TARGETING THE PATHWAY

# Evolving Roles of MEK Inhibitors in NF1-Associated PN




Supported by an independent educational grant from Alexion Pharmaceuticals.



The Society for Neuro-Oncology has reviewed and approved this symposium as appropriate for presentation as an Independent Supported Symposium. The symposium constitutes the content and views of the sponsor and is not part of the official SNO Annual Meeting program.




In support of improving patient care, Creative Educational Concepts LLC (CEC) is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.

# Activity Credit Types

IPCE CREDIT™

This activity was planned by and for the healthcare team, and learners will receive 1.0 Interprofessional Continuing Education Credit for learning and change.

**Physicians**
(ACCME)

Creative Educational Concepts LLC designates this live activity for a maximum of 1.0 *AMA PRA Category 1 Credit(s)*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

**Nurses**
(ANCC)

This activity is designated for 1.0 contact hours.

*Note to Nurse Practitioners: The content of this CNE activity pertains to Pharmacology.*

ONCC
Credibility. Contribution. Care.

This activity is designated for 1.0 contact hours.

The program content has been reviewed by the Oncology Nursing Certification Corporation (ONCC) and is acceptable for recertification points.

**OCN**
Care Continuum
Oncology Nursing Practice
Symptom Management, Palliative Care, Supportive Care Treatment

**CBCN**
Care Continuum
Symptom Management, Palliative Care, Supportive Care Treatment

**CPHON**
Care Continuum
Pediatric Hematology and Oncology Nursing Practice
Symptom Management, Palliative Care, Supportive Care Treatment

**AOCNP**
Care Continuum
Care of the Pediatric Hematology and Oncology Patient
Disease Related Biology
Symptom Management, Palliative Care, Supportive Care Treatment

PA AAPA CATEGORY 1 CME

Creative Educational Concepts LLC has been authorized by the American Academy of PAs (AAPA) to award AAPA Category 1 CME credit for activities planned in accordance with AAPA CME Criteria. This activity is designated for 1.0 AAPA Category 1 CME credits. PAs should only claim credit commensurate with the extent of their participation.

Through an agreement between the Accreditation Council for Continuing Medical Education and the Royal College of Physicians and Surgeons of Canada, medical practitioners participating in the Royal College MOC Program may record completion of accredited activities registered under the ACCME's "CME in Support of MOC" program in Section 3 of the Royal College's MOC Program.

U.E.A.M.S.

Through a mutual recognition agreement between the AMA and the UEMS-EACCME, European physicians completing an e-learning activity from a US-based ACCME-accredited CME provider can use AMA PRA Category 1 Credit™ toward their credit requirements. Creative Educational Concepts is based in Radnor, Pennsylvania, USA. Please retain your certificate as proof of completion.

CME for MIPS
IMPROVEMENT ACTIVITY

Completion of this accredited CME activity meets the expectations of an Accredited Safety or Quality Improvement Program (IA_PSPA_28) for the Merit-based Incentive Payment Program (MIPS). Clinicians should submit their improvement activities by attestation via the CMS Quality Payment Program website.

ABIM CME MOC ACCREDITED

Successful completion of this CME activity, which includes participation in the evaluation component, enables the participant to earn up to 1.0 MOC points in the American Board of Internal Medicine's (ABIM) Maintenance of Certification (MOC) program. It is the CME activity provider's responsibility to submit participant completion information to ACCME for the purpose of granting ABIM MOC credit.

cecONCOLOGY

This activity will include discussions of products or devices that are not currently labeled for use by the U.S. Food and Drug Administration (FDA).

The faculty have been informed of their responsibility to disclose to the audience when they discuss off-label or investigational uses (any uses not approved by the FDA) of products or devices.





## **JAISHRI BLAKELEY, MD** (co-chair)

Professor of Neurology, Neurosurgery and Oncology
The Marjorie Bloomberg Tiven Professor
of Neurofibromatosis
Executive Director, Neurofibromatosis Therapeutic
Acceleration Program
Director, Johns Hopkins Comprehensive
Neurofibromatosis Program
The Johns Hopkins University School of Medicine
Baltimore, Maryland




## **ANGELA HIRBE, MD, PHD** (co-chair)

Associate Professor of Medicine and Pediatrics
Director, Adult Neurofibromatosis Clinical Program
Division of Oncology, Sarcoma Section
Washington University School of Medicine
St. Louis, Missouri




# DARREN HARGRAVE
# MB.CHB (HONS), MD, MRCP, FRCPCH

Clinical Professor in Paediatric Neuro-Oncology
University College London Great Ormond Street
Institute of Child Health
Honorary Consultant Paediatric Oncologist
Great Ormond Street Hospital for Children
London, United Kingdom

# Disclosures

## FACULTY

**Jaishri Blakeley, MD, MD,** reports the following financial relationships:

*Consultant*—Alexion Pharmaceuticals Inc., and SpringWorks Therapeutics Inc.

*Research support*—Bristol Myers Squibb Company

**Angela Hirbe, MD, PhD,** reports the following financial relationships:

*Advisory board*—Aadi Subsidiary Inc.

*Consultant*—Aadi Subsidiary Inc., Alexion Pharmaceuticals Inc., AstraZeneca, and SpringWorks Therapeutics Inc.

*Grants*—Tango

*Other financial or material support*—Boehringer Ingelheim

**Darren Hargrave, MB.Chb (Hons), MD, MRCP, FRCPCH,** reports the following financial relationships:

*Advisory board and consultant*—Alexion Pharmaceuticals Inc./AstraZeneca, Day One Biopharmaceuticals Inc., Ipsen Pharma, Novartis, and SpringWorks Therapeutics Inc.

*Grants*—Alexion/AstraZeneca

*Speakers bureau*—Alexion Pharmaceuticals Inc./AstraZeneca, Ipsen Pharma, and SpringWorks Therapeutics Inc.

## PATIENT ADVOCATE AND CAREGIVER/PLANNER

**Renie Moss** reports no financial relationships to disclose

## PEER REVIEWERS

**Alaa Bawaneh, MD, PhD,** reports no financial relationships to disclose

**Jessica Giddens, DNP, APRN, FPMHNP-BC, RN-BC,** reports no financial relationships to disclose

**THE FOLLOWING CEC STAFF** have no financial relationships to disclose:

- David Modrak, PhD (planning committee)
- Alexis Oneca (planning committee)
- Nichole Lainhart (planning committee)
- Thomas Mitchell, MSW, LSW (planning committee)
- Scott J. Hershman, MD, FACEHP, CHCP (planning committee)
- Sandra Caballero, PharmD (planning committee)
- Sharon Tordoff (planning committee)

*All identified conflicts of interest have been mitigated.*




Assess neuro-oncologic features of neurofibromatosis type 1 (NF1), including tumor types and neurological signs, to support early recognition and guide clinical decision-making




Integrate MEK inhibitors in the management of NF1-associated plexiform neurofibromas (PNs) in adult and pediatric patients




Develop evidence-based, interprofessional care plans for patients with NF1 that reflect current clinical standards and support individualized, longitudinal management

## To Ask a Question

To submit a question, please go to the *Ask Question* tab at the bottom of the screen.



# Neurofibromatosis Type 1

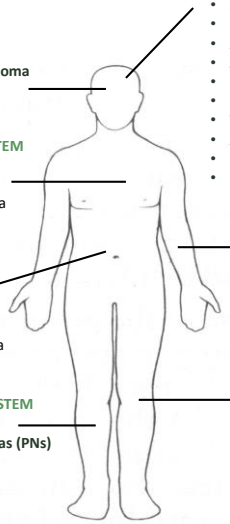
## Clinical Features and Diagnostic Criteria



# The Neurofibromatoses

## NEUROFIBROMATOSIS TYPE 1 (NF1)

**1 in 2,800 people worldwide**



**CENTRAL NERVOUS SYSTEM**
- Gliomas
- Seizures
- Learning disabilities
- Attention deficit
- Autism
- Headaches
- Precocious puberty
- Vascular abnormalities (Moyamoya)
- Aqueductal stenosis
- Sleep disturbances
- Multiple sclerosis

**EYES and VISION**
- **Optic nerve glioma**
- **Lisch nodules**

**CARDIOVASCULAR SYSTEM**
- Heart valve defects
- Aortic coarctation
- Renal artery dysplasia
- Hypertension

**SKIN**
- **Café-au-lait macules**
- **Skinfold freckling**
- Juvenile xanthogranulomas
- Melanoma

**GI SYSTEM**
- GISTs

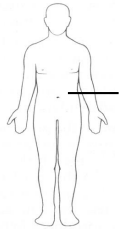
**ENDOCRINE SYSTEM**
- Pheochromocytoma

**PERIPHERAL NERVOUS SYSTEM**
- **Neurofibromas**
- **Plexiform neurofibromas (PNs)**

**SKELETAL SYSTEM**
- **Dysplasia of long bones**
- **Pseudarthrosis**
- **Sphenoid wing dysplasia**
- Dystrophic scoliosis
- Scalloping of vertebrae
- Pectus excavatum
- Macrocephaly
- Short stature
- Osteoporosis

## NON-NF2 SCHWANNOMATOSIS

1 in 158,000 people worldwide



**PERIPHERAL NERVOUS SYSTEM**
- Spinal schwannomas
- Peripheral schwannomas

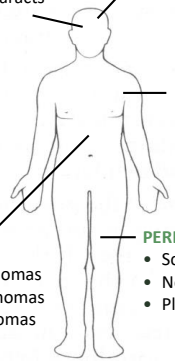
**PAIN**

## NF2-RELATED SCHWANNOMATOSIS (NF2)

1 in 67,700 people worldwide

**EYES and VISION**
- Epiretinal membranes
- Retinal hamartomas
- Juvenile cataracts

**CENTRAL NERVOUS SYSTEM**
- Meningiomas
- Cranial nerve schwannomas



**SKIN**
- Schwannomas
- Café-au-lait macules

**SPINE**
- Schwannomas
- Ependymomas
- Meningiomas

**PERIPHERAL NERVOUS SYSTEM**
- Schwannomas
- Neurofibromas
- Plexiform schwannomas

GIST, gastrointestinal stromal tumors.

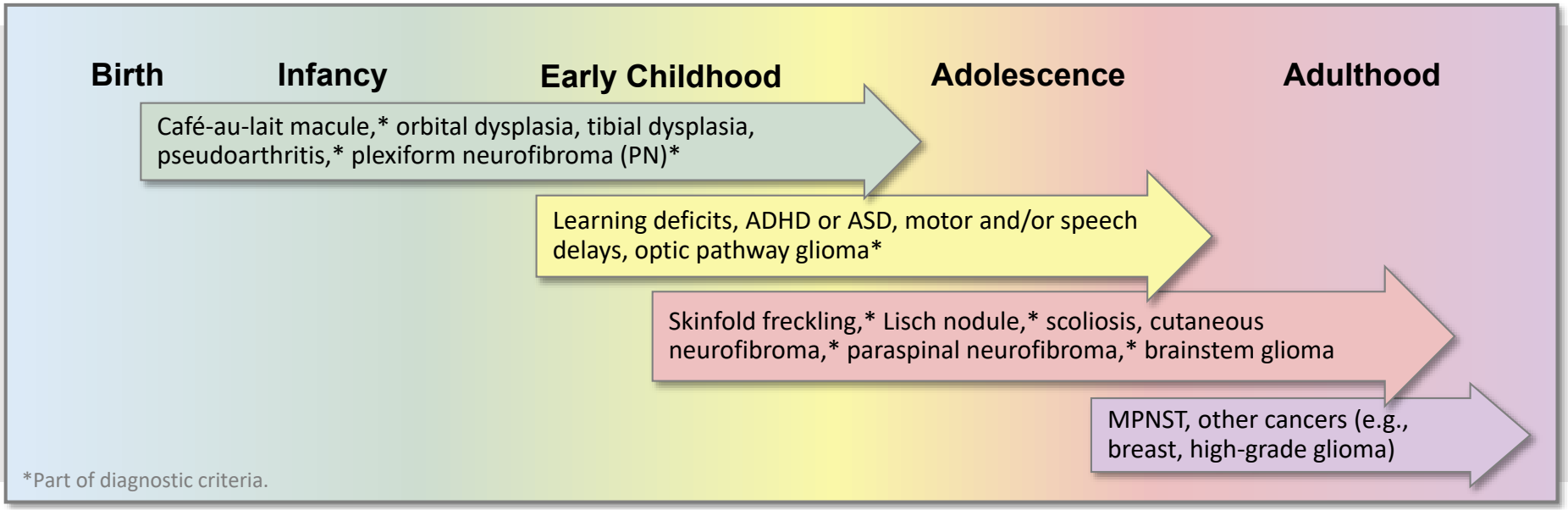
Friedman JM. Neurofibromatosis 1. In: *GeneReviews*. Updated April 3, 2025. https://www.ncbi.nlm.nih.gov/books/NBK1109/.
Moodley M, et al. *Semin Pediatr Neurol*. 2024;52:101172. Lee TJ, et al. *Orphanet J Rare Dis*. 2023;18(1):292.

cecONCOLOGY

# Development of Clinical Features of NF1

## *Timing and Severity Varies*

Neurofibromin expression largely restricted to the nervous system and adrenal medulla, with little or no expression in other tissues




*Part of diagnostic criteria.

