Access and prices across the EU
Affordability and sustainability of innovative medicines

Carin Uyl-de Groot

European Parliament, December 4, 2019

Erasmus University Rotterdam
Policy goals in health care

System objectives

Goal:
Ensuring affordable and equitable access for (all) patients to effective therapies in a sustainable manner
The good news (1).....

Cancer survival in Europe 1999–2007 by country and age: results of EUROCARE-5—a population-based study

Roberta De Angelis, Milena Sant, Michel P Coleman, Silvia Franksa, Paolo Balli, Daniela Pierannunzio, Annalisa Trama, Otto Visser, Hermann Brenner, Eva Ardanza, Magdalena Bialo-Lasota, Gerda Engholm, Alice Nennecke, Sabine Siesling, Franco Berrino, Riccardo Capocaccia, and the EUROCARE-5 Working Group*

Summary

Background Cancer survival is a key measure of the effectiveness of health-care systems. EUROCASE—the largest cooperative study of population-based cancer survival in Europe—has shown persistent differences between countries for cancer survival, although in general, cancer survival is improving. Major changes in cancer diagnosis, treatment, and rehabilitation occurred in the early 2000s. EUROCASE-5 assesses their effect on cancer survival in 29 European countries.

Methods In this retrospective observational study, we used data from 107 cancer registries or more than 10 million patients with cancer diagnosed up to 2007 and followed up to 2009. Uniform study control procedures were applied to all datasets. For patients diagnosed 2000–07, we calculated 5-year relative survival for 46 cancers weighted by age and country. We also calculated country-specific and age-specific survival for 10 common cancers, together with survival differences between time periods (1992–99, 2000–04, and 2005–07).

Findings Five-year relative survival generally increased steadily over time for all European regions. The largest increases from 2000 to 2005–07 were for prostate cancer (73.4% [95% CI 72.9–73.9] vs 81.7% [81.3–82.1]), non-Hodgkin lymphoma (53.8% [53.3–54.4] vs 60.4% [60.0–60.9]), and rectal cancer (52.1% [51.6–52.6] vs 57.6% [57.1–58.1]). Survival in eastern Europe was generally low and below the European mean, particularly for cancers with good or intermediate prognosis. Survival was highest for northern, central, and southern Europe. Survival in the UK and Ireland was intermediate for rectal cancer, breast cancer, prostate cancer, skin melanoma, and non-Hodgkin lymphoma, but low for kidney, stomach, ovarian, colon, and lung cancers. Survival for lung cancer in the UK and Ireland was much lower than for other regions for all periods, although results for lung cancer in some regions (central and eastern Europe) might be affected by overestimation. Survival usually decreased with age, although to different degrees depending on region and cancer type.

Findings 5-year relative survival generally increased steadily over time for all European regions.
The good news (2):
Many innovative (cancer) drugs
The bad news (1):
Rise in health expenditures 2000-2015 as share Gross Domestic Product (GDP)

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Austria</td>
<td>9.2</td>
<td>9.6</td>
<td>10.1</td>
<td>10.4</td>
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<tr>
<td>Czech Republic</td>
<td>5.7</td>
<td>6.4</td>
<td>6.9</td>
<td>7.5</td>
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<tr>
<td>Denmark</td>
<td>8.1</td>
<td>9.1</td>
<td>10.4</td>
<td>10.6</td>
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<tr>
<td>France</td>
<td>9.5</td>
<td>10.2</td>
<td>10.7</td>
<td>11.0</td>
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<tr>
<td>Germany</td>
<td>9.8</td>
<td>10.2</td>
<td>11.0</td>
<td>11.1</td>
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<tr>
<td>Ireland</td>
<td>5.9</td>
<td>7.7</td>
<td>10.6</td>
<td>9.4</td>
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<tr>
<td>Netherlands</td>
<td>7.1</td>
<td>9.4</td>
<td>10.4</td>
<td>10.8</td>
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<td>Norway</td>
<td>7.7</td>
<td>8.3</td>
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<td>9.9</td>
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<td>Poland</td>
<td>5.3</td>
<td>5.8</td>
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<td>6.3</td>
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<tr>
<td>Spain</td>
<td>6.8</td>
<td>7.7</td>
<td>9.0</td>
<td>9.0</td>
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<tr>
<td>United Kingdom</td>
<td>6.3</td>
<td>7.4</td>
<td>8.5</td>
<td>9.8</td>
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<tr>
<td><strong>Average EU</strong></td>
<td><strong>7.3</strong></td>
<td><strong>8.2</strong></td>
<td><strong>8.9</strong></td>
<td><strong>9.0</strong></td>
</tr>
</tbody>
</table>
The bad news (2):
Huge differences within EU, unequal access

Costs of cancer treatment: € 102 per person in Europe

Figure 1: Health-care costs of cancer per person in European Union countries in 2009, by health-care service category.
Data not adjusted for price differentials.

