New Paradigms in Drug Discovery:
How Genomic Data Are Being Used to Revolutionize
the Drug Discovery and Development Process

Pharmacy Benefit Management and Pharmacogenomics

March 21, 2012

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Drug Discovery and Development: Pre- and Post Approval Worlds

Current paradigm is static

Assessor body

Regulators

Payers

Evidence focus

- Quality, safety, efficacy
- Benefit-risk profile

- Relative efficacy/effectiveness
- Cost vs. health benefit
- Budget impact

Studies / Data

- Emphasis on RCT, most often placebo-controlled

- Active controlled RCT
- Observational studies
- Cost effectiveness / utility analyses
- Budget impact analyses

Adapted from Eichler et al, Nature Rev Drug Disc, 2010
Drug Discovery and Development: Pre- and Post Approval Worlds Are Colliding

Future paradigm is dynamic

Approval

Assessor body

Regulators

Payers

Dedicated relative efficacy / effectiveness assessment?

Evidence focus

• Quality, safety, efficacy
• Benefit-risk profile

• Cost vs. health benefit
• Budget impact

• Relative efficacy/effectiveness

Studies / Data

• Emphasis on RCT, most often placebo-controlled

• Cost effectiveness / utility analyses
• Budget impact analysis

• Active controlled RCT
• Adaptive Ph III-IV trials
• Observational studies
• Meta analysis

Adapted from Eichler et al, Nature Rev Drug Disc, 2010
A more practical view

Clinical Utility

Homogeneity determined by inclusion and exclusion criteria of clinical protocol

Clinical Effectiveness

Heterogeneity of real world exposure

Approval
A more practical view

Clinical Utility

Approval

Clinical Effectiveness

Homogeneity determined by inclusion and exclusion criteria of clinical protocol

Heterogeneity of real world exposure

Pharmacogenomics, Personalized Medicine
Efficacy, Safety and Effectiveness is mostly a stakeholder perspective …

- As regulators and payers have different perspectives, responsibilities, and incentives for decision making, the need for evidence varies
  
  > **Regulatory agencies** focus on **efficacy and safety**
    
    – Increasing safety hurdles (e.g., REMS in US, RMP in EU)
    
    – Cost assessment no part of decision-making
  
  > **Payer / HTA body** focus on **effectiveness**
    
    – Cost can play a critical role in decision-making
    
    – Off label use (e.g., Avastin v. Lucentis for macular degeneration)

- Drug development programs are under pressure to meet growing and divergent demands of different stakeholders, but…

REMSS = Risk evaluation and mitigation strategies; RMP = Risk Management Plan
… but the lines are starting to blur.

- Regulators (US and Europe alike) are increasingly interested in comparative data and outcomes research

- Demand for more (post-market) safety data cannot be met by RCTs
  - FDA (Sentinel network)
  - EMA (European Network for Centers for Pharmacoepidemiology and Pharmacovigilance, ENCePP)

- Reimbursement bodies call for value-based pricing…tied to demonstration of comparative effectiveness in real-world
  - Germany: Federal Joint Committee requires drug makers to demonstrate greater efficacy for a new compound in order to charge more
  - UK: NHS to introduce value-based pricing in 2014 that includes factors such as therapeutic innovation, burden of illness, wider societal benefits (whatever that means…)

**Notes:**
- EMA = European Medicines Agency; UK = United Kingdom; NHS = National Health Service
Strategic Partnerships Emerge

Pfizer's Deal with Medco's UBC Could Shed Light on New Personalized Rx Opportunities

November 02, 2011

Pfizer’s Deal with Medco’s UBC Could Shed Light on New Personalized Rx Opportunities

By Turna Ray

Pfizer’s new research collaboration with Medco subsidiary United BioSource Corporation is in line with a growing trend among drug developers to work with companies that house large databases of patient data in an effort to advance personalized therapies.

The Pfizer deal is the second such agreement that UBC has signed in the last six months. In June, Sanofi-Aventis announced that it would conduct comparative effectiveness research with UBC in order to make strategic decisions about which drugs to advance in its pipeline. The deal may also help Sanofi opportunistically develop personalized medicines (PGx Reporter 6/29/2011).
PBM: Leverage of Database and Patient Access

What if …?

Retrospective Research

Prospective Research

Impact of Proton Pump Inhibitors on the Effectiveness of Clopidogrel After Coronary Stent Placement: The Clopidogrel Medco Outcomes Study

Rolf P. Kretz, M.D., Eric J. Stanek, Pharm.D., Ronald Aubert, Ph.D., Jianying Yao, M.S., Jeffrey A. Broall, M.D., Ph.D., FACC, Zeruemenay Desta, Ph.D., Todd C. Skaar, Ph.D., J. Russell Teagarden, D.M.H., Felix W. Fruch, Ph.D., Robert S. Epstein, M.D., and David A. Flockhart, M.D., Ph.D.

Clinical News

Medco Launches Plavix®, Effient® Comparative Effectiveness Study Examining Role of Genetics

Study to determine whether effectiveness of Plavix is similar to Effient based on patient’s genetic makeup

Genetics for Generics™ - with Plavix going generic in 2011 a financial savings may be found with widely used blood thinner

FRANKLIN LAKES, NJ, Oct. 20, 2009 – Medco Health Solutions, Inc. (NYSE:MHS) today announced it will conduct a head-to-head study of Plavix® (clopidogrel) and Effient® (prasugrel) that will examine the effectiveness of these drugs in heart patients is impaired by their genetic makeup.
Example:
Safety and efficacy of clopidogrel vs. prasugrel

Clopidogrel versus Prasugrel all comers

Safety: clopidogrel has better profile

Example: Safety and efficacy of clopidogrel vs. prasugrel

Clopidogrel versus Prasugrel all comers

Clopidogrel 2C19 stratified

Example:
Study Comparative Effectiveness

Do patients who are CYP2C19 extensive metabolizers benefit from clopidogrel therapy similar to patients who are on prasugrel?

Not just clinical, also economical impact

- Clopidogrel going generic in May 2012
  > Medco has approx. 0.9mm patients on clopidogrel → approx. 4.5mm total US
  > Approx. cost /patient /day = $4 → $18mm drug spend /day or ~$6.5b /year
  > Assume 75% generic savings → approx $5b in annual savings

- At the same time prasugrel sales are slow:

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- Personalized Medicine
  > Assume genetic test costs $200 → approx. $1b annual cost
  > 5 – 25% of patients are PM or IM
Personalized Medicine Example:
Delay need, then when needed find right biologic

1. Delay cycling to and between biologic therapy.
2. Increase chance of being on the right drug at the right time.
3. Reduce Rx waste and toxicity exposure without therapeutic benefit

Access to longitudinal pharmacy and medical claims data critical
What would happen if payers were to...

- Require comparative effectiveness data based on personalized medicine?
- Pay only if a drug actually works?
- Initiate coverage with evidence development (CED) strategies?
- Identify and encourage patients to participate in clinical trials?
- Co-sponsor clinical trials?
- Provide pharmacy, lab and outcome data for research?
- Partner with industry to develop more personalized medicines faster?
Thank You!

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