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Management of neurofibromatosis: Optimizing treatment and care from childhood to adult life

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Practice aid for supporting the management of patients with NF1

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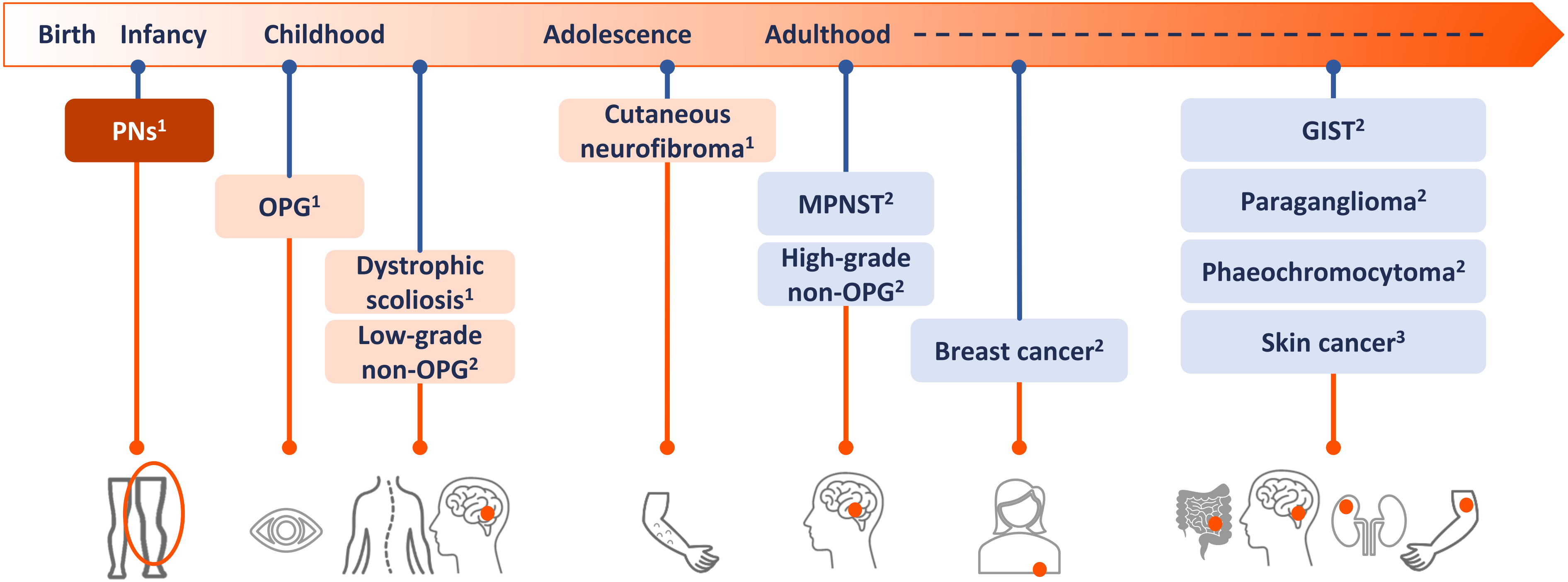
Overview of key manifestations of NF1 over the lifespan



PNs[1]

OPG[1]

Dystrophic scoliosis[1]

Low-grade non-OPG[2]

Cutaneous neurofibroma[1]

MPNST[2]

High-grade non-OPG[2]

Breast cancer[2]

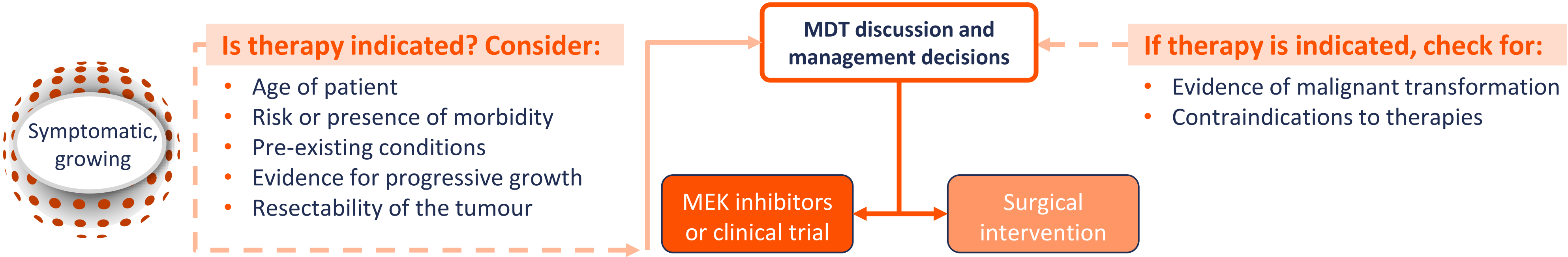
GIST[2]

Paraganglioma[2]

Phaeochromocytoma[2]

Skin cancer[3]

Management of PNs[2,4]



Symptomatic, growing

Is therapy indicated? Consider:

- Age of patient
- Risk or presence of morbidity
- Pre-existing conditions
- Evidence for progressive growth
- Resectability of the tumour

MDT discussion and management decisions

If therapy is indicated, check for:

- Evidence of malignant transformation
- Contraindications to therapies

MEK inhibitors or clinical trial

Surgical intervention

Patients should be monitored for PNs at every visit. Asymptomatic PNs showed be kept under observation.

