The value of new oncology drugs

A personal perspective on the value of oncology drugs
Brussels, February 28, 2018
How much do we currently pay for oncology drugs in Europe?
Cost of cancer drugs per capita in the EU

38 euro
Predicted 2020 oncology medicines sales in Belgium

Predicted 2020 oncology medicines sales in Belgium

Drugs for colorectal cancer cost 4.4 euro per capita

1,203,943 colon cancer survivors

An additional 30,000 people with colorectal cancer survived last year who would have been dead ten years ago (average +7% overall survival rate)
Success & High Unmet Medical Needs

Current treatments for colorectal cancer are insufficient to offer a solution to patients. The probability to survive stage IV colon cancer are between 10 to 20% depending on the country.

153,000 people die from colon cancer in the European Union, every year.
Value = Quality/Cost
Different perspectives on value

**Investors**
- Return on investment

**Payers/governments**
- Cost-effectiveness

**Patient**
- Medical Value

**Science**
- Incentives for insights

**Citizens/Tax payers**
- Willingness to pay?
Investments in cancer research

The European pharmaceutical industry invests 7.7 billion euro per year in oncology research, which is 54 times more than all non-commercial funding of research in the entire European Union.

Current success rate Phase I - Phase III is 5%.

Time frame is approx 10 years.

Pharmaceutical R&D investments (in $bln) vs number of NME’s approved by FDA

Source: EvaluatePharma, FDA
Value = Quality/Cost

R&D cost failure

R&D cost product A

Mfg cost

A

Standard of Care
Value = Quality/Cost

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Value = Quality/Cost

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Standard of Care
Value = Quality/Cost

- Better overall survival
- Better quality of life
- Economic value
  - less hospitalisation
  - productive years
  - number of patients
  - current prices
  - ...

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Negotiation

LIST Price

Standard of Care

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Mfg cost
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Better overall survival
Better quality of life
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- less hospitalisation
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- ...

LIST Price

Discount Price = confidential

Negotiation

R&D cost failure

R&D cost product A

Mfg cost

Standard of Care
Value = Quality/Cost

Better overall survival
Better quality of life
Economic value
- less hospitalisation
- productive years
- number of patients
- current prices
- ...

Product B has no medical value above standard of care, but costs a lot in development

Would you price it the same?
What is health economic value?

Calculation of Quality Adjusted Life Years = One QALY equates to one year in perfect health

**Product 1**
Median overall survival rate = 2 months
Treatment costs 20,000€
Cost/QALY = 120,000€

**Product 2**
Overall survival rate = 10 years
Treatment costs 200,000€
Cost/QALY = 20,000€
The price of a drug is determined by its value, not by its costs.
Pricing - the sky is the limit?

Kymriah - $475,000 for Acute lymphoblastic leukemia (ALL)

Spinraza - $750,000 for the first year and $375,000 each year after for the treatment of spinal muscular atrophy

Soliris - $542,000 each year to treat paroxysmal nocturnal hemoglobinuria and atypical hemolytic uremic syndrome.

Brineura - $702,000 per year to treat the ultrarare CLN2 disease.
Pricing - the sky is the limit?

Kymriah - $475,000

“It is difficult to determine if it is too high by fivefold or too low by half”

Anna Kaltenboeck, senior health economist and Peter B. Bach, M.D., director of the Drug Pricing Lab at Memorial Sloan Kettering Cancer Center in New York

“Kymriah was found to be cost effective in the pediatric ALL setting”

“Curative CAR-T cell therapy can be over £500,000 indication per patient”
Health Technology Assessment

Medical value - Quality Adjusted Life Year
Economic value - what is the cost versus the standard of care?

Problems with this:
- many different ways of calculation QALYs
- what is the value of a human life?
- is it ethical to put a value on human life?
- what is quality of life?
- what is the cost, and what is economic value?
- what is the standard of care?
- what if there is no standard of care?
- what with new mechanisms of action?
- ignores long term innovation
- ignores the effect of loss of exclusivity
- ignores incremental innovation
- ignores investment dynamics
What is value?

