

# Response Evaluation In Neurofibromatosis Schwannomatosis INTERNATIONAL COLLABORATION

- If sharing any data or information from these slides generated by the REiNS International Collaboration, please acknowledge the authors, group chairs, and specific working group.
- If using any information presented with a citation, please reference the primary source.

# REiNS 2021 Winter Meeting

“Developing skeletal outcomes for NF Clinical Trials”

*Welcome and Direction*

---

Brigitte Widemann, MD

Scott Plotkin, MD, PhD

Jonathan Rios, PhD



Response Evaluation In Neurofibromatosis Schwannomatosis  
INTERNATIONAL COLLABORATION

# Disclosures

- SRP: co-founder of NFlection Therapeutics and NF2 Therapeutics; consulting for AstraZeneca, Akouos, and SonALAsense
- BW: no disclosures
- JR: no disclosures



# Best practices for this call

- Please keep yourself on mute
- Direct questions through the chat, if possible
- Speak slowly and clearly, please – the meeting is being captioned for individuals who are hard of hearing
- Live captioning can be activated within the Zoom app
  - Click on “More” (or CC icon) – click on “live transcript”
- Speakers – please do your best to stay on time

# What is REiNS?

*Response Evaluation in NF and Schwannomatosis*

- Established in 2011 by team of investigators
- International collaboration to develop standardized response criteria and outcome measures for clinical trials in NF1, NF2, and schwannomatosis
- Collaboration across medical specialties; includes experts in NF and other areas (including patient representation)
- Response criteria are a work in progress
- Criteria will improve our ability to determine and compare treatment efficacy
- Moving towards regulatory approvals





We will be

# Celebrating the 10<sup>th</sup> Birthday of REiNS in 2021

- 2011 Children's Tumor Foundation Meeting:
  - Jackson Hole, WY
- Thank you Scott for your leadership, vision, direction and persistence



# Engaging stakeholders

- Investigators, clinicians
- Patient representatives
- NF Foundations
- Food and Drug Administration
- NCI, Cancer Therapy Evaluation Program
- NIH/Department of Defense
- Pharma- Astra Zeneca, Dermavant, NFlection, Pierre Fabre, Springworks, Infixion Bio, and more



# Response Evaluation in Neurofibromatosis and Schwannomatosis (REiNS) Collaboration

## Working groups

- **Tumor Imaging/WBMRI** (Ahlawat, Dombi)
- Functional outcomes (Plotkin)
- **Patient reported outcomes** (Merker)
- Visual outcomes (Avery)
- Disease Biomarkers (Bettegowda/Hanemann)
- Neurocognitive outcomes (Janusz)
- Cutaneous neurofibromas (Cannon/Sarin)
- Patient Representation (Gross/Merker)