MEK inhibitors for treating PNs in NF1

SELUMETINIB (Approved)[5,6]	MIRDAMETINIB[7] (Investigational, under review[8])
Paediatric patients	Paediatric or adult patients
Oral capsule, 25 mg/m^2 BID; ± food	Capsule/dispersible tablet, 2 mg/m^2 (max 4 mg) BID; ± food; 3 weeks on/1 week off
Confirmed PR*: 68% (34/50) **Durable PR**: 56% (28/43)	**Confirmed ORR†**: Adults, 41%; Children, 52%
Nausea, vomiting, diarrhoea; CPK increase (asymptomatic); acneiform rash; paronychia	**Adults**: Acneiform rash, diarrhoea, nausea, vomiting **Children**: Diarrhoea, acneiform rash, vomiting

Direct comparisons between trials should not be made due to differences in trial design.

*PR = Target PN volume decrease from BL ≥20% (MRI-assessed); confirmed PR = PR on consecutive restaging examinations ≥3 months apart; durable PR = PR for ≥12 cycles (≈1 year). †% patients with reduction of target PN volume ≥20% (MRI-assessed) by BICR within the 24-cycle treatment phase.

Recommended monitoring protocols when treating patients with MEK inhibitors[9]

Prior to initiating therapy	Monitoring after initiating therapy
Physical examination with vital signs	Monthly
Dermatological examination	Monthly
Laboratory evaluation (CBC, CK, electrolytes, creatinine, glucose and ALT/AST)	Monthly
Cardiac assessment (echocardiogram)	At 1 month, then every 3–6 months
Ophthalmological evaluation (visual acuity)	At 1 month, then every 3–6 months
Imaging (MRI of the affected area)	Every 3–6 months

Barriers to successful transition from paediatric to adult health care[10]

Family/patient

- Poor understanding of NF1 and the importance of medical care
- Difficulty finding HCPs with experience of NF1
- Lack of self-advocacy skills
- Financial concerns
- Discomfort with accepting transfer of responsibility of care

Shared

- Poor communication
- Lack of trust
- Difficulty establishing new relationships
- Cultural differences

Provider

- Lack of understanding of patient transition needs
- Lack of understanding of NF1 and its special care needs
- Poor communication about the transition process
- Difficulties transferring medical records
- Differences in adult vs paediatric care models

Committed clinicians and a structured HCT programme are necessary to effectively transition AYAs with NF1 into the adult healthcare system. Recognition of barriers and identification of high-risk individuals are also important considerations.

Key points to consider when facilitating transition

- Start early plan ahead
- Provide patient-/family-appropriate education
- Develop collaborative relationships between the providers
- Prepare comprehensive medical records for transfer
- Ensure awareness of resources and support, e.g. patient organizations (Children's Tumor Foundation)

Abbreviations and references

Abbreviations

ALT, alanine aminotransferase; AST, aspartate aminotransferase; AYA, adolescents and young adults; BICR, blinded independent central review; BID, two times daily; BL, baseline; CBC, complete blood count; CK, creatine kinase; CPK, CPK, creatine phosphokinase; GIST, gastrointestinal stromal tumour; HCP, health care professional; HCT, healthcare transition; MDT, multidisciplinary team; MEK, mitogen-activated protein kinase; MPNST, malignant peripheral nerve sheath tumour; MRI, magnetic resonance imaging; NF1, neurofibromatosis type 1; OPG, optic pathway glioma; ORR, overall response rate; PN, plexiform neurofibroma; PR, partial response.

References

1. Friedman, JM. *GeneReviews*® [Internet]. 2022. Available from: www.ncbi.nlm.nih.gov/books/NBK1109/; 2. Carton, C. et al. *Lancet*. 2023;56:101818; 3. Trinh P, et al. *JAMA Dermatol*. 2022;158:1214–6; 4. Fisher MJ, et al. *Neuro Oncol*. 2022;24:1827–44; 5. Gross AM, et al. *N Engl J Med*. 2020;382:1430–42; 6. FDA. Selumetinib PI. Available at: https://bit.ly/48ZxsP9 (accessed 3 January 2025); 7. Moertel CL, et al. *J Clin Oncol*. 2024;42(Suppl. 16):3016; 8. OncLive. FDA Grants Priority Review to Mirdametinib for NF1-Associated Plexiform Neurofibromas. Available at: https://bit.ly/3Z1bO8G (accessed 3 January 2025); 9. Klesse, L.J, et al. *Oncologist*. 2020;25:e1107–16; 10. Radtke HB, et al. *Pediatric Health Med Ther*. 2023;14:19–32.