Luengo-Fernandez et al. Lancet Oncology 2013;14:1165-1174
Result budget problems

The Netherlands (2014): € 530 million spent on new cancer drugs
Maximum growth budget per year: 1.2%

<table>
<thead>
<tr>
<th>New cancer drugs</th>
<th>Estimated costs per patient</th>
<th>ICER</th>
<th>Estimated budget impact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nivolumab</td>
<td>€ 80,000</td>
<td>€ 134,000</td>
<td>€ 200 mln</td>
</tr>
<tr>
<td>Pertuzumab</td>
<td>€ 78,000</td>
<td>€ 150,000</td>
<td>€ 40 mln</td>
</tr>
<tr>
<td>Ibrutinib</td>
<td>€ 70,000</td>
<td>Unknown</td>
<td>€ 100 mln</td>
</tr>
<tr>
<td>Palbociclib</td>
<td>Unknown</td>
<td>Unknown</td>
<td>€100 mln</td>
</tr>
<tr>
<td>CAR-T cells</td>
<td>€300-400,000</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>
Affordable (expensive) therapies

Thanks to Matthijs Versteegh
3,000 patients

€80,000 per patient

Survival gain of 3 months (median)

Too expensive?
Opportunity costs

What we give to patient A, we cannot give to patient B.

Given a limited health care budget (or a limited willing to pay a higher premium) it is unethical not to make a societal decision.

Problem is a EU / worldwide problem
Why is it expensive?
Development phase: a long and winding road to registration

Pfizer -- http://www.pfizer.co.uk/pfizer_uk/navigation/research_frame.htm
Development phase
From discovery to patient

0 years
10 years of research
2 to 3 years of administrative procedures
20 years
Patent expiry

Source: “Recherche & Vie”, LIM (AGIM)
Costs of development new drug

Cost factors:

• R&D (including failures)
• Manufacturing
• Marketing and promotion

• Estimation: 300 million - 2.6 billion dollars
### Worldwide Total Revenues of Leading Pharmaceutical Companies in 2014 (in billion dollars)

<table>
<thead>
<tr>
<th>Company</th>
<th>Total Revenue ($)</th>
<th>R&amp;D Costs ($)</th>
<th>Sales and Marketing Costs ($)</th>
<th>Other Activities Costs* ($)</th>
<th>Profit ($)</th>
<th>Profit Margin (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Johnson &amp; Johnson</td>
<td>71.3</td>
<td>8.2</td>
<td>17.5</td>
<td>31.8</td>
<td>13.8</td>
<td>19</td>
</tr>
<tr>
<td>2. Novartis</td>
<td>58.8</td>
<td>9.9</td>
<td>14.6</td>
<td>25.1</td>
<td>9.2</td>
<td>16</td>
</tr>
<tr>
<td>3. Pfizer</td>
<td>51.6</td>
<td>8.6</td>
<td>11.4</td>
<td>11.6</td>
<td>22.0</td>
<td>43</td>
</tr>
<tr>
<td>4. Hoffmann-La Roche</td>
<td>50.3</td>
<td>9.3</td>
<td>9.0</td>
<td>20.0</td>
<td>12.0</td>
<td>24</td>
</tr>
<tr>
<td>5. Sanofi</td>
<td>44.4</td>
<td>6.3</td>
<td>9.1</td>
<td>20.5</td>
<td>8.5</td>
<td>11</td>
</tr>
<tr>
<td>6. Merck</td>
<td>44.0</td>
<td>7.5</td>
<td>9.5</td>
<td>22.6</td>
<td>4.4</td>
<td>10</td>
</tr>
<tr>
<td>7. GSK</td>
<td>41.4</td>
<td>5.3</td>
<td>9.9</td>
<td>17.7</td>
<td>8.5</td>
<td>21</td>
</tr>
<tr>
<td>8. AstraZeneca</td>
<td>25.7</td>
<td>4.3</td>
<td>7.3</td>
<td>11.5</td>
<td>2.6</td>
<td>10</td>
</tr>
<tr>
<td>9. Eli Lilly</td>
<td>23.1</td>
<td>5.5</td>
<td>5.7</td>
<td>7.2</td>
<td>4.7</td>
<td>20</td>
</tr>
<tr>
<td>10. AbbVie</td>
<td>18.8</td>
<td>2.9</td>
<td>4.3</td>
<td>7.5</td>
<td>4.1</td>
<td>22</td>
</tr>
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**Total Top 10 Global Companies**

