touch™ NEUROLOGY

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

Practice aid for supporting the management of patients with NF1

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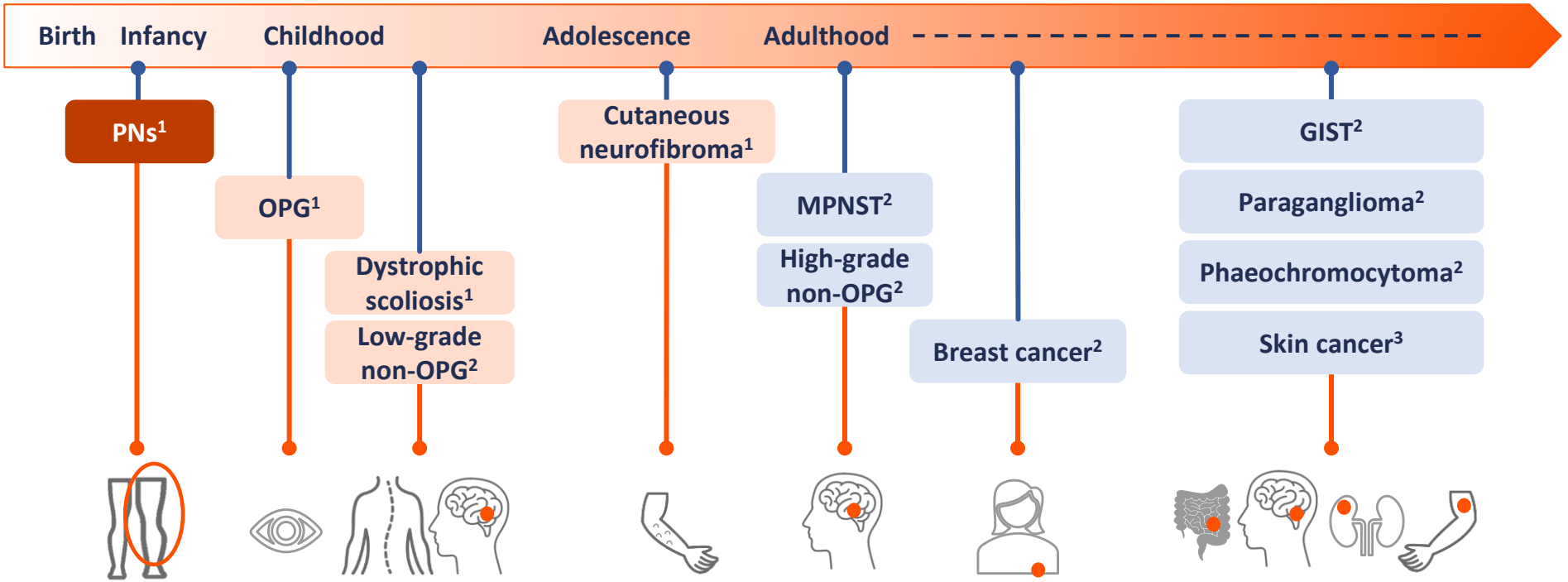
Overview of key manifestations of NF1 over the lifespan



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.

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MEK inhibitors for treating PNs in NF1

SELUMETINIB (Approved)[5,6]

- Paediatric patients
- Oral capsule, 25 mg/m^2 BID; ± food
- **Confirmed PR***: 68% (34/50)
  Durable PR: 56% (28/43)
- Nausea, vomiting, diarrhoea; CPK increase (asymptomatic); acneiform rash; paronychia

MIRDAMETINIB[7] (Investigational, under review[8])

- Paediatric or adult patients
- Capsule/dispersible tablet, 2 mg/m^2 (max 4 mg) BID; ± food; 3 weeks on/1 week off
- **Confirmed ORR†**:
  Adults, 41%; Children, 52%
- **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

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