

REiNS 2018 Winter Meeting

“Designing Clinical Trials for Cutaneous Neurofibromas, an Unmet Need for Patients with Neurofibromatosis Type 1”

Welcome and Direction

Ana-Maria Vranceanu, Peter de Blank &
Heather Thompson, PhD CCC-SLP
On behalf of the REiNS
Meeting Organizing Committee



Response Evaluation In Neurofibromatosis Schwannomatosis
INTERNATIONAL COLLABORATION

Disclosures

- No disclosures to report



What is REiNS?

Response Evaluation in NF and Schwannomatosis

- Established in 2011 by team of 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 with stakeholders will help facilitate approval of, and therefore access to, drugs for these rare conditions
- Response criteria are a work in progress and will continue to be modified as we gain experience in trials for NF
- Criteria will improve our ability to determine and compare treatment efficacy



Engaging stakeholders

- Investigators
- Patient representatives
- NF Foundations
- Food and Drug Administration
- Cancer Therapy Evaluation Program
- NIH/DOD
- Pharma- Dermavant, Nflection, Pierre Fabre, Springworks



Response Evaluation in Neurofibromatosis and Schwannomatosis (REiNS) Collaboration

Working groups

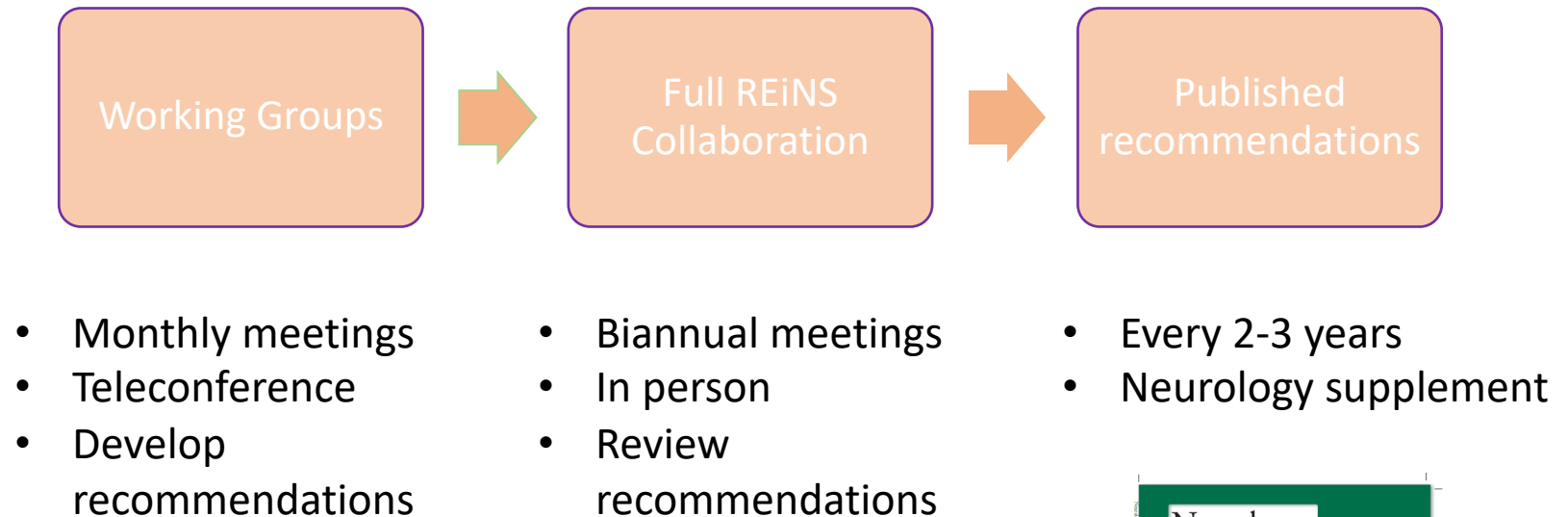
- Tumor Imaging/WBMRI (Ahlawat, Dombi)
- Functional outcomes (Plotkin)
- Patient reported outcomes (Wolters)
- Visual outcomes (Avery, Fisher)
- Disease Biomarkers (Bettegowda/Hanemann)
- Neurocognitive outcomes (Janusz)
- Cutaneous neurofibromas (Cannon/Pichard)
- Patient Representation (Plotkin)

- 9 working groups
- Over 160 active members
- Over 70 institutions and organizations

The REiNS working groups are open to all participants

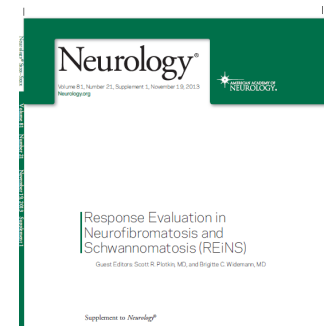


How REiNS Works



Collaborators:

- CTF and other foundations
- Food and Drug Administration
- Cancer Therapy Evaluation Program
- National Institutes of Health



REiNS publications (2013-present)

