Exploring the future of pharmacotherapy

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Declaration of interests

- Professor of Pharmacoepidemiology, Utrecht Institute of Pharmaceutical Sciences, 0.4 FTE.
- Chairman of the Dutch Medicines Evaluation Board (MEB), since mid 2007.
- Co-opted member of EMA PhVWP, 2006-2009; 2009-2015 co-opted member of EMA CHMP.
- Scientific Director WHO-Utrecht Collaborating Centre for Pharmaceutical Policy and Regulation, since 2008.
- This talk reflects my personal views; I am being inspired and challenged on a daily basis by many colleagues from these ‘environments’.
Edvard Munch: The dance of life, 1900

Gustav Klimt: Death and Life, 2010
A lot of future thinking, personal view

- Over the **last 15 years**, pharmacotherapy has made fascinating progress in terms of better products, diagnostics, in-process controls, better PK/PD, more data on effectiveness and safety, factoring in pharmacogenomics or HTA,

- but we still discuss the dosing of TNF blockers, safety of anticoagulants, use of antipsychotics in the elderly, strategies to beat AMR and many other therapeutic gaps, etc.

- Over the **next 15 years** the field will continue to blossom, both in science and clinical impact, but the future will be shaped primarily by socio-economic change and global health developments and challenges,

- rather than better molecules, biomarkers, roboting in supply chain management, e-health, or biosimilars, etc.

From ‘blur’ to learning about futures

- With all this emerging science, transformative products will enter the clinic very soon
- This cancer drug shows promise, but at a price that many can’t pay
- We’ll see more biomarker/personalized therapies
- I am sitting here day after day at the EMA talking about future medicines my patients will never get access to
- Game changing advances in science represent just 10 percent of the key trends impacting health futures
- Biosimilars have the future, we need to convince doctors
- As a payer I only want to spend money on products that have shown clear OS benefit, I don’t care about PFS

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### Early spread of HIV-1 in human populations


### Ebola origin and transmisson during 2014 outbreak


#### Exposure to HIV/Ebola

<table>
<thead>
<tr>
<th>Time/space</th>
<th>Viral biology/evolution</th>
<th>Susceptibility factors</th>
<th>Social change</th>
<th>Economics</th>
<th>Transport/mobility</th>
<th>Political/religious</th>
</tr>
</thead>
</table>

#### Exposure to medicines

<table>
<thead>
<tr>
<th>Time/space</th>
<th>Pharmacology of drug</th>
<th>Patient characteristics</th>
<th>Indication</th>
<th>Prescribing/adherence</th>
<th>Health care/regulatory</th>
<th>Pharmaceutical market</th>
</tr>
</thead>
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**Pharmacotherapy as a ‘social construct’**

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Scenario analysis of the future of medicines
Hubert Leufkens, Flora Haaijer-Ruskamp, Albert Bakker, Graham Dukes

Planning future policy for medicines poses difficult problems. The main players in the drug business have their own views as to how the world around them functions and how the future of medicines should be shaped. In this paper we show how a scenario analysis can provide a powerful teaching device to adjust peoples' preconceptions. Scenarios are plausible, not probable or preferable, portraits of alternative futures. A series of four of alternative scenarios were constructed: “sobriety in sufficiency,” “risk avoidance,” “technology on demand,” and “free market unfettered.” Each scenario was drawn as a narrative, documented quantitatively wherever possible, that described the world as it might be if particular trends were to dominate development. The medical community and health policy makers may use scenarios to take a long term view in order to be prepared adequately for the future.

Figure 1 | A matrix of four scenarios for the pharmaceutical sciences in 2020.