“Folfox costs more than 20 times the traditional regimen, which is quite an enormous cost” (Gary Lyman MD, MPH, an oncologist and health outcomes researcher at the Duke University Comprehensive Cancer Center)

Folfox “was the least expensive with 56€ per month of progression-free survival (PFS)” (study presented at the annual congress of the American Society of Clinical Oncology (ASCO))

Andrea Bonetti, Jcopo Giuliani - Cost-effectiveness of front-line trials in metastatic colorectal cancer: Integrating the European Society for Medical Oncology Magnitude of Clinical Benefit Scale (ESMO-MCBS) with the costs of drugs. Journal of Clinical Oncology 35, 2017
Innovative treatments are only more expensive for a short while
Evaluation of oncology drugs by European HTA agencies

<table>
<thead>
<tr>
<th>Drug</th>
<th>England</th>
<th>France</th>
<th>Germany</th>
<th>Italy</th>
<th>Poland</th>
<th>Spain</th>
<th>Sweden</th>
<th>Netherlands</th>
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<td>Xalkori (crizotinib)</td>
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<td>Teysuno (combination: tegafur, gimeracil, and oteracil)</td>
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<td>Caprelsa (vandetanib)</td>
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<td>Halaven (eribulin)</td>
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<td>Inlyta (axitinib)</td>
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<td>Jevtana (cabazitaxel)</td>
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<td>Adcetris (brentuximab vedotin)</td>
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<td>Yervoy (ipilimumab)</td>
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<td>Zelboraf (vemurafenib)</td>
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<td>Pixuvri (pixantrone dimaleate)</td>
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<td>Gilenya</td>
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Rejected  Approved  Approved with conditions/restrictions

(Source: “Variation in Health Technology Assessment and Reimbursement Processes in Europe” in: Value In Health, 2017)
Evaluation of oncology drugs by European HTA agencies

Conclusions

The main conclusion that we can draw from this research is that it is challenging even for those with considerable personal experience in European HTA processes to establish what is really happening in market access for new drugs, and why there are differences among countries. Although some of the variation can be understood, it appears that issues and forces (including budget impact and political factors) other than the HTA processes of various countries can contribute to decisions and to time to patient access. Although it is important to measure delays in patient access resulting from differences in HTA processes, we recommend that efforts should be directed toward improving transparency in HTA, which should, in turn, lead to more effective processes.

(Ronald L Akehurs, Eric Abadie, Noël Renaudin, François Sarkozy “Variation in Health Technology Assessment and Reimbursement Processes in Europe” in: Value In Health, 2017)

“All countries assess similar types of evidence; however, the specific criteria/endpoints used, their level of provision and requirement, and the way they are incorporated (e.g. explicitly vs. implicitly) varies across countries, with their relative importance remaining generally unknown. Incorporation of additional ‘social value judgements’ (beyond clinical benefit assessment) and economic evaluation could help explain heterogeneity in coverage recommendations and decision-making”. (“Using health technology assessment to assess the value of new medicines: results of a systematic review and expert consultation across eight
Trends

Drugs will become more expensive

- more targeted
- used in smaller patient populations
- more efficacy
- more cost-effective
- combination treatments
Different perspectives on value

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**Incentives for insights**
The law of affordability & sustainability

Patients need
- access today
- new treatments for tomorrow

Therefore a more coherent approach is needed
- cost-reduction through prevention, early diagnosis and early-stage treatment
- more investments in basic research
- high prices for high medical value to encourage high risk research
- strong pressure on prices once loss-of-exclusivity has been reached
Recommendations

• High need for new treatments - so all incentives for high risk research should be encouraged
• Patient involvement must be strengthened to ensure that it is meaningful and impacts upon patient access
• HTA should not be the be-all-and-end-all: more clarity, more harmonised, with long term perspective on health & innovation
• Price flexibility and more creative approaches must be introduced to increase access to medicines
• The system must be faster to allow quicker access
• Sustainability = high prices for high medical value, low prices after loss of exclusivity + increased screening and early detection

Adapted from “International comparisons of Health Technology Assessment”, A report from Breast Cancer Now and Prostate Cancer UK
Thank you!
Limited number of patients

5 years

Time
What is wrong with current value evaluation?

• It ignores
  • patient inputs in QoL evaluation
  • long term perspective of price decrease and loss of exclusivity
  • solidarity principle
  • investor dynamics and future research incentives

Instead of caring about fighting the disease in the long term, HTA is primarily concerned about fiscal control
Clinical Value Evolves Over Time: Trastuzumab

Trastuzumab was originally approved by the FDA in 1998 to treat metastatic breast cancer in patients whose tumors expressed the HER2 protein. Approval was based on data showing that treatment slowed disease progression but long term survival data was unknown.

- 2001 data showed that median overall survival increased by 25% with the addition of trastuzumab.
- In 2008, the benefit of earlier treatment initiation was proven, giving trastuzumab an additional indication as early adjuvant therapy for breast cancer.
- Subsequent indications for use in combination to treat other types of gastric and gastroesophageal cancers followed.

