

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

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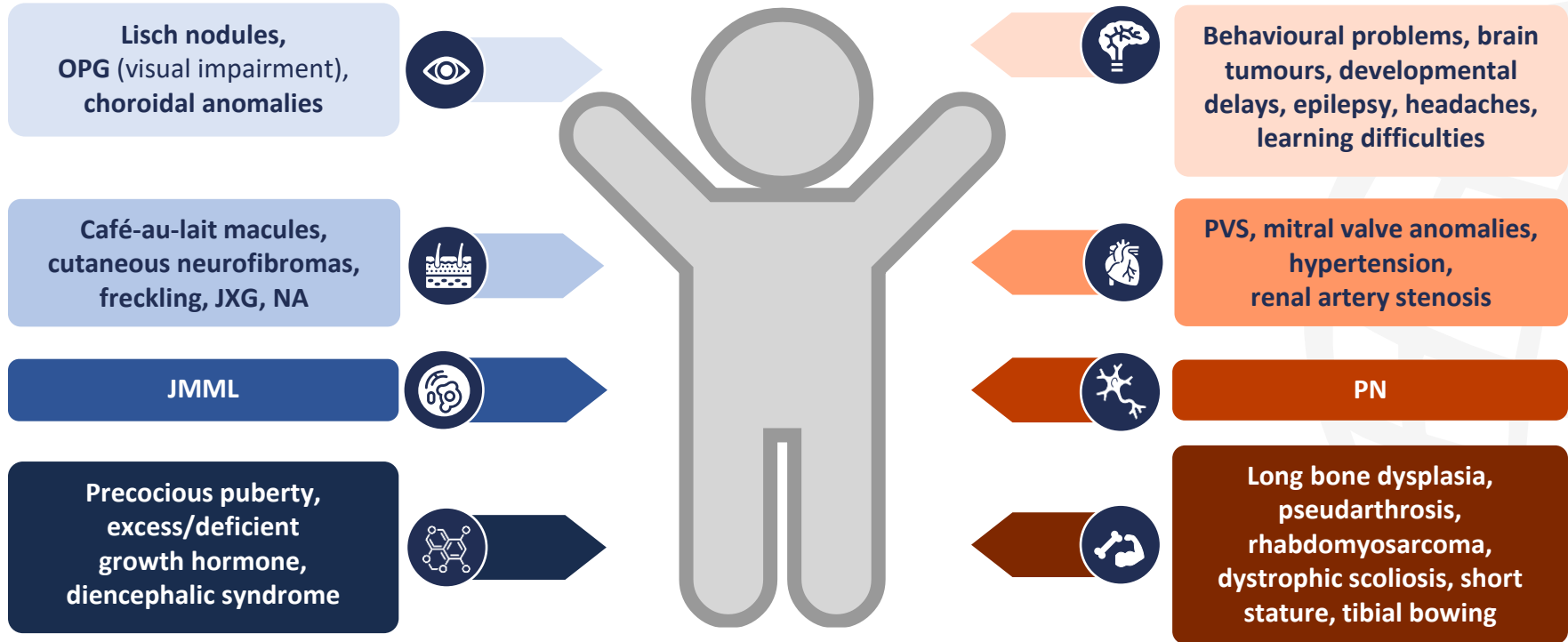
Navigating treatment options for NF1 in paediatric patients