ADHD, attention-deficit hyperactivity disorder; ASD, autism spectrum disorder; MPNST, malignant peripheral nerve sheath tumors.

Kerashvili N, et al. *Expert Rev Neurother*. 2024;24:409–420. Botero V, et al. *J Neurodev Disord*. 2024;16:49.

cecONCOLOGY

# NF1
## *Diagnostic Criteria*

### 1988

Diagnostic criteria for NF1 are met if **two or more** of the following are found:

1. Six or more café-au-lait spots (in the greatest diameter)
   - 1.5 cm or larger after puberty
   - 0.5 cm or larger before puberty
2. Freckling in the axilla or groin
3. Two or more Lisch nodules
4. Two or more neurofibromas OR one plexiform neurofibroma
5. Optic pathway glioma
6. A distinctive osseous lesion, such as sphenoid dysplasia or thinning of long bone cortex with or without pseudoarthrosis
7. First-degree relative with NF1

### 2021

Diagnostic criteria for NF1 are met in an individual who **does not have a parent diagnosed with NF1** if **two or more** of the following are found:

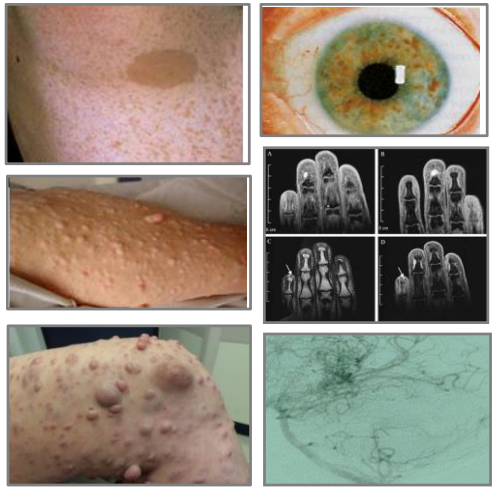
1. Six or more café-au-lait spots (in the greatest diameter)
   - 1.5 cm or larger after puberty
   - 0.5 cm or larger before puberty
2. Freckling in the axilla or groin
3. Two or more neurofibromas OR one plexiform neurofibroma
4. Optic pathway glioma
5. Two or more iris Lisch nodules OR **two or more choroid abnormalities**
6. A distinctive osseous lesion, such as sphenoid dysplasia, anterolateral bowing of tibia or pseudoarthrosis of a long bone
7. **Heterozygous pathogenic *NF1* variant with a variant allele fraction of 50% in apparently normal tissue**

If a **parent meets the above diagnostic criteria**, the individual only requires one or more of the above criteria to merit an NF1 diagnosis

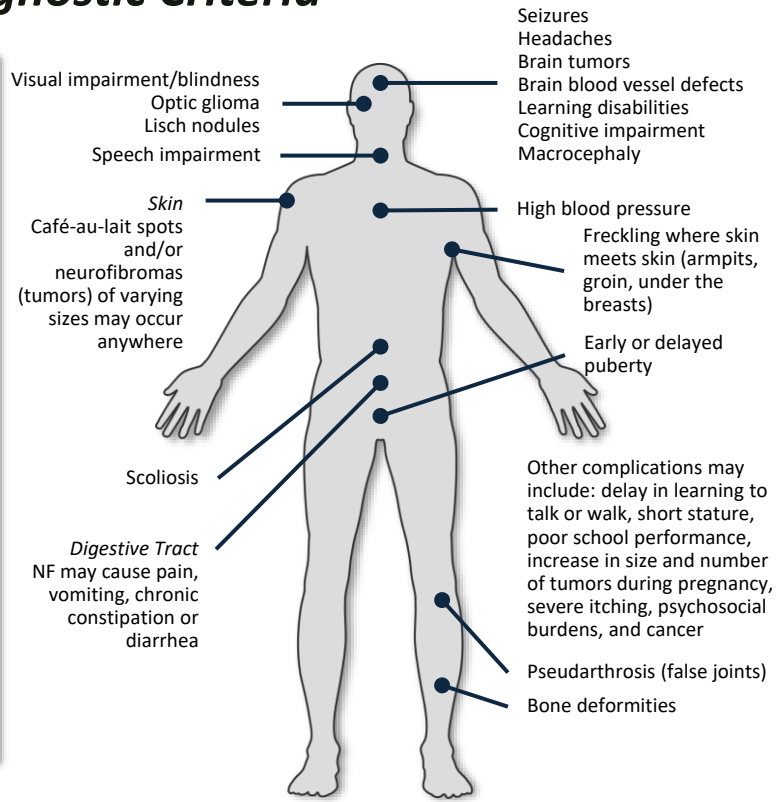
NIH Consensus Development Conference. *Neurofibromatosis.* 1988;1(3):172–178. Legius E, et al. *Genet Med.* 2021;23:1506–1513.

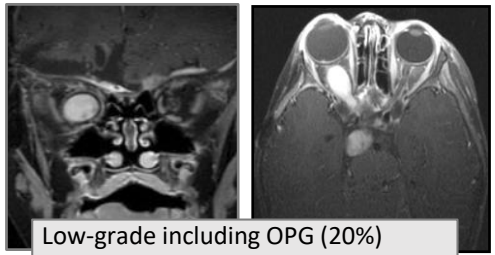
# Neurofibromatosis Type 1

## *Manifestations and Diagnostic Criteria*

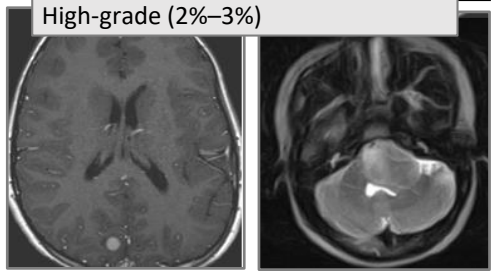


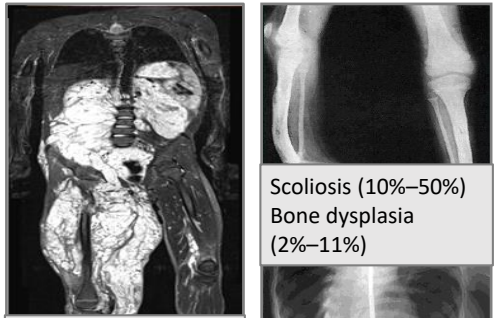
Lisch nodules (>90% of adults; by 10 years)
Café-au-lait macules (~100%)
Cutaneous neurofibromas (>95%)
Cognitive manifestations (~30%–-70%)
Vascular manifestations (~2%–5%)



Low-grade including OPG (20%)
High-grade (2%–3%)





PN (30%–50%)
ANNUBP and
MPNST (8%–13%)



Scoliosis (10%–50%)
Bone dysplasia
(2%–11%)


Carton C, et al. *EClinicalMedicine*. 2023;56:101818.
Legius E, et al. *Genet Med.* 2021;23(8):1506–1513. Toro G, et al. *Healthcare (Basel).* 2021;9(7):881.
Well L, et al. *Sci Rep*. 2021;11(1):16889. Baudou E, et al. *Front Neurol*. 2019;10:1373.
Kim A, et al. *Sarcoma*. 2017;2017:7429697. Korf BR. *Handb Clin Neurol*. 2013;111:333–340.
Stevenson DA, et al. *J Pediatr Orthop*. 2013;33(3):269–275. Ferner RE. *Pract Neurol*. 2010;10(2):82–93.


cecONCOLOGY

# Irene “Renie” Moss



**Renie Moss**
*Patient Advocate and Caregiver*

Renie Moss lives in Alabama with her husband of 24 years, Philip Sr., and two children, Philip Jr. (age 20) and Helen (age 17), all three of whom have NF1. Ms. Moss is an avid advocate for the neurofibromatosis patient and research communities.

- Former chair of the Children’s Tumor Foundation (CTF) Volunteer Leadership Council
- Former patient liaison to the Synodos NF1 Research Consortium
- Patient representative for Response Evaluation in Neurofibromatosis and Schwannomatosis International Collaboration (REiNS)
- Member of the University of Alabama–Birmingham (UAB) NF Clinic Patient Advisory Board
- Member of the UAB Genetic Counseling Program’s advisory board

Renie Moss. Interview with CE Concepts. August 2025.

# Challenges of Accessing NF1 Care



**Renie Moss**
*Patient Advocate and Caregiver*



cecONCOLOGY

# Case: Sam G.



Sam G. is a 7-year-old male who has experienced some mild learning difficulties and clumsiness in school, which has been attributed to behavioral issues and not formally evaluated. He has a younger brother (4 years) and sister (2 years).

At his annual physical examination, his pediatrician notes axillary freckling and small, soft cutaneous nodules. Ophthalmologic exam finds Lisch nodules. NF1 is diagnosed based on clinical criteria. Parents do not have clinical characteristics of NF1.

Examination reveals:

- 9 café-au-lait spots >0.5 cm (largest 1.5 cm, multiple smaller spots), initially referred to as "birth marks" without follow up investigation
- Bilateral axillary freckling, no neurofibromas palpable
- Mild hypotonia, coordination difficulty noted
- No scoliosis on a forward bend test; no long bone abnormalities
- Visual-spatial and processing deficits, attention and executive function concerns

# Sam G. (…continued)



## Recommendations

- Comprehensive ophthalmologic exam
- Baseline neurological evaluation and developmental/ behavioral monitoring and support
- Genetic counseling to discuss inheritance, family testing, reproductive planning
- Continue occupational therapy and speech therapy per IEP
- Initiate parent support via Children's Tumor Foundation and/or local NF1 support networks
- Annual follow-up appointments for NF1 surveillance: neurological exam, skin, ophthalmology, growth and development

# Neurofibromatosis Type 1

## MEK Inhibitors for the Treatment of Symptomatic, Inoperable Plexiform Neurofibromas in Children



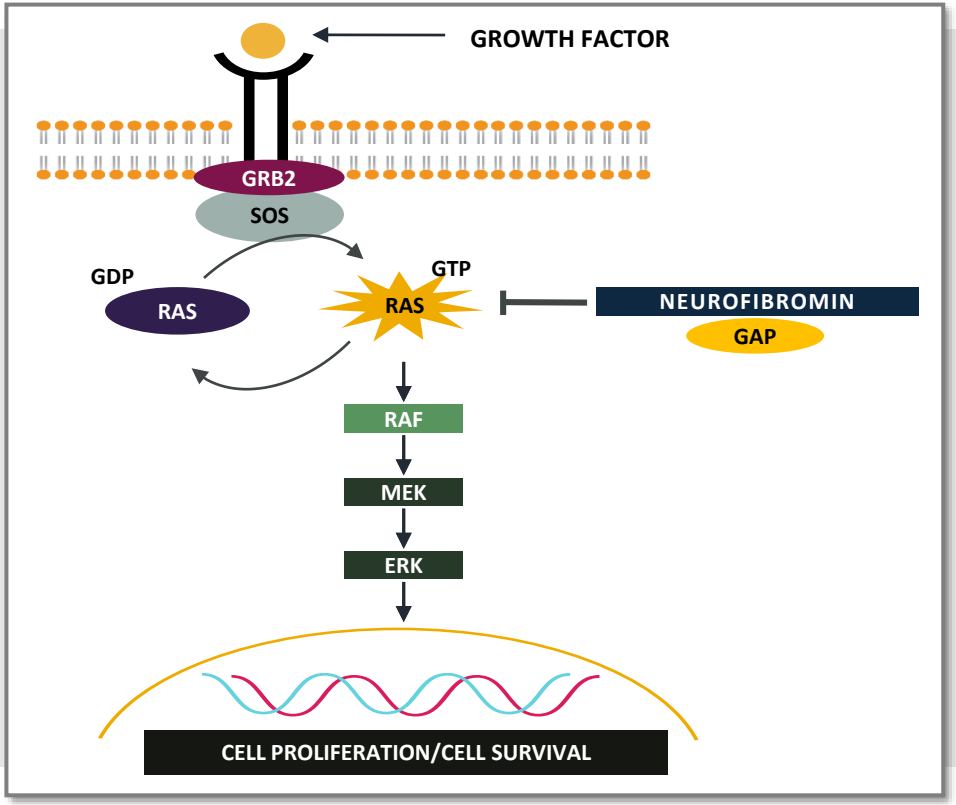
# Tumors Associated with NF1

Common

- Dermal neurofibromas
- Plexiform neurofibromas (PNs)
- Optic pathway gliomas and other low-grade tumors

Rare (<10%–15% of all people with NF1)

- Malignant peripheral nerve sheath tumors (MPNSTs)
- High-grade glioma
- Breast cancer
- Gastrointestinal stromal tumors (GISTs)
- Pheochromocytoma and/or paragangliomas
- Rhabdomyosarcomas




ERK, extracellular signal-regulated kinase; GAP, GTPase-activating proteins; GDP, guanosine diphosphate; GRB2, growth factor receptor-bound protein 2; GTP, guanosine triphosphate; MEK, mitogen-activated kinase; RAF, rapidly accelerated fibrosarcoma; RAS, rat sarcoma; SOS, Son of Sevenless.