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

***The REiNS working groups are open to all participants***





# Response Evaluation in Neurofibromatosis and Schwannomatosis (REiNS) Collaboration

## Working groups

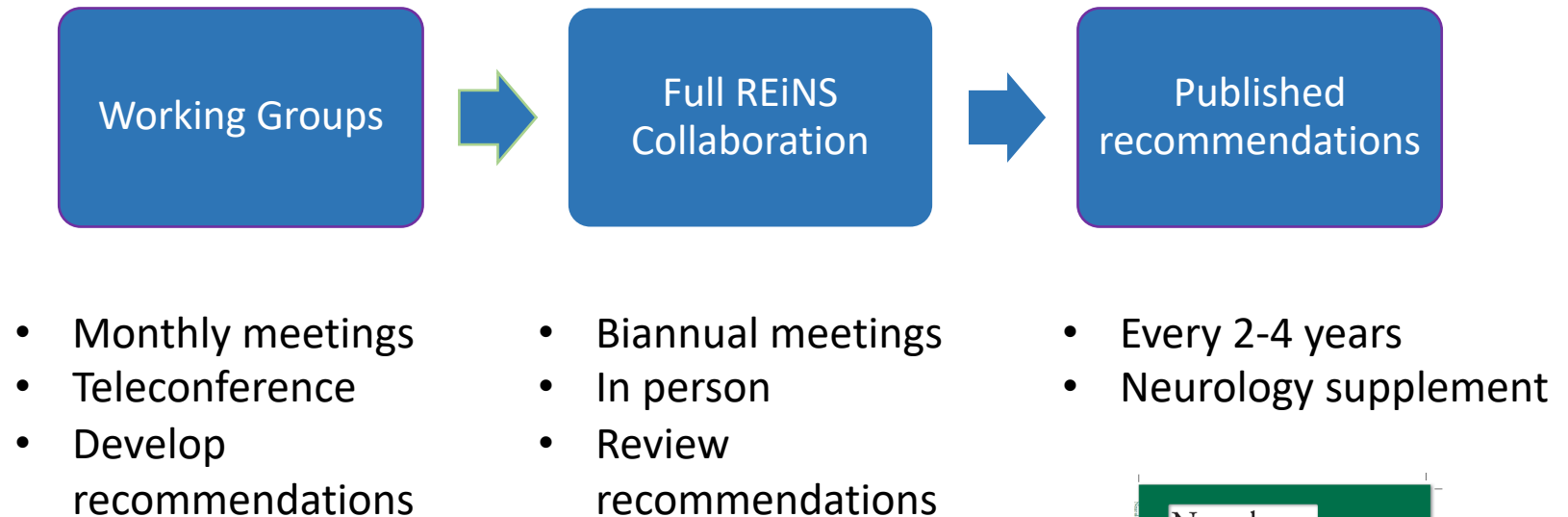
- Tumor Imaging/WBMRI (Ahlawat, Dombi)
- **Functional outcomes** (Plotkin)
- Patient reported outcomes (Merker)
- **Visual outcomes** (Avery)
- Disease Biomarkers (Bettegowda/Hanemann)
- Neurocognitive outcomes (Janusz)
- Cutaneous neurofibromas (Cannon/Sarin)
- Patient Representation (Gross/Merker)

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

***The REiNS working groups are open to all participants***

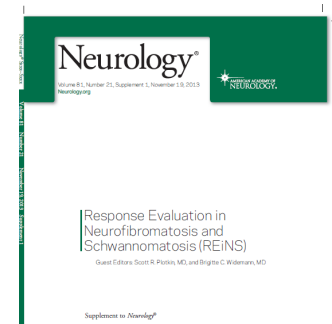


# How REiNS Works



## Collaborators:

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



# REiNS publications (2013-2020)

- 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



# 2021 Neurology supplement

## **Use of SkinDex to assess patients with NF1: a report from US and Australian Clinics**

*Christopher Moertel, Mimi Berman for the REiNS Cutaneous Neurofibroma Working Group*

## **Reliability of digital calipers, photography, and ultrasound to measure cutaneous neurofibromas in patients with neurofibromatosis 1**

*Scott Plotkin for the REiNS Cutaneous Neurofibroma Working Group and Neurofibromatosis Therapeutic Acceleration Program (NTAP)*

## **Patient Views Regarding Cutaneous Neurofibromas and Treatment**

*Ashley Cannon and Dominique Pichard for the REiNS Cutaneous Neurofibroma Working Group and Neurofibromatosis Therapeutic Acceleration Program (NTAP)*

## **Evaluating satisfaction, barriers, and successes of patient engagement in REiNS**

*Vanessa Merker, Renie Moss for the REiNS Patient Representative Working Group*

## **Assessing general and disease-specific quality of life in neurofibromatosis clinical trials (depending on title length restrictions)**

*Pamela Wolters for the REiNS Patient Reported Outcomes Working Group*

## **Measures of Quality of Life and function for hearing in patients with neurofibromatosis 2**

*Heather Thompson for the REiNS Patient Reported Outcomes Working Group*



# 2021 Neurology supplement

## **Social skills outcomes for patients with neurofibromatosis 1**

*Jennifer Janusz for the REiNS Neurocognitive Working Group*

## **Measurement of attention as a clinical trials outcome in preschoolers with neurofibromatosis 1**

*Bonnie Klein-Tasman for the REiNS Neurocognitive Working Group*

## **Genotype-Phenotype correlations in neurofibromatosis and their potential clinical use**

*Chetan Bettegowda and Oliver Hanemann for the REiNS Biomarkers Group*

## **Biomarkers for cutaneous neurofibroma**

*Kavita Sarin for the REiNS Cutaneous Neurofibroma Working Group*

## **Reliability of strength testing using hand held dynamometry in patients with neurofibromatosis 1 and 2.**

*Vandana Akshintala, Kaleb Yohay for the REiNS Functional Endpoints Working group*

