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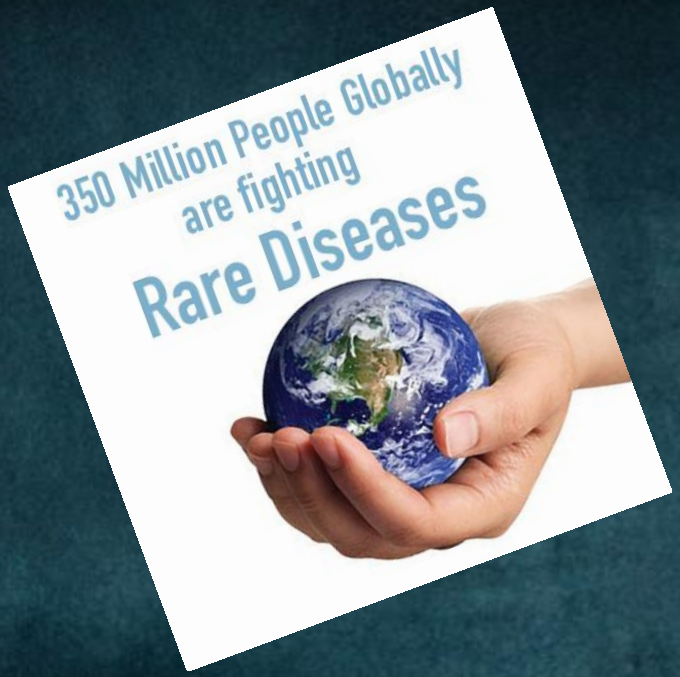
Clinical & Regulatory Challenges for Drug Development in Rare Diseases


350 Million People Globally
are fighting
Rare Diseases


30% of children with Rare & Genetic Diseases
will not live to see their 5th birthday
www.globalgenes.org
hope.
starts
here.


1 IN 10
AMERICANS LIVE WITH A RARE DISEASE


80 percent
of rare diseases
are caused by
faulty genes
globalgenes.org

Rare Diseases

- Definition varies by country and legislation - 1:2000 in the EU; < 200,000 in the US; <50,000 in Japan; <2,000 in all of Australia...
- Affect all body systems. Perhaps most common are:
  - –cancers
  - –neurology
  - –metabolic endocrine
  - –large % pediatrics with genetic origin

History of “Rare Diseases”

- Orphan drug legislation/regulation had, as its basis, tighter regulation of drugs following Thalidomide in the 1960’s
- Rare diseases are not “new;” have always been around just needed laws and regulation, along with political will
- US Orphan Drug Act Passed - first in the World followed by Singapore, Japan, Australia, EU, and many more

RARE DISEASES BY THE NUMBERS

A disease is defined as orphan in the U.S. when it affects fewer than

200,000 people

There are approximately

7,000 types of rare diseases and disorders

95% of rare diseases have no FDA-approved drug treatment

80% of rare diseases are genetic in origin

Approximately **50%** of those affected by rare diseases are children

30% of children with a rare disease will not live to see their fifth birthday

8: Average number of physicians visits before diagnosis

3: Average number of misdiagnoses

7+ years: Average time until diagnosis

SOURCES: National Organization for Rare Diseases, Global Genes Project

Studying a Rare Disease

- Small # of patients
- Live all over the country/world - rare diseases do not recognize country borders
- Drugs to treat Rare Diseases must be Safe and Effective for the disease
  - know a bit about efficacy at time of approval
  - know less about safety at time of approval
- What is known about the Natural History of the Disease

Studying a rare disease:

- Patient Awareness
  - Using Social Media not only to educate but as a means to study the natural history of a disease
- Difficult to Diagnose often misdiagnosed
  - Training future health care workers
  - Newborn screening
- Variations in the diseases - homogeneous / heterogeneous
  - Biomarkers

Clinical Trial Design

- Large double blind likely not possible
- Numbers of available/eligible patients limited
  - engage advocacy groups and social media
- May be competition for patients for some “in” diseases
- Multinational studies may be needed - but is there clinical expertise available in some areas of the world
- Small studies more susceptible to the effects of variability

Clinical Trial Design

- Careful design of the Study - power
- Carefully select the endpoint
- Seek early involvement of FDA/EMA/Regulatory Authorities
- Involve PATIENTS in planning the Clinical Trial!!
- Centers for Rare Diseases proposed

Designing the Clinical Trial

- Seek Scientific Advice/Pre-IND meeting
- Frequent interaction with Regulators - ask questions
  - avoids redundancy and saves “patients”
- If have sufficient power and effective therapy may have only one pivotal trial. Emphasis on MAY
- Attention to unmet medical need – flexibility by regulators

Designing the Clinical Trial

- In EU adaptive licensing an emerging concept
- New approaches for clinical studies being funded in 7th Framework Program
- In US NIH consortia studying certain diseases and groups of diseases
- New validated statistical design being explored
- Continual manufacturing concepts

How Safe is Safe

- Rare Safety Signals will manifest late
  - Took 20 years for first safety signals to appear - EPO
  - Tysabri - removed and then reintroduced to the market
  - More to be described
- Need for post marketing studies to determine safety signals as early as possible
- Always attention to Risk vs Benefit

Balance between regulation and cost and statistics

- Ethics and social mores
  - Vary in different parts of the world
- Subsidies - government/philanthropy/Venture capital
  - What will it be tied to?
- Bring the “payors” to the table
- Improving technology without increasing the cost
  - Finding difference uses for current therapies
- Coordinating Investments

Do We Need To SHARE More

- Partnerships
  - Public-private partnerships
  - Nations/states
    - Regulatory Agencies
    - Decrease Territorial imperative
  - Patient groups - Listen to the Patient. Patient involvement VERY important
  - Rare Disease Organizations - can assist with recruitment, education, cultural nuances
  - Data/Publications
- Development
  - Races between companies

Future

- Personalized Medicine
  - Gene Therapy
  - Will it alter regulation
- Data Analysis improvements

¿Questions?

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