The Antiretroviral Pregnancy Registry (APR): Industry Perspective On a Successful Collaboration

by

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ILF/CIPHER Thematic Roundtable on Paediatric ARVs
Room St. Moritz, Starling Hotel, Geneva, Switzerland
Monday, 7 March 2016, 13:00 – 16:30 CET
The APR: Purpose

• International registry jointly sponsored by manufacturers of FDA approved and marketed antiretroviral (ARV) drugs indicated for the treatment of HIV and Hepatitis B
  • FDA Mandated

• Key Objectives of the APR:
  o Provide early warning signal of major teratogenicity
  o Estimate risk of major birth defects and compare to that of general population
  o Supplement data from animal toxicology, clinical, and other epidemiologic studies
  o Assist clinicians and patients in weighing potential risks and benefits of treatment
The APR: Mechanism

- Prospective exposure-registration cohort study
- Voluntary registration of prenatal exposures by treating healthcare providers
- Prospective reporting of pregnancies prior to knowledge of pregnancy outcomes

- Healthcare providers:
  - Register pregnant women exposed to ARV
  - Report data on ARV exposure throughout pregnancy
  - Provide fetal/neonatal outcome data
The APR: Mechanism

Prospective

Retrospective

Clinical Studies

Timing, Dosage, Type of Antiretroviral Drug Use, Concomitant Exposures, and Pregnancy Outcome/Birth Defect at Time of Delivery

Primary Analysis

Prevalence = \frac{\text{number of defects}}{\text{number of live births}}

*MACDP 3/100 live births
^TBDR 4/100 live births
1st trimester vs 2nd & 3rd trimester

Secondary Review for Clusters and Patterns

Secondary Analyses

*MACDP = Metropolitan Atlanta Congenital Defects Program;
^TBDR = Texas Birth Defects Registry
The APR: Mechanism

• 26 current Sponsors representing 94 products
  o 45 brand named single entity drugs or fixed dose combinations (FDC)
  o 49 generic versions

• Primary Analyses: Birth defects data are reviewed, analyzed and interim report published every six months

• Data Dissemination: Interim report available to the public through APR website: APRegistry.com

• Ad Hoc Analyses: Reviewed for scientific merit and approved by publication committee
  • Sponsoring companies can request additional analyses on their products
  • Advisors can lead additional analysis of interest if data permits
  • Publication committee can recommend additional analyses of general interest
The APR: Funding and governance

- Funded in equal parts by all the sponsoring companies

- Overseen by independent Advisory Committee with members from CDC, NIH, FDA, Office of the Global AIDS Coordinator, patient advocate and practicing physician specialists

- Policy document details governance and operations
  - Changes are ratified by the steering committee

- INC Research Coordinating Center runs the registry on behalf of the sponsors
The APR: Governance

Sponsors

Advisors

Co-Ordinating Center

APR Steering Committee

Subcommittees

- Birth Defects
- Publications
- Methods
- Data Integration
- Improve reporting
- Ad Hoc analyses of general interests

Funding

Operations
INC Research Coordinating Center

The coordinating Center is responsible for:

- Providing case management, reporting, data analysis, and generation of Interim Reports
- All day-to-day functions associated with the conduct of the Registry
- Forward reports containing maternal and/or fetal adverse events to the Sponsors as documented in the AEMP (via AE email notifications)
- Coordination and organization of regular and ad hoc meetings
- IRB submissions and updates
- Assisting with or writing abstracts, manuscripts, and other documents
- Management of and updates to the APR website
- Other duties as agreed upon by the Steering Committee
The APR: Successes

• 25 years of unique collaboration
• Pooling of resources is efficient and cost effective
  • The only registry to include all drugs used in treatment of a disease
• Comprehensive, single point of reference & resource for patients, physicians, regulators and researchers

• The first to develop an Advisory Committee blending government, consumers and the scientific community
  • Independent advisory committee to maintain data rigor and scientific integrity
The APR: Challenges

• Stakeholders are also market competitors with competing interests
• Managing requests to data mine with ‘checks and balances’ via registry policies
• Sustaining Registry awareness activities to maintain enrolment
• Regulating rising operational costs
• The continued success of the Registry depends on active participation by healthcare providers
The APR: Summary

• Include all stakeholders in the program
• Engage the industry scientists from the outset
• Multipronged approach to problem solving
• Publish reports that are critical to patients, healthcare providers and scientists
  • e.g. APR interim report
  • (Potential) CIPHER reports on pediatric HIV epidemiology
• Program awareness activities are key to success
Questions
# The Antiretroviral Pregnancy Registry

*Ongoing since January 1989*

**Collaborative Project Sponsored by:**

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Submission of Data

• Registry data forms and instructions for completion are available on the Registry website: APRegistry.com
  – Completed data forms are submitted to the Registry via toll free fax, email, mail, or the electronic data collection (EDC)

• For additional information or to enroll a patient, please contact the Registry Coordinating Center by email at SM_APR@incresearch.com or by phone at 1-800-258-4263.
  – The process is easy and our knowledgeable, friendly staff are available to answer your questions.
The Antiretroviral Pregnancy Registry
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