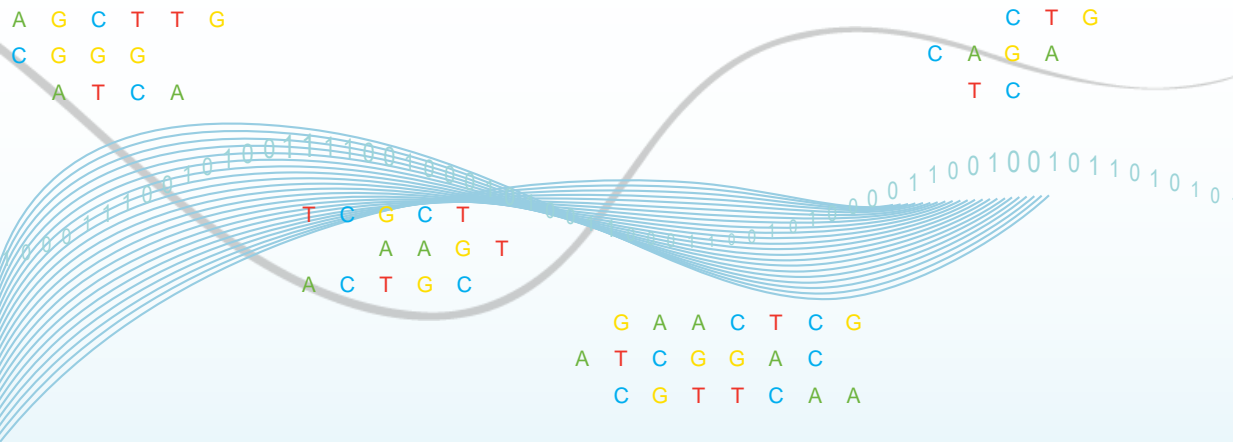


New Paradigms in Drug Discovery: **How Genomic Data Are Being Used to Revolutionize the Drug Discovery and Development Process**

Pharmacy Benefit Management and Pharmacogenomics



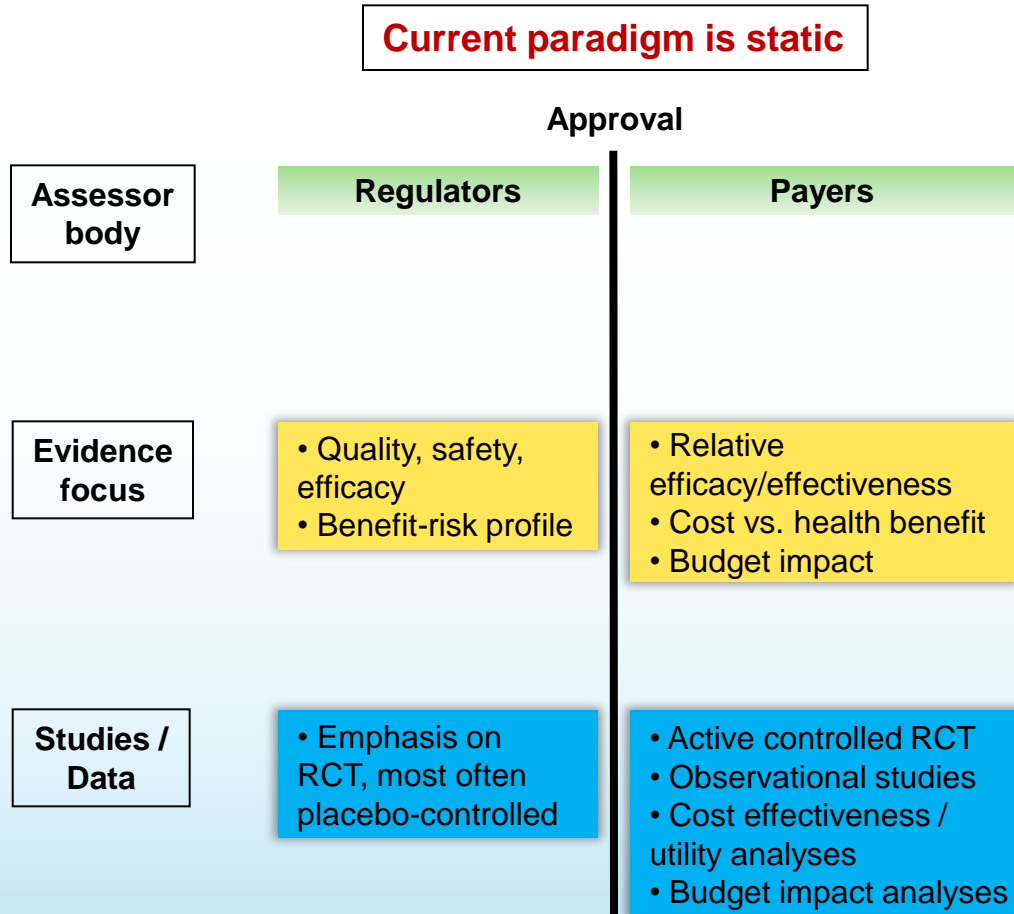
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UBC
United BioSource Corporation
Evidence Matters®