Lalvani S, et al. *J Multidiscip Healthc*. 2024;17:1803–1817.
Acar S, er al. *Expert Opin Investig Drugs*. 2022;31:31–40. Kerashvili N, et al. *Expert Rev Neurother*. 2024;24:409–420. Botero V, et al. *J Neurodev Disord*. 2024;16:49.

# NF1-PNs

- Develop in up to 50% of patients with NF1
  - Typically, congenital or manifest in early childhood
  - Grow most rapidly in children <5 years of age
- Highly infiltrative, most frequently located in trunk or extremities
  - Can obstruct major organs, potentially life-threatening

Lalvani S, et al. *J Multidiscip Healthc*. 2024;17:1803–1817.
Acar S, er al. *Expert Opin Investig Drugs*. 2022;31:31–40. Kerashvili N, et al. *Expert Rev Neurother*. 2024;24:409–420.

# NF1-PNs

- Most patients have ≥1 PN-associated morbidity
  - Most common: pain, disfigurement, and motor dysfunction
  - Other comorbidities of note: defects in vision, airway, and bowel/bladder function
- Symptomatic PNs tend to be larger than asymptomatic PNs
  - Asymptomatic and symptomatic often coexist
- Benign, but may progress to atypical neurofibromas and then undergo transformation to MPNST
  - Estimated lifetime risk of MPNST in patients with NF1 is 8%–13%

Lalvani S, et al. *J Multidiscip Healthc*. 2024;17:1803–1817. Armstrong AE, et al. *BMC Cancer*. 2023;23(1):553.
Acar S, er al. *Expert Opin Investig Drugs.* 2022;31:31–40. Kerashvili N, et al. *Expert Rev Neurother*. 2024;24:409–420.

# NF1-PN Management
## *Observation vs Treatment*

### INTERTWINED CONSIDERATIONS
- Age of patient
- PN growth status
- Growth rate
- Present/impending morbidity
- Progressive nature of tumor

### OBSERVATION
- Not all patients with NF1-PN require treatment
- Most stable tumors do not cause morbidity
- May not progress or cause symptoms
- Management involves regular monitoring

### TREATMENT
- Goal (most cases) to improve or prevent PN-associated morbidity
- Consider when evidence shows/ suggests PN-related morbidity or tumor growth with impending morbidity

Lalvani S, et al. *J Multidiscip Healthc.* 2024;17:1803–1817.
Armstrong AE, et al. *BMC Cancer*. 2023;23(1):553. Fisher MJ, et al. *Neuro Oncol*. 2022;24:1827–1844.

# NF1-PN Management

## *Surgery vs Medical Treatment*

### PRIOR TO TREATMENT

- Rule out malignant transformation of PN
- Assess change in tumor growth rate (i.e., new onset or recent change in PN-related pain)
- Biopsy if clinical concern
- Multidisciplinary input needed
- Note
  - Medical therapy for NF1-PN does not prevent transformation to MPNST
  - Treatment is different for MPNST vs NF1-PN

### SURGERY

- Preferred if resection can be achieved without significant morbidity
- Complete tumor excision: ~15% of cases
- NF1-PN regrowth (post partial or subtotal resection): ~43%
- Permanent sequelae (neurologic): 5%–18% of patients

### MEDICAL TREATMENT

- Preferred if specific contraindications or pre-existing conditions
- Concerns related to a therapeutic option
- Assess logistics, adverse events, formulation, compliance, long-term safety, etc.

Lalvani S, et al. *J Multidiscip Healthc.* 2024;17:1803–1817.
Armstrong AE, et al. *BMC Cancer*. 2023;23(1):553. Fisher MJ, et al. *Neuro Oncol.* 2022;24:1827–1844.

# To Treat or Not to Treat NF1-PNs?



- Symptomatic, inoperable PNs
- Recent or ongoing PN growth
- Significant pain or functional impact
- PNs in high-risk locations
- Younger age or earlier in disease course





- Toxicities (skin, cardiac, gastrointestinal, ocular)
- Duration of treatment
- Long-term sequela
- Long-term data lacking for some agents

Armstrong AE, et al. *BMC Cancer*. 2023;23(1):553.

# Sam G. (…continued)



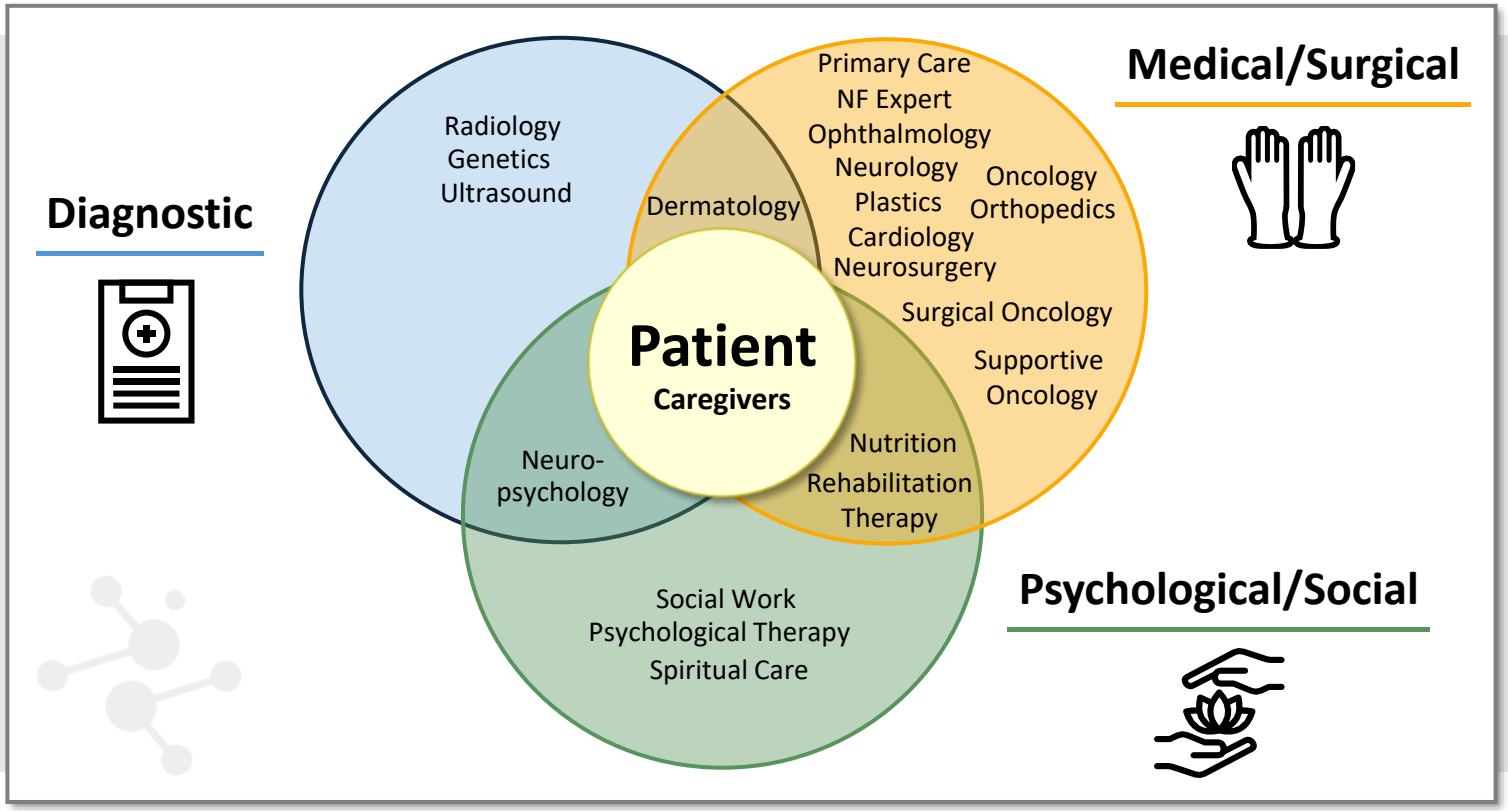

At 10 years of age, he develops a slowly enlarging, diffuse swelling along the lower left jaw and neck. This area feels rubbery, is sometimes tender, and grows steadily but unpredictably. The mass is non-resectable due to its size and location and causes cosmetic deformity and periodic discomfort. MRI confirms a plexiform neurofibroma.

Over several years, the lesion causes noticeable facial asymmetry and mild difficulty with chewing and speech. He begins to experience neuropathic pain and occasional airway discomfort by age 13–14. Function and quality of life (QoL) decline, and the mass becomes increasingly prominent.



At 15 years of age, progressive pain, impaired function, and disfigurement are negatively impacting his QoL.

# Multidisciplinary Care for Patients with NF1




Lalvani S, et al. *J Multidiscip Healthc*. 2024;17:1803–1817. Armstrong AE, et al. *BMC Cancer*. 2023;23(1):553.



## Recommendations

- Complete resection is not possible
- In consultation with his parents, it is decided that he receive systemic therapy

# Targeted Medical Therapy for NF1-PN

Several MEK inhibitors and tyrosine kinase inhibitors (TKIs) have demonstrated activity against NF1-PN.

Outcome measures in clinical trials:

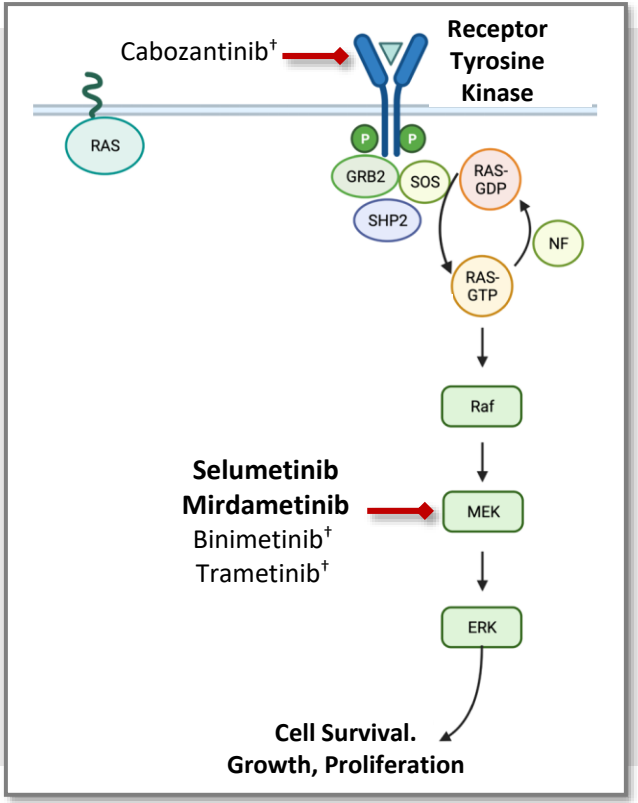
- Assessed PN growth and response via 3D volumetric analysis
- Patient-reported and functional outcome assessments

**SELUMETINIB***

**FDA-approved in *adult and pediatric*** patients 1 year of age and older with NF1 who have symptomatic, inoperable PN

**MIRDAMETINIB***

**FDA-approved in *adult and pediatric*** patients 2 years of age and older with NF1 who have symptomatic PN not amenable to complete resection




†Not FDA approved for the treatment of NF1-PN.

*Approval specifics vary by country.

NF, neurofibromin; SHP2, Src homology-2 protein tyrosine phosphatase.

