



Response Evaluation In Neurofibromatosis Schwannomatosis INTERNATIONAL COLLABORATION

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REiNS 2023 Winter Meeting

Welcome and Introduction

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Response Evaluation In Neurofibromatosis Schwannomatosis
INTERNATIONAL COLLABORATION

What is REiNS?

Response Evaluation in NF and Schwannomatosis

- Established in 2011 by team of NF investigators
- International collaboration to develop standardized response criteria for determining treatment response in patients with NF1 and schwannomatosis
- Collaboration across institutions and medical specialties; includes experts in NF1-SWN and other areas and patient representatives
- Proactive discussion of endpoints and outcome measures with stakeholders will facilitate access to new therapies for these rare conditions, identify activity in clinical trials and ultimately gain regulatory approval
- We believe that consensus response criteria
 - will improve our ability to determine and compare treatment efficacy
 - are a work in progress and will continue to be modified as we gain experience in trials for NF1-SWN



Engaging stakeholders is a key principle of REiNS

- Investigators
- Patient representatives
- NF and other Foundations
- Food and Drug Administration
- European Medicines Agency
- NIH
- Department of Defense
- Pharma/Biotech



Organization and Membership of REiNS International Collaboration

Working groups:

- Cutaneous neurofibromas (Sarin/Cannon)
 - Disease biomarkers (Sundby/Bettegowda)
 - Functional outcomes (Gross)
 - Gene-directed therapy (Plotkin)
 - Neurocognitive outcomes (Janusz)
 - Patient reported outcomes (Thompson)
 - Patient representation (Merker)
 - Tumor imaging/WBMRI (Ahlawat, Dombi)
 - Visual outcomes (Avery)
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- 9 working groups
 - Over 370 active members
 - Over 70 institutions and organizations



EUROPEAN
MEDICINES
AGENCY



ACADEMIC
MEDICAL CENTERS



PHARMACEUTICAL
COMPANIES

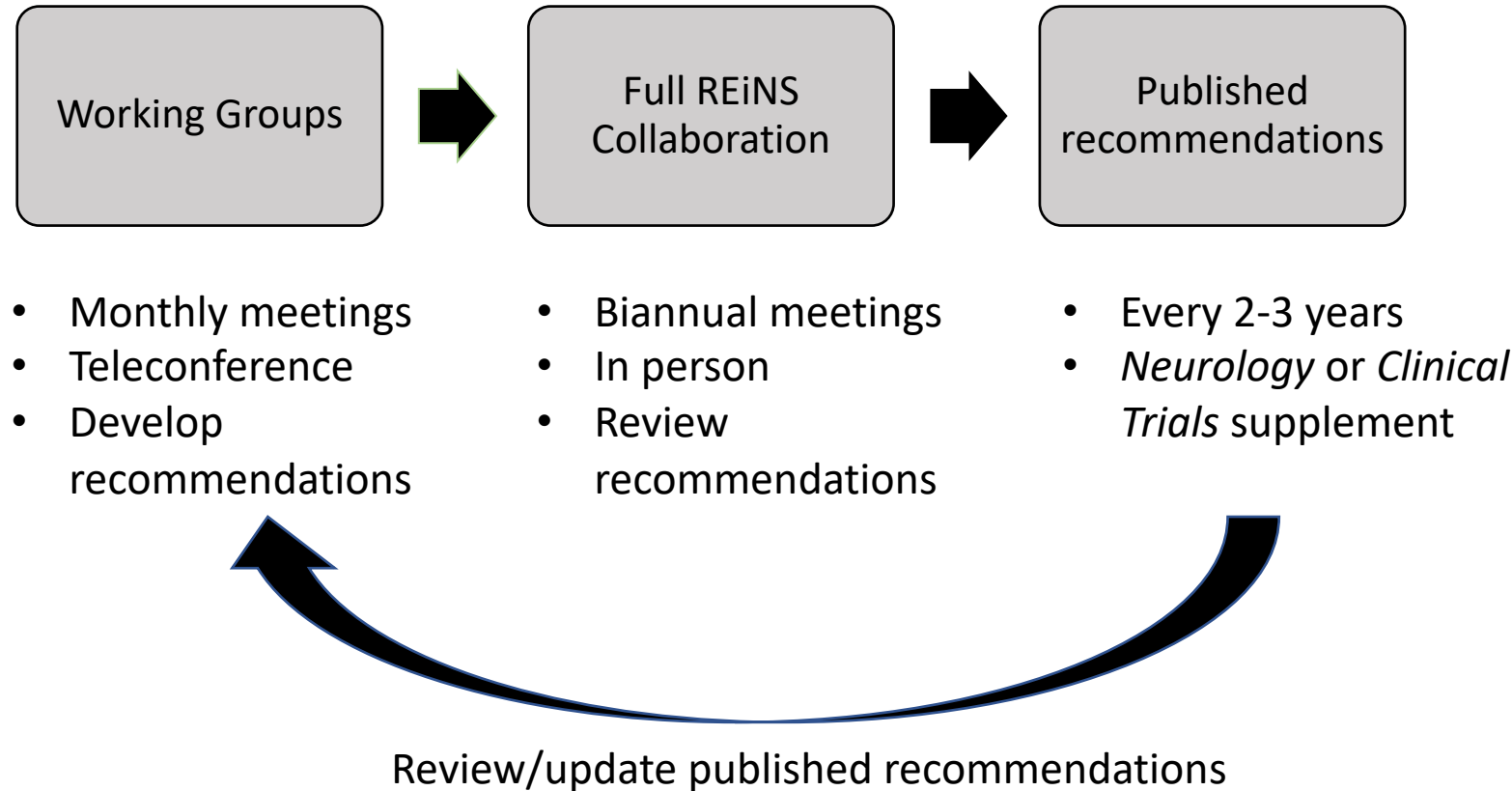
The REiNS working groups are open to all participants