## **Implementation and performance of REiNS clinical trial endpoints in SPRINT trial**

*Andrea Gross for the REiNS Functional Endpoints Working and PRO Working group*



# Brief working group updates

- Tumor Imaging/WBMRI (Ahlawat, Dombi)
  - No updates → upcoming meetings to decide next steps
  - Considering study of WBMRI and pain localization
- Functional outcomes (Plotkin)
  - Supplement on measuring strength with HHD
  - Current meeting focused on skeletal outcomes
- Patient reported outcomes (Merker)
  - Working on ratings for disfigurement, tinnitus, and scoliosis
- Visual outcomes (Avery)
  - No updates



# Brief working group updates

- Disease Biomarkers (Bettegowda/Hanemann)
  - No updates, working to expand committee
- Neurocognitive outcomes (Janusz)
  - Working on measures of social cognition, academic function, and psychosocial function
- Cutaneous neurofibromas (Cannon/Sarin)
  - Submitted multiple manuscripts to supplement
  - Launching an eDelphi process in collaboration with IDEOM to arrive at consensus endpoints for cNF
- Patient Representation (Gross/Merker)
  - Successful recruitment of second group of 51 patient reps
  - Providing feedback on clinical trial design
  - Hoping to increase diversity



# How REiNS is supported

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





# REiNS 2021 Winter Meetings

---

- “Developing skeletal outcomes for NF Clinical Trials”
- Focus on an 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
- Focus on discussion among stakeholders



# Agenda (1)

---

12:00 -12:15 pm            **Welcome and introduction**

Scott Plotkin (Mass General Hospital), Brigitte Widemann (National Cancer Institute), Jonathan Rios (UT Southwestern)

12:15 – 12:45 pm            **Currently available techniques and endpoints for study of osteoporosis**

David Stevenson, MD (Stanford University)

12:45 - 1:00 PM            **Natural history study of bone density in children with NF1**

Andrea Gross, MD (National Cancer Institute)

1:00 - 1:30 PM            **Endpoints for study of scoliosis**

Noelle Larson, MD (Mayo Clinic)

1:30 - 1:45 PM            **Radiation risks of imaging studies**

Shivani Ahlawat, MD (Johns Hopkins University)



# Agenda (2)

---

**1:45 - 2:15 PM Application of x-ray, MRI, qCT, and DEXA in a natural history study of scoliosis progression in children with NF1**

David Viskochil, MD, PhD (University of Utah)

**2:15 - 2:30 PM Break**

**2:30 – 2:45 PM Can routine MRI be used to measure scoliosis in NF1 patients? A retrospective study of the correlation between standing x-ray and MRI**

Andrea Gross, MD (National Cancer Institute)

**2:45 - 3:00 PM How scoliosis in NF can lead down a difficult path**

Herb Sanoff (patient representative)

**3:00 - 3:30 PM Patient reported outcomes for NF1-related scoliosis: domains of interest**

Vanessa Merker, PhD (Mass General Hospital) and Heather Thompson, PhD (California State University)



# Acknowledgements

- Welcome to our patient representatives (16 veterans and 51 new members)
- Thanks to the leaders of the Skeletal Outcomes Working group: Jonathan Rios, Andrea Gross, and David Stevenson
- Thanks to Jennifer Da (MGH) for her technical support and tireless work on behalf of REiNS



# Critical feedback!

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



# Upcoming 2021 Summer meeting

- “Gene therapy for NF1, NF2, and SWN”
- Wednesday, June 16, 2021
- 1:30 pm – 3:30 pm EST