Dr AeRang Kim

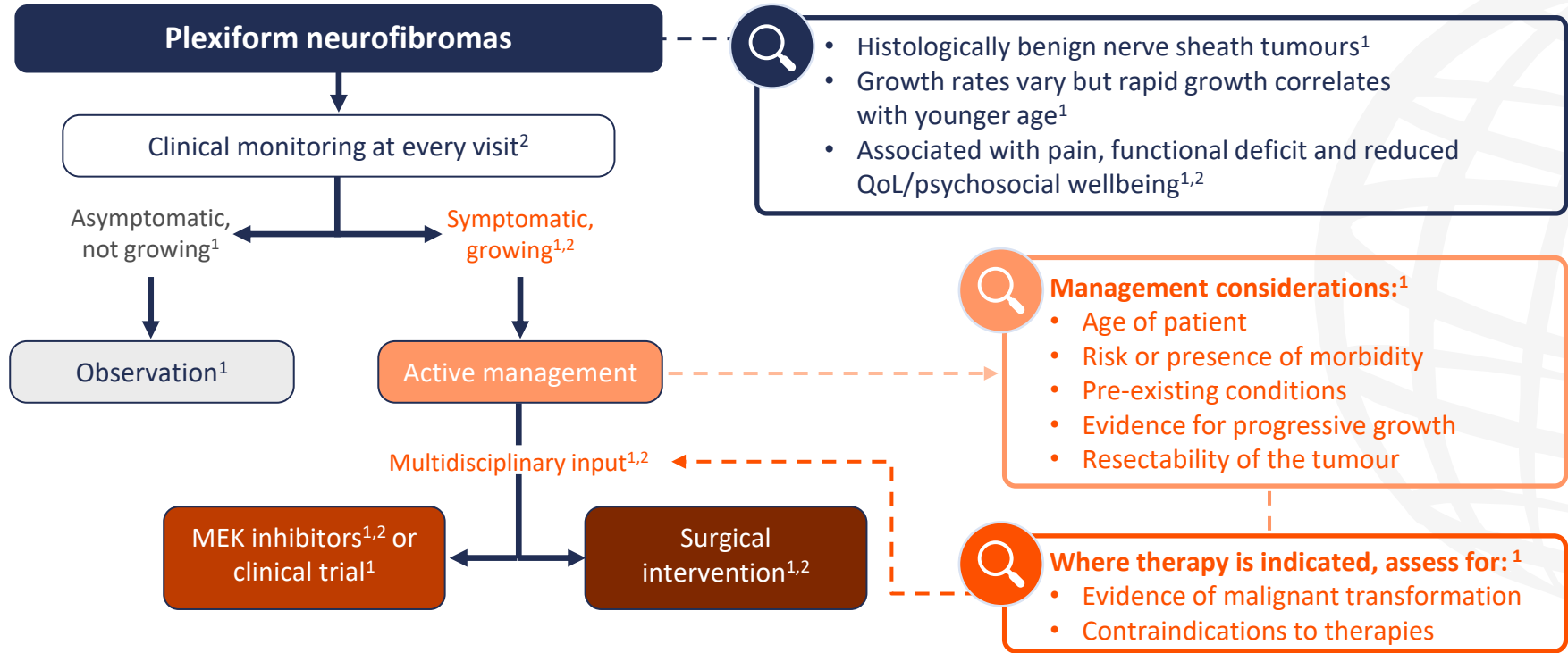
Children's National Hospital,
Washington, DC, USA



