Poster RWD163

Medication Adherence and Persistence on Selumetinib Treatment in Pediatric Patients: A US Claims Database Analysis

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OBJECTIVE

- The primary objective of this closed claims database study was to evaluate real-world adherence, persistence/discontinuation, and reinitiation among pediatric patients treated with selumetinib

CONCLUSIONS

- Most pediatric patients were adherent to selumetinib treatment, with 70% of patients adherent at 6 months; the probability of adherence appeared to decrease with age
- Persistence was high, with probability estimates at 3 and 6 months of 95.6% and 85.5%, respectively
- Approximately 20% of patients who discontinued selumetinib treatment for ≥84 days subsequently reinitiated treatment; most reinitiations occurred within 6 months

PLAIN LANGUAGE SUMMARY

Why did we perform this research?

Neurofibromatosis type 1 (NF1) is a genetic condition that can cause a range of signs and symptoms, including the growth of tumors called plexiform neurofibromas (PN) along a person's nerves. PN can be painful and cause other problems due to their size and location; often it is not possible to remove PN completely with surgery. Selumetinib is a medication that was approved by regulators in the USA on April 10, 2020, for treating children at least 2 years old with NF1 and symptomatic, inoperable PN. Selumetinib has since been approved by regulators in multiple other countries/regions (including the EU, China, and Japan) for the treatment of children at least 3 years old with the same condition. Currently, there is limited published information on how long children stay on selumetinib after they first start taking it.

How did we perform this research?

The aim of this study was to use a research database of medical insurance claims to assess whether children who were prescribed selumetinib between April 10, 2020 and December 31, 2022, continued on this treatment. This was measured by finding the percentage of days children took selumetinib in the time between their first prescription and the study cut-off date.

What were the findings of this research?

The results showed that most children continued taking selumetinib; the average proportion of days a child had taken selumetinib in the 6 months after their first prescription was 83.6%. Older children (12–18 years old) were less likely to adhere to their selumetinib treatment compared with younger children (2–11 years old). It was estimated that 85.5% of children would persist with selumetinib treatment during the initial 6 months of treatment. The average (median) time children persisted with selumetinib treatment was 2 years and 3 months. Although some children stopped persisting with selumetinib treatment (14.5%), about one-fifth of these children restarted taking selumetinib at a later date.

Poster | Plain language summary | Supplementary material

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https://rarediseaseresource.com/2024/ISPOR-05-05/NF1_Med_Adherence_and_Persistence_Poster

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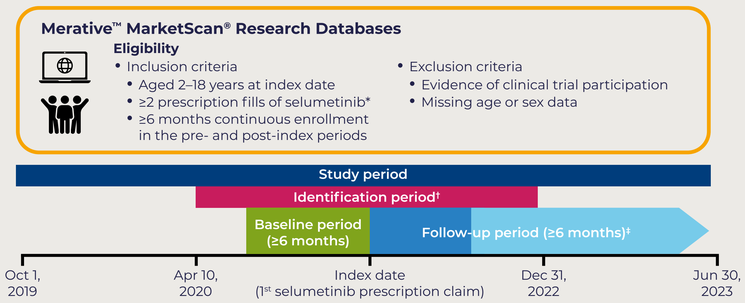
INTRODUCTION

- Neurofibromatosis type 1 (NF1) is a genetic disorder with diverse clinical manifestations[1]
  - Plexiform neurofibromas (PN) are nerve sheath tumors that arise in up to 50% of people with NF1,[2,3] and can cause pain and functional limitations[4]
- Selumetinib received U.S. Food and Drug Administration (FDA) approval on April 10, 2020, for the treatment of pediatric patients aged ≥2 years with NF1 and symptomatic, inoperable PN[5,6]
  - Selumetinib has since been approved to treat pediatric patients aged ≥3 years with NF1 and symptomatic, inoperable PN by multiple other regulatory bodies, including those in the EU, China, and Japan[7–9]
- Data on real-world selumetinib treatment patterns in pediatric patients with NF1-PN are limited
  - Results from the pivotal SPRINT trial showed that mean adherence to selumetinib among pediatric patients with NF1-PN was 96.7% during the first 12 months of treatment[10]
  - Although adherence (61.3% in the first 6 months) and persistence (64.2% during the first 6 months) to selumetinib were determined in a real-world study by Yang et al., 2024, these could have been underestimated, because the analysis was based on an open claims database; therefore, some prescriptions may not have been captured[11]

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 is the date selumetinib received FDA approval for pediatric patients with NF1 and symptomatic, inoperable PN; ‡The light blue arrow indicates that follow-up could vary as it continued for as long as a patient was enrolled. FDA, Food and Drug Administration; NF1, neurofibromatosis type 1; PN, plexiform neurofibroma.

- Adherence, discontinuation, persistence, and time to reinitiation were assessed (**Table 1**)
- To evaluate the association between proportion of days covered (PDC) and age, PDC (outcome variable) was analyzed using a logistic regression (LR) against age (exposure)
  - The LR was adjusted for sex, cognitive deficits and Charlson Comorbidity Index
  - LR analyses were also performed with age as continuous and categorical variables

Table 1: List of assessed metrics and their definitions

Term	Definition
Adherence	• Patients were adherent if PDC (days covered ÷ days in specified time frame) was ≥80%
Discontinuation	• A gap of ≥84 days from the end of the supply of the prior prescription fill to the start of the next prescription fill (or end of study period)
Persistence*	• The proportion of patients who did not discontinue their selumetinib treatment • Measured by the cumulative number of days of continuous use of selumetinib without discontinuation
Time to discontinuation*	• Defined as the time from the date of the first prescription fill to the last day covered by the last prescription filled prior to discontinuation
Time to reinitiation*	• The number of days between the end of the 84-day discontinuation window and treatment reinitiation

*This was evaluated using Kaplan–Meier analysis. PDC, proportion of days covered.