EMA Annual Report 2014

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<table>
<thead>
<tr>
<th>Product discussions</th>
<th>Learning dimensions</th>
</tr>
</thead>
<tbody>
<tr>
<td>ERT products rare diseases</td>
<td>B/R, dose/duration of therapy, registry building</td>
</tr>
<tr>
<td>ATMPs (cel, gene)</td>
<td>Quality, pharmaceutical formulation, GMP</td>
</tr>
<tr>
<td>Repositioning ‘old’ molecules (alfa-2 agonist, antioxidant, anticholinergic)</td>
<td>Quality, pharmaceutical formulation, clinical data</td>
</tr>
<tr>
<td>Biosimilar</td>
<td>Similarity exercise &gt; quality, preclinical, clinical</td>
</tr>
<tr>
<td>Inhibitors of HDAC, Hh, MEK, BRAF, VEGF, proteasome</td>
<td>System biology, epigenetics, biomarkers, B/R</td>
</tr>
<tr>
<td>Liposome formulation of antibiotic</td>
<td>Pharmaceutical formulation, GMP</td>
</tr>
<tr>
<td>Extension to pediatric use (HIV, immune modulating products, insulins)</td>
<td>PK/PD, posology, pharmaceutical formulation</td>
</tr>
<tr>
<td>MABs (IL17, VEGF, HER2, CD30+, PD1)</td>
<td>System biology, immunology, biotechnology, B/R</td>
</tr>
<tr>
<td>Vaccins, blood factors</td>
<td>Pharmaceutical formulation, immunology, B/R</td>
</tr>
<tr>
<td>Targeted therapy based on CFTR, exon skipping</td>
<td>Cell/system biology, protein science, genomics</td>
</tr>
<tr>
<td>NOACs, SGLT2 inhibitors, obesity products</td>
<td>B/R, safety monitoring, long-term CV outcomes</td>
</tr>
<tr>
<td>MS products</td>
<td>B/R, PML risk</td>
</tr>
</tbody>
</table>
Outlook for 2020 ..........

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Key drivers for the future ....

- Non-data space (regulatory, HTA, clinical) becomes more critical.
- Increasing variance in access to medicines across Europe.
- Response to global needs and challenges.
Key questions in the lifecycle of a medicine

<table>
<thead>
<tr>
<th>Question</th>
<th>Today’s challenges</th>
</tr>
</thead>
<tbody>
<tr>
<td>Robust definition and diagnosis of disease?</td>
<td>Psychiatric morbidities, sepsis, somatic functional disorders</td>
</tr>
<tr>
<td>Clinically relevant endpoints to evaluate drug effects?</td>
<td>6-MWT in PAH, HbA1C in diabetes, PFS/OS in cancer</td>
</tr>
<tr>
<td>Identifiable target population (indication) that may benefit?</td>
<td>Biomarkers to identify responders and non-responders</td>
</tr>
<tr>
<td>What kind of comparison is useful, needed and feasible?</td>
<td>Placebo, active controls and dynamics in treatment options</td>
</tr>
</tbody>
</table>

Possible Type I error: 42 products showed a confirmatory phase with pertinent uncertainties; still 24/42 were approved.

Possible Type II regulatory error: 26 products showed a convincingly positive confirmatory phase; still 5/26 were not approved.
Adaptive licensing opens a window for observational studies, registries and pragmatic trials


Adaptive licensing: stakeholder perceptions

Variability use TNF alpha blockers


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Uptake of new medicines in Europe: availability of 2004 approvals


Policy measures and economic stability, EU 2008-2011

Leopold C et al. Effect of the economic recession on pharmaceutical policy and medicine sales in eight European countries. WHO Bull 2014; 92(9):630-640.
How to navigate to a sustainable future of medicines in a global context?

Spending on medicines per geographic region

There is more than one approach in medicine.....
Design-driven innovations need ‘interpreters’, i.e. actors who listen, connect, translate, give meaning to things (MEDICINES) and come with innovative, meaningful proposals.

The future of pharmacotherapy?

- The fundamentals will probably not change dramatically, further sophistication, technology platforms.

- Much better taxonomy of the ‘critical uncertainties’ (both efficacy/effectiveness and safety) of modern medicines.

- Increasing awareness and understanding that pharmacotherapy is a ‘social construct’; diversification of the culture of medicines’ use.

  Strong future of ‘integrative’ pharmacotherapy: the hospital pharmacist as interpreter.