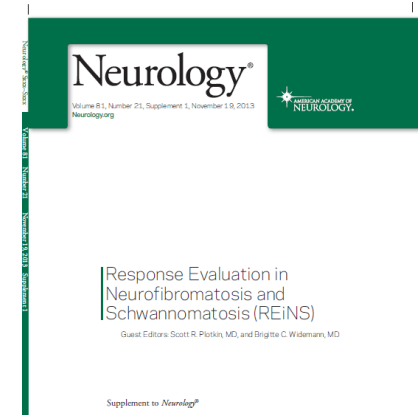
REiNS Philosophy



How REiNS Works: From Concept to Published Recommendation



<https://ccrod.cancer.gov/confluence/display/REiNS/Home>



REiNS publications (2013-2021)

Functional outcomes

- Functional outcome measures ([vision](#)) for NF1-associated optic pathway glioma clinical trials
- Patient Report of [Hearing in NF2](#): Recommendations for Clinical Trials
- [Sleep](#) and [pulmonary](#) outcomes for clinical trials of airway plexiform neurofibromas in NF1
- Reliability of [strength](#) testing using hand held dynamometry in patients with neurofibromatosis 1 and 2.

Cutaneous neurofibroma

- Measuring the Effect of Cutaneous Neurofibromas on [Quality of Life](#) in Neurofibromatosis Type 1
- Validating Techniques for [Measurement of Cutaneous Neurofibromas](#): Recommendations for Clinical Trials
- [Perspective of Adults](#) With NF1 and Cutaneous Neurofibromas: Implications for Clinical Trials

Patient reported outcomes

- Patient-Reported Outcome Measures Assessing Domains of [Quality of Life](#) in NF Clinical Trials
- Outcomes of [Pain and Physical Functioning](#) in NF Clinical Trials
- Assessing general and disease-specific [quality of life](#) in NF clinical trials
- Measures of Quality of Life and function for [hearing](#) in patients with neurofibromatosis 2

Imaging

- Current [Whole-Body MRI](#) Applications in the Neurofibromatoses: NF1, NF2 and Schwannomatosis
- Recommendations for imaging [tumor response](#) in neurofibromatosis clinical trials

Neurocognitive outcomes

- Neurocognitive Outcomes in Neurofibromatosis Clinical Trials: Recommendations for the Domain of [Attention](#)
- Recommendations for [Social Skills](#) End Point for Clinical Trials in NF1
- Recommendations for Measurement of [Attention Outcomes](#) in Preschoolers With Neurofibromatosis

Biomarkers

- Current status and recommendations for biomarkers and biobanking in neurofibromatosis
- Status and Recommendations for Incorporating Biomarkers for Cutaneous Neurofibromas Into Clinical Research
- Genotype-Phenotype correlations in neurofibromatosis and their potential clinical use

Patient engagement

- Enhancing Neurofibromatosis Clinical Trial Outcome Measures Through Patient Engagement

REiNS Supplement 2023



Merker

Gross

- Gene-targeted therapies for neurofibromatosis and schwannomatosis
- Perspective of Adolescents With Neurofibromatosis 1 and Cutaneous Neurofibromas: Implications for Clinical Trials
- Perspectives of adults with NF1, NF2, and schwannomatosis on psychosocial clinical trials: results from an international online survey
- Recommendations for Assessing Appearance Concerns Related to Plexiform and Cutaneous Neurofibromas in Neurofibromatosis 1 Clinical Trials
- Patient Report of Tinnitus in Neurofibromatosis Type 2: Recommendations for Clinical Trials
- Methodologies for Assessment of Bone Health in Neurofibromatosis Type 1 with a Focus on Use in Clinical Trials
- Recommendations for the prospective collection of biosamples for analysis of biomarkers in NF clinical trials

Winter 2023 Meeting: Objectives

- Map the benefits and challenges of decentralized trial designs for a variety of NF1, *NF2-SWN*, *LZTR1-SWN*, *SMARCB1-SWN* related manifestations
- Understand current FDA and EMA guidance on the conduct of decentralized trials
- Identify whether and how REINS-recommended outcome measures and endpoints can be adapted to be administered in participants' homes or local communities

Quality improvement for REiNS



REiNS Future: Expanded interactions with FDA / EMA

As conceived summer 2023

- Innovative trial designs for NF: Have the end goal in mind
 - Fit for purpose trials
 - **Decentralized trials**
 - Therapeutic and prevention trials
 - Biomarkers in trials
 - Novel endpoints: Employment, education, marriage, living independently
- Patient registries
 - Real world data
 - External control for non randomized interventional trials
- Reaching underrepresented populations
- Source of agents for clinical trials
- Revisit REiNS working groups:
 - Do we need a REiNS “Trial Design” working group?



REiNS Summary

- Highly productive international working group
- Recommendations have been critical to regulatory approvals
- Designs of meaningful clinical trials
- Better comparisons of trial outcomes
- More consistent collection data collection
- New members are always welcome

REiNS 2024 Summer Meeting!

June 20, 2024 (??)

Belgium (Venue TBD!)

+ Virtual participation



Thank you



Danielle (Dani) Silverman, MS