- Achieving consensus for clinical trials: The REiNS International Collaboration
- Patient-reported outcomes in neurofibromatosis and schwannomatosis clinical trials
- Functional outcome measures for NF1-associated optic pathway glioma clinical trials
- Hearing and facial function outcomes for neurofibromatosis-2 clinical trials
- Recommendations for imaging tumor response in neurofibromatosis clinical trials
- Conclusions and future directions for the REiNS International Collaboration
- Consensus for NF Clinical Trials: Recommendations of the REiNS Collaboration
- Outcomes of Pain and Physical Functioning in NF Clinical Trials
- Sleep and pulmonary outcomes for clinical trials of airway plexiform neurofibromas in NF1
- Neurocognitive Outcomes in Neurofibromatosis Clinical Trials: Recommendations for the Domain of Attention
- Current Whole-Body MRI Applications in the Neurofibromatoses: NF1, NF2 and Schwannomatosis
- Current status and recommendations for biomarkers and biobanking in neurofibromatosis



How REiNS is supported

- Through volunteerism of hundreds of investigators and patient representatives!
- Financial support from Children's Tumor Foundation and Mass General Hospital
- Grant support (R13) through National Cancer Institute, National Center for Advancing Translational Sciences (NCATS)



New Leadership Structure: Directors Council

Name	Role
Brigitte Widemann	Imaging group
Eva Dombi	Imaging group
Scott Plotkin	Functional/Patient representation groups
Jaishri Blakeley	At large
Michael Fisher	At large
Oliver Hanemann	Biomarkers
Karin Walsh	At large
Pam Wolters	Patient reported outcomes
Shivani Ahlawat	Whole body MRI
Jennifer Janusz	Neurocognitive
Ashley Cannon	Cutaneous neurofibroma
Dominique Pichard	Cutaneous neurofibroma
Rob Avery	Visual outcomes
Chetan Bettegowda	Biomarkers
TBD	Patient representation
TBD	Patient representation
Peter de Blank	Meetings and grants
Heather Thompson	Meetings and grants
Ana-Maria Vranceanu	Meetings and grants
Andrea Gross	Patient representation



Enhanced communication

- Working groups meet monthly and communicate with individual members
- Leadership has instituted a new monthly email using MailChimp – includes news, upcoming meetings, member profile



REiNS 2018 Winter Meeting

- “Designing Clinical Trials for Cutaneous Neurofibromas, an Unmet Need for Patients with Neurofibromatosis Type 1”
- Focus on a longstanding and important unmet need
- Uniquely suited to our work in determining clinical endpoints
- Drawing from multiple groups and prior experience
 - Patient representation
 - Patient Reported Outcomes, Quality of Life
 - Measures of tumor size



Meeting organization committee

- Peter de Blank, MD, MSCE
NeuroOncology, Cincinnati Children's Hospital Medical Center
- Ana-Maria Vranceanu, PhD
Psychology, Massachusetts General Hospital
- Heather Thompson, PhD CCC-SLP
Speech-Language Pathologist
Communication Sciences and Disorders, California State University, Sacramento



NIH Meeting Support

- R13 grant awarded
 - \$10,000 from NCI and NCATS
 - PI: Scott Plotkin, MD, PhD
 - Many thanks to Brigitte Widemann and the Meeting Organizing Committee for helping to draft the application
- Meeting Aims
 - 1) to assemble key stakeholders (investigators, patient representatives, pharmaceutical companies, and members of the FDA) to examine strategies for clinical trials in cNF
 - 2) to achieve consensus on recommended primary and secondary endpoints for clinical trials of cNF
 - 3) to define key aspects of clinical trial design (including patient eligibility, tumor characteristics, frequency of assessments, duration of safety evaluation, and acceptability of corollary biomarkers) unique to cNF trials



Agenda (1)

- **8:15-8:45 FDA Perspective on Establishing Novel Endpoints for Clinical Trials of Skin Disease**
 - Melissa Reyes, MD (Medical Officer, FDA) - discussion
- **9:00-9:30 Results of a Survey of NF1 Patients— Defining the Symptom Burden of Cutaneous Neurofibromas**
 - Gregg Erickson (patient representative)
- **9:45-10:15 Recommendations of the cNF Summit Sponsored by NTAP**
 - Jaishri Blakeley, MD (JHU) for cNF Working Group



Agenda (2)

- **11:00-11:30 Ongoing Studies of cNFs: Trial Design and Endpoints**
 - Ashley Cannon, PhD (UAB) for the cNF Working Group
- 12-1:30 Lunch at local venues
- **1:30-2:00 What Constitutes Clinical Benefit for Trials of cNF?**
 - Dominique Pichard, MD (NIAMS)
- **2:00-2:15 PROs for Trials of cNF: Measuring Itch, Pain and Visibility**
 - cNF Working Group



Agenda (3)

- **2:30-3 Measuring Change in cNF Size—Novel Techniques and Endpoints**
 - Scott Plotkin, MD, PhD (MGH) for the cNF Working Group
- **3:30-4 Recommended Biomarker Studies for Trials of cNF**
 - Kavita Sarin, MD, PhD (Stanford) for the Disease Biomarker Working Group
- **4-5:30 Panel Discussion**



Feedback

- We need your feedback to improve the meeting and for grant purposes
- Please fill out survey at the end of the day (or earlier if you leave before the end)



Acknowledgments

- Dr. William Timmer, Program Director, Cancer Therapy Evaluation Program (CTEP)
- Children's Tumor Foundation
- NTAP
- Patient Representatives
- cNF working group
- Raquel Thalheimer
- All attendees