Developing New Medicines in a Time of Cost Containment

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Swiss HLG Winter Conference
Flüeli Ranft, 29.01.2017
Disclaimer

• The explanations, opinions and facts expressed relate to the personal point of view of the lecturer.

• The perspective hereby represented does not particularly correspond to the official point of view of Helsana or the University of Basel and is accordingly not binding in any way for Helsana or the University of Basel.
Changing healthcare landscape
Full pipelines
New Drug (NME) Approvals by FDA
Orphanisation: Increase in FDA orphan drug approvals
Pharma business model in flux

- Precision medicines
- Orphan drugs
- Speciality pharma
# Expensive drugs in US

<table>
<thead>
<tr>
<th>Drug (company)</th>
<th>Treats</th>
<th>Typical/Annual cost</th>
<th>Target patient population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soliris (Alexion)</td>
<td>PNH</td>
<td>$440‘000</td>
<td>10‘-12‘000 world-wide</td>
</tr>
<tr>
<td>Naglazyme (BioMarin)</td>
<td>Rare enzyme disorder</td>
<td>$400‘000</td>
<td>1‘00 in developed countries</td>
</tr>
<tr>
<td>Elaprase (Shire/Sanofi)</td>
<td>Rare enzyme disorder</td>
<td>$375‘000</td>
<td>2‘000 worldwide</td>
</tr>
<tr>
<td>Cinryze (Shire)</td>
<td>Hereditary angioedema</td>
<td>$350‘000</td>
<td>6‘000 in US</td>
</tr>
<tr>
<td>Gattex (NPS)</td>
<td>Short bowel syndrome</td>
<td>$295‘000</td>
<td>3‘-5‘000 in US</td>
</tr>
<tr>
<td>Harvoni (Gilead)</td>
<td>Hepatitis C</td>
<td>$94‘500</td>
<td>3.2 mio in US</td>
</tr>
</tbody>
</table>
Neglected diseases: 485 compounds in the pipeline
Healthcare reform as Hydra
From problem to solution
Better R&D process
New molecules (NMEs), FDA 2000-2012

- 332 NMEs
- 302 Submissions
  - 151 Approvals
  - 151 First-cycle declines
Deficiencies in efficacy (FDA)

302 molecules
2000-2012

First rejection n=151
Dosing n=24 (16%)
Inadequate endpoint n=20 (13%)
Insufficient efficacy in comparison to standard n=20 (13%)
Inconsistent results in different studies /centers n=17 (11%)

Approval after resubmission n=71
Dosing n=9 (13%)
Insufficient efficacy in comparison to standard n=7 (9.9%)
Inadequate endpoint n=5 (7%)
Deficiencies in safety (FDA)

302 molecules
2000-2012

First rejection n=151
Cardiovascular n=14 (9%)
Total mortality n=11 (7%)
Neuropsych n=9 (6%)

Approval after resubmission n=71
Cardiovascular n=3 (4%)
Neuropsych n=3 (4%)
Renal n=3 (4%)
Infections n=3 (4%)
Regulatory science

„Discoveries in biomedical research are slow to find their way into patient care because the agency (FDA) relies on 20th-century methods to evaluate 21st-century science.“

- Dr. Margaret Hamburg,
  Past FDA Commissioner
Innovation and efficiency

Old = efficient
New = inefficient
Old = not innovative
New = innovative
Cave hypes!
If it does not work, we should not be paying for it (any more)!!!
Definitions

**Replacement**
New practice is better than standard

**Back to the drawing board**
New practice is not better than standard

**Reaffirmation**
An existing practice is better than an inferior standard

**Reversal**
An existing practice is not better than an inferior practice
Examples for medical reversal

- Antibiotics in diabetic women with asymptomatic bacteriuria (Harding 2002)
- Conventional adjuvant chemotherapy with or without high-dose chemotherapy and autologous stem cell transplantation in high risk breast cancer (Tallman 2003)
- Methylprednisolone, valaciclovir, or the combination in vestibular neuritis (Strupp 2004)
Waste
Inadequate vial sizes
Example Bortezomib (Velcade®)
Example Pembrulizumab (Keytruda®)