Clinical manifestations of NF1 in paediatric patients



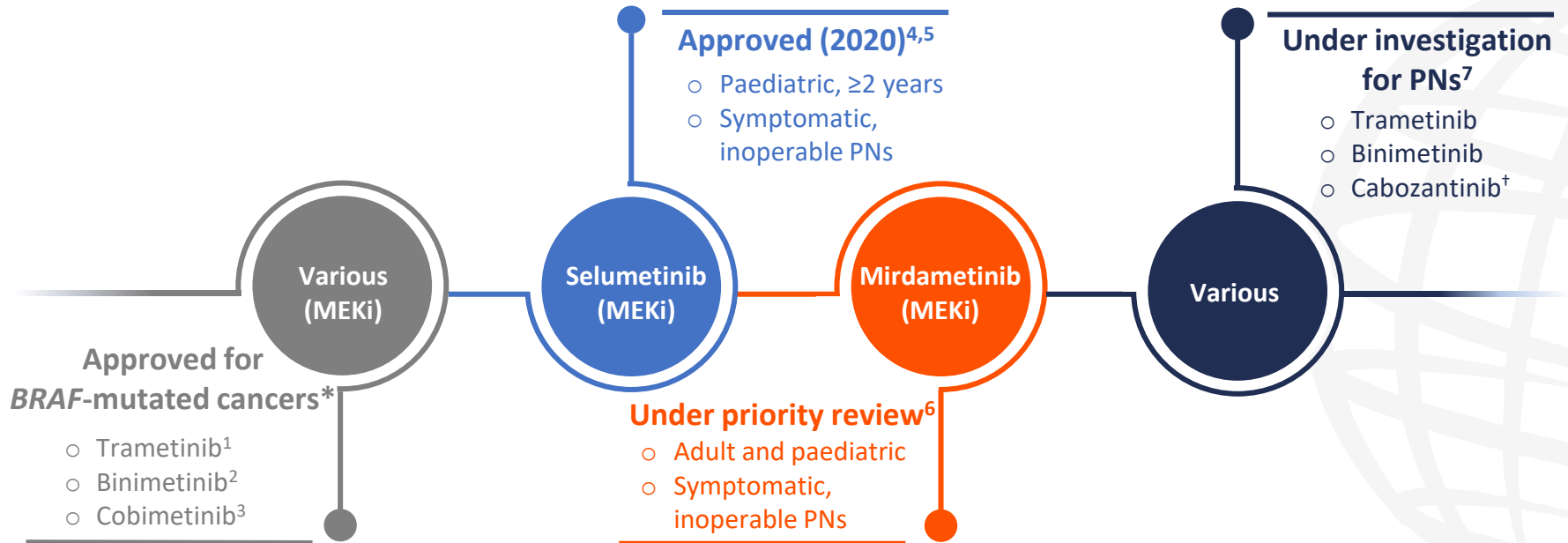
Treatment approach for plexiform neurofibromas



MEK, mitogen-activated protein kinase; QoL, quality of life.

1. Fisher MJ, et al. *Neuro-Oncol.* 2022;24:1827–44; 2. Carton C, et al. *Lancet.* 2023;56:101818.

The evolving therapeutic landscape for NF1



*See individual PI for specific indications. †Cabozantinib is a tyrosine kinase inhibitor that targets MET and vascular endothelial growth factor receptor 2, among others.

MEKi, mitogen-activated protein kinase inhibitor; NF1, neurofibromatosis type 1; PI, prescribing information; PN, plexiform neurofibroma.

1. FDA. Trametinib PI. Available at: <https://bit.ly/3ZfgEd4> (accessed 3 January 2025); 2. FDA. Binimetinib PI. Available at: <https://bit.ly/414vmMh> (accessed 3 January 2025);

3. FDA. Cobimetinib PI. Available at: <https://bit.ly/4fT763l> (accessed 3 January 2025); 4. FDA. Selumetinib PI. Available at: <https://bit.ly/48ZxsP9> (accessed 3 January 2025);

5. EMA. Selumetinib SmPC. Available at: <https://bit.ly/3Zf7vYR> (accessed 3 January 2025); 6. OnLive. FDA Grants Priority Review to Mirdametinib for NF1-Associated Plexiform Neurofibromas. Available at: <https://bit.ly/3Z1bO8G> (accessed 3 January 2025); 7. Armstrong AE, et al. *BMC Cancer*. 2023;23:553.

MEK inhibitors: Side effects and toxicities

Frequent, typically mild



Gastrointestinal

- Abdominal pain
- Diarrhoea
- Nausea/vomiting



Constitutional

- Elevated creatinine kinase
- Fatigue
- Weight gain

Potentially severe, dose limiting



Dermatological

- Acneiform rash
- Eczematous rash
- Folliculitis
- Hand foot syndrome
- Paronychia