Na B, et al. *Curr Oncol Rep*. 2024;26:706–713. Armstrong AE, et al. *BMC Cancer*. 2023;23(1):553.
Fischer MJ, et al. *Neuro Oncol*. 2022;24:1827–1844. de Blank PM, et al. *Neuro Oncol*. 2022;24:1845–1856.
Mirdametinib (package insert). Revised February 2025.
https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/219379Orig1s000lbl.pdf.
Selumetinib (package insert). Revised September 2025 (updated package insert for new indication is pending on FDA website, as of November 20, 2025). https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/219943Orig1s000lbl.pdf.
U.S. Food and Drug Administration (FDA). News release. Published November 19, 2025. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-selumetinib-adults-neurofibromatosis-type-1-symptomatic-inoperable-plexiform.

# MEK Inhibitors in Pediatric Patients



# SPRINT Trial
## *Selumetinib in Children with Inoperable PN*

- Phase 2, open-label
- Children (2–18 years of age)
- NF1 + symptomatic inoperable PN
- No evidence of MPNST, an optic glioma, malignant glioma, or other cancer requiring treatment with chemotherapy or radiation therapy

**Baseline Demographics** (median values)
- Age: 10 years
- Male: 60%
- Volume of target NF: 487 mL
- Progression status (progressive/not/data lacking): 42%/30%/28%
- Location of target NF
  - Neck + trunk (24%), trunk + limbs (24%), head (18%), head + neck (16%), trunk (10%), limbs (8%)
- NF-related comorbidities (median number: 3)
  - Disfigurement (88%), motor dysfunction (66%), pain (52%), airway (32%), vision (20%), bowel or bladder (20%), other (22%)

**Selumetinib 25 mg/m$^2$ BID** (n=50)
Treatment cycle: 28 days (no rest between cycles)

Up to 2 years if no drug-related toxicity or progressive disease
(≥20% volume increase in target PN)

### Primary Endpoint
- Partial response (≥20% volume reduction in target PN by 3D analysis of MRI)
  - Confirmed (2 consecutive)
  - Durable (lasting ≥12 cycles)

### Secondary Endpoints
- Duration of response
- Safety
- Patient-observer reported outcomes

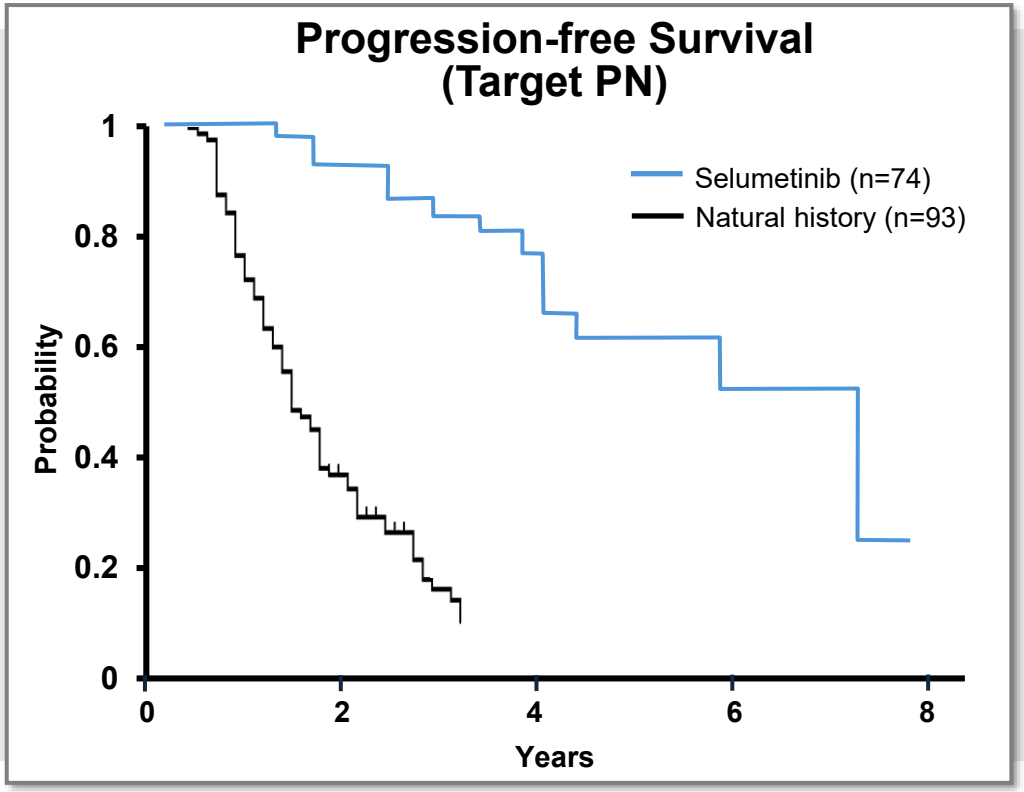
BID, twice daily.

Gross AM, et al. *N Engl J Med*. 2020;382:1430–1442.

# Combined 5-Year Progression-Free Survival

## *SPRINT + Phase I*

- Combined cohort (n=74)
  - Continuous selumetinib dosing (median duration: 57.5 cycles)
  - Remaining on treatment at data cutoff (n=31)
- Partial response
  - Confirmed and durable: 70% and 59%
- Time to response (median)
  - Initial: 8 cycles (range 4–40)
  - Best response: 18 cycles (range 4–94)
- Median PFS
  - 88 cycles (6.7 years)
- 1-year probability of being progression-free after
  - 60 cycles: 61% (95% CI, 46–73)




Gross AM, et al. *Neuro Oncol*. 2023;25:1883–1894.

# Selumetinib Adverse Events

| All Grade (Grade 3–4) | Gastrointestinal | Skin and Subcutaneous Tissue | Other Toxicities |
|---|---|---|---|
| ≥80% | Vomiting (6%) | All rashes* (6%) | |
| 50%–79% | Abdominal pain<br>Diarrhea (16%)<br>Nausea (2%)<br>Stomatitis | Dry skin<br>Rash acneiform (4%) | Increased CPK (7%)<br>Musculoskeletal pain<br>Fatigue<br>Pyrexia (8%) |
| 20%–49% | Constipation | Paronychia (6%)<br>Pruritus<br>Dermatitis (4%)<br>Hair changes | Headache (2%)<br>Epistaxis<br>Hematuria (2%)<br>Proteinuria<br>Decreased appetite<br>Decreased ejection fraction<br>Sinus tachycardia<br>Skin infection (2%)<br>Edema |

Adverse events (AEs) occurring in ≥20% of patients.
*Rash (all) includes dermatitis acneiform, rash maculo-papular, erythema, rash pustular, rash, urticaria, exfoliative rash, rash pruritic, and rash erythematous.
CPK, creatine phosphokinase.



Selumetinib (package insert). Revised September 2025 (updated package insert for new indication is pending on FDA website, as of November 20, 2025). https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/219943Orig1s000lbl.pdf.

# Selumetinib AEs of Special Interest

| Ocular | | | |
|---|---|---|---|
| **Adverse Event, n** | **Grade 1** | **Grade 2** | **Grade 3** |
| Blurred vision | 4 | 0 | 0 |
| Cataract | 1 | 0 | 0 |
| Dry eye | 1 | 1 | 0 |
| Eye disorders (other) | 2 | 0 | 0 |
| Eye pain | 1 | 0 | 0 |
| Photophobia | 1 | 0 | 0 |
| Photosensitivity | 2 | 1 | 0 |
| Retinopathy | 1 | 0 | 0 |
| Watering eyes | 1 | 0 | 0 |

| Cardiac | | | |
|---|---|---|---|
| **Adverse Event, n** | **Grade 1** | **Grade 2** | **Grade 3** |
| Ejection fraction decreased | 0 | 14 | 1 |
| Hypertension | 6 | 2 | 0 |
| Sinus bradycardia | 2 | 0 | 0 |
| Sinus tachycardia | 2 | 0 | 0 |

Safety population, N=74

No grade 4 ophthalmological or cardiac AEs reported

Gross AM, et al. *Neuro Oncol*. 2023;25:1883–1894.

# Selumetinib*
## *Warnings and Precautions*

- Ocular toxicity: blurred vision, photophobia, cataracts, and ocular hypertension
  - 15% of pediatric population (resolved in 82%)
- Cardiomyopathy
  - Decreased LVEF of ≥10% occurred in 23% of pediatric patients (all were identified during routine echocardiography); decreased LVEF resolved in 71% of these patients
- Skin toxicity
  - Rash occurred in 91% of pediatric patients (8% Grade 3); the most frequent rashes included dermatitis acneiform (54%), maculopapular rash (39%), and eczema (28%)
- Gastrointestinal toxicity
  - Diarrhea in 77% of pediatric population (15% Grade 3)
- Increased creatine phosphokinase
  - Occurred in 76% of pediatric population (9% Grade 3 or 4)
- Risk of bleeding
  - Vitamin E is excipient and can inhibit platelet aggregation and antagonize vitamin K-dependent clotting factors
- Embryo-fetal toxicity

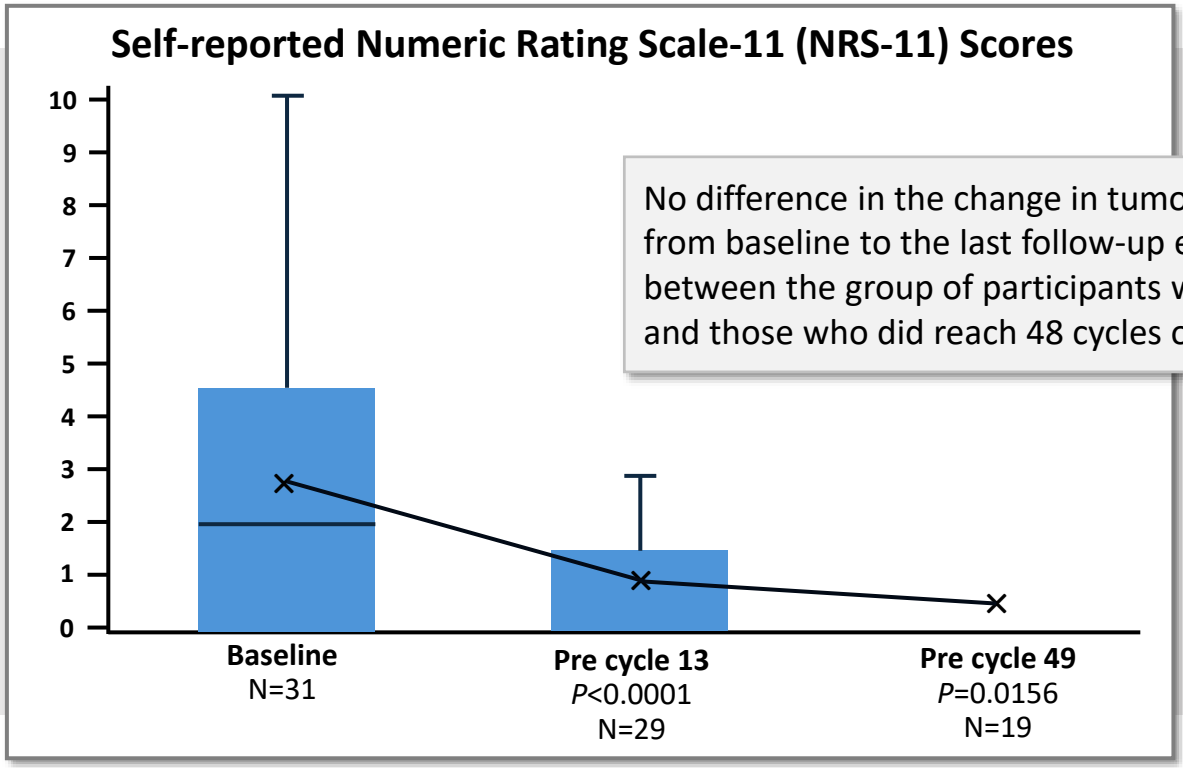
Toxicities seen in an unapproved adult population* with multiple tumor types who received selumetinib as a single agent or in combination with other anti-cancer agents:

- Retinal vein occlusion (RVO) and retinal pigment epithelial detachment (RPED)
- Intestinal perforation, colitis, ileus, and obstruction
- Cardiomyopathy (decreased left ventricular ejection fraction [LVEF])
- Severe palmar-plantar erythrodysesthesia syndrome
- Rhabdomyolysis

*Selumetinib is FDA approved in patients ≥1 year of age who have a PN; EMA approved in patients ≥3 years of age; other countries may vary.

