Qualitative Insights into Disease Burden and Meaningful Change Associated with Cutaneous Neurofibromas (cNFs) in Adults with Neurofibromatosis Type 1

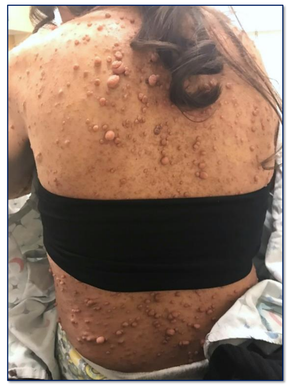
PCR142

McCool-Myers M [1], Raither L [2], Hughes M [2], Kochendoerfer G [3], Bradshaw M [3], Horwath P [3], Mathias S [4], Burbridge C [2]

[1]Clinical Outcomes Solutions LLC, Chicago, IL, USA, [2]Clinical Outcomes Solutions, Ltd., Folkestone, Kent, UK, [3]NFlection Therapeutics Inc, Boston, MA, USA, [4]Health Outcomes Solutions, Palm Beach Gardens, FL, USA

Background and Objectives

- Neurofibromatosis type 1 (NF1), a rare autosomal dominant disorder, causes cutaneous neurofibromas (cNFs) that can appear all over the body. Although benign, cNFs can be associated with pain, anxiety, and depression, and can interfere with physical, social and emotional functioning.
- To support development of a novel treatment for cNFs with NFX-179 Topical Gel, NFlection sought to understand what is most important to individuals with respect to their cNFs and to explore the participant experience of meaningful change in cNFs within a Phase 2b clinical trial.
- In the clinical trial, approximately 200 adults with NF1 in the US were randomized to either: a 1.5% concentration of NFX-179 Topical Gel, a 0.5% concentration of NFX-179 Topical Gel, or Vehicle Topical Gel. A total of 10 Target cNFs were treated once daily on the face, upper extremities, and anterior trunk for a 6-month period.



"We live in such a vain society, and everybody is so quick to say, 'Oh my God, what's wrong with you?' It was getting to a point where you didn't wanna wear… short sleeves, you just wanted to cover your arms or wear lots of makeup or not even go outside." *(Female, aged 46 years)*

"I had quite a few, quite a few of them removed because they were getting very bothersome and very painful… Up to the point where I was, I was in tears because of how painful they were." *(Male, aged 56 years)*

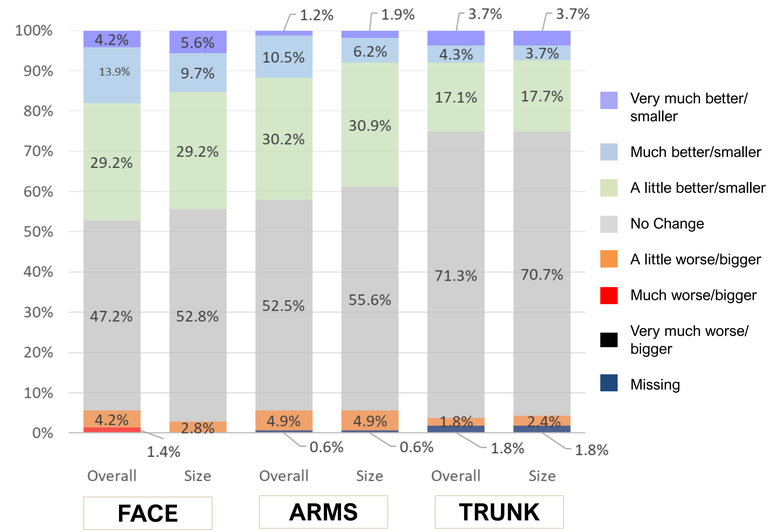
Methodology

- To meet the objectives, two qualitative interview studies were conducted between 2020-2023 with individuals with NF1 and presenting with cNFs.
- **Concept elicitation (CE) interviews** (N=10), conducted prior to the Phase 2b clinical trial, explored:
  - The lived experience of people with NF1
  - The development of two 7-point Patient Global Impression of Change (PGI-C) rating scales capturing Overall cNF Change and Change in cNF Size, including an additional follow-up item for meaningful change (yes/no) for each scale
- **Blinded qualitative exit interviews (EI)** (N=40) were conducted within 14 days of completion of the 6-month treatment. During the EI, the PGI-C scales were completed for each of the 10 Target cNFs. Discussions explored:
  - Any perceived changes (improvement/worsening) in the 10 cNFs in Overall Change and Change in Size
  - If the change was meaningful and why
  - The smallest level of meaningful change on the PGI-C scales (e.g. 1-category, 2-category, etc.)