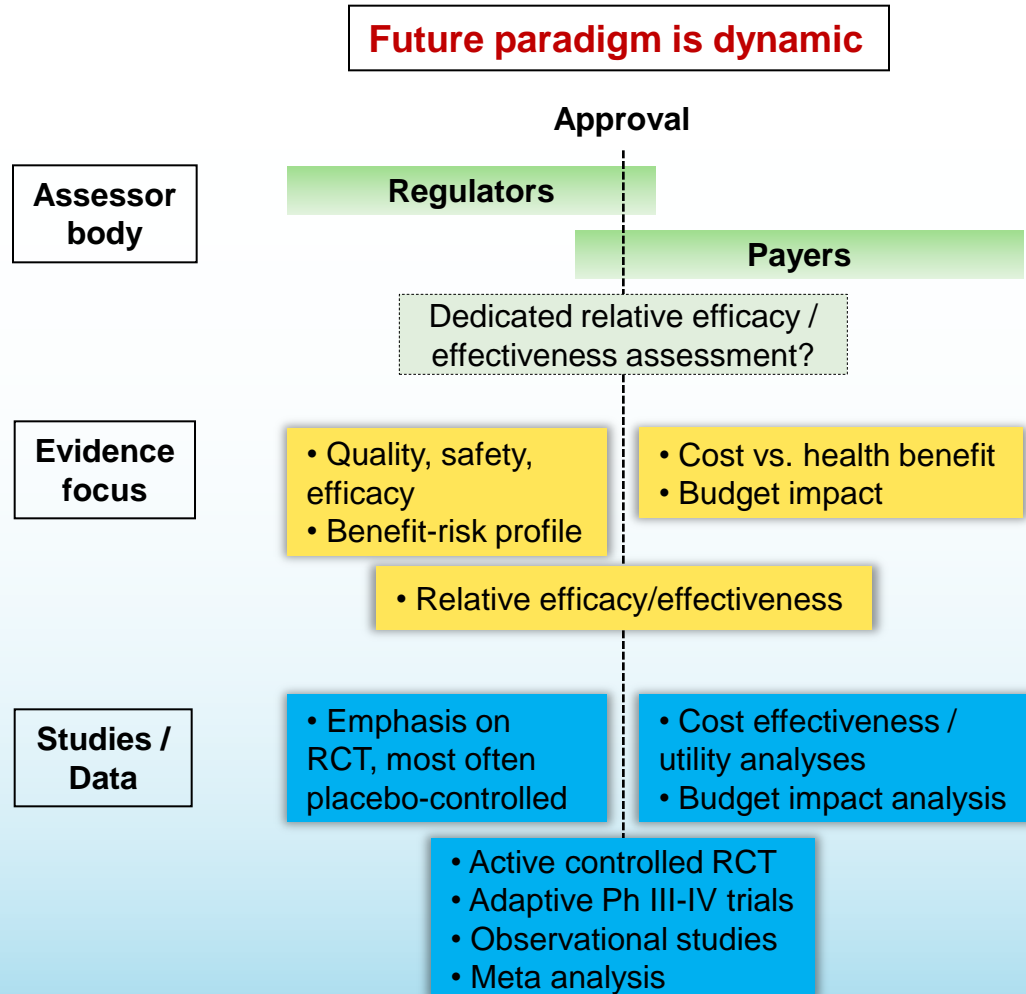
March 21, 2012

Felix W. Frueh, PhD
President
Medco Research Institute

Drug Discovery and Development: Pre- and Post Approval Worlds



Drug Discovery and Development: Pre- and Post Approval Worlds **Are Colliding**



A more practical view

Approval

Clinical Utility



Homogeneity determined by inclusion and exclusion criteria of clinical protocol

Clinical *Effectiveness*



Heterogeneity of real world exposure

A more practical view

Approval

Clinical Utility



Homogeneity determined by inclusion and exclusion criteria of clinical protocol

Clinical *Effectiveness*



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...**

... 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...)

Strategic Partnerships Emerge