Selumetinib (package insert). Revised September 2025 (updated package insert for new indication is pending on FDA website, as of November 20, 2025). https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/219943Orig1s000lbl.pdf.

# Selumetinib
## *Patient-Reported Pain*




No difference in the change in tumor pain intensity from baseline to the last follow-up evaluation between the group of participants who did not reach and those who did reach 48 cycles of treatment

Gross AM, et al. *Neuro Oncol*. 2023;25:1883–1894.

# ReNeu Trial

## *Mirdametinib in Children and Adults with Inoperable PN*

- Phase 2, open-label
- Age-based cohorts
  - Pediatric (2–17 years)
  - Adults (≥18 years)
- NF1 + inoperable progressive and/or symptomatic PN

**Baseline Demographics** (pediatric [n=56]/adults [n=58])

- Median age: 10/58 years
- Male: 46%/36%
- Location of NF
  - Head + neck (50%/48%), lower-upper extremities (14%/29%), paraspinal (7%/9%), other (29%/14%)
- NF-related complications
  - Pain (70%/90%), disfigurement-major deformity (50%/52%), motor dysfunction or weakness (27%/40%), airway dysfunction (13%/5%), other (21%/17%)
- Target PN progressing: 63%/53%

**Mirdametinib 2 mg/m² BID (max 4 mg)**

Treatment cycle: 28 days (3 weeks on, 1 week off)

Up to 2 years



**Primary Endpoint**

- Partial response (≥20% volume reduction in target PN by volumetric MRI)

**Secondary Endpoints**

- Duration of response
- Safety
- QoL and physical functioning

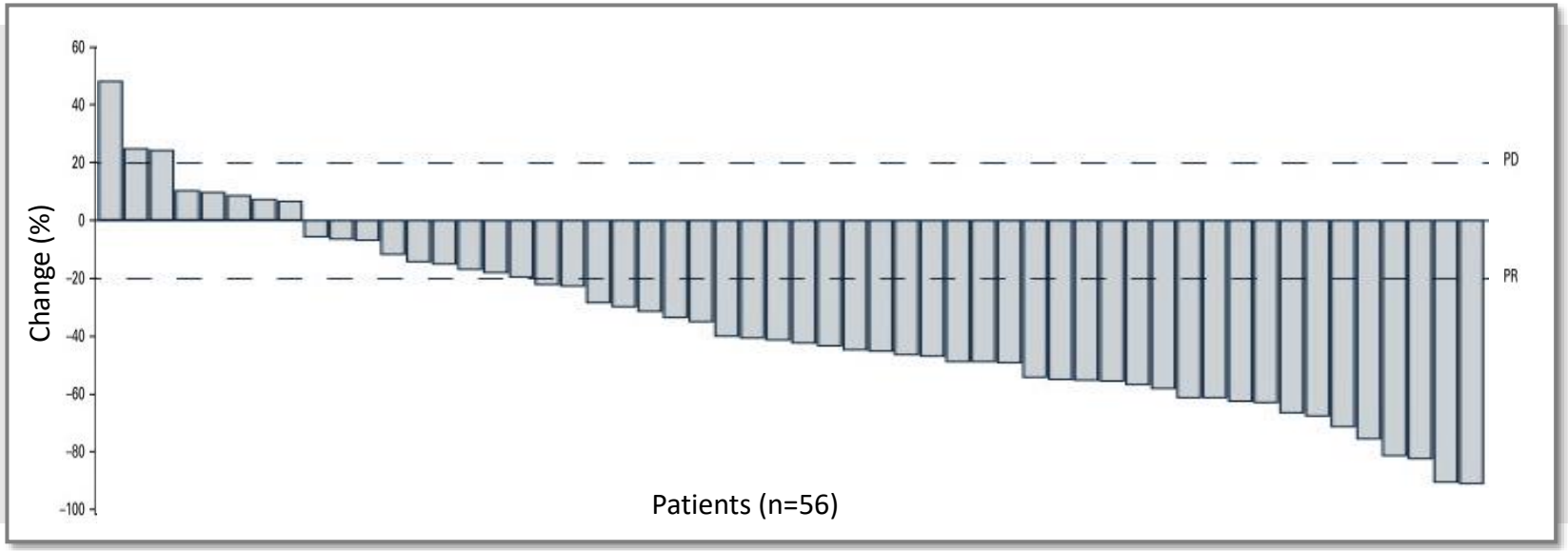
Moertel CL, et al. *J Clin Oncol*. 2025;43(6):716–729.

cecONCOLOGY

# ReNeu (Pediatrics)

## *Best Change from Baseline in Target PN Volume per Patient*

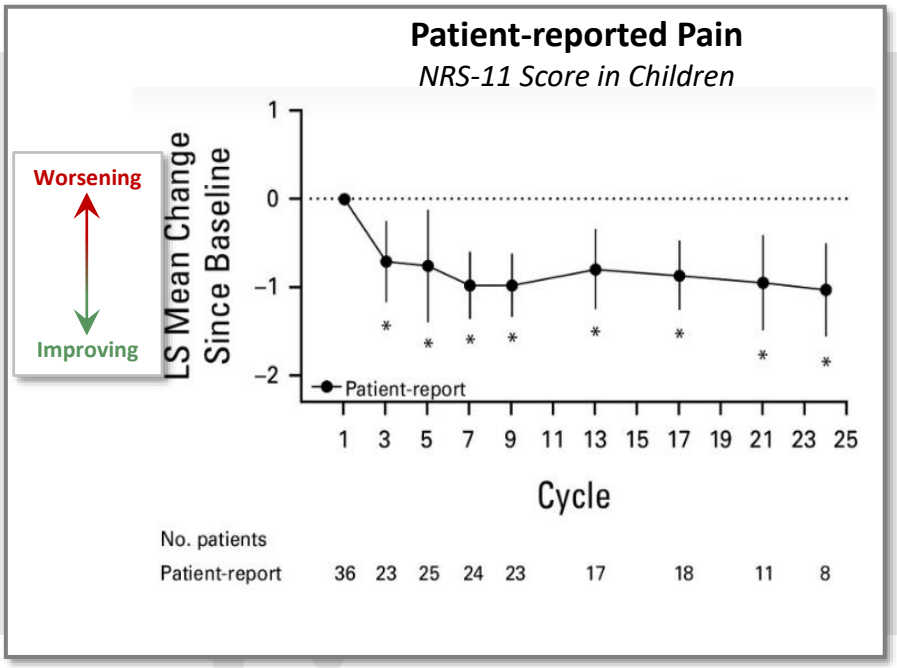
**Best Percent Change in Target PN Volume**

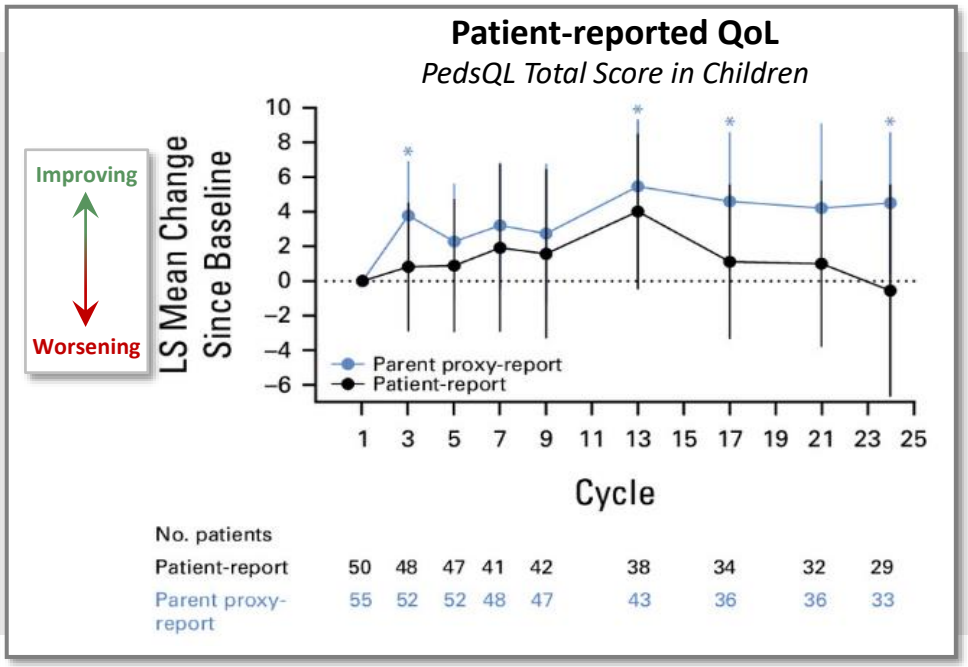



Moertel CL, et al. *J Clin Oncol*. 2025;43(6):716–729.

# ReNeu (Pediatrics)

## *Pain and QoL*




Moertel CL, et al. *J Clin Oncol*. 2025;43(6):716–729.

# ReNeu Adverse Events (Pediatrics)

| All Grade (grade 3–4) | Skin and Gastrointestinal | Other Toxicities |
|---|---|---|
| ≥80% | | |
| 50%–79% | Rash* (4%)<br>Diarrhea (5%) | Increased CPK (5%) |
| 20%–49% | Nausea<br>Vomiting<br>Abdominal pain (4%)<br>Stomatitis | Musculoskeletal pain (2%)<br>Headache (2%)<br>Paronychia<br>Left ventricular dysfunction (2%)<br>Increased triglycerides, creatinine, alk-phos, ALT<br>COVID-19<br>Upper respiratory tract infection<br>Decreased glucose, calcium, bicarbonate<br>Cough<br>Pyrexia<br>Decreased hemoglobin, leukocytes, neutrophils, lymphocytes<br>Increased lymphocytes |

alk-phos, alkaline phosphatase; ALT, alanine aminotransferase.
AEs occurring in ≥20% of patients; data for adult patients is not included.
*Rash includes dermatitis acneiform, eczema, maculo-papular rash, pustular rash, dermatitis, erythematous rash, palmar-plantar erythrodysesthesia syndrome, exfoliative rash, skin exfoliation, pruritic rash, papule, papular rash, and macular rash.



Mirdametinib (package insert). Revised February 2025. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/219379Orig1s000lbl.pdf.

# Mirdametinib
## *Warnings and Precautions*

- Ocular toxicity: retinal vein occlusion (RVO), retinal pigment epithelium detachment (RPED), and blurred vision
  - Occurred in 25% of patients; 20% Grade 1, 3.8% Grade 2, and 0.8% Grade 3
- Left ventricular dysfunction
  - Decreased LVEF of 10%–<20% occurred in 20%, and decreased LVEF of ≥20% occurred in 0.9% of patients (all were identified during routine echocardiography); decreased LVEF resolved in 75% of these patients
- Dermatological AEs
  - Rash occurred in 84% of patients (31% Grade 2; 6% Grade 3); the most frequent rashes (≥2%) included dermatitis acneiform (65%), rash (11%), eczema (8%), maculo-papular rash (4.5%) and pustular rash (3.8%)
- Embryo-fetal toxicity

Mirdametinib (package insert). Revised February 2025. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/219379Orig1s000lbl.pdf.

## Sam G. (…continued)



Sam is now 19 years old and has been receiving selumetinib continuously for symptomatic PN. The tumor shrank and is now stable. His pain also improved.  However, the indication for selumetinib is for "pediatric patients 1 year of age and older."

# Which do you recommend for this patient?

A. Stop therapy
B. Switch to mirdametinib
C. Stay on selumetinib

# Neurofibromatosis Type 1

## Transition of Care



# The Role of Peers in the Transition from Pediatric to Adult Care



**Renie Moss**
*Patient Advocate and Caregiver*



cecONCOLOGY

# Clinical Perspective
## *Transition from Pediatric to Adult Care*

### Pediatric Needs

- Developmental delays
- Scholastic concerns
- Plexiform neurofibromas
- Autism/ADD
- Optic pathway gliomas
- Bone abnormalities

### Adult Needs

- Dermal neurofibromas
- Malignant progression
- Pain
- Glioblastoma
- Breast cancer
- Family planning

**Birth** → **18 years** → **Adult**

### Multidisciplinary Care Throughout the Lifespan

- Neurology
- Medical oncology
- Orthopedics
- Neurosurgery
- Plastic surgery
- Dermatology
- Psychiatry
- PT/OT

The transition of care is a process of moving from pediatric-centered to adult-centered care with or without transition to a new clinician.

ADD, attention deficit disorder; OT, occupational therapy; PT, physical therapy.
*Based on Dr. Angela Hirbe's clinical experience and opinion.

