



Response Evaluation In Neurofibromatosis Schwannomatosis INTERNATIONAL COLLABORATION

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REiNS 2023 Summer Meeting

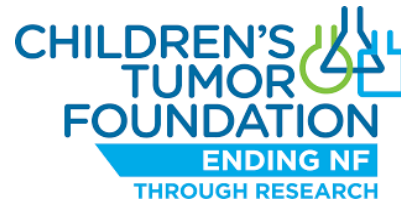
Welcome and Introduction

Brigitte Widemann, M.D., National Cancer Institute

Scott Plotkin, M.D., Ph.D., Massachusetts General Hospital



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, NF2, and schwannomatosis
- Collaboration across institutions and medical specialties; includes experts in NF and other areas (including patient representation)
- 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 NF



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 (Cannon/Sarin)
- Disease biomarkers (Bettegowda/Sundby)
- 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)

- 9 working groups
- Over 370 active members
- Over 70 institutions and organizations



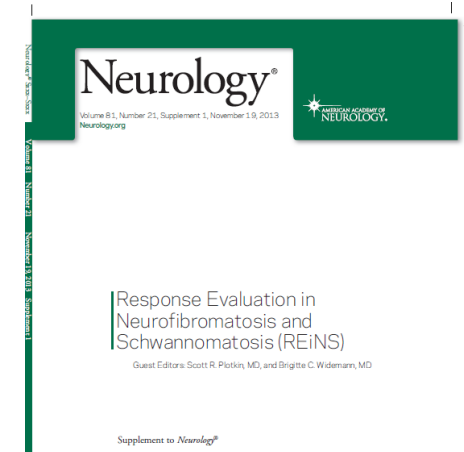
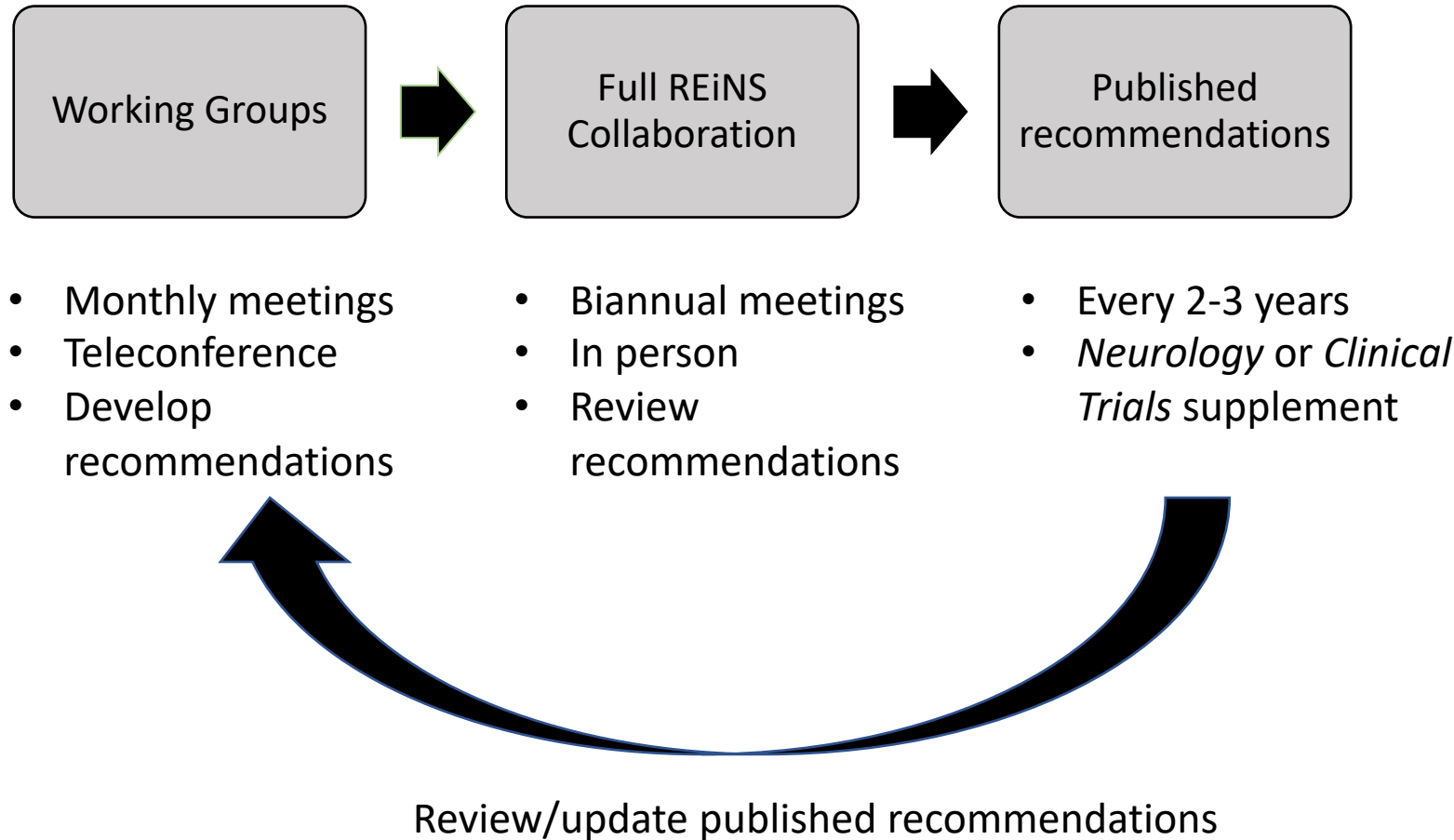
The REiNS working groups are open to all participants



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

Summer 2023 Meeting: Objectives

- To update REiNS members about ongoing activities for selected working group
- To inform REiNS members about types of FDA-sponsored meetings that encourage feedback from the community
- provide information to REiNS members about an upcoming natural history study for skeletal issues in NF1



REiNS Mini-symposium: Expanding collaborations with the Food and Drug Administration

Opportunities for FDA Advice: CPIM and NOTE Meetings

Diana Bradford, M.D.

Clinical Team Leader, US Food and Drug Administration (virtual talk)

Guided discussion about “Prospective evaluation of skeletal disease manifestations in NF1”

Andrea Gross, M.D., National Cancer Institute

Laura Klesse, M.D., Ph.D., UT Southwestern



Quality improvement for REiNS



REiNS Award for Outstanding Service - 2023

And the nominees are:

- Dale Berg
- Andrea Gross
- Andres Lessing
- Miranda McManus
- Vanessa Merker
- Pam Wolters

The winners for 2023 are:

- **Vanessa Merker**
- **Miranda McManus**

And a happy birthday to Jaishri Blakeley 😊



REiNS Future: Expand interactions with FDA / EMA

- Patient registries
 - Real world data
 - External control for non randomized interventional trials
- 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
- 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 2023 Winter Meeting!

Monday, December 4, 2023

Baltimore/DC Area (Venue TBD!)

+ Virtual participation



EUROPEAN
MEDICINES
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