Cardiac

- Decreased LVEF



Ocular

- Dry eye
- Periorbital oedema
- Retinopathy

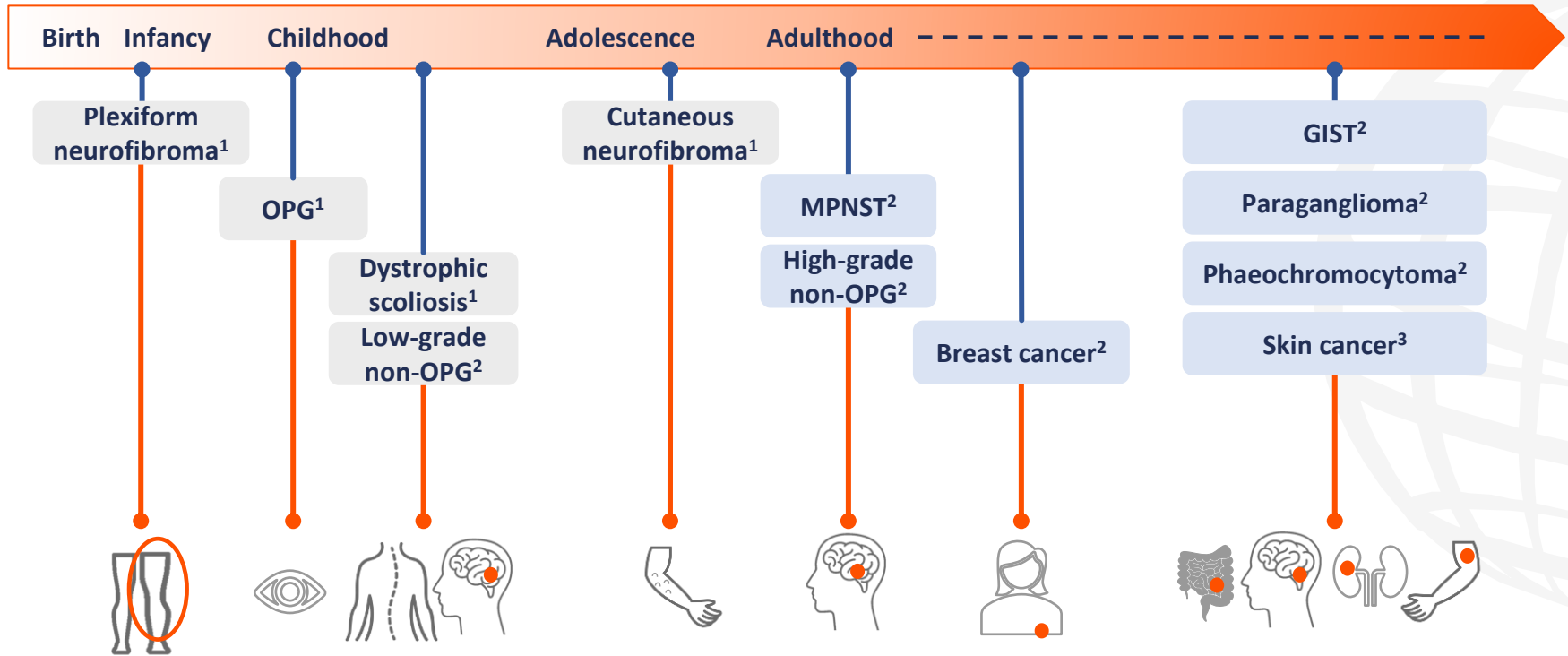
Optimal care for adult patients with NF1

