CHALLENGE ALEXION

Sponsors Goal

Alexion, AstraZeneca Rare Disease, is committed to ensuring that all children and adolescents who suffer from neurofibromatosis type 1 (NF1) and plexiform neurofibromas (PNs) have the best quality of life, both phyisically and psychologically.

The problem

Overview of NF-1 PN

Neurofibromatosis (NF) is a rare genetic disorder that involves the **development of tumors of the central or peripheral nervous system that may affect the brain, spinal cord, and nerves, among others.** The most common type of NF is NF1, which affects approximately **1 in 3,000 people** worldwide.[1,2] NF1 is commonly recognized in **early childhood** and is a lifelong and progressive condition. The severity of NF1 manifestations can vary significantly and people with the disease may not develop every symptom.[2,3]

The **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 present:[4]

A:

1. Six or more café-au-lait macules
2. Freckling in the axillary or inguinal regions
3. Two or more neurofibromas of any type or one PN
4. Optic glioma (optic pathway glioma)
5. Two or more Lisch nodules (iris hamartomas)
6. A distinctive osseous lesion such as sphenoid dysplasia, anterolateral bowing of the tibia, or pseudarthrosis of a long bone
7. A heterozygous pathogenic NF1 variant with a variant allele fraction of 50% in apparently normal tissue such as white blood cells

B: A child of a parent who meets the diagnostic criteria specified in A merits a diagnosis of NF1 if one or more of the criteria in A are present.

PN can occur in 30–50% of patients with NF1 and can cause comorbidities that worsen over time.[5,6] The effect of PN on paediatric patients' quality of life (QoL) can vary **depending on PN volume, quantity, location** and **degree of encroachment on surrounding tissues**.[7]

The context

Currently, there is limited psychological support to mitigate the consequences of living with NF1 PN, due to National Health System overload and little resources dedicated to mental health.

The presence of PN and their associated comorbidities can significantly impact the QoL of patients, caregivers, and their families[8-10]

A cross-sectional survey (N=143) involving 61 paediatric patients with NF1-PN aged 8–18 years and their caregivers, and 21 additional caregivers of paediatric patients (aged 2–7 years) with NF1-PN (proxy-reported) found that:[8]

- **64,6%** described experiencing **pain or discomfort**
- **32,9%** reported having **disfigurement**
- **28,0%** had **motor dysfunction**
- Commonly reported conditions included **Attention-Deficit/Hyperactivity Disorder (ADHD)** (56,1%) and **headaches** (47,6%)

Additionally, another study evaluating QoL of paediatric patients aged 8–17 years (N=140) via an online platform found that:[9]

- Children with NF1-PN reported significantly **worse scores than the general population** on 8 of 10 domains
- The domains where children with NF1-PN performed significantly worse included **anxiety, depression, stigma, psychological stress, meaning and purpose, mobility, peer relationships, positive affect, wellbeing, and upper extremity function**

A cross-sectional study involving caregivers (N=95) of paediatric patients aged 2–18 years with NF1-PN found that:[10]

- **48,4%** reported having **anxiety**
- **34,7%** of caregivers were found to have **depression**

The challenge

How can we develop an effective and empathetic system to provide psychological support for children with NF1 and PNs, leveraging technology to address their diverse needs and enhance their QoL?

Idea words

Psychological support; social media; patient communities; technologies; telehealth; app; virtual reality, gamification, artificial intelligence, wearable devices; schools; NF1; PN; quality of life; psychological burden

References

1. **Lammert M,** Friedman JM, Kluwe L, Mautner VF. Prevalence of neurofibromatosis 1 in German children at elementary school enrollment. Arch Dermatol. 2005;141(1):71-4.
2. **Evans DG,** Howard E, Giblin C, Clancy T, Spencer H, Huson SM, Lalloo F. Birth incidence and prevalence of tumor-prone syndromes: estimates from a UK family genetic register service. Am J Med Genet A. 2010;152A(2):327-32.
3. **Tonsgard JH.** Clinical Manifestations and Management of Neurofibromatosis Type 1. Semin Pediatr Neurol. 2006;13(1):2-7.
4. **Legius E**, Messiaen L, Wolkenstein P, et al. Revised diagnostic criteria for neurofibromatosis type 1 and Legius syndrome: an international consensus recommendation. Genetics in Medicine. 2021;23(8):1506-1513.
5. **Nguyen R**, Kluwe L, et al. Plexiform neurofibromas in children with neurofibromatosis type 1: frequency and associated clinical deficits. J Pediatr. 2011 Oct;159(4):652-5.e2.
6. **Mautner VF**, et al. Assessment of benign tumor burden by whole-body MRI in patients with neurofibromatosis 1. Neuro Oncol. 2008 Aug;10(4):593-8.
7. **Hersh JH**; American Academy of Pediatrics Committee on Genetics. Health supervision for children with neurofibromatosis. Pediatrics. 2008 Mar;121(3):633-42.

8. **Yang X, Yoo HK, Amin S. et al.** Clinical and humanistic burden among pediatric patients with neurofibromatosis type 1 and plexiform neurofibroma in the USA. Childs Nerv Syst. 2022;38:1513–1522.
9. **Lai J-S, Jensen SE, Charrow J, et al**. Patient Reported Outcomes Measurement Information System and Quality of Life in Neurological Disorders Measurement System to Evaluate Quality of Life for Children and Adolescents with Neurofibromatosis Type 1 Associated Plexiform Neurofibroma. J Pediatr. 2019;206:190–196.
10. **Yang X, Yoo HK, Amin S, et al**. Burden Among Caregivers of Pediatric Patients with Neurofibromatosis Type 1 (NF1) and Plexiform Neurofibroma (PN) in the United States: A Cross-Sectional Study. Neurol Ther. 2022;11:1221–1233.