

Overview

QuickTime™ and a
decompressor
are needed to see this picture.

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Disclosures

- Consultant: Actelion Pharmaceuticals, Shire HGT - honoraria donated to Mayo Clinic.
- Grant support: Miglustat in Niemann-Pick disease, type C – Actelion Pharmaceuticals, Inc. (PI)
- Honoraria: Stem Cells, Inc. (Chair, DMSB); Up-To-Date (Editor).
- Unlabeled drug use: Isofagamine and miglustat in LSDs

Topics

- Epidemiology
- Biology
- Perception
- Resources

Rare Diseases - Definition

- Prevalence < 200,000 US persons (Orphan Drug Act)
- Prevalence > 200,000 and “...there is no reasonable expectation that the cost of developing and making available in the U.S. a drug for such disease or condition will be recovered from sales in the U.S. of such drug”
- Orphan Drug Act, Pub. L. No 97-414, 96 Stat. 2049 (1984 as amended)

Diseases and patients

- ~ 7,000 rare diseases
- Most are genetic, most are IEMs
- 25-30 million affected in the US (i.e. > the population of Australia)
- The prevalence in affected individuals and their families is 100%

- Griggs RC, et al. MGM 2009; 96:20-6

Biology

- Mechanistic understanding is variable
 - Modifier genes
 - Epigenetic factors
- Highly variable phenotypes within diseases (even in siblings)
- Nervous system disease burden may be irreversible at diagnosis

Biology example: LSDs

- 50+ diseases
- Severe phenotypes expressed in CNS
- Multisystem manifestations
- Most result from enzyme deficiency
- Insidiously progressive
- Transducing the gene product has limited direct effect in CNS
 - ERT
 - EET
 - HSCT

LSDs - II

- Animal models helpful, but may not reproduce subtleties of human disease
- Interventions in animal models may not translate to humans
- Limited pool of candidates for human studies
- Few validated outcome measures or biomarkers for NS disease

Perception - classic quotes

- “You will never see this”
- “We were told that we were the only family in the * with this disease”
- “There is no treatment”
- “They said at the ER that they could not help”
- (*state/region/country/world)

Perception

- IEMs are poorly understood by physicians and the public
 - Delayed diagnosis
- Misperceived as “untreatable”
 - Failure to refer
- Symptoms often inappropriately attributed to the IEM
 - Burden of disease further increased

Perception II

- Lack of awareness limits competitiveness for resources
 - Reduced research and clinical funding

Resources

- Biology - technical tools
- Lay organizations
- Legislation
 - Orphan Drug Act
 - Safe Medical Devices Act
(Humanitarian Device Exemption)

Resources II

- Funding and related resources
 - ORD/NIH
 - CETT(collaboration, education, test translation) program
 - OPD grants
 - Academic-Industry partnerships
 - RDCRN
 - Repositories, core facilities

Responses

- Education
- Advancing basic science
- Partnerships (patients-physicians-investigators-regulators-industry)
- Creative approaches to clinical investigations (networks - natural history and trials)
- Data management

Questions, comments?