Dr Rebecca Brown

University of Alabama School of Medicine
Birmingham, AL, USA



Manifestations of NF1 vary across the lifespan



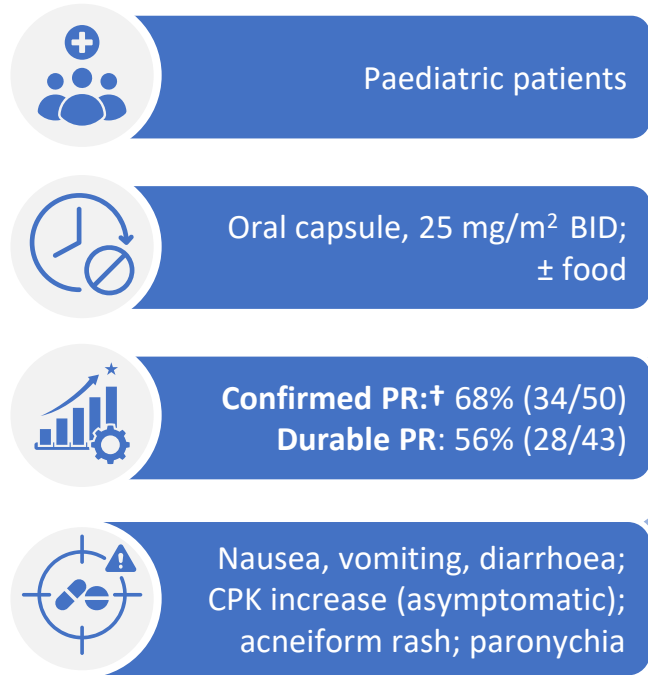
GIST, gastrointestinal stromal tumour; MPNST, malignant peripheral nerve sheath tumour; NF1, neurofibromatosis type 1; OPG, optic pathway glioma.

1. Friedman, JM. *GeneReviews*® [Internet]. 2022. Available from: www.ncbi.nlm.nih.gov/books/NBK1109/; 2. Carton, C. et al. *Lancet*. 2023;56:101818;

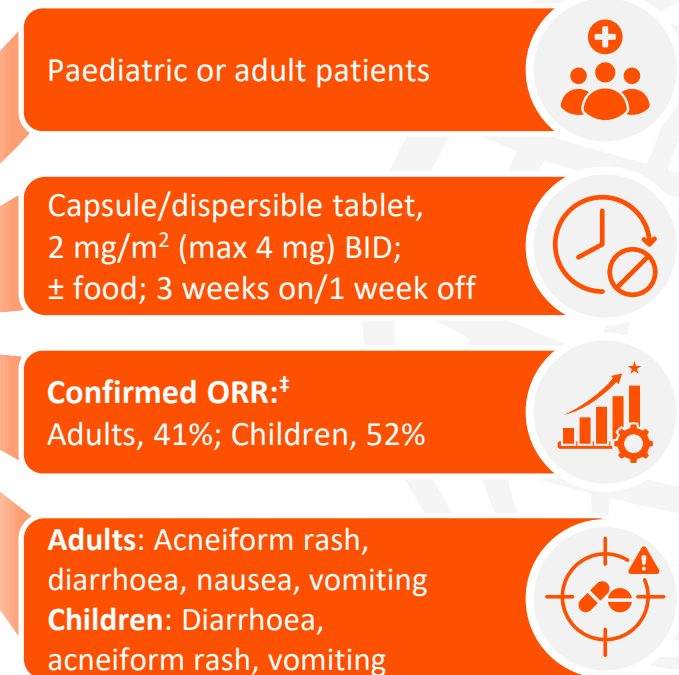
3. Trinh P, et al. *JAMA Dermatol*. 2022;158:1214–6.

MEK inhibitors for treating PNs in NF1

SELUMETINIB (Approved)^{1,2}



MIRDAMETINIB^{3*}



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

*Investigational, under review for FDA approval.⁴ †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 blinded independent central review within the 24-cycle treatment phase. BID, two times daily; BL, baseline; CPK, creatine phosphokinase; MRI, magnetic resonance imaging; ORR, overall response rate; PN, plexiform neurofibroma; PR, partial response.

1. Gross AM, et al. *N Engl J Med.* 2020;382:1430–42; 2. FDA. Selumetinib PI. Available at: <https://bit.ly/48ZxsP9> (accessed 3 January 2025); 3. Moertel CL, et al. *J Clin Oncol.* 2024; 42(Suppl. 16):3016; 4. Onclive. FDA Grants Priority Review to Mirdametinib for NF1-Associated Plexiform Neurofibromas. Available at: <https://bit.ly/3Z1b08G> (accessed 3 January 2025).

Monitoring parameters for MEK inhibitor therapy

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

Best practices for continuity of care for patients with NF1 from childhood to adulthood

Dr Kaleb Yohay

NYU Langone Health
New York, NY, USA



Transitioning to adult services: A multifaceted challenge



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