Clinical Trials in Rare Diseases – General Resources

Here we provide some general resources relevant to clinical trials in rare diseases, including a list of relevant articles and website links. We have also included a few key references specific to research in Batten disease. Please note that we cannot directly post the published articles. However, wherever available, we have provided a link to a free, downloadable version of the article. Please contact us if you wish to suggest other materials to be shared here.

Published Articles and Books

1. Biomarkers Definitions Working Group. Biomarkers and surrogate endpoints: Preferred definitions and conceptual framework. *Clinical Pharmacology & Therapeutics*. 2001; 69(3):89-95

2. Cialone J, Adams H, Augustine EF, Marshall FJ et al. Females experience a more severe disease course in Batten disease. *J Inherit. Metab. Dis.*2012; 35:549-555

3. Ciccetti D, Bronen R, Spencer S, et al. Rating scales, scales of measurement, issues of reliability: resolving some critical issues for clinicians and researchers. *J Nerv Ment Dis.* 2006;194(8):557-64.

4. Day, S. Dictionary for Clinical Trials. Second Edition. 2007. John Wiley & Sons, Ltd. West Sussex, England

5. Food and Drug Administration. Guidance for Industry: Qualification Process for Drug Development Tools

6. Gliklich RE, Dreyer NA, eds. Registries for Evaluating Patient Outcomes: A User's Guide. 2nd ed. Agency for Health Care Research and Quality. September 2010.

7. Griggs RC, Batshaw M, Dunkle M. Clinical research for rare disease: Opportunities, challenges, and solutions. *Molecular Genet and Metab*. 2009;96:20-26.

8. Hobart JC, Cano SJ, Zajicek JP, Thompson, AJ. Rating scales as outcome measures for clinical trials in neurology: problems, solutions, and recommendations. *Lancet Neurol.* 2007;6(12):1094-1105.

9. Kairalla JA, Coffey CS, Thomann MA, & Muller KE. Adaptive trial designs: a review of barriers and opportunities. *Trials*. 2012;13:145-153

10. Katz R. Evidentiary standards for drug development and approval. *NeuroRx*. 2004;1(3), 307-316
Free full text available via PubMed Central.

11. Kohlschuetter A & Schulz A. Towards understanding the neuronal ceroid lipofuscinoses. *Brain and Dev*. 2009: 499-502.

12. Kwon JM, Adams H, Rothberg PG, et al. Quantifying physical decline in juvenile neuronal ceroid lipofuscinosis (Batten disease). *Neurology*. 2011; 77(20):1801-1807

13. Marshall FJ, de Blieck EA, Mink JW, et al. A clinical rating scale for Batten disease. Reliable and relevant for clinical trials. *Neurology.* 2005;65:275-279

14. Lebrun A-H, Moll-Khosrawi P, Pohl S, Makrypidi G, et al. Analysis of the potential biomarkers and modifier genes affecting the clinical course of CLN3 disease. *Mol Med.* 2011; 17(11-12):1253-1261.

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Published Articles and Books (*cont'd*)

15. Lojewski X, Staropoli JF, Biswas-Legrand S, Simas, AM, et al. Human iPSC models of neuronal ceroid lipofuscinosis capture distinct effects of TPP1 and CLN3 mutations on the endocytic pathway. *HMG*

16. Murphy SM, Puwanant A, Griggs RC, et al. Unintended effects of orphan product designation for rare neurological diseases. *Ann Neurol*. 2012;72:481-490.

17. Patient Registries in the Field of Rare Diseases: Overview of the issues surrounding the establishment, management, governance, and financing of academic registries (free PDF available); Orphanet Report Series: Rare Disease Task Force report (June 2011)

18. Perlmutter J. Understanding Clinical Trial Design: A Tutorial for Research Advocates. *Research Advocacy Network – Advocacy Institute*

19. Rare Diseases and Orphan Products: Accelerating Research and Development; Institute of Medicine

20. Rubinstein YR, Groft SC, Bartek R. Creating a global rare disease patient registry linked to a rare diseases biorepository database: Rare Disease-HUB (RD-HUB). *Contemporary Clinical Trials.*2010;31:394-404.

21. Small Clinical Trials: Issues and Challenges; National Academy of Sciences

22. Strimbu K & Tavel JA. What are biomarkers? *Curr Opin HIV AIDS*. 2010;5(6):463-466

Websites / Online Resources

U.S. Food and Drug Administration (FDA)

- Clinical Trials and Human Subject Protection
- Center for Drug Evaluation and Research (CDER)
- Center for Biologics Evaluation and Research (CBER)
- Office of Orphan Products Development \
- Rare Disease Program
- Clinical Outcome Assessment Qualification Program
- Roadmap to Patient-Focused Outcome Measurement in Clinical Trials
- Qualification of Clinical Outcome Assessments (COAs)

National Institutes of Health (NIH)

- Patient Reported Outcomes Measurement Information System (PROMIS)
- Office of Rare Disease Research
- National Center for Advancing Translational Research (NCATS)

Clinical Trials in Rare Diseases – General Resources

Websites / Online Resources (*cont'd*)

Clinical Trials.gov

ClinicalTrials.gov is a registry and results database of publicly and privately supported clinical studies of human participants conducted around the world. Learn more About Clinical Studies and About This Site, including relevant History, Policies, and Laws.

National Organization for Rare Disorders (NORD)

"The National Organization for Rare Disorders (NORD), a 501(c)(3) organization, is a unique federation of voluntary health organizations dedicated to helping people with rare "orphan" diseases and assisting the organizations that serve them. NORD is committed to the identification, treatment, and cure of rare disorders through programs of education, advocacy, research, and service."

EU Clinical Trials Register

The EU Clinical Trials Register website contains information on interventional clinical trials on medicines. The information available dates from 1 May 2004 when national medicine regulatory authorities began populating the EudraCT database, the application that is used by national medicine regulatory authorities to enter clinical trial data. The EU Clinical Trials Register website launched on 22 March 2011 enables users to search for information which has been included in the EudraCT database

European Commission – Clinical Trials

This website provides access to policies, requirements, and guidelines for clinical trials conducted within the European Union. The site also links to other websites relevant to the conduct of clinical trials within the EU.

EveryLife Foundation

- Workshop on Clinical Evaluation of Rare Disease Treatments
- Rare Disease Workshop Series

Orphanet – Rare Disease Task Force

- Patient Registries in the Field of Rare Diseases

World Health Organization International Clinical Trials Registry Platform (ICTRP)

The mission of the WHO International Clinical Trials Registry Platform is to ensure that a complete view of research is accessible to all those involved in health care decision making. This will improve research transparency and will ultimately strengthen the validity and value of the scientific evidence base. The registration of all interventional trials is a scientific, ethical and moral responsibility.