# BARRIERS to Successful NF1 Health Care Transitions

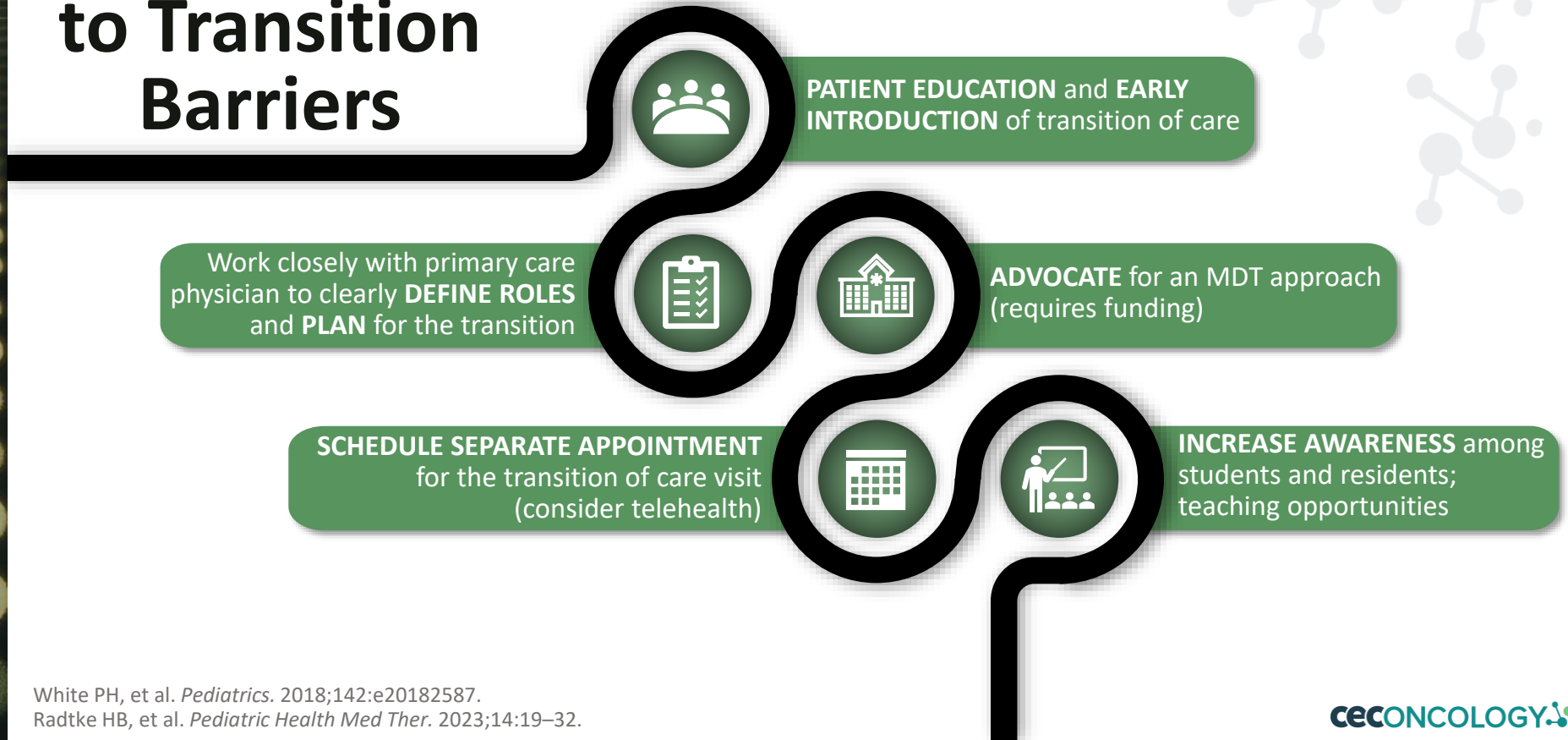



GC, genetic counselling; SW, social work.

White PH, et al. *Pediatrics*. 2018;142:e20182587.
Radtke HB, et al. *Pediatric Health Med Ther*. 2023;14:19–32.

cecONCOLOGY

# Potential SOLUTIONS to Transition Barriers



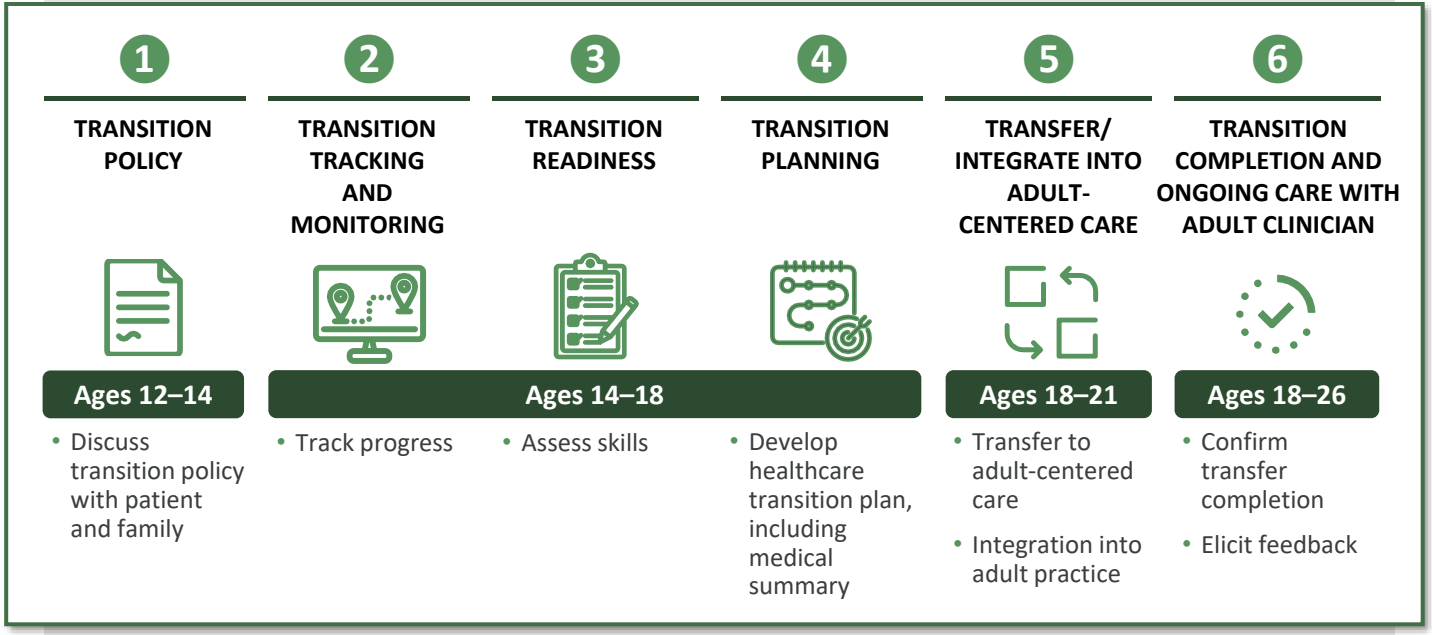

White PH, et al. *Pediatrics.* 2018;142:e20182587.
Radtke HB, et al. *Pediatric Health Med Ther.* 2023;14:19–32.

cecONCOLOGY

# Core Elements of Health Care Transition

## Key Elements for Transition to Adulthood Program

- Annual assessments to plan transition
- Establishment of yearly personal goals
- Bi-monthly adolescent and young adult transition planning meetings
- Dedicated collaborative specialists across the lifespan




White PH, et al. *Pediatrics.* 2018;142:e20182587. Radtke HB, et al. *Pediatric Health Med Ther.* 2023;14:19–32.

cecONCOLOGY

# Tools to Aid Transition of Care

**GOT TRANSITION** is a national resource center on health care transition in the United States. Its aim is to “improve transition from pediatric to adult health care through the use of evidence-driven strategies for health care professionals, youth, young adults, and their families.”




Got Transition website. 2025. https://www.gottransition.org/.

cecONCOLOGY

# Neurofibromatosis Type 1

## MEK Inhibitors for the Treatment of Symptomatic, Inoperable Plexiform Neurofibromas in Adults



# Case: Mary G.




Mary G. is a 45-year-old female with a painful facial PN that is also causing significant deformity. The pain is similar to what it has been for years (i.e., no new/changing pain). Her MRI does not demonstrate concerning features of the tumor.

# ReNeu Trial

## *Mirdametinib in Children and Adults with Inoperable PN*

- Phase 2, open-label
- Age-based cohorts
  - Pediatric (2–17 years)
  - Adults (≥18 years)
- NF1 + inoperable progressive and/or symptomatic PN

**Baseline Demographics** (pediatric [n=56]/adults [n=58])

- Median age: 10/58 years
- Male: 46%/36%
- Location of NF
  - Head + neck (50%/48%), lower-upper extremities (14%/29%), paraspinal (7%/9%), other (29%/14%)
- NF-related complications
  - Pain (70%/90%), disfigurement-major deformity (50%/52%), motor dysfunction or weakness (27%/40%), airway dysfunction (13%/5%), other (21%/17%)
- Target PN progressing: 63%/53%

**Mirdametinib 2 mg/m² BID (max 4 mg)**

Treatment cycle: 28 days (3 weeks on, 1 week off)

Up to 2 years



**Primary Endpoint**

- Partial response (≥20% volume reduction in target PN by volumetric MRI)

**Secondary Endpoints**

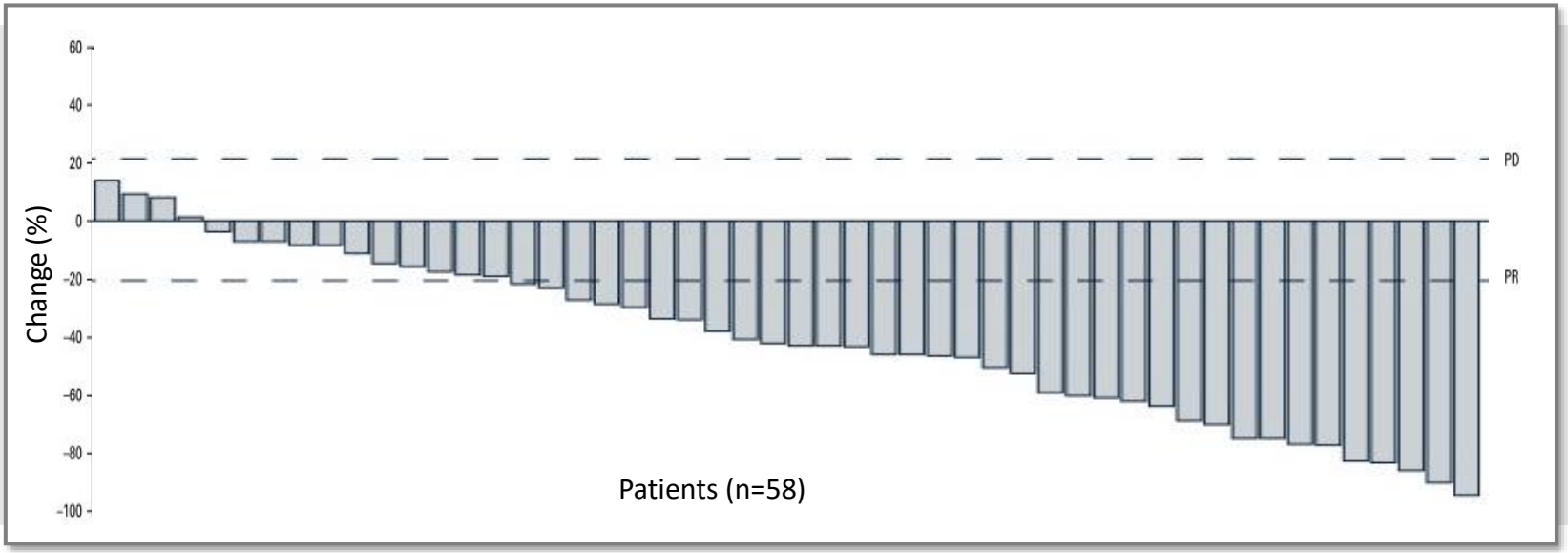
- Duration of response
- Safety
- QoL and physical functioning

Moertel CL, et al. *J Clin Oncol*. 2025;43(6):716–729.

