Comparative Effectiveness Research (CER) and Pharmaceutical Companies

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CER represents:

1. The next logical step in the progression of more rigorous information about new healthcare technologies

2. A necessary input for a value-driven healthcare system
History of Pharmaceutical R&D

**CLINICAL PRACTICE**

- **Early 20th Century**
  - Flexner Report led to dominance of biomedical model of medical care in the US (Education, Research, Practice)

- **Mid-Late 20th Century**
  - Rapid growth in biomedical science and new technologies
  - Physicians primary decision makers
    - Lack of coherent synthesis of knowledge enables practice variation
      - Wennberg/Dartmouth Atlas

**PHARMACEUTICAL R&D**

- **Early 20th Century**
  - Little Regulation
  - Few Effective Medicines

- **Mid-Late 20th Century**
  - Growth of Modern Pharmaceutical Industry
  - Regulation of Pharmaceutical Marketing & Sales
    - Safety & Efficacy – RCTs
  - Limited barriers to market access
    - MD as learned intermediary
End of 20th Century

**CLINICAL PRACTICE**

- Emergence of Evidence-based Medicine
  - Cochrane Collaboration
  - AHCPR $\rightarrow$ AHRQ
  - NCQA, USPSTF
- Appearance of Practice Guidelines and Performance Metrics (downward pressure on practice variation)
  - Pay-for-Performance
- Exploding Health Care Costs
  - Health Technology Assessment to permit greater restriction on coverage and reimbursement
    - Australia, Ontario
    - UK (NICE)

**PHARMACEUTICAL R&D**

- More information required by regulatory bodies on the efficacy and safety of new products
  - New tools for R&D
- Outcomes Research Studies & Health Economic Models provide additional information on value and therapeutic role for new technology
  - Disease Management tools & programs to ensure that providers and payers obtain value from new technologies
The 21st Century

- **Mitigating the continued rise of healthcare costs is now a public priority**
  - The pharmaceutical industry is being asked to be part of the solution in US Healthcare Reform
  - Payers and providers are “managing” access to new and expensive technologies through a variety of methods that will increase downward pressure on industry ROI
    - HTA is widely adopted by payers
      - Europe, Growing in Asia
      - Managed Care in US
      - MedCAC
    - Tiered Formularies and Benefits
    - Coverage with evidence development
    - Risk sharing Contracts
**Early Efforts in the US in the Application of CER to Health Policy decisions**

- **MMA**
  - Comparative effectiveness (e.g., EBM) – Section 1013 (AHRQ)

- **CMS**
  - CMS endorsement of HECON in MMA formulary design
  - Coverage with Evidence Development
  - Coverage with Conditions

- **DERP (17 State Consortium - Medicaid)**
  - Evidence-based Drug Class Reviews

- **AHRQ**
  - Centers for Research & Education in Therapeutics (CERTs)
  - Evidence-based Practice Centers (EPCs)
  - Effectiveness Health Care Program
    - Comparative Effectiveness (EPCs and DeCIDE)
    - Network of Research Centers (DEcIDE)
    - Eisenberg Center for Clinical Decisions and Communications (Oregon)
How will the Pharmaceutical Industry Adapt?

- Some ("enlightened") companies will develop new strategies for:
  - Research & Development
  - Commercialization
  - Industry Policy Initiatives

ENHANCE VALUE DERIVED BY PATIENTS, PROVIDERS, & PAYERS
The Evolving Paradigm of Drug Development

- Basic Science
- Clinical Research
- Outcomes Research
- Disease Management

Traditional

- Value-based Development
  - Sub-populations that benefit most
  - Stratified / Personalized Medicine
    - Biomarker / Genetic Diagnostics to Target Treatments

1990’s

2007 & Beyond
Strategy for Traditional Drug Discovery

**MICRO Considerations**
- Understand the molecular basis of the disease
- Select a therapeutic target
- Link the therapeutic target to a defined mechanism of action
- Discover a lead compound that is safe, effective, and novel
- Always have backup compounds with structural diversity

