Management of NF1-related PNs: Approaches for delivering state-of-the-art care

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When should systemic and targeted therapies be considered for adults with NF1-PN?

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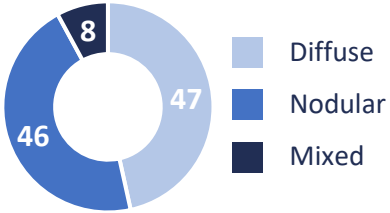
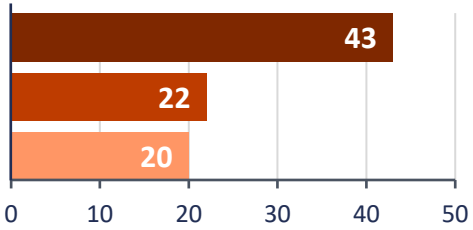
Clinical burden of NF1-PN in adults

Dutch national expertise center on NF1, retrospective study, 2004–2025
Adult NF1 cohort (N=1,067, 57% female; NF1-PNs, n=501 [47%])

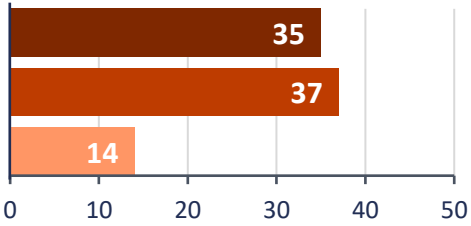
PN type (%)



PN-related symptoms (%)



Indications for treatment (%)



Key
- Disfigurement
- Pain
- Neurological deficits*

≥1 surgery for symptomatic PNs: 46%†
- >1 resection for the same tumor: **12%**
- Peri/post-operative complications: **13%‡**
- Growth after resection: **36%**

Surgical management comes with post-operative complications, and radiotherapy is associated with a risk of secondary malignancies; the introduction of MEK inhibitors for managing NF1-PNs is a major step forward

*Neurological deficits in the PN-related symptoms graph comprise motor (12%) and sensory (8%) deficits. †Partial/debulking was more common than complete resection.
‡Hemorrhage, 4%; neurological deficit, 5%; other, 6%.
NF1-PN, neurofibromatosis type 1-associated PN; PN, plexiform neurofibroma; NF1, neurofibromatosis type 1.
Noordhoek CD, et al. *Neuro-Oncol Pract*. 2026; https://doi.org/10.1093/nop/npag063.

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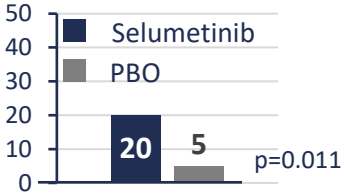
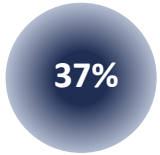
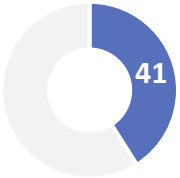
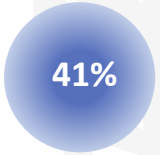
MEK inhibitors for NF1-PNs in adults

	Selumetinib (25 mg/m^2, orally, BID)[1]	Mirdametinib (2 mg/m^2, orally, BID)[2]
Trial	**KOMET** (NCT04924608), phase III (N=145) Selumetinib (n=71) vs PBO (n=74)	**ReNeu** (NCT03962543), phase IIb, N=58 Adults; separate pediatric cohort not shown
Cycles (C)	28 days (continuous)	28 days, 3 weeks on/1 week off (intermittent)
Efficacy	**ORR (%) at C16***  **Mean PN volume reduction** (post hoc analysis) 	**ORR (%) at C24†,‡**  **Median best reduction in target PN volume** 
AEs ≥ grade 3 (%)	**Overall** / **Related to intervention** **Selumetinib** 32 / 20 **PBO** 18 / 1	**Overall** 16

Efficacy data should not be compared directly because of differences in the trial designs.
*ORR (CR+PR). CR, disappearance of the target PN; PR, ≥20% decrease in target PN volume vs baseline (both confirmed by consecutive scans 3–6 months after the first response).
†ORR, ≥20% reduction of target PN volume from baseline on consecutive scans during the 24-cycle treatment phase.
‡The observed ORR was significantly higher (p<0.001) than the predefined minimum clinically relevant response rate of 23% for adults.
AE, adverse effect; BID, twice a day; CR, complete response; MEK, mitogen-activated protein kinase; NF1-PN, neurofibromatosis type 1-associated PN; ORR, overall response rate; PBO, placebo; PN, plexiform neurofibroma; PR partial response.

1. Chen AP, et al. *Lancet*. 2025;405:2217–30; 2. Moertel CL, et al. *J Clin Oncol*. 2024;43:716–29.

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How can adverse effects be monitored and managed to maximize therapeutic benefit?

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MEK inhibitor-associated adverse effects

MEK, mitogen-activated protein kinase.
Armstrong AE, et al. *Neuro Oncol.* 2026;28:847–63.

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How can pain, function and quality of life guide shared decisions in NF1-PN care?

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Care provision within the MDT to optimize HRQoL

Drivers of reduced HRQoL in adults with NF1-PNs[1]

Chronic pain → Functional decline → Risk of MNPST → Psychosocial stressors* → Persistent or worsening HRQoL

Community care[2–4]

- General patient needs
- Coordination with the specialist NF1 care team
- Patient monitoring and evaluation where access to a specialist team is limited

MDT led by an NF1 specialist with a nurse coordinator[4,5]

- Medical and surgical oncology
- Neuro- and plastic surgery
- Pain management
- Genetic counseling
- Social work

HRQoL challenges evolve across developmental stages, underscoring the need for continuous, age-appropriate supportive care, and management within an MDT[1]

*Including employment challenges, sexual self-esteem and social isolation.
HRQoL, health-related quality of life; MDT, multidisciplinary team; MNPST, malignant peripheral nerve sheath tumor; NF1, neurofibromatosis type 1; NF1-PN, NF1-associated plexiform neurofibroma.

1. Armstrong AE, et al. *Neuro Oncol*. 2026;28:847–63; 2. Stewart DR, et al. *Genet Med*. 2018;20:671–82; 3. Abate D, et al. Presented at: The 2026 NF Conference, Denver Co, USA. June 26–30, 2026. Poster no. 406; 4. Lipinski LJ, et al. *Orphanet J Rare Dis*. 2026;21:219; 5. Lalvani S, Brown RM. *J Multidiscip Healthc*. 2024;17:1803–17.

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