Average patient: 70 kg
Required dose of Keytruda: 140mg

Treatment cost: $6,440
Waste: $460

Treatment cost: $6,440
Waste: $2,760

Treatment cost: $9,200
Waste: $0

Treatment cost: $6,440
Waste: $0
Waste in healthcare

Berwick D. JAMA. 2012;307(14):1513-1516
Take-Back Day is on April 30th

- In last 10 years DEA took back 2750 tons of medicines

2015: 350 tons
Speed, speed, speed...
Measures to reduce the use of services

- No benefit
- Marginal benefit
- Unclear benefit
- Not desired by the patient
- Duplicated services
- Equally effective, cheaper, existing alternatives
Less is often more (*therapeutic nihilism*)
Stacie Al-Chokhachi, second from right, and her son, Dalton, right, who has Duchenne muscular dystrophy, traveled from Memphis to Hyattsville, Md., to attend an F.D.A. meeting.
Reality of multiple sclerosis

About 40 people testified – mostly patients, some physicians
Increase medication safety


Based on our estimate, medical error is the 3rd most common cause of death in the US

Behandlungsfehler mit Todesfolge

All causes: 2,597k
- Cancer: 585k
- Heart disease: 611k
- COPD: 149k
- Suicide: 41k
- Motor vehicles: 34k
- Firearms: 34k

Makary MA 2016
Interesting, however challenging: pay-per-use

Indication \( x = \text{price } X \)
Indication \( y = \text{price } Y \)
Genomic medicine as catalyst
Hedgehog inhibitor itraconazole in basalioma

Kim DJ et al (2014)
Analysis of 589,306 genomes identified individuals who were resistant against severe pediatric mendelian diseases

Chen R 2016
Candidates of the resilience project

Smith Lemli Opitz Syndrome  
Epidermolysis bullosa simplex  
Pfeiffer Syndrome

Familial Dysautonomia

Chen R 2016
Changing role of the payor

TIME TO ADAPT
Helsana Strategy: From Payer to Player …

Yesterday…  …Today…  …Tomorrow?

“Mutual"  Health Insurer  Health Player
Payor’s choices drive the market

24.11.2015

CVS Health

CVS Health Corp. (NYSE:CVS) has selected Repatha evolocumab from Amgen Inc. (NASDAQ:AMGN) as its exclusive PCSK9 inhibitor in exchange for undisclosed discounts on the lipid-lowering mAb.

“We have determined that choosing a single PCSK9 inhibitor for our commercial formularies allows us to get the best price possible for clients and preserves our commitment to deliver the best care available,” CMO Troyen Brennan said in a statement.

The PBM said its pharmacy and therapeutics (P&T) committee determined that Repatha and the competing Praluent alirocumab PCSK9 inhibitor from Regeneron Pharmaceuticals Inc. (NASDAQ:REGN) and Sanofi (Euronext:SAN; NYSE:SNY) were therapeutically equivalent.

09.11.2015

Harvard Pilgrim Health Care

Regional insurance company Harvard Pilgrim Health Care Inc. granted Repatha evolocumab from Amgen Inc. (NASDAQ:AMGN) exclusive preferred status on its formulary in exchange for undisclosed discounts on the lipid-lowering drug.

