Pediatric Onset Opsoclonus Myoclonus Ataxia Syndrome (POOMAS) Registry:

Progress towards an international registry

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Background

- OMS is an ultra-rare condition, affecting approximately 1 in 5 million children/year
- Most studies on OMS have had limited sample sizes, geographic representations, and data points
- Biospecimens and MRI imaging from OMS patients are scarce
  - When available, material is mostly stored in local biobanks and radiology systems at treating hospitals, not accessible to outside researchers
- Through a previous, three-nation study examining neuropsychological outcomes in OMS, our team demonstrated the feasibility of conducting OMS research on an international scale

OMS Study Group Database Task Force

- Founded at the 2016 OMS International Workshop (Abingdon, England), charged with building an international OMS database
  - France (Kumaran Deiva, MD, PhD, Hôpitaux Universitaires Paris Sud)
  - Germany (Barbara Hero, MD University Children's Hospital Cologne)
  - United Kingdom (Ming Lim, MD, PhD, Evelina London Children's Hospital)
  - Switzerland (Andrea Klein, MD, University Children's Hospital Basel)
  - USA (Mark Gorman, MD, Boston Children's Hospital)
- Critical advice provided by Marc Tardieu and Anne Berg

Specific Aims

- To determine the course of illness, prognostic factors, and treatment efficacy in an international database of children with OMS
- To create a registry of available biological material and MRI linked with clinical information in children with OMS
- Establish possibility, patient base to contact subjects for future studies
- To encourage further academic study, initiative, and publication, accelerating the future of OMS research

Study Design

- Longitudinal, observational natural history of consecutive subject visits at participating study sites
- Data collected only at clinically indicated visits (i.e. no study specific visits)
  - Subjects on immunotherapy: data entry anticipated every ~3 months
  - Subjects off immunotherapy: data entry anticipated every ~12 months
  - If no data entry within these time frames, automated query is sent to sites
- 'Tiered' enrollment structure
  - "Prospective": enrolled with 24 months of OMS onset
  - "Retrospective": enrolled >24 months after OMS onset
- Screening, recruitment plans
  - Query medical records for subjects with OMS onset within ~10 years
  - Where applicable, subjects will be contacted to offer enrollment

Inclusion Criteria

- Formal diagnosis of Opsoclonus Myoclonus Syndrome
  - Primarily based upon *Genoa Criteria*
  - Allows for “limited” forms of OMS
    - (opsoclonus and/or myoclonus/ataxia with neural crest cell tumor)
- Age of onset < 18 years old

Case Report Forms

- Initial Registry Visit
- Follow-up Registry Visit
- Biological Material/MRI Form

Initial Registry Visit

- Inclusion Criteria
- Demographic Data
- Autoimmune Disease History (patient, 1st degree relatives)
- Birth and Developmental History
- OMS Onset History
- OMS Relapse History

Initial Registry Visit

- Clinical Exam
- Tumor Assessment and Treatment
- Brain MRI Review
- CSF and Serum Studies
- Treatment Data
- Neuropsychological Assessment History
- Biological Material/MRI Imaging

Clinical Evaluation Data

- OMS Rating Scales
  - Mitchell and Pike OMS Severity Scale
    - Evaluates stance, gait, arm/hand function, opsoclonus, mood/behavior, speech
  - Scale for the Assessment and Rating of Ataxia (SARA)
    - Evaluates stance, gait, sitting, speech, finger chase, nose-finger test, fast-alternating hand movements, heel-shin slide
    - Aligned with the European Childhood Ataxia and Cerebellar Group
    - Validated in children ≥ 4 years old
- Interim course of illness, recovery, relapse
  - Relapse data of pivotal importance
    - Relapse: worsening of OMS symptoms lasting ≥ 72 hours (without better explanation)
    - Detailed information collected on possible relapse cause, pre-relapse OMS Score, maximum OMS score at relapse, treatment escalation, outcome

Brandsma et al Developmental Medicine & Child Neurology 2014, 56: 556–563

Additional Measures

- Developmental history
- Neuropsychological assessments
  - Composite score, outcomes recorded (where available)
  - WPPSI-IV, WISC-V, DAS, Bayley, Stanford-Binet
  - Suggested time points and scales

Follow-up Registry Visits

- Separate case report form, to be completed at each follow-up clinic evaluation

- Allows for continuous, accurate collection of data, as newly-acquired information is updated in each section

Biological Material/MRI Form

- As mentioned, biospecimens and MRI imaging data from OMS patients are incredibly limited
  - When available, material is mostly stored in local biobanks and radiology systems at treating hospitals, not accessible to outside researchers

- Our ‘virtual biorepository’ intends to capture:
  - Location and type of biological samples (collected specifically for research purposes) available to access for future research studies
  - Location of MRI imaging available to access for future research studies

Progress (to date)

- Regular conference calls with task force over past 2-3 years
- Evaluation of database structure, logistics
  - Location of central database
  - Budget calculations, differing scenarios
- Full-time program manager (Lauren Kerr) hired at Boston Children's Hospital using existing philanthropic funds
  - Mantz Fund for OMS Research, OMS Life Foundation, BCH Fund for OMS Research
  - Based within BCH Translational Neuroscience Center
- Finalized database protocol, case report forms (March 2018)
- Obtained IRB (ethics) approval (May 2018)

Progress (to date)

- Programmed REDCap database
  - Data collection, storage through REDCap (https://www.project-redcap.org/)
    - Electronic data capture system for clinical data management
    - Currently used in >100 countries to support >450,000 projects
    - Over 4000 active projects at Boston Children's Hospital alone
  - Supported through BCH Clinical Research Information Technology (CRIT)
  - Database testing, editing to be conducted as needed

- Nearly finalized registry policies
  - Data sharing and access
  - Inclusion of new sites
  - Expectations for participation
  - Authorship

Progress (to date)

- Status: Active enrollment!
  - Enrolled first subject on July 18, 2018
  - Currently have enrolled 16 subjects, total

Next Steps

- Identification, approval, and start-up of additional sites
  - Additional sites anticipated across US, Europe, UK
  - Onboarding initiatives to be led by current sites in each nation
  - In US, will use IRB reliance agreements as much as possible
- Obtain additional funding

Ongoing Challenges

- Funding & Support
  - Boston Children's responsible for primary fundraising efforts
    - To minimize costs, administrative and technical work will be centralized at Boston Children's, currently supported through philanthropic measures
  - Grant funding for OMS/rare diseases is limited
    - Applied for Pablove Foundation seed grant (not awarded)

Future Vision

- Once operational, we anticipate future studies will utilize our database as a “core” for research/recruitment
- Through these studies, we will seek additional funding to maintain and expand database capabilities
- Focus of anticipated studies: mechanisms of disease, clinical outcomes, MRI findings, biomarkers, surrogate markers, treatment efficacy
- Overarching goal: accelerate future of OMS research

Questions / Comments?