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Drupal.behaviors.print = function(context) {window.print();window.close();}>
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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. Kreutz, M.D., Eric J. Stanek, Pharm.D., Ronald Aubert, Ph.D., Jianying Yao, M.S., Jeffrey A. Breall, M.D., Ph.D., FACC, Zeruesenay Desta, Ph.D., Todd C. Skaar, Ph.D., J. Russell Teagarden, D.M.H., Felix W. Frueh, Ph.D., Robert S. Epstein, M.D., and David A. Flockhart, M.D., Ph.D.

Clinical News

medco®

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

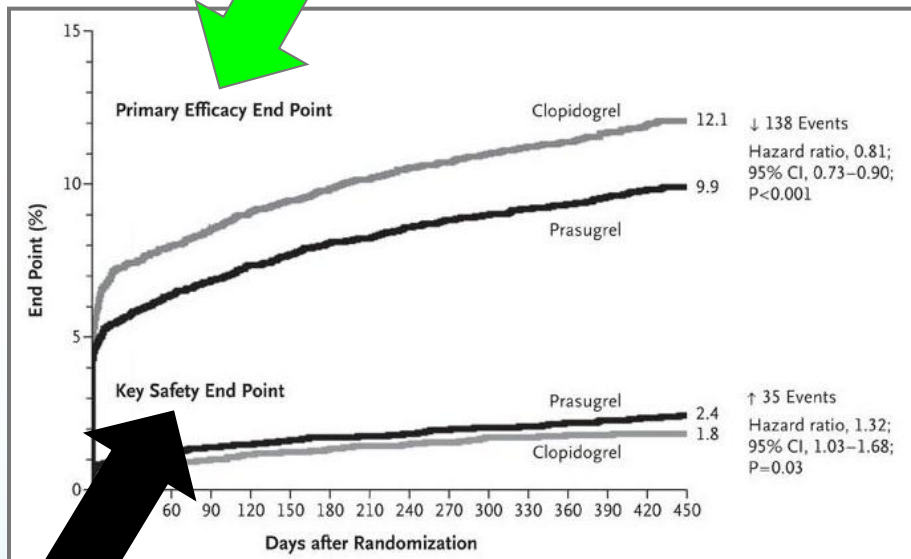
Genetics for Generics™ - with Plavix going generic in 2011 a financial savings may be found with widely used blood thinner

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 the effectiveness of these drugs in heart patients is impacted by their genetic makeup.