![Graph showing the evolution of clinical value over time for Trastuzumab.](chart.png)
New scientific insights & willingness to pay drive research investments

Number of molecules in development

SOURCE: PharmaProjects 2014; McKinsey analysis
Cancer survival rates in Europe
What is value?

- Value = Quality/Cost

- Who determines value? Who gives them the right to make that assessment?

- Who determines the time-frame?

- Who determines
The importance of research

Current treatments for colorectal cancer are insufficient to offer a solution to patients. Mortality rates are high, and the probability to survive stage IV colon cancer are between 10 to 20% depending on the country.

A lot of research is being conducted at the moment. There are 1604 clinical trials being conducted around the world in the area of colorectal cancer, of which 704 in Europe.
5-Year colon cancer survival rate in the European Union

CONCORD-3 Study - The Lancet, January 2018
\[ \text{VALUE} = \frac{\text{QUALITY}}{\text{COST}} \]

- Therapeutic value for patient
- Health economic outcomes
- Consistent product quality: purity, stability, ...
- Cost of research of this medicine
- Shareholder reward (in line with high financial risks)
- Cost of goods
Value or Price?

The medicines budget for disease X is 100. Because of a breakthrough innovation bringing substantial benefits to patients, the medicines budget for that disease will increase to 110, but once off-patent, the overall budget for that disease will be lower than ever .... Forever.
The value of pharmaceutical innovation over a long term period
The value of pharmaceutical innovation over a long term period

Costs to society without medical innovation

Number of patients

Time

Costs
The value of pharmaceutical innovation over a long term period

Costs to society without medical innovation

Costs to society with medical innovation

Number of patients
Price comparisons with generics

A company launched a great innovation with Product A, which was sold at a price of 100. After patent expiry, generics offered it at a price of 40. Now this company comes with a new innovation for the same disease with a price of 120, so 3 times more than the generic.
The overview of 2004 immuno-oncology (IO) agents. Six classes of IO agents are identified on the basis of different mechanisms of actions.

<table>
<thead>
<tr>
<th>Class</th>
<th>Number of Agents</th>
<th>Clinical Stage Breakdown</th>
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</thead>
<tbody>
<tr>
<td>T-cell targeted immunomodulator</td>
<td>199</td>
<td>Approved: 54, Phase III: 12, Phase II: 22, Phase I/II: 5, Preclinical &amp; Discovery: 5</td>
</tr>
<tr>
<td>Other immunomodulator</td>
<td>284</td>
<td>Approved: 72, Phase III: 24, Phase II: 42, Phase I: 24, Preclinical &amp; Discovery: 9</td>
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<tr>
<td>Cancer vaccine</td>
<td>261</td>
<td>Approved: 130, Phase III: 33, Phase II: 33, Preclinical &amp; Discovery: 77</td>
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<tr>
<td>Cell therapy</td>
<td>179</td>
<td>Approved: 112, Phase III: 12, Phase II: 96, Preclinical &amp; Discovery: 4</td>
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<tr>
<td>Oncolytic virus</td>
<td>95</td>
<td>Approved: 34, Phase III: 12, Phase I/II: 16, Preclinical &amp; Discovery: 49</td>
</tr>
<tr>
<td>CD3-targeted bispecific antibody</td>
<td>46</td>
<td>Approved: 29, Phase III: 8, Preclinical &amp; Discovery: 9</td>
</tr>
</tbody>
</table>

From: Comprehensive analysis of the clinical immuno-oncology landscape
Ann Oncol | © The Author 2017. Published by Oxford University Press on behalf of the European Society for Medical Oncology.
The health economist’s quadrant

No Discussion - reject

Is there a need?

No discussion - accept

High

Low

Price

Standard of care

Medical value

Product A

Product B
What is the burden of colon cancer?

Total colorectal cancer treatment cost in EU is 14 € per capita

Paul Hanly, Isabelle Soerjomataram, Linda Sharp : Measuring the societal burden of cancer: The cost of lost productivity due to premature cancer-related mortality in Europe - International Journal of Cancer, September 2014
The drug pricing process

European Medicines Agency

European Commission

National P&R authorities/Health Technology Assessment

Opinion about efficacy & safety

Formal approval

Cost-effectiveness evaluation

National negotiation on price

List price may differ significantly from confidential discount price

Source: QuintilesIMS Consulting Services analysis