REiNS 2019 Winter Meeting

“Clinical Trial Design for Cutaneous Neurofibromas”

Welcome and Direction

Scott Plotkin, MD, PhD
Brigitte Widemann, MD
Disclosures

• SRP: co-founder of NFlection Therapeutics and NF2 Therapeutics; consulting for AstraZeneca
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

- Monthly meetings
- Teleconference
- Develop recommendations

- Biannual meetings
- In person
- Review recommendations

- Every 2-3 years
- Neurology supplement

Collaborators:
- CTF and other foundations
- Food and Drug Administration
- Cancer Therapy Evaluation Program
- National Institutes of Health
• 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
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
2020 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
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 2018/2019 Winter Meetings

• “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
• Focus on discussion among stakeholders
Agenda (1)

8:00 -8:10 am Welcome and introduction
Scott Plotkin (Mass General Hospital), Brigitte Widemann (National Cancer Institute)

8:10-9:00 am Review of proposed outcome measures for cNF: tumor size, PROs, global assessment of change
Dominique Pichard (NCI) and Scott Plotkin (MGH)

9:00 -9:30 am Selumetinib for cutaneous neurofibroma: preliminary findings and lessons learned
Ashley Cannon (UAB) and Brigitte Widemann (NCI)

9:30 – 10:00 am Proposed design for a pilot activity trial using local therapy (topical formulation/injection): inclusion criteria, endpoints, and go/no go decisions
Scott Plotkin (Mass General Hospital)
10:00 - 10:30 am  Group discussion
10:30 – 11:00 am  Coffee Break
11:00 – 11:30 am  Proposed design for a screening trial using systemic therapy: inclusion criteria, endpoints, and go/no go decisions
  Brigitte Widemann (National Cancer Institute)
11:30 - 12:00 pm  Group discussion
12:00-1:00 pm      Sponsored lunch by NF Northeast, NF Midwest, and Texas NF
1:00 -1:45 pm      Next steps in designing trials for cNF: what do we need as a community? A panel discussion
Agenda (3)

1:45-2:30 pm Assessing the strengths and weaknesses of the REiNS patient representation program
Vanessa Merker (VA) and Andres Lessing (Patient Representative)

2:15 -2:45 pm Small group discussions: next steps for the REiNS patient representation program

2:45-3:15 pm Small group debriefing/large group discussion
cNF Working Group

• Thanks to Ashley Cannon and Dominique Pichard for their leadership these last 2 years

• Leadership transition
  • Dominique Pichard to become Chief Scientific Officer for International Rett Syndrome Foundation
  • Kavita Sarin to join leadership of Working Group
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)
Future meetings

• Skeletal endpoints
• Gene therapy
• Your thoughts?
Acknowledgments

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• NTAP
• Patient Representatives
• cNF working group
• Jennifer Da
• All attendees