Poster CO119

Natural history, management, and burden of disease in adults with NF1 and symptomatic inoperable plexiform neurofibroma in France

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STUDY OBJECTIVE

- The objectives of this study were to describe the natural history, clinical characteristics, disease burden, and treatment patterns among adults with NF1 and symptomatic inoperable PN managed in French NF1 specialist centers

CONCLUSIONS

- Adults with NF1 and symptomatic, inoperable PN experience persistent morbidity and have limited treatment options
- Management of NF1-PN has previously relied on partial resection and symptomatic care, highlighting unmet needs for effective systemic therapies and standardized pain assessment

PLAIN LANGUAGE SUMMARY

Why did we perform this research?
Neurofibromatosis type 1 (NF1) is a genetic disorder, which can cause tumors called plexiform neurofibromas (PN) to grow around nerves. The symptoms associated with PN growth can substantially impact a person's quality of life. Until 2025, there were no approved pharmacological treatments for adults with PN. Researchers carried out this study to better understand how the presence of PN affects adult patients with NF1-PN in France, and how the signs and symptoms of NF1-PN are managed in these patients.

How did we perform this research?
Adult patient data were collected from medical records of people in France with NF1 and symptomatic, inoperable PN. Information on patients' PN-related complications, as well as details of PN treatment, management, and imaging, were collected. Information on how adult patients use healthcare resources was also collected. Patients were selected between January 1, 2010 and December 30, 2018, after which patient data were collected until December 2023.

What were the findings of this research and what are the implications?
The study found that most patients experienced PN-related complications, the most common of which was pain. Throughout the study, the most common treatment used to manage PN was analgesics/non-steroidal anti-inflammatory drugs (NSAIDs), and dermatologists were the most common specialists that patients had at least one consultation with. The study also showed that adult patients used healthcare resources substantially more over time. The most commonly used healthcare resource was consultation, which was generally reported more than emergency visits, hospitalizations, procedures, or treatments. The findings presented here aid in better understanding the problems adult patients with NF1-PN face.

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Poster
Supplementary material
Plain language summary

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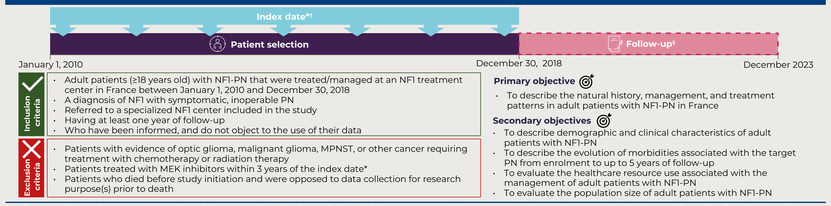
BACKGROUND

- Neurofibromatosis type 1 (NF1) is a multisystem genetic disorder that affects approximately 1 in 3000 people worldwide and can result in a wide range of clinical manifestations, such as nerve sheath tumors called plexiform neurofibromas (PN)[1]
- PN can grow anywhere in the body and occur in up to 50% of people with NF1[1,2]
  - PN are often associated with a range of morbidities, including pain, disfigurement, and motor dysfunction, and impact quality of life[3,4]
  - Malignant transformation of PN occurs in approximately 10% of adults with NF1-PN[5]
- Most adult patients with NF1-PN experience PN-related pain that interferes with their daily functioning,[6] and, in one US study, approximately 40% of patients reported taking either over-the-counter or prescription pain medication[7]
- PN that cannot be completely removed without risk of substantial morbidity due to encasement of, or close proximity to, vital structures, invasiveness, or high vascularity of the PN, are considered inoperable[8]
  - In one study, approximately one-third of adult patients with NF1-PN had a PN that was considered inoperable[9]
- In 2025, selumetinib, a mitogen-activated protein kinase kinase 1/2 inhibitor, was approved by the European Medicines Agency (EMA) for the treatment of adults with NF1 and symptomatic and inoperable PN[10]
  - At the time of this study, there were no pharmacologic treatments approved by the EMA for the treatment of NF1-PN in adults
  - Before this approval, available treatments for adults primarily focused on pain management and symptom relief, as well as maximal feasible surgical debulking of PN
  - There is an unmet need for studies that examine burden of disease and PN management in adult patients with NF1-PN in France