**MACRO Considerations**
- **Target Populations**
  - Prevalence / Incidence
  - Unmet medical need
- **Economic Considerations**
  - Willingness-to-pay
  - Competitiveness of market environment in disease area
New R&D Paradigm Goals

- **Enhanced Efficiency**
  - Decrease Cycle Time
    - Adaptive Clinical Trials
  - Decrease Late Stage Failures

- **Enhanced perception of value to payers, providers and patients**
  - Greater product differentiation
    - Biomarkers, Outcomes
  - Stratified / Personalized Medicine
    - Targeting of therapy to those patients who will benefit most
      - Biomarkers, Diagnostics (responders/non-responders)
    - Decrease toxicity
Building Blocks of R&D Strategy

- Deep Disease Understanding – Unmet/Unsatisfied Medical Need and Patient Heterogeneity (Natural Hx, Response to Tx)
- Patient Subpopulation Identification (Biomarkers, PK/PD, Gene Arrays)
- HTA/EBM Comparative Framework Analysis of Potential Value vs SOC
- Research Studies to Support Registration and Demonstrate Value in Targeted Subpops
- Tailored Tx
- HTA
- Q-Pharm
- Epi/HSR
Strategies for the New Paradigm

- **Early Development**
  - Greater reliance on biomarkers including genomics combined with modeling for predictive efficacy and toxicity
  - Combine dose-finding and POC studies

- **Late Development**
  - Simulated clinical trials
  - Adaptive clinical trial designs
  - Large simple trials
  - Stratified Phase III development
  - Parallel timelines
  - Active comparators in Phase III studies

- **Life Cycle Development**
  - Effectiveness Studies
  - Treatment Registries
  - Novel reimbursement and contracting strategies

Ongoing Consultation with Regulatory Authorities and Payers
Commercialization Opportunities

- Increased consultation with scientific and payer thought-leaders during development can create true champions to enhance the “pull” in the market at launch.

- Better differentiation of the value of new products will mitigate downward pressure on price.
  - Need to develop value story tailored to payers that enable payers to “do the right thing” and provide access.
  - Understanding value story across sub-populations opens the door to novel contracting and pricing strategies.
    - Risk Sharing
    - Benefit-based coverage
Enhancing the Value Proposition for the Patient and Payer

**Goal:** Improve *individual* patient outcomes and health outcome predictability through *tailoring* of treatment.

**One size fits all**  
*Lower predictability of health outcomes*  
(e.g. most pharma products today)

**Degree of Tailoring**  
Assess spectrum of patient response to therapy;  
Stratify patient populations;  
Optimize benefit / risk based upon biomarkers including Imaging, Clinical Observation, Patient Self-report.

**Targeted Therapy**  
*Higher predictability of health outcomes*  
(e.g. oncology products comprising drug and companion diagnostic)
The Patient Therapeutic Continuum

Mark R. Trusheim, M.S., Ernst R. Berndt, Ph.D., and Frank L. Douglas, Ph.D., M.D.,
“Stratified Medicine: Strategic and Economic Implications of Combining Drugs and Clinical Biomarkers”,
One view: Large Revenues Are Possible

(trillions of patients, average yearly price in $thousands)

Trusheim et al.
My view: Substantial ROI is Possible

- Greater value may translate into:
  - Some price premium
  - More rapid access and uptake
  - Better adherence and compliance

- This can offset decreases in revenues associated with smaller target populations
Industry Transformation: A New and Sustainable Business Model

- More Valued Treatments
- More Efficient Development
- Stronger Partnership with Payers and Providers

- Restructuring to provide greater flexibility to manage R&D risk
  - Fully Integrated Pharmaceutical Network (FIPNET)
Challenges

- Industry needs consistent “rules of the road” to succeed in its transformation
  - CER
    - Transparency, Reproducibility, Limitations of Bias
    - How are gaps in evidence handled \(\rightarrow\) translation into policy
- CER can both assist healthcare improvement and appropriately shape the evolution of pharmaceutical R&D
  - Broad stakeholder involvement (ex patients, industry)
  - Broad scope (not just focus on drugs)
  - Explicitly address patient heterogeneity
  - Translation of into health policy decisions should be put into appropriate context (ex. uncertainty, unmet medical need)