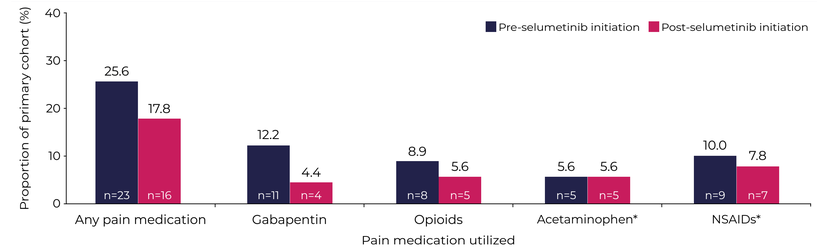
Table 1: Patient baseline characteristics and demographics

Patient characteristic	N=90
Mean age (SD), years	12.0 (4.3)
Sex, n (%)	
Male	59 (65.6)
Female	31 (34.4)
Payor type, n (%)	
Commercial	61 (67.8)
Medicaid	29 (32.2)
Region, n (%)	
Northeast	9 (10.0)
North Central	13 (14.4)
South	29 (32.2)
West	10 (11.1)
Unknown*	29 (32.2)
CCI, mean (SD)	2.0 (2.4)
NF1-PN-related comorbidities, n (%)†	
ADHD	26 (28.9)
Scoliosis	24 (26.7)
Headache	22 (24.4)
Abnormalities of gait and mobility	17 (18.9)
Dorsalgia (back pain)	15 (16.7)
Constipation	15 (16.7)
Muscle weakness	14 (15.6)
Abdominal pain	12 (13.3)

*Medicaid patients did not provide regional data; †Comorbidities reported in ≥10% patients are presented here. Other NF1-PN-related comorbidities included: congenital heart disease, epilepsy/seizures, anxiety disorders, autism, depression/bipolar disorder, hypertension (and uncontrolled hypertension), malignant peripheral nerve sheath tumor, and leukemia. ADHD, attention deficit hyperactivity disorder; CCI, Charlson Comorbidity Index; NF1, neurofibromatosis type 1; PN, plexiform neurofibroma; SD, standard deviation.

- Post-index utilization decreased versus pre-index utilization for opioids, gabapentin, and NSAIDs; no change was seen in acetaminophen utilization (**Figure 2**)
  - The largest decrease in utilization was observed for gabapentin (PMU decrease of 67%; adjusted OR 0.33; 95% confidence interval [CI]: 0.10, 1.09; p=0.07) (**Figure 3**)

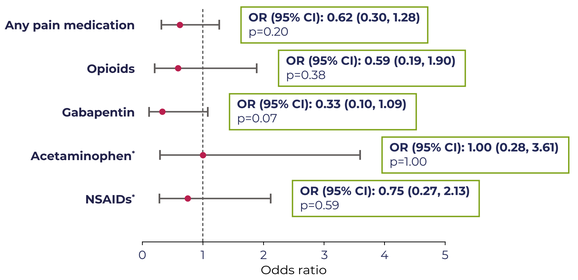
Figure 2: Patients with ≥1 pain medication prescribed pre- and post-index in the primary cohort (N=90)



*Prescription only. NSAID, non-steroidal anti-inflammatory drug.