METHODS

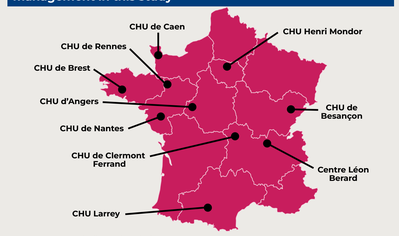
- This retrospective, multicenter, observational study included adults (aged ≥18 years) with NF1 and symptomatic, inoperable PN who had been identified between January 2010 and December 2018 (**Figure 1**) across 10 specialized centers that manage NF1 across France (**Figure 2**)
- Patient data were extracted from medical records and analyzed descriptively at baseline and over a follow-up period of up to 5 years
  - Results for the 'whole follow-up' visit summarize data for all available follow-up visits per patient, excluding baseline
  - Follow-up for data collection ended in December 2023
- The target PN was defined as the most clinically relevant tumor, i.e., the biggest and/or most symptomatic PN, according to the surgeon or as agreed at the time of the multidisciplinary meeting or documented in the patient's medical record that the PN was symptomatic (pain, disfigurement, functional mobility issues)
  - This choice was at the investigator's discretion

Figure 1. Study design



*Defined as: 1. The earliest documented date, within the patient selection period, on which the symptomatic PN was deemed inoperable by a national or local MDT or 2. The first date when the evaluation of the symptomatic PN was recorded as inoperable based on the opinion of a surgeon or physician or 3. The date on which the target PN was first reported as symptomatic without any mention of surgery. †The index date could have occurred at any point during the patient selection period. ‡Follow-up varied between individuals.
MDT, multidisciplinary team; MEK, mitogen-activated protein kinase kinase; MPNST, malignant peripheral nerve sheath tumor; NF1, neurofibromatosis type 1; PN, plexiform neurofibroma.

Figure 2. Specialized centers in France for NF1-PN management in this study



CHU, Centre Hospitalier Universitaire.

RESULTS

Patient disposition

- Overall, 84 patients were enrolled in the study, and 83 patients were included in the analysis population (**Supplementary Figure 1**)

Patient demographics and baseline disease characteristics

- In this population, 57.8% (48/83) of patients enrolled in the study were female, with an overall mean (standard deviation [SD]) age at enrolment of 36.3 (12.2) years and a median age of 34.3 years (range: 18.4–62.6) at enrollment
- The mean (SD) age at target PN diagnosis was 30.1 (14.5) years
- The most frequently met NF1 diagnosis criteria were six or more café-au-lait macules over 5 mm and two or more neurofibromas or one PN, each reported in 95.2% (79/83) of patients
- Target PN were most commonly located in the lower extremities (27.7% [23/83]) and trunk (18.1% [15/83])

Table 1. NF1-PN characteristics at baseline

NF1-PN characteristic	Patients (N=83)
Type of NF1, n (%)	
Sporadic	41 (49.4)
Hereditary	36 (43.4)
Not reported	6 (7.2)
Type of target PN, n (%)	
Internal only	30 (36.1)
External only	24 (28.9)
Both internal and external	28 (33.7)
Segmental	1 (1.2)
Reason for target PN inoperability, n (%)	
Location	72 (86.7)
Risk of complications or hemorrhage	17 (20.5)
Too small	3 (3.6)
Patient or caregiver preference	1 (1.2)
Number of non-target PN, n (%)	n=78
0	17 (21.8)
1	40 (51.3)
2	12 (15.4)
≥2	9 (11.5)

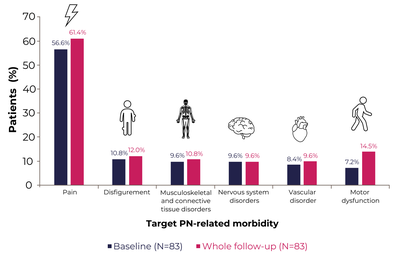
NF1, neurofibromatosis type 1; PN, plexiform neurofibroma.

Inoperability of target PN was primarily due to location (86.7% [72/83]; Table 1)

Target PN-associated morbidities

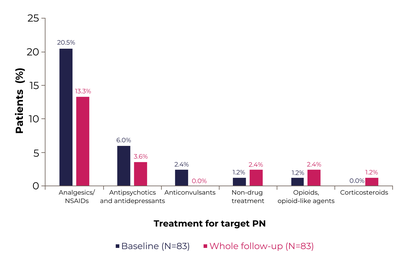
- At baseline, 80.7% had a target PN-related morbidity
  - The most commonly reported target PN-related morbidity was pain (56.6% [47/83]; **Figure 3**)
- Over the whole follow-up, 89.2% (74/83) of patients had a target PN-related morbidity
  - The most commonly reported target PN-related morbidities were pain, which persisted in 61.4% (51/83) patients, and motor dysfunction, which doubled from 7.2% (6/83) at baseline to 14.5% (12/83; **Figure 3**)

Figure 3. Target PN-related morbidities experienced by ≥10%* patients at baseline and follow-up



*At either baseline or whole follow-up.
PN, plexiform neurofibroma.

Figure 4. Treatments used to manage target PN at baseline and follow-up



'Whole follow-up' visit describes treatment received at the latest follow-up visit performed.
NSAID, non-steroidal anti-inflammatory drug; PN, plexiform neurofibroma.