RESULTS

- Overall, 90 patients with ≥2 selumetinib prescription fills were identified (**Table 2**)

Table 2: Patient baseline demographics and clinical characteristics

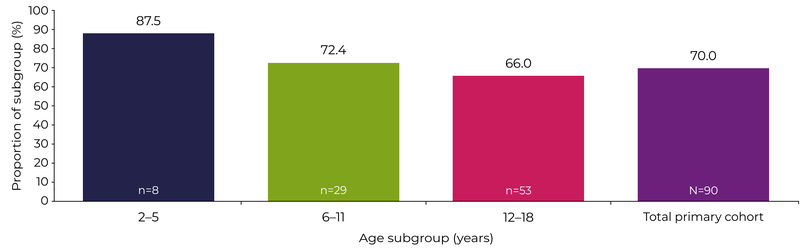
Patient characteristic	N=90
Mean age (SD), years	12.0 (4.3)
Age subgroup, years, n (%)	
2–5	8 (8.9)
6–11	29 (32.2)
12–18	53 (58.9)
Sex, n (%)	
Male	59 (65.6)
Female	31 (34.4)
Payor type, n (%)	
Commercial	61 (67.8)
Medicaid	29 (32.2)
CCI, mean (SD)	2.0 (2.4)

Please scan the QR code for table of all baseline demographics and clinical characteristics **(Supplementary Table 1)**.
CCI, Charlson Comorbidity Index; SD, standard deviation.

Adherence

- At 6 months post-index, mean (SD) PDC was 83.6% (19.0), and 70% of patients were adherent (PDC ≥80%)
- Younger patients (aged 2–5 years; n=8; PDC ≥80%: 87.5%) were more likely to be adherent than those in the 6–11 years (n=29; PDC ≥80%: 72.4%) and 12–18 years (n=53; PDC ≥80%: 66.0%) age subgroups; these were not statistically significant differences (**Figure 2; Table 3**)
- LR analysis, for which age was a continuous variable, showed that each 1 year increase in age was associated with a 10% decrease in the probability of being adherent to treatment; the difference did not reach statistical significance
  - Unadjusted: odds ratio [95% confidence interval] 0.90 [0.80, 1.00], p=0.063
  - Adjusted: odds ratio [95% confidence interval] 0.90 [0.79, 1.02], p=0.098

Figure 2: Proportion of patients adherent to treatment (PDC ≥80%) by age subgroup



PDC, proportion of days covered.

Table 3: Odds ratios on adherence to selumetinib treatment by age subgroup using LR

Age subgroup, years	Unadjusted		Adjusted*	
	OR (95% CI)	p-value	OR (95% CI)	p-value
2–5	3.60 (0.58, 70.02)	0.248	2.06 (0.30, 41.32)	0.527
6–11	1.35 (0.51, 3.79)	0.554	1.25 (0.45, 3.65)	0.678
12–18	Ref	Ref	Ref	Ref

*Adjusted for sex, cognitive deficits and Charlson Comorbidity Index. CI, confidence interval; LR, logistic regression; OR, odds ratio; Ref, reference.

Table 4: Discontinuation and persistence probability estimates

Probability estimates, % (95% CI)	N*	Discontinuation	Persistence
3 months	87	4.4 (1.7, 11.4)	95.6 (88.6, 98.3)
6 months	76	14.5 (8.7, 23.6)	85.5 (76.4, 91.3)
9 months	59	23.2 (15.6, 33.6)	76.8 (66.4, 84.4)
12 months	45	34.8 (25.3, 46.5)	65.2 (53.5, 74.7)
18 months	25	38.2 (28.2, 50.3)	61.8 (49.7, 71.8)
24 months	14	47.8 (35.2, 62.4)	52.2 (37.6, 64.8)
Median TTD (Kaplan–Meier method), years		2.25 (1.23, NA)	

*Patients 'at risk' of discontinuing selumetinib treatment (i.e. the number of patients who were still continuously enrolled and had not yet discontinued selumetinib treatment). CI, confidence interval; NA, not available; TTD, time to discontinuation.

Persistence

- Persistence was observed in 95.6% and 85.5% of patients at the first 3 (n=87) and 6 (n=76) months of follow-up, respectively (**Table 4**)
- Median time to discontinuation was 2.25 years, and at 6 months post-index, the probability of discontinuation was 14.5% (**Table 4; Supplementary Figure 1**)
  - Approximately 20% of patients (n=7) who discontinued treatment (for ≥84 days) reinitiated treatment; most reinitiations of selumetinib (~80%) occurred within 6 months (**Supplementary Figure 2**)

STUDY LIMITATIONS

- Reasons for treatment discontinuation and reinitiation were not collected
  - A patient may have paused selumetinib treatment for several reasons (e.g. symptom relief did not meet expectations)
- Only prescription fill behavior was evaluated and not direct measures of treatment adherence
- The sample sizes were generally small; when quantifying by age subgroup the analysis is underpowered, particularly in the youngest age subgroup (2–5 years, n=8)

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