# ReNeu (Adult)

## *Best Change from Baseline in Target PN Volume per Patient*

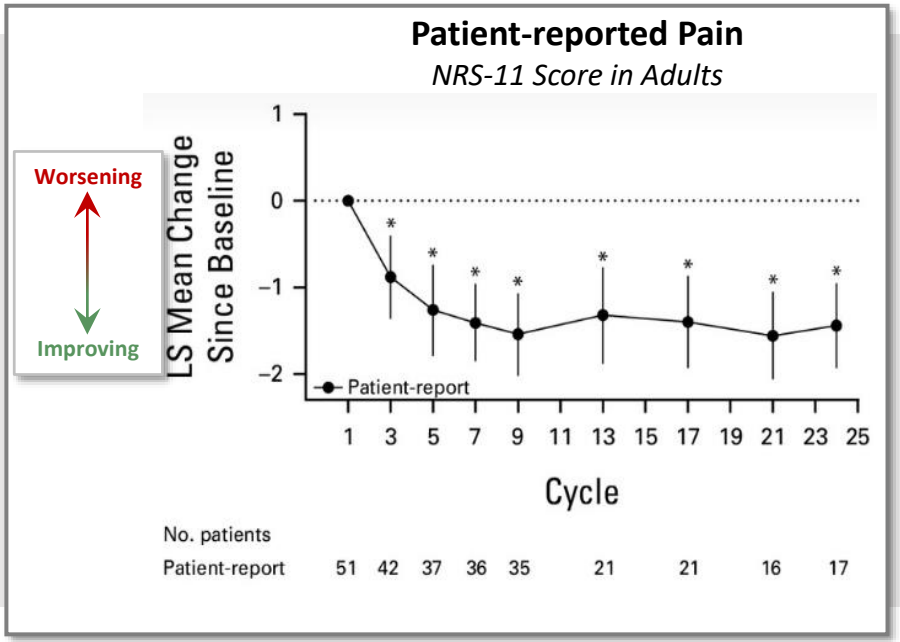
**Best Percent Change in Target PN Volume**

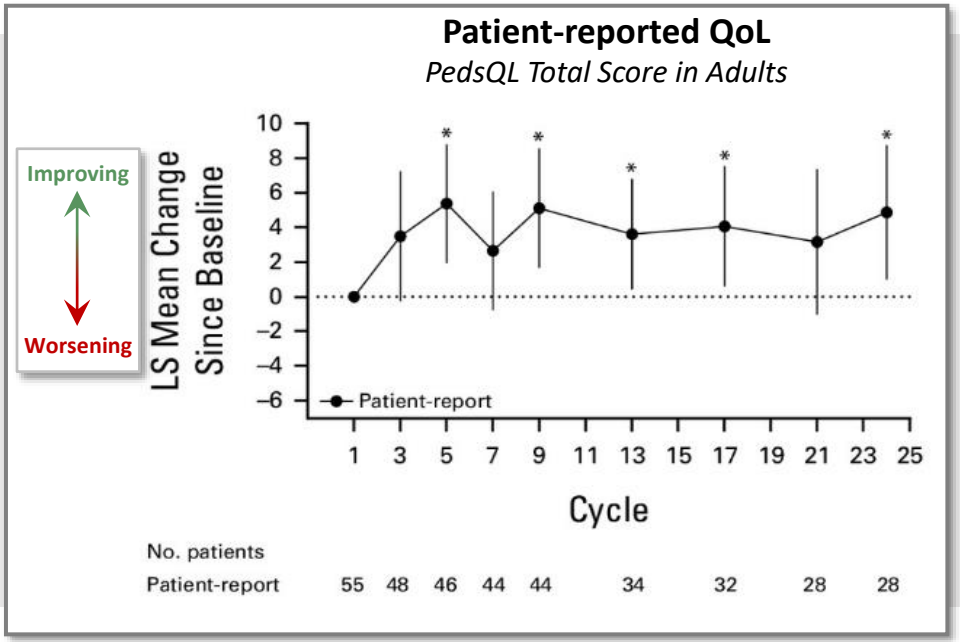



Moertel CL, et al. *J Clin Oncol*. 2025;43(6):716–729.

# ReNeu (Adult)

## *Pain and QoL*




Moertel CL, et al. *J Clin Oncol*. 2025;43(6):716–729.

# ReNeu Adverse Events (Adult)

| **All Grade** (grade 3–4) | **Skin and Gastrointestinal** | **Other Toxicities** |
|---|---|---|
| ≥80% | Rash* (10%) | |
| 50%–79% | Diarrhea<br>Nausea | Increased CPK (4%) |
| 20%–49% | Vomiting<br>Abdominal pain (3%) | Musculoskeletal pain (5%)<br>Headache (2%)<br>COVID-19 (5%)<br>Fatigue (2%)<br>Peripheral neuropathy<br>Increased triglycerides, cholesterol<br>Decreased calcium<br>Anemia<br>Decreased hemoglobin |

AEs occurring in ≥20% of patients; data for adult patients is not included.
*Rash includes dermatitis acneiform, eczema, maculo-papular rash, pustular rash, dermatitis, erythematous rash, palmar-plantar erythrodysesthesia syndrome, exfoliative rash, skin exfoliation, pruritic rash, papule, papular rash, and macular rash.



Mirdametinib (package insert). Revised February 2025. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/219379Orig1s000lbl.pdf.

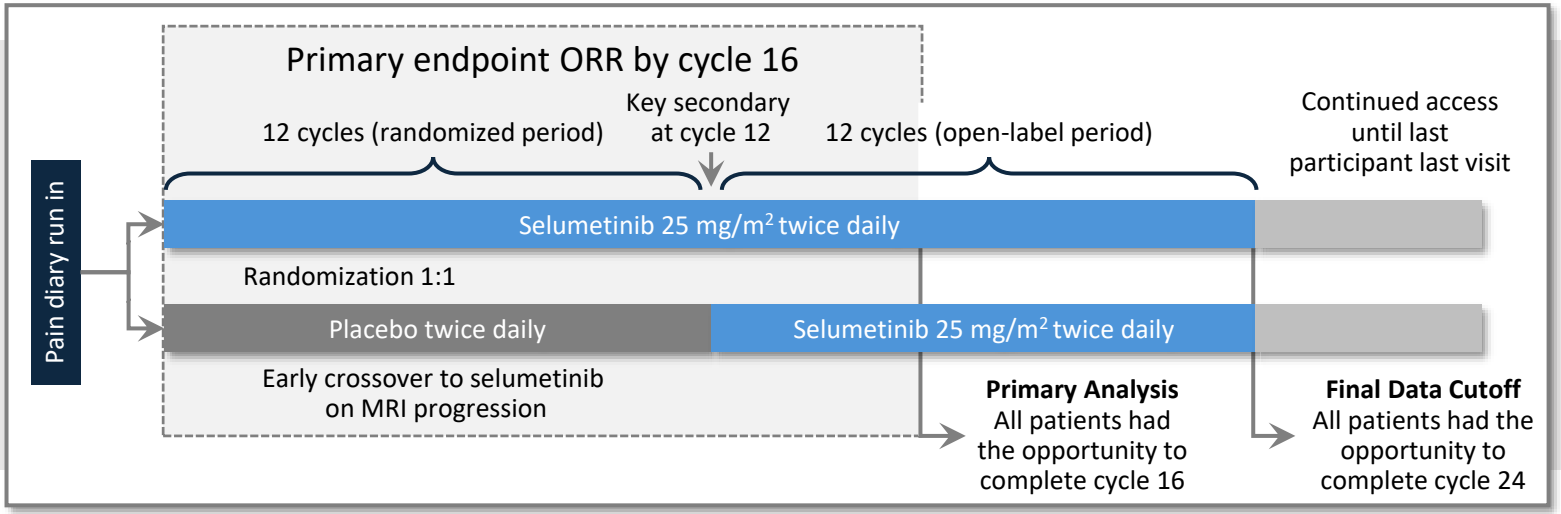
# KOMET Trial

## *Selumetinib* in Adults with Symptomatic Inoperable PN*

- Phase 3, placebo-controlled
- Adults ≥18 years of age
- NF1 + symptomatic inoperable PN
- A completed PAINS-pNF diary with a documented chronic target plexiform neurofibroma pain score on ≥4 of 7 days over ≥2 weeks during screening; stable chronic pain medication at baseline

**Baseline Demographics** (median values)

- Age: 29.5 years
- Male: 49%
- Volume of target PN: 92.0 mL selumetinib, 221.9 mL placebo
- Location of target PN
  - Neck + trunk (24%), trunk + limbs (24%), head (18%), head + neck (16%), trunk (10%), limbs (8%)
- Patients were stratified by chronic target plexiform neurofibroma pain score and geographical region

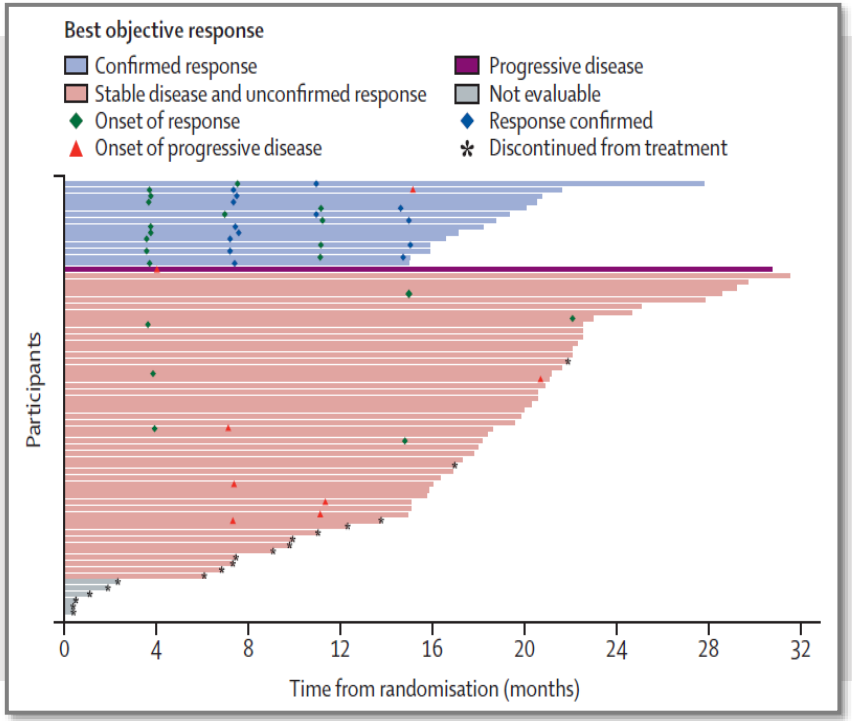


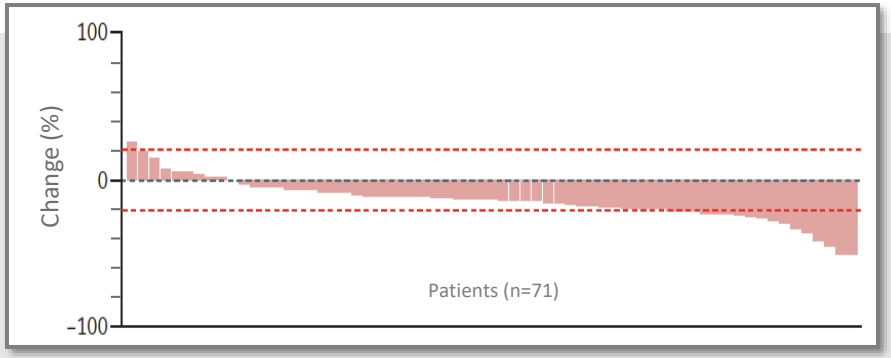

*Selumetinib is FDA approved in patients ≥1 year of age who have a PN; EMA approved in patients ≥3 years of age; other countries may vary.

Chen AP, et al. *Lancet*. 2025;405(10496):2217–2230.

# KOMET Trial: Efficacy

## *Selumetinib* in Adults with Symptomatic Inoperable PN*




| Participants randomly assigned to selumetinib | Target plexiform neurofibroma volume, best percentage change | |
|---|---|---|
| | Participants with an objective response by C16 (n=14) | Participants who had not reached an objective response by C16 (n=51) |
| Mean | −36·6 | −9·9 |
| Median (minimum, maximum) | −33·9 (−58·1 to −22·6) | −11·4 (−26·7 to 24·0) |

*Selumetinib is FDA approved in patients ≥1 year of age who have a PN; EMA approved in patients ≥3 years of age; other countries may vary.