Results

- CE interviews demonstrated that cNF size was the most salient aspect of cNFs and the driving factor in concerns about appearance.
- EI sample was primarily female (60.0%), Non-Hispanic White (87.5%), with a mean age of 51.5 years [range 21-78]. This generally aligned with the total clinical trial population. Participants reported that their cNFs were generally of moderate severity, with most participants reporting having at least 100 cNFs.
- PGI-C ratings for Overall Change and Change in Size were obtained during EI for each Target cNF (N=398 total cNFs). Figure 1 illustrates patient-reported changes in cNFs by body location (Face, Arms, Trunk) and by scale (Overall, Size). Interviewers and participants were blinded to treatment arm in EI.

Figure 1. PGI-C Ratings for Overall Change and Change in Size by Body Location (N=398 Target cNFs)



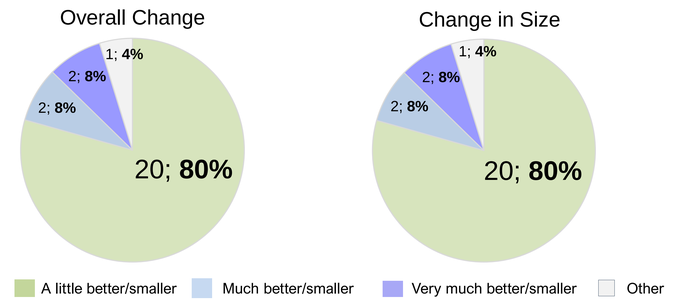
- **More than one-third of all treated cNFs rated as better** on PGI-C Overall (35.9%, n=143) **or smaller** on PGI-C Size (34.2%, n=136). Twenty-five of 40 (62.5%) EI participants reported improvement in at least 1 cNF after treatment (active or placebo) on either the PGI-C Overall or Size scale.
  - Improvement Group: at least 1 cNF improved on either PGI-C scale
  - No Improvement Group: no cNF improved on either scale
- **Flattening of cNFs** was the most commonly-reported change in the Improvement Group (88.0%, 22/25). Participants described how reductions in cNF size were associated with positive impacts including less noticeability:

"Especially the ones on my face, I'm very self-conscious about. So, I appreciate that those were the ones that flattened out and that are less noticeable…I feel slightly more attractive as they flatten out." *(Female, aged 57 years)*

"They've definitely flattened out - they don't stick out as much, so I think that makes them less noticeable." *(Female, aged 54 years)*

- Of the EI participants reporting improvement in their cNF(s), 80.0% (20/25) reported that a **1-category change** of either "a little better" or "a little smaller", represented **the smallest level of meaningful change** on the PGI-C scales, regardless of body location (Figure 2).

Figure 2. Smallest Level of Change on the PGI-C Scales in the Improvement Group (N=25)



"I would say... a little smaller makes you feel better… Just the fact knowing that it did shrink and became flatter is meaningful." *(Female, aged 58 years)*

"It was meaningful, because it did appear to be better and, I guess, looked better and, and maybe less distracting." *(Male, aged 76 years)*

- Participants who reported no change in cNFs (15/40), i.e. "No Improvement Group", discussed hypothetical change; 9/15 stated that a **1-category change would be meaningful to them**.

"Oh my God, it'd be a game changer! Would it have given me more self-confidence? Would it have improved my mood to not have these on my face? Absolutely!" *(Male, aged 49 years)*

Conclusions and Next Steps

- Reduction in cNF size, i.e. flattening, is important to people living with NF1.
- The PGI-C scales captured changes in cNF Overall and in cNF Size. For both, a 1-category improvement on the PGI-C was reported by participants to reflect meaningful change.
- PGI-C responses collected during the Phase 2b trial strongly correlated with objective measurements of cNF volume and height reduction; PGI-C items are being considered for inclusion as patient-reported outcome measures in the Phase 3 trial.

Limitations: 1) This was a US-only population; Phase 3 will be an international study. 2) The experience of meaningful change may differ if more severe and symptomatic cNFs had been included in the Target cNF selection. 3) PGI-C ratings were collected in the EI since PGI-C ratings collected at the End of Treatment Visit could not be provided to Clinical Outcomes Solutions in sufficient time for interview conduct.

ISPOR 2024, May 5-8, 2024, Atlanta, GA: Poster session 3, Tuesday May 7, Poster ID: PCR142

Disclosures: GK, MB and PH are employees of NFlection Therapeutics.

This research was funded by NFlection Therapeutics but undertaken by Clinical Outcomes Solutions which is a third-party independent research company.