Example:

Safety and efficacy of clopidogrel vs. prasugrel

Clopidogrel versus Prasugrel all comers



Safety: clopidogrel has better profile

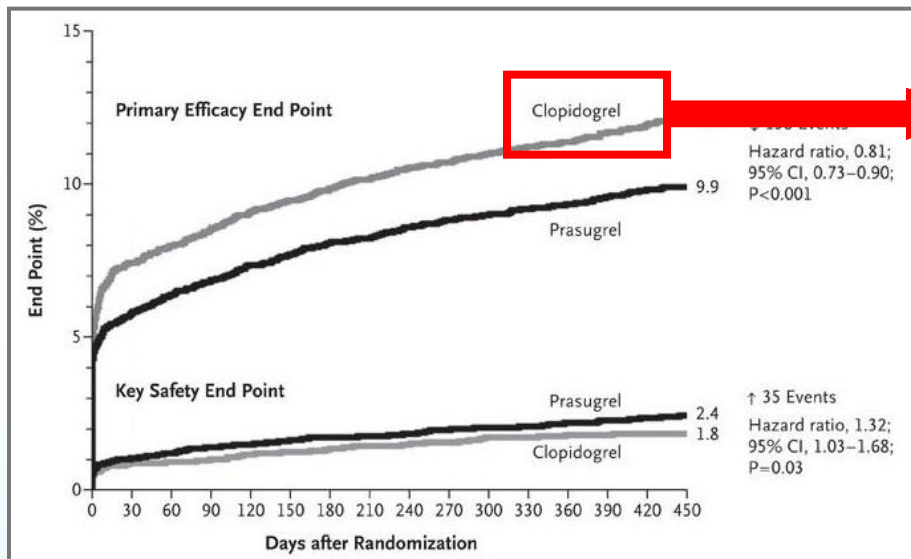
Source: N Engl J Med 2007;357:2001-15. and N Engl J Med 2009;360:354-62.

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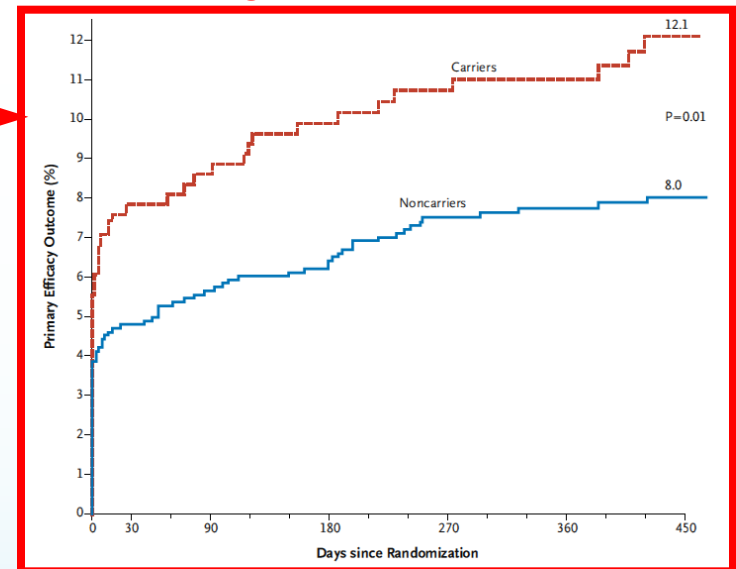
Example:

Safety and efficacy of clopidogrel vs. prasugrel

Clopidogrel versus Prasugrel all comers



Clopidogrel 2C19 stratified

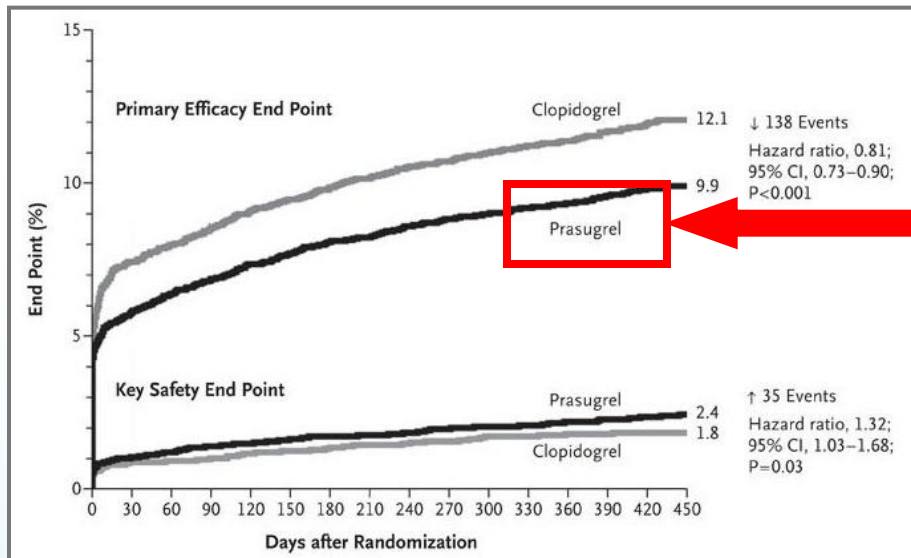


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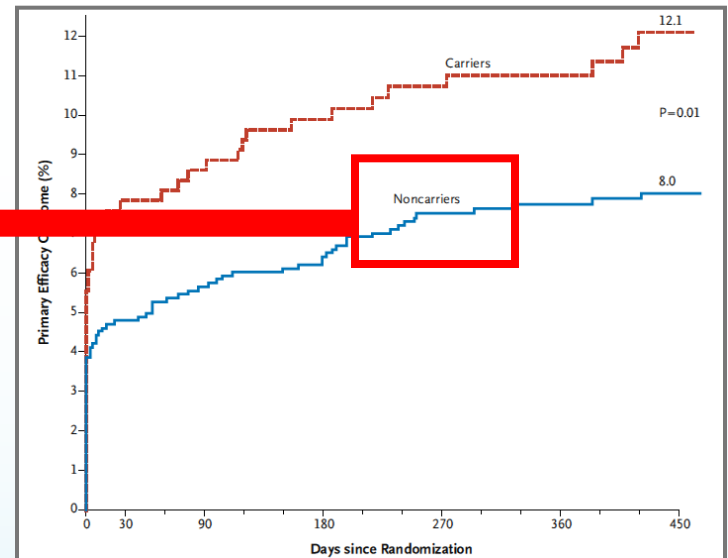
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Example: Study Comparative Effectiveness

Clopidogrel versus Prasugrel all comers



Clopidogrel 2C19 stratified



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:

Q4 2010	Q1 2011	Q2 2011	Q3 2011
\$47mm	\$56mm	\$72mm	\$84mm

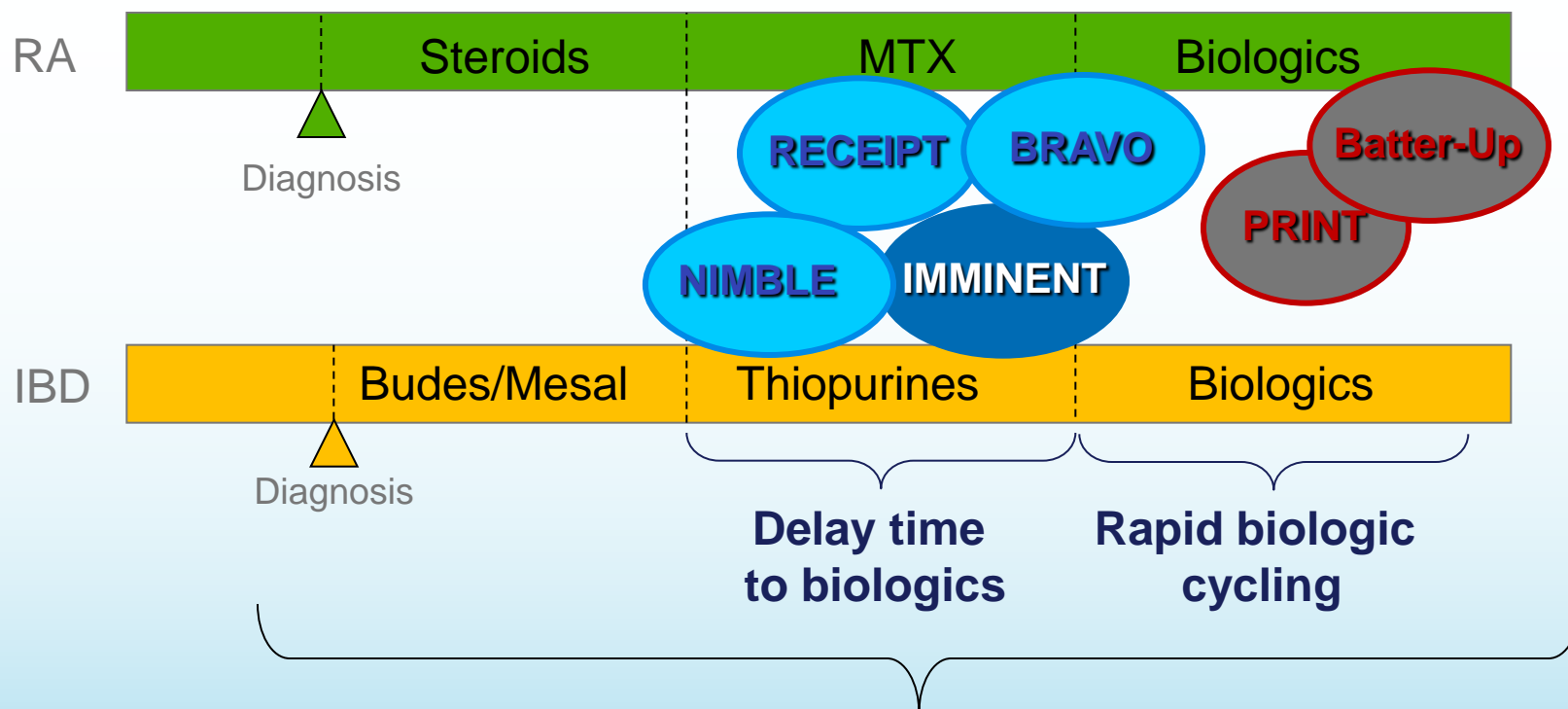
■ Personalized Medicine

- > 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

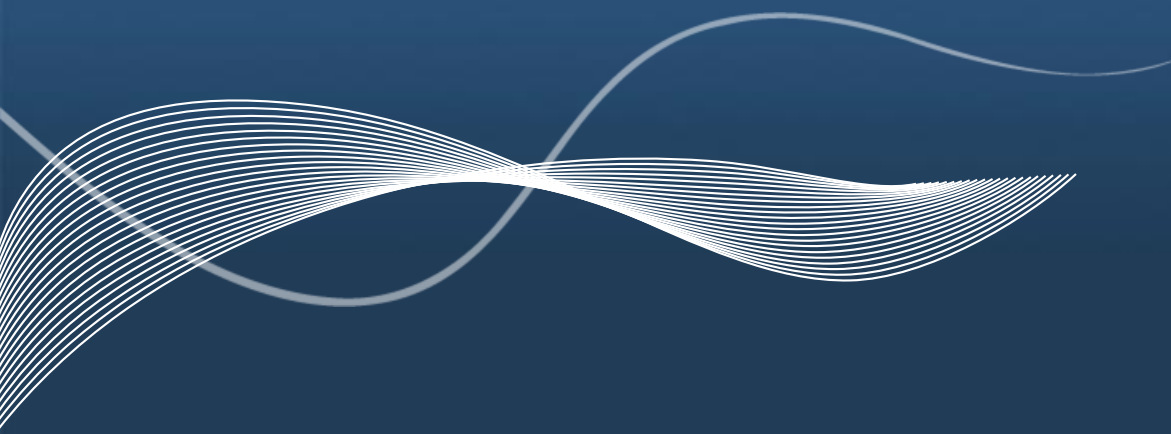


**Access to longitudinal pharmacy
and medical claims data critical**

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 !



Felix_Frueh@medco.com