Chen AP, et al. *Lancet*. 2025;405(10496):2217–2230.

cecONCOLOGY

# KOMET Trial: Adverse Events

| | Selumetinib* n=71 | Placebo n=74 |
|---|---|---|
| Any AEs (grade ≥3) | 100% (32%) | 92% (18%) |
| Serious AE | 14% | 12% |
| AE leading to discontinuation | 13% | 7% |
| AE leading to dose modification | 38% | 14% |
| Any AE special interest | 66% | 22% |
| Maximum reported CTCAE grade | | |
| 1 | 23% | 30% |
| 2 | 45% | 45% |
| 3 | 27% | 15% |
| 4 | 6% | 3% |

| | Selumetinib* n=71 | Placebo n=74 |
|---|---|---|
| Gastrointestinal disorders | 75% | 43% |
| Skin and subcutaneous tissue disorders | 90% | 35% |
| Musculoskeletal/connective tissue disorders | 27% | 23% |
| General disorders | 51% | 28% |
| Investigations | 62% | 28% |
| Infections and infestations | 54% | 45% |
| Eye disorders | 17% | 12% |

| All Grade (Grade 3–4) | Gastrointestinal | Skin and Subcutaneous Tissue | Other Toxicities |
|---|---|---|---|
| ≥80% | | | |
| 50%–79% | Diarrhea (12%) | Dermatitis acneiform (11%) | Increased CPK (5%) |
| 20%–49% | Nausea (16%)<br>Vomiting (8%) | | |

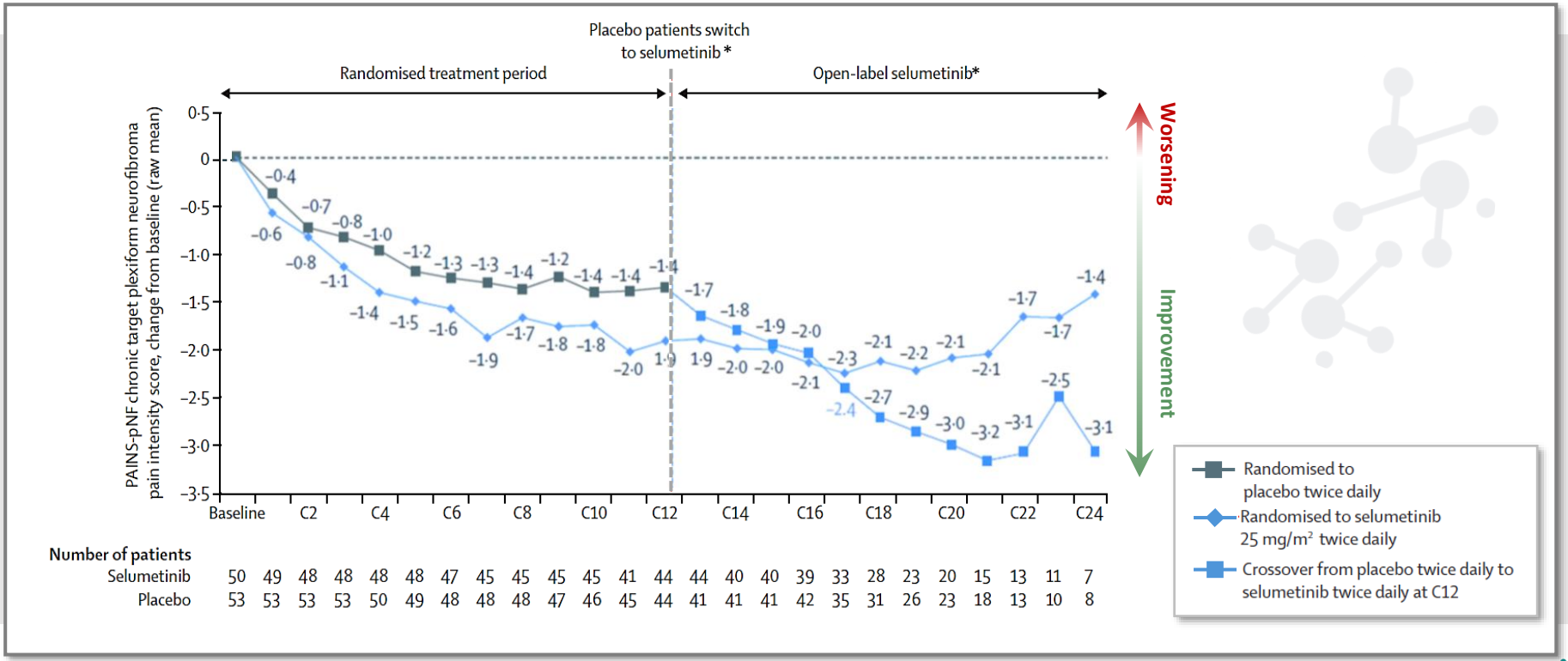
*Selumetinib is FDA approved in patients ≥1 year of age who have a PN; EMA approved in patients ≥3 years of age; other countries may vary.

CTCAE, Common Terminology Criteria for Adverse Events.

Chen AP, et al. *Lancet.* 2025;405(10496):2217–2230.

# KOMET Trial: Pain Scores

## *Selumetinib* in Adults with Symptomatic Inoperable PN*




*Selumetinib is FDA approved in patients ≥1 year of age who have a PN; EMA approved in patients ≥3 years of age; other countries may vary.

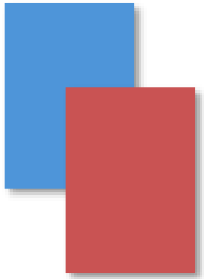


Chen AP, et al. *Lancet*. 2025;405(10496):2217–2230.

# MEKi Options

## SELUMETINIB*

- Pediatric and adult patients
- Pill and granular (sprinkle) dosing
- Continuous therapy
- 6.2-hour serum half life
- Avoid CYP3A4 inhibitors



## MIRDAMETINIB

- Pediatric and adult patients
- Capsule and dispersible tablet
- 3 weeks on, 1 week off
- 28-hour serum half life

**No head-to-head comparisons**
**No data on MEKi switching**

*Selumetinib is FDA approved in patients ≥1 year of age who have a PN; EMA approved in patients ≥3 years of age; other countries may vary.

Selumetinib (package insert). Revised September 2025 (updated package insert for new indication is pending on FDA website, as of November 20, 2025). https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/219943Orig1s000lbl.pdf.
Mirdametinib (package insert). Revised February 2025. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/219379Orig1s000lbl.pdf.

# Neurofibromatosis Type 1

## Managing Patients Utilizing Long-Term MEK Inhibitor Therapy



## Mary G. (…continued)



Mary receives mirdametinib. Her facial tumor shrinks to approximately half of its original size and the pain improves substantially. However, she develops grade 4 CPK increase.

# Which do you recommend for this patient?

A. Assess for symptoms, if asymptomatic continue therapy
B. Switch to selumetinib
C. Withhold until grade ≤1 and resume at lower dose
D. Permanently discontinue treatment
E. Continue irrespective of CPK increase

# NF1-PN and MEKi Therapy Monitoring

| Exam | Monitoring |
|---|---|
| Review of systems and physical examination (including GI, vision, skin, oral mucosa, and nails) | • Every visit (generally monthly) |
| Ophthalmologic examination | • Baseline, then every 6–12 months<br>• Consider increased frequency with new symptoms |
| Echocardiogram/ejection fraction | • Baseline, every 3–6 months |
| Electrocardiogram | • Baseline, then as clinically indicated |
| Pregnancy status | • Baseline, then per institutional standards |
| Laboratory examinations | • Baseline, then every 3–6 months: creatine kinase, metabolic panel, liver function tests, CBC<br>• Baseline, then as clinically indicated: amylase, lipase |

CBC, complete blood count; GI, gastrointestinal.

Friedman JM. Neurofibromatosis 1. In: Adam MP, et al., eds. *GeneReviews*. Seattle (WA): University of Washington, Seattle; 1993 (updated 2025).
Moodley M, et al. *Semin Pediatr Neurol*. 2024;52:101172. Na B, et al. *Curr Oncol Rep*. 2024;26:706–713.
Lee TJ, et al. *Orphanet J Rare Dis*. 2023;18(1):292.

# General MEKi Safety Experience in Clinical Trials

## Pediatric/Children

- Mild rash
- Paronychia
- Hypotonia or muscle weakness
- Retinal damage
- Impact on developmental changes are unknown

## Adolescents/Adults

- Severe acne rash
- Paronychia
- Weight gain
- Fatigue
- GI problems

Gross AM, et al. *Nat Med.* 2025;31(1):105–115. Solares I, et al. *ESMO Open*. 2021;6(4):100223.
Gross AM, et al. *Neuro Oncol*. 2023;25:1883–1894. Moertel CL, et al. *J Clin Oncol*. 2025;43(6):716–729.

# Summary

- Patients with NF1 are at risk for tumor and nontumor manifestations, necessitating care from a multidisciplinary team
- PNs are one of the most common tumor manifestations in patients with NF1 and carry a significant risk of malignant transformation
- PN can be managed surgically, with MEKis, or on clinical trial
- Many areas of ongoing research to improve therapy for patients with NF1-PN
- The goal of transition of care is to maintain optimal healthcare, which can only be achieved when each person, at every age, receives medically and developmentally appropriate care

# Unanswered Questions

- How long is MEKi therapy needed?
- Does it help to switch between MEKi?
- What is the realistic vs optimal surveillance of a person on MEKi for PN?
- Is there a role for MEKis in preventing MPNST in people with high burden of PN?

# The Future

| NCT Number | Phase II Study Title | Study Status | Conditions | Primary Outcome Measures | Age Group |
|---|---|---|---|---|---|
| NCT05331105 | HL-085 in Adults with Neurofibromatosis Type 1 (NF1) and Inoperable Plexiform Neurofibromas | Recruiting | NF1-PN | ORR | Adult, older adult |
| NCT06541847 | NF119 (INSPIRE): A Phase 2, Open-Label Study to Evaluate the Safety and Effects of HLX-1502 in Patients with Neurofibromatosis Type 1 | Recruiting | NF1 | PN response rate | Child, adult, older adult |
| NCT06188741 | NF114: Selumetinib for the Prevention of Plexiform Neurofibroma Growth in NF Type 1 | Not yet recruiting | NF1-PN | PFS | Child |
| NCT06502171 | Study of Cabozantinib with Selumetinib for Plexiform Neurofibromas | Not yet recruiting | NF1-PN | Dose limiting toxicity, safety | Adult (≥16 yrs) |

ClinicalTrials.gov.




## Put information into action!

Takeaways from this program can be implemented into your practice to improve patient care.

- *Refer patients to NF1 centers.* NF1 is a complex disease that requires support from many specialists. NF1 centers offer access to experts with experience in managing the specific needs of these patients.
- *Develop a robust multidisciplinary team for NF1 patient care.* Clinicians should have a low threshold for calling in support from specialists in neurology, cardiology, nephrology, pulmonology, genetics, and other specialties.
- *Implement strategies to improve transitions from pediatric care and integration into adult care.* Patients with NF1 are typically diagnosed in childhood and will need to transition to managing their own care as adults, which may be challenging for a young person. Remember, it is not too early to plan for the future.

## To Ask a Question

To submit a question, please go to the *Ask Question* tab at the bottom of the screen.





## Additional Resources

Visit *www.ceconcepts.com* for clinical information and certified educational activities.

# Claim Credit

Scan the appropriate QR code for your mode of participation in this activity and create or log in to a Creative Educational Concepts learner account. Complete the necessary requirements (e.g., pre-test, post-test, evaluation) and then claim your credit.*

Thank you for your participation!

*To receive credit, participants must register an account and apply for credit within 10 days of the live activity. For questions or technical difficulties, please contact info@ceconcepts.com.

## In-Person

## Livestream

# Claim ABIM MOC Credit

*3 Steps to Complete*

1. Actively participate in the discussion today by **responding to questions** and/or **asking the faculty questions**
   *(MOC credit can be claimed even if a question goes unanswered or an incorrect response is entered)*
2. Complete the post-test and evaluation at the conclusion of the webcast
3. Enter your **ABIM ID number** and **DOB** (MM/DD) on the evaluation, so credit can be submitted to ABIM

ABIM CME MOC ACCREDITED

# CME for MIPS Improvement Activity

*How to Claim This Activity as a CME for MIPS Improvement Activity*

- Actively participate today by responding to ARS questions and/or asking the faculty questions
- Complete the post-test and activity evaluation at the link provided
- Over the next 3 months, actively work to incorporate improvements from this presentation into your clinical practice
- In approximately 3 months, complete the follow-up survey from Creative Educational Concepts

CME for MIPS IMPROVEMENT ACTIVITY

CEC will send you confirmation of your participation to submit to CMS attesting to your completion of a CME for MIPS Improvement Activity.

TARGETING THE PATHWAY

# Evolving Roles of MEK Inhibitors in NF1-Associated PN




Supported by an independent educational grant from Alexion Pharmaceuticals.