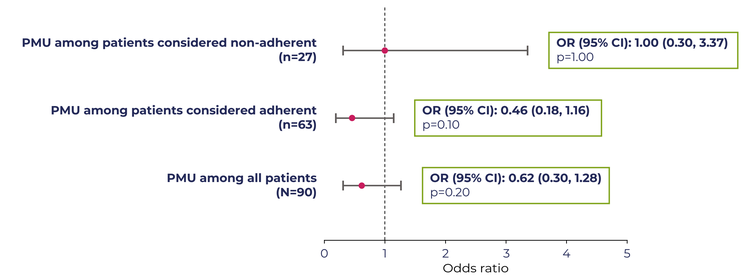
- Utilization of any pain medication was reported in 25.6% of the primary cohort pre-index, compared with 17.8% post-index (**Figure 2**)
  - PMU decreased by 38% in the post-index compared with the pre-index period (adjusted OR 0.62; 95% CI: 0.30, 1.28; p=0.20), mostly driven by a reduction in gabapentin and opioid use (**Figure 3**)
- In the primary cohort (N=90), 70% patients were considered adherent (n=63; ≥80% proportion of days covered)
  - In patients considered adherent to selumetinib treatment, PMU decreased by 54% from the pre- to post-index periods (adjusted OR 0.46; 95% CI: 0.18, 1.16; p=0.10); no difference in PMU was observed in non-adherent patients pre- and post-index (adjusted OR 1.00; 95% CI: 0.30, 3.37; p=1.00) (**Figure 4**)

Figure 3: Adjusted odds ratios for PMU in the primary cohort pre- and post-index (N=90)



*Prescription only. ORs were adjusted for sex, age, and CCI. ORs less than 1 represented a decrease in PMU post-index/first selumetinib prescription claim. Please scan the QR code for results of the unadjusted analysis (**Supplementary Figure 1**). CCI, Charlson Comorbidity Index; CI, confidence interval; NSAID, non-steroidal anti-inflammatory drug; OR, odds ratio; PMU, pain medication utilization.

Figure 4: Adjusted odds ratios for PMU in the primary cohort pre- and post-index, stratified by adherence (N=90)



ORs were adjusted for sex, age, and CCI. Patients with ≥80% proportion of days covered (days covered ÷ days in time frame) were considered adherent. ORs less than 1 represented a decrease in PMU post-index/first selumetinib prescription claim. Please scan the QR code for results of the unadjusted analysis (**Supplementary Figure 2**). CCI, Charlson Comorbidity Index; CI, confidence interval; OR, odds ratio; PMU, pain medication utilization.

STUDY LIMITATIONS

- As this analysis was based on prescription fills, it can only be assumed that patients had taken their medications
- It was only possible to assess prescription PMU; utilization of over-the-counter pain medications was not evaluated
- Pain medication used to relieve NF1-PN-related pain could not be distinguished from those that were used for other sources of pain
- The sample sizes were generally small, although this is typical for rare disease studies

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Conflicts of Interest
GL, TD, ME, BG and AA are employees of, and have stocks in, Alexion, AstraZeneca Rare Disease. JM is a consultant for Alexion and has been paid consulting fees by Alexion, AstraZeneca Rare Disease. JM has received payment/honoraria from the American Society of Pediatric Hematology/Oncology and has received support for attending meetings/travel from the Children's Oncology Group. JM also declares participating on a Data Safety Monitoring Board or Advisory Board for Alexion, AstraZeneca Rare Disease.

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1. Alexion. Koselugo (selumetinib) Prescribing Information. 2024; 2. FDA. FDA approves selumetinib for neurofibromatosis type 1 with symptomatic, inoperable plexiform neurofibromas. (accessed April 2024); 3. AstraZeneca. Koselugo approved in the EU for children with neurofibromatosis type 1 and plexiform neurofibromas. (accessed April 2024); 4. AstraZeneca. Koselugo approved in Japan for paediatric patients with plexiform neurofibromas in neurofibromatosis type 1. (accessed April 2024); 5. AstraZeneca. Koselugo approved in China for paediatric patients with neurofibromatosis type 1 and plexiform neurofibromas. (accessed April 2024); 6. Bergqvist C et al. *Orphanet J Rare Dis* 2020;15:37; 7. Blakeley JO and Plotkin SR. *Neuro Oncol* 2016;18(5):624-638; 8. Iheanacho I et al. *Neurol Sci* 2022;43:1281–1293; 9. Wolters PL et al. *Am J Med Genet A* 2015;167A:2103–2113.

Please scan the QR code to access the **Supplementary Material** for full reference links.