Multidisciplinary team (MDT)

At baseline, 62.7% (52/83) had received advice from an MDT relating to their target PN. Over the whole follow-up, 45.8% (38/83) of patients received advice from an MDT relating to their target PN at least once

Management of target PN

- Overall, 20.5% (17/83) patients had a previous history of PN surgery at baseline, all of which were partial resections (**Supplementary Table 1**)
  - Overall, 23.3% (17/83) underwent surgery for their target PN during follow-up, all of which were partial resections (100.0% [17/17])
- Analgesic use was recorded in 13.3–20.5% of visits; systemic therapies were rarely used (**Figure 4**)

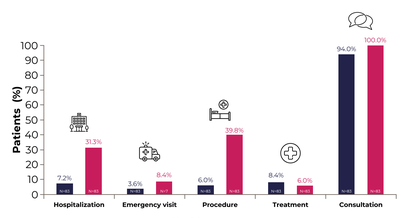
Imaging

- Imaging results of target PN were available for 32.9% (27/83) and 57.8% (48/83) of the population at baseline and follow-up, respectively
  - Magnetic resonance imaging (MRI) was the most common imaging type (baseline: 85.2% [23/27]; follow-up: 85.4% [41/48]), with the less frequent use of positron emission tomography scans (baseline: 25.0% [1/4]; follow-up: 100.0% [7/7]) and ultrasound (baseline: 25.0% [1/4]; follow-up: 0.0% [0/7]) by those who did not have an MRI scan
  - Biopsies were performed in some patients (25.3% [21/83]), mostly due to suspicion of malignant transformation of the PN (95.2% [20/21])

Healthcare resource utilization

- Consultation was the most commonly reported healthcare resource utilized by patients for NF1-PN at baseline and follow-up (**Figure 5**)
  - At baseline, 7.2% (6/83) patients had one or more NF1-PN-related hospitalizations vs 31.3% (26/83) patients over the entire follow-up period
    - Patients who underwent at least one surgical procedure for their NF1-PN at baseline and over the entire follow-up period were 6.0% (5/83) vs 39.8% (33/83), respectively

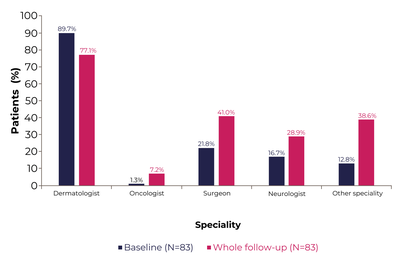
Figure 5. Healthcare resource utilization for NF1-PN at baseline and follow-up



NF1, neurofibromatosis type 1; PN, plexiform neurofibroma.

Dermatologists were the most common specialist that patients had at least one consultation with at both baseline (89.7% [70/83]) and during follow-up (77.1% [64/83]; Figure 6)

Figure 6. Specialties of physicians seen by patients at baseline and follow-up



LIMITATIONS

- Data were collected retrospectively from medical records
  - Relevant information may not have been documented consistently in the past, potentially leading to underreporting of certain conditions or complications
- Sample size was small for some analyses, including those assessing consultations or specific morbidities, as these were difficult to obtain
- The robustness of the findings in some categories was limited, due to a significant amount of missing data

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Conflicts of interest

L.F. declares receiving consulting fees, payment/honoraria for lectures, presentations, speaker bureaus, medical writing support or educational events from Alexion AstraZeneca Rare Disease. **L.F.** also declares payment from Alexion AstraZeneca Rare Disease to their institution. **M.A-A.** declares grants or contracts from Pierre Fabre and Bristol Myers Squibb to their institution, as well as consulting fees, and payment or honoraria for lectures, presentations, speaker bureaus, medical writing support or educational events, from Pierre Fabre, Alexion AstraZeneca Rare Disease, and MSD. **M.A-A.** also declares payments made to their institution from Bristol Myers Squibb, Pierre Fabre, Alexion AstraZeneca Rare Disease, and MSD for support in attending meetings and/or travel, and declares payment to their institution from Alexion AstraZeneca Rare Disease for participation on a Data Safety Monitoring Board or Advisory Board. **M.A-A.** also declares receipt of equipment, materials, drugs, medical writing support, or other services from Pierre Fabre. **J.R.** declares that their company, IQVIA Operations France, was contracted by, and received payment from, Alexion AstraZeneca Rare Disease to undertake this study. **S.B.** declares receiving support for this poster, and support for attending meetings and/or travel from Alexion AstraZeneca Rare Disease. **A.A.** is an employee of, and has stock/stock options in, Alexion AstraZeneca Rare Disease. **E.A.** and **T.R.** are employees of Alexion AstraZeneca Rare Disease.