Stratified Medicines and Companion Diagnostics

An Industry Viewpoint

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About IML

- Formed in February 2003, ex-GSK Predictive Medicine Group
- Work within industry, government, other stakeholders

1. Align test and drug Product profiles
2. Establish value of Combined Product profiles
3. Identify test technology and broker relationship
4. Manage integrated programmes to deliver CDx and SRx

Value Proposition Calculator
- Added value of companion programme
- Business relationship
- Portfolio Management

IP Generation & Exploitation
- GSK & Smarthaler
- SE & tuneable magnetic proteins
- TSB SBRI on sepsis care
**Stratified Medicines**

![Diagram showing the components of stratified medicines](image)

- Right Medicine
- Right Patient
- Right Disease
- Right Time
- Right Dose
- Right Response

**Stakeholders**

- Healthcare Providers
  (clinicians, primary practitioners, hospital workers)
- Patients
  (consumer and beneficiary of healthcare)
- Industry
  (Pharma co’s & associated value-chain, eg, Dx Co, CRO)
- Government/Regulators/Payors
Keys issues with medicines today are .....

Safety and efficacy

New market models for pharma*

<table>
<thead>
<tr>
<th>Cost of medicines</th>
<th>Hi volume, low price</th>
<th>Low volume, hi price</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High</td>
<td></td>
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BLOCK-BUSTER  
One drug fits all; poor response rates (20-80%) & risk of SAEs (>1%)  
SEGMENT-BUSTER  
Drug responses monitored for efficacy and SAEs using diagnostic-type test (CDx)  
NICHE-BUSTER  
Drug given to specific patients determined by predictive tests (Mol Dr.; PGx)

Hi volume, low price  
Low volume, hi price  
Billion dollar sales line

Number of patients treated

*Blair (2009)
CDx offers increased revenue through better commercialization*

*Agarwal PharmExec.com (Jan, 2009)

Opportunity Map for CDx*

MIT Stratified Medicine Model*
Linking Development & Biomarker Performance to Patients & Markets

Biomarker Performance
Efficacy & Population Enrichment
Adoption Rate & Market Share

Patient Benefits & AEs
Pricing: Drug & Diagnostic
Cash Flow & NPV

Market Size

*Trusheim et al Nature 2011

PharmaCo-DxCo Relationships*

<table>
<thead>
<tr>
<th>Relationship Structure</th>
<th>Outcome</th>
<th>Investment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Pfizer maraviroc and Monogram trofile test</td>
<td>Product Rescue</td>
<td>$1.8bn (90% R, 10% D)</td>
</tr>
<tr>
<td>2. Amgen panitumumab and KRAS test</td>
<td>Market Expansion</td>
<td>$1.3bn (99% R, 1% D)</td>
</tr>
<tr>
<td>3. GSK abacavir and HLA SNP test</td>
<td>Market Penetration</td>
<td>$1.9bn (98% R, 2% D)</td>
</tr>
<tr>
<td>4. AZ/ Prom budesonide and Prometheus Serology 7 test</td>
<td>Integrated</td>
<td>$1.8bn (97% R, 3% D)</td>
</tr>
</tbody>
</table>

*Blair (2008), Blair (2010); Blair & Blakemore (2011)

