REiNS collaboration seeks common outcome measures for neurofibromatosis clinical trials

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As potentially effective new treatments for neurofibromatosis (NF) are developed, standardized research approaches—including outcome measures specific to NF—are needed. The first report from the Response Evaluation in Neurofibromatosis and Schwannomatosis (REiNS) International Collaboration has been published as a supplement to *Neurology*, the Official Journal of the American Academy of Neurology (AAN).

The (REiNS) Collaboration was formed to achieve consensus regarding the design of clinical trials for treatments of NF and related disorders, with a focus on developing a standard set of appropriate and meaningful outcome measures. "This supplement presents the initial progress of several of the working groups and includes the first series of consensus recommendations for NF clinical trial endpoints by the REiNS International Collaboration," according to an introduction by Dr Scott R. Plotkin and colleagues. The full supplement is freely available on the journal website.

Initial Reports on Consensus Approach to NF Clinical Trials

The REiNS Collaboration was established at the 2011 meeting of the Children's Tumor Foundation. The neurofibromatoses—NF1, NF2, and schwannomatosis—are a group of related genetic diseases in which

patients are predisposed to developing multiple tumor types, particularly tumors of the nerve sheath. Other manifestations may occur as well, including learning problems in patients with NF1 and cataracts in those with NF2. Especially for NF1, the disease is usually diagnosed in childhood.

Traditionally, surgery has been the standard treatment for NF tumors. But recent advances in scientific understanding of the biology and development of NF have raised the promise of new targeted antitumor agents. An ambitious research agenda has been developed for rapid evaluation of these emerging NF treatments.

Most early NF studies used designs similar to those for cancer treatments. But these research designs—often focusing on tumor size or overall survival—may not be relevant to NF. Neurofibromatosis tumors are typically benign, rather than malignant, and patients face unique clinical and functional problems. "The NF community continues to struggle with the optimum design of clinical trials for this group of patients," Dr Plotkin and coauthors write.

A major goal of the REiNS Collaboration is to develop standardized outcome measures for use in NF clinical trials. The collaborators are organized into seven working groups, focusing on imaging of tumor response, functional outcomes, visual outcomes, patient-reported outcomes, neurocognitive outcomes, and whole-body magnetic resonance imaging (MRI), and disease biomarkers. The new supplement includes initial working group reports addressing:

- Patient-reported outcomes, especially pain.
- Functional outcomes affecting vision—important because of the high rate of tumors affecting the optic nerve in NF1.
- Hearing and facial function outcomes, addressing the high rate of hearing loss and facial weakness in NF2.

- Imaging tumor response—MRI with volumetric analysis is recommended to show changes in tumor size.

By developing consensus outcome measures relevant to NF, the REiNS collaborators hope to promote rapid evaluation of treatments that may benefit individuals affected by these disorders. "Ultimately, we plan to engage industry partners and national regulatory agencies in this process to facilitate approval of drugs for patients with NF," Dr Plotkin and coauthors write.

They add that the recommendations will likely be modified over time, as more data on NF-specific endpoints become available. Future modifications to the recommendations and other updates will be shared with the NF research community through the REiNS website: http://www.reinscollaboration.org.

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