Additionally, the parties agreed to a pay-for-performance deal whereby Amgen will provide Harvard Pilgrim with an "enhanced discount" if the reduction in LDL levels for Harvard Pilgrim members is less than what was observed during clinical trials. The size of the discount is not disclosed.
3 drugs account for 53% of Medicare Part B drug expenditure

<table>
<thead>
<tr>
<th>Drug proprietary name</th>
<th>Approved use</th>
<th>Total expenditures (in millions)</th>
<th>Expenditures per beneficiary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lucentis</td>
<td>Ophthalmologic</td>
<td>$1,369</td>
<td>$9,423</td>
</tr>
<tr>
<td>Eylea</td>
<td>Ophthalmologic</td>
<td>1,088</td>
<td>9,936</td>
</tr>
<tr>
<td>Prolia</td>
<td>Orthopedic</td>
<td>665</td>
<td>2,776</td>
</tr>
<tr>
<td>Treanda</td>
<td>Cancer</td>
<td>332</td>
<td>21,685</td>
</tr>
<tr>
<td>Lexiscan</td>
<td>Diagnostic Imaging</td>
<td>257</td>
<td>215</td>
</tr>
</tbody>
</table>

Source: GAO analysis of CMS and FDA data. I GAO-16-12
Innovation report of German health plan Techniker Krankenkasse
Find the balance act to a system which is…

available

affordable
Options for reimbursement
Comparing prices among countries is difficult and complex

- Most price agreements of medicines are bound to confidentiality, therefore, what is generally public is the reference price
- Contractual conditions are frequently rather complex and not in public domain
Elements to define the optimal target price of a pharmaceutical

- Socially responsible
- Politically acceptable
- Financially sound
- Medical-scientifically sustainable
If it's not affordable, what are the options?

- Reduce price
- Limit access
- Increase efficiency
Cost-sharing
High cost sharing reduces adherence

RAND researchers found that doubling co-pays reduced patients’ adherence to prescribed medicines by 25% to 45% and increased emergency room visits and hospitalizations.

Source: D.P. Goldman, et al.22
Risk-sharing
Promising: Performance-based reimbursement schemes

Performance-based schemes

Non-outcome-based schemes
- Population level
  - Price-volume
  - Market share

Patient level
- Utilization caps
- Manufacturer funded treatment initiation

Health outcomes-based schemes
- Conditional coverage
  - Coverage with evidence development
- Performance linked reimbursement
  - Outcomes guarantee
  - Pattern or process of care

Outcomes
- Based on
- Pattern or
  - Process of care
- Guarantee
- Approval
- Development
- Evidence
- With
- Coverage
- Conditional
- Approval
- Treatment
- Manufacturer funded
- Initiation
- Utilization caps
- Market share
- Price-volume
- Population level
- Performance linked
- Reimbursement
- Conditional coverage
- Health outcomes-based schemes
- Non-outcome-based schemes
- Performance-based schemes
New models

1. High-cost drug mortgages
2. High-cost drug re-insurance
3. High-cost drug patient rebates
Challenges: The very UGLY
NBI post Turing

Price gouging like this in the specialty drug market is outrageous. Tomorrow I'll lay out a plan to take it on. -H

The New York Times @nytimes
Overnight, the price of a 62-year-old drug jumped to $750 a tablet from $13.60 nyKme1PjuC92
The Turing Case

1 $ /pill

750 $ /pill

DARAPRIM PRICE HIKE

<table>
<thead>
<tr>
<th>PREVIOUSLY</th>
<th>NOW</th>
</tr>
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<tbody>
<tr>
<td>$13.50</td>
<td>$750</td>
</tr>
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</table>

imprimis PHARMACEUTICALS vs. TURING PHARMACEUTICALS
Share buybacks 2005-2014

19 big pharma companies in S&P 500:

97% of net income went into share buybacks
A general question remains…

Which services shall be financed out of *solidarity*?
Paramount "non-equation" in health policy

Solidarity ≠ Equality ≠ Justice
Is the glass half empty or half full?

New drugs in

Obsolete drugs out
Take home messages

• Value determination is paramount
• We need fair and transparent rules
• Value changes over time
• We need to free space
• Breakthrough innovations (e.g. HCV drugs) are a reality – more to come
• Medical community must get involved in discussions on value determination
Finally...
Questions?