

Day one-presentation-session III
Ron Christensen

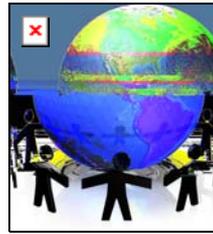
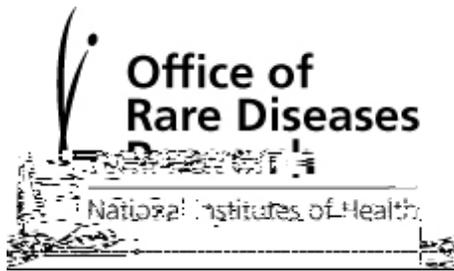
III Clinical Research, Patient Registries, Patient Care and Disease Management

Clinical Research and Patient Registries in Rare Diseases

Ron Christensen (REGISTRAT-MAPI)

Individuals with rare diseases have opportunities to participate in various types of clinical research programs that advance scientific knowledge and improve patient care. Clinical investigators are increasingly recruiting patients with rare diseases to enroll in academic and drug development clinical trials. Patient registries are clinical research tools with a wide variety of applications and benefits. These and other types of clinical research programs in which patients with rare diseases may participate, such as expanded access programs, will be presented in this session.

- Clinical trials
 - Biopharmaceutical product development
 - Academic/governmental research
 - Investigator initiated studies
- Patient registries
 - Registry sponsorship
 - Types of registries
 - Benefits to participants
- Expanded access programs
- Post-marketing requirement studies
- Direct-to-patient programs



Uniting Rare Diseases

Advancing Rare Disease Research: The Intersection of Patient Registries, Biospecimen Repositories and Clinical Data

Session III Clinical Research, Patient Registries, Patient Care and Disease Management

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Clinical Research & Patient Registries for Rare Diseases

Clinical Research for Rare Diseases

- Clinical Trials
 - Biopharmaceutical product development
 - Academic / governmental research
 - Investigator initiated studies (IIS)
- Expanded Access Programs
- Post-marketing Requirement Studies

Orphan Drug Development

- 339 approved orphan drugs in the U.S.
- FDA is approving approximately 14 applications per year
- Total of 139 between January 1, 2000 & October 31, 2009.
- In 2008, 38% of all NME's approved by the FDA were orphans.

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Pharma's Increased Investment in Orphan Drug Development

- Several big pharma companies have expanded their development pipelines to include orphan diseases.
- Biotech companies with orphan products are acquisition targets for big pharma companies.
- Biotech companies have demonstrated that orphan drug development is a viable business model.
- Orphan drugs may turn out to be “blockbusters.”
- A “safety first” regulatory mindset makes finding blockbuster markets more difficult.

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Pharma's Increased Investment in Orphan Drug Development (cont.)

- Healthcare reform legislation is likely to include a number of features that will make development of orphan products more attractive.
- Genomics and orphan drug development may help companies adapt to the broader demands of personalized medicine.
- Engaging in orphan drug research brings much needed public relations benefits.

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NIH Programs

- Therapeutics For Rare & Neglected Diseases Program (TRND)
 - \$24 million in 2009 NIH budget.
 - NIH will take on early stage drug development to “de-risk” compounds intended to treat rare diseases.
 - Goal is to entice private sector partners to develop drugs by making the economics more attractive.
- NIH Challenge Grants for rare diseases and registries
- Comparative effectiveness research (CER)
 - \$400 million from the American Recovery and Reinvestment Act of 2009 for CER
 - \$48 million for registries

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Expanded Access Programs

- Also called compassionate use programs or named patient programs.
- Allows patients to receive promising, but not fully studied or approved therapies, when no other treatment option exists.
- Generally implemented after evaluation of Phase III data and prior to product approval, i.e., under the IND.
- Safety data required; clinical and product utilization data varies.

Post-Marketing Requirement Studies

- May be mandated as a condition of product approval (FDAAA 2007).
- Identify new safety signals & quantify adverse event rates.
- Evaluate treatment outcomes and disease status.
- Evaluate real world product use, including off-label use.
- Monitor adherence to treatment guidelines.
- Provide product & disease-related information to physicians & patients.
- Often observational studies / registries.

Patient Registries for Rare Diseases

Definition of a Registry

Guidance for Industry: Good Pharmacovigilance Practice and Pharmacoepidemiologic Assessment

<http://www.fda.gov/cder/guidance/index.htm>

“an organized system for the collection, storage, retrieval, analysis and dissemination of information on individual persons exposed to specific medical intervention who have either a particular **disease**, a **condition** (e.g., a risk factor) that predisposes [them] to the occurrence of a health-related event, or prior **exposure** to substances (or circumstance) known or suspected to cause adverse health events.”

Definition of a Registry

AHRQ

Registries for Evaluating Patient Outcomes: A User's Guide

“A patient registry is an **organized system** that uses observational study methods to collect uniform data (clinical and other) to evaluate specified outcomes for a population defined by a particular **disease, condition, or exposure**, and that serves one or more predetermined scientific, clinical, or policy purposes.”

Registry Sponsorship

- Biopharmaceutical industry
- Academic / governmental
- Investigator initiated
- Advocacy groups
- Professional societies

Registry Designs

- Disease (naturalistic, natural history)
- Product or medical device
- Product safety
- Pregnancy
- Patient (caregiver) reported
- Comparison groups (e.g., internal, external, historical)

Benefits of Registries

- Obtain “real world” therapeutic effectiveness and safety data
- Rare adverse events can be detected with large patient numbers
- Flexible, multi-faceted, e.g., applications, sub-studies
- Heterogeneity among numerous investigative sites
- Registry subjects are heterogeneous
 - Various treatments
 - Concomitant medications
 - Co-morbidities

Benefits of Registries (cont.)

- Usual diagnostic and follow-up procedures can be used rather than “research” procedures
- Can be conducted in any phase of product development or independently
- Research collaboration with interactive communication & data reporting to investigators & patients
- Hypothesis generation when an “a priori” hypothesis is undefined
- Supportive data for product label extensions
- Evidence-based medicine for outcomes & reimbursement

Applications of Patient Registries

- Effectiveness & safety of treatment
- Identification of patients for clinical trials
- Repository for biospecimens & clinical data
- Humanistic & economic outcomes
 - Patient reported outcomes / quality of life
 - Compliance / tolerability / satisfaction
 - Cost effectiveness
 - Reimbursement
 - Healthcare utilization
- Treatment patterns & product utilization
- Continuous quality improvement & standards of care

Clinical Research & Patient Registries for Rare Diseases

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