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REiNS 2021 Summer Meeting

Scott Plotkin, MD, PhD
Brigitte Widemann, MD
Disclosures

- SRP: co-founder of NFlection Therapeutics, NF2 Therapeutics; consulting for AstraZeneca, SonalaSense, Akouos
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 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, others
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)
• Neurocognitive outcomes (Janusz)
• Cutaneous neurofibromas (Cannon/Sarin)
• Patient Representation (Gross)

• 8 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
<table>
<thead>
<tr>
<th>2013 Neurology Supplement</th>
<th>2016 Neurology Supplement</th>
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<tbody>
<tr>
<td>Achieving consensus for clinical trials: The REiNS International Collaboration</td>
<td>Consensus for NF Clinical Trials: Recommendations of the REiNS Collaboration</td>
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<tr>
<td>Patient-reported outcomes in neurofibromatosis and schwannomatosis clinical trials</td>
<td>Outcomes of Pain and Physical Functioning in NF Clinical Trials</td>
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<tr>
<td>Functional outcome measures for NF1-associated optic pathway glioma clinical trials</td>
<td>Sleep and pulmonary outcomes for clinical trials of airway plexiform neurofibromas in NF1</td>
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<tr>
<td>Hearing and facial function outcomes for neurofibromatosis-2 clinical trials</td>
<td>Neurocognitive Outcomes in Neurofibromatosis Clinical Trials: Recommendations for the Domain of Attention</td>
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<tr>
<td>Recommendations for imaging tumor response in neurofibromatosis clinical trials</td>
<td>Current Whole-Body MRI Applications in the Neurofibromatoses: NF1, NF2 and Schwannomatosis</td>
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<tr>
<td>Conclusions and future directions for the REiNS International Collaboration</td>
<td>Current status and recommendations for biomarkers and biobanking in neurofibromatosis</td>
</tr>
</tbody>
</table>
2021 Neurology supplement

Introduction
NF Clinical Trials – REiNS Collaboration 2020 Recommendations: Looking Back and Moving Ahead
Andrea M. Gross, MD, Brigitte C. Widemann, MD, and Scott R. Plotkin, MD, PhD, on behalf of the REiNS Leadership Council

Patient engagement
Enhancing NF Clinical Trial Outcome Measures Through Patient Engagement: Lessons from REiNS
Vanessa L. Merker, PhD, for the REiNS Patient Representative Working Group

Cutaneous neurofibroma
Perspective of Adults with Neurofibromatosis 1 and Cutaneous Neurofibromas: Implications for Clinical Trials
Ashley Cannon, PhD, MS, and Dominique C. Pichard, MD, for the REiNS Cutaneous Neurofibroma Working Group and Neurofibromatosis Therapeutic Acceleration Program (NTAP)

Measuring the Impact of Cutaneous Neurofibromatosis on Quality of Life in Neurofibromatosis Type 1
Christopher Moertel, MD, and Yemima Berman, BMBS, PhD, for the REiNS Cutaneous Neurofibroma Working Group

Validating Techniques for Measurement of Cutaneous Neurofibromas: Recommendations for Clinical Trials
Scott R. Plotkin, MD, PhD, for the REiNS Cutaneous Neurofibroma Working Group and Neurofibromatosis Therapeutic Acceleration Program (NTAP)

Status and Recommendations for Incorporating Biomarkers for Cutaneous Neurofibromas into Clinical Research
Kavita Y. Sarin, MD, PhD, for the REiNS Cutaneous Neurofibroma Working Group
2021 Neurology supplement

**Patient reported outcomes**

**Current Recommendations for Patient-Reported Outcome Measures Assessing Domains of Quality of Life in Neurofibromatosis Clinical Trials**
*Pamela L. Wolters, PhD, for the REiNS Patient Reported Outcomes Working Group*

**Patient Report of Hearing in Neurofibromatosis Type 2: Recommendations for Clinical Trials**
*Heather L. Thompson, PhD, CCC-SLP, for the REiNS Patient Reported Outcomes Working Group*

**Recommendations for Social Skills Endpoints for Clinical Trials in Neurofibromatosis Type 1**
*Jennifer A. Janusz, PsyD, for the REiNS Neurocognitive Working Group*

**Recommendations for Measurement of Attention Outcomes in Preschoolers with Neurofibromatosis**
*Bonita P. Klein-Tasman, PhD, for the REiNS Neurocognitive Working Group*

**Biomarkers**

**Genotype-Phenotype Correlations in Neurofibromatosis and Their Potential Clinical Use**
*Chetan Bettegowda, MD, PhD, and C. Oliver Hanemann, MD, PhD, for the REiNS Biomarkers Working Group*

**Functional outcomes**

**Reliability of Hand-held Dynamometry to Measure Focal Muscle Weakness in Neurofibromatosis Types 1 and 2**
*Srivandana Akshintala, MBBS, MPH, for the REiNS Functional Endpoints Working Group*

**Imaging**

**Imaging Evaluation of Plexiform Neurofibromas in Neurofibromatosis 1: A Survey-Based Assessment**
*Shivani Ahlawat, MD, for the REiNS Imaging Working Group*
<table>
<thead>
<tr>
<th>Time</th>
<th>Topic and Speaker</th>
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| 1:30 – 1:45 pm  | Introduction and REiNS Updates  
*Scott Plotkin, M.D., Ph.D., Mass General Hospital*  
*Brigitte Widemann, M.D., National Cancer Institute* |
| 1:45 – 2:00 pm  | Update from neurocognitive working group  
*Karin Walsh, Psy.D., Children’s National Medical* |
| 2:00 – 2:15 pm  | Update from patient reported outcomes (PRO) working group  
*Heather Thompson, Ph.D., California State University*  
*Staci Martin, Ph.D., National Cancer Institute* |
| 2:15 – 2:30 pm  | Questions and discussion for neurocognitive and PRO working groups  
*Vanessa Merker, Ph.D., Mass General Hospital*  
*Andrea Gross, M.D., National Cancer Institute* |
| 2:30 – 2:45 pm  | Update from patient representation working group  
*Vanessa Merker, Ph.D., Mass General Hospital*  
*Andrea Gross, M.D., National Cancer Institute* |
| 2:45 – 3:00 pm  | Update from functional outcomes working group  
*Jonathan Rios, Ph.D., UT Southwestern*  
*Andrea Gross, M.D., National Cancer Institute* |
| 3:00 – 3:15 pm  | Questions and discussion for patient representation and functional outcomes working groups  
*Vanessa Merker, Ph.D., Mass General Hospital*  
*Andrea Gross, M.D., National Cancer Institute* |
| 3:15 – 4:15 pm  | REiNS Mini-symposium:  
Identifying clinical, genetic, and radiologic features associated with increased risk for MPNST  
3:15-3:25 pm: Brigitte Widemann, MD (clinical features)  
3:25-3:35 pm: Shivani Ahlawat, MD (imaging features)  
3:35-4:15 pm: Discussion |
| 4:15 pm         | Plans for December meeting and closing comments  
*Scott Plotkin, M.D., Ph.D. (Mass General Hospital)*  
*Brigitte Widemann, M.D. (National Cancer Institute)* |
Acknowledgments

- Dr. William Timmer, Program Director, Clinical Investigations Branch, NCI, Cancer Therapy Evaluation Program (CTEP)
- Children’s Tumor Foundation, NF Northeast, NF Midwest, and Texas NF
- NTAP
- Patient Representatives
- Jennifer Da
- All attendees