*Trusheim et al Nature 2011
**NPV* Matrix v2**

<table>
<thead>
<tr>
<th>Revenue Scenarios</th>
<th>NPV A</th>
<th>NPV B</th>
<th>NPV C**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full Risk-Sharing (5% drug royalty)</td>
<td>Costs to Dx Co = FULL</td>
<td>Rx revenues to Dx Co = $5%</td>
<td>Costs to Dx Co = FULL</td>
</tr>
<tr>
<td>Hybrid Risk &amp; Fee (2% drug royalty)</td>
<td>Dx Co Rx risk = Exposed</td>
<td>Dx Co Rx risk = Exposed</td>
<td>Dx Co Rx risk = Exposed</td>
</tr>
<tr>
<td>Fee-for-Service (No royalty)</td>
<td>NPV D</td>
<td>NPV E**</td>
<td>NPV F</td>
</tr>
<tr>
<td>Costs to Dx Co = $PART</td>
<td>Costs to Dx Co = $PART</td>
<td>Costs to Dx Co = $PART</td>
<td></td>
</tr>
<tr>
<td>Rx revenues to Dx Co = $X+2%</td>
<td>Rx revenues to Dx Co = $X+2%</td>
<td>Rx revenues to Dx Co = $X+2%</td>
<td></td>
</tr>
<tr>
<td>Dx Co Rx risk = Part Exposed</td>
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<td>Dx Co Rx risk = Part Exposed</td>
<td></td>
</tr>
</tbody>
</table>

New Test Co-Developed with New Drug
Existing Test Made/Used to Order for New-to-Market Drug
Relationship Scenarios

*NPV discount factor varied (10%, 12.5%, 15%) as surrogate for relative risk
**Red text is most-likely revenue-relationship scenario intersection

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**The Price vs Value Imbalance***

<table>
<thead>
<tr>
<th>Targeted Therapy</th>
<th>Annual Price</th>
<th>Companion Diagnostic</th>
<th>Test Price</th>
<th>Model</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xalkori (critozinib, Pfizer)</td>
<td>$115,200</td>
<td>Vysis ALK Break Apart In Situ Hybridisation FISH Probe Kit (Abbott Molecular)</td>
<td>$1,500</td>
<td>Turnaround (ALK positivity ~7%)</td>
<td>TBD</td>
</tr>
<tr>
<td>Zelboraf (vemurafenib, Plexikon/ Diachi-Sankyo/ Roche)</td>
<td>$56,400</td>
<td>Cobas 4800 BRAF V600 Mutation Test (Roche Molecular)</td>
<td>$120 - $150</td>
<td>Integrated (BRAF V600E mutation ~40%)</td>
<td>$144M ($213M***)</td>
</tr>
<tr>
<td>Herceptin (trastuzumab, Genentech/ Roche)</td>
<td>$70,000</td>
<td>HercepTest (Dako)</td>
<td>$500</td>
<td>Turnaround (HER-2 expression score 3+ ~10%)</td>
<td>$620M**</td>
</tr>
</tbody>
</table>

** Projected Annual Sales 2012 based on HY12 – roche.com
Mitigating Delays – Platform Bridging*

**A**
- **CDx development**
  - Based on phase II samples upon agreement with Regulators
- **Phase III trial**
  - CDx clin. trial assay
- **IND submission/ co-approval**
  - Delayed, but with CDx for patient selection

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**B**
- **Phase III trial**
  - Platform A
- **CDx bridging study**
  - Platform B based on phase III samples upon agreement with Regulators
- **IND submission/ approval**
  - Delayed, but with Plat B CDx for patient selection

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**C**
- **Phase III trial**
  - Platform A
- **CDx development**
  - Based on phase II samples upon agreement with Regulators
- **CDx bridging study**
  - Platform B based on phase III samples upon agreement with Regulators
- **IND submission/ approval**
  - Label change: Plat B CDx for patient selection

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*Martina Kaufmann, IML

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Stakeholders

- **Healthcare Providers**
  - (clinicians, primary practitioners, hospital workers)
- **Patients**
  - (consumer and beneficiary of healthcare)
- **Government/ Regulators/ Payors**
- **Industry**
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Modified from Brandenburger & Nalebuff, 1996
Relationships

Predictive Medicine

Earlier diagnosis + effective treatment = better long term outcome

1. Insult/ trigger
2. Inflammation
3. Tissue remodelling
4. Symptomatic disease
Observations

- If patient is not obviously ill, how will benefit be measured and compensated?
- How will clinical studies demonstrate preventative benefit in timescale of drug development?
- Will prevention of one disease merely postpone eventual burden on healthcare system?
- How will insurers and other parties view risk based on prediction and prevention?

Bibliography