<table>
<thead>
<tr>
<th>Percentage of Total Revenue – Profit</th>
</tr>
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<tbody>
<tr>
<td>Total</td>
</tr>
<tr>
<td>(%)</td>
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<tr>
<td>Revenue</td>
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<tr>
<td>(%)</td>
</tr>
<tr>
<td>Profit</td>
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<tr>
<td>(%)</td>
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</tbody>
</table>

*Other activities' costs = Total revenue – R&D costs – Sales and marketing costs. Overhead costs are included in R&D, sales and marketing and other activities.*

**Pharma highest profit: 20%, followed by banks 10%**
Systems are not sustainable so:

How to reduce spending?

• Shift from expensive to cheap technologies
• Make patients or the insurance pay a larger part
• Reduce the **prices of drugs**
• Reduce the total use of drugs

• Focus on reduction of prices
• However, also issue of **unequal access across Europe**
Availability of 2 cancer drugs
Source: ECL report, October 2018
Example uptake new cancer drug across Europe
PATIENT ACCESS PATHWAY

Regional Authorization

Regulatory Approval

Assessment & Reimbursement

National Market Access

Pricing & Financing

National Patient Access

Prescription & Use

Patient Value
Value based pricing

Incremental cost-effectiveness ratios: Cost per QALY gained

Thresholds
- NICE: £ 30.000, US: US$ 50-100.000
- WHO threshold: depend on WHO region and Gross Domestic Product (GDP)

Still budget impact problem.

Pay for performance (P4)
- Reimbursement dependent on treatment success

Volume-price arrangements
- sales < Y price P1; sales > Y lower price P2
Rationale for adapting the business model of (cancer) drug pricing

Issues:
1. A free market does not work for innovative (cancer) drugs
   - *Informational imbalance*
   - *Failure of competition*
2. Current cancer drug prices not justified by Research and Development (R&D)
3. Country specific solutions did not solve the problem
   - EUNeHTA
4. Restricted access to innovative drugs
New pricing model innovative (cancer) drugs:

https://www.youtube.com/watch?v=znTgYPRWyrA

News and Views  |  7 May 2018

Sustainability and affordability of cancer drugs: a novel pricing model

Carin A. Uyl-de Groot & Bob Löwenberg

Nature Reviews Clinical Oncology 15, 405–406
The algorithm

$$\text{Fair Cost of New Medicine} = \left[ \frac{\text{R&D costs}}{\text{nr. of patients} \times \text{years of patent left}} + \frac{\text{production costs per patient per year}}{\text{profit margin}} \right] \times (1+\text{profit margin})$$

Outline adapted business model of (cancer) drug pricing

Registration of new drug for certain indication (FDA, EMA, other)

Central level (US, EU, other)

Calculation of maximum price of new cancer drug

Calculation maximum price of new cancer drug based on algorithm

Algorithm includes:
- Research & development (R&D) cost including abandoned drugs
- New drug (manufacturing, sales, marketing, overheads) costs
- Profit margin linked to clinical benefit
- Number of patent years after registration
- Number of patients worldwide

Establishment of proposed price for new cancer drug by e.g. an EU or USA agency (subject to adjustment to national circumstances)
Ongoing debate and progress

Meetings with the European Parliament
• Resolution: transparency R&D costs, discounts (2017)
• White paper access to medicines (October 2018)

Dutch Ministry of Health: BeNeLuxAI
ESMO: access to medicine hot topic
EHA: task force fair prices

Patient organizations: e.g. Inspire2Live

Pharmaceutical companies (improving access/uptake)

Collaboration with other organizations:
• Fair Medicine
Measures needed at different levels (national, European), but barriers and limitations

Access issue is broader than discussion about drug prices

Change health systems/legislation: will take years

Patient’s right to health – right to have access to optimal quality of cancer care

Collaboration between all stakeholders, including pharmaceutical companies

Encourage joint negotiations
Health systems:
Take home message

• Faster access to new (cancer) therapies
• Better access to new (cancer) therapies
• Lower prices for new (cancer) therapies

It is not a utopia.
THANK YOU