Studying Value and Health Economics in GI Cancer

Thursday, 4 July 08:00 - 08:20

Speaker(s)

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ESO Task Force Advisory Board on Access to Innovative Treatment in Europe

European School of Oncology
Dr Paul Cornes  
Disclosures June 2019

- Honoraria received:
  - Accord Healthcare
  - Amgen
  - Astro Pharma
  - Biogen
  - European Commission
  - Generics& Biosimilar Medicines Association Australia
  - Global Academy of Health Sciences
  - Medicines for Europe/European Generics Association
  - Merck Serono
  - Mylan
  - Napp
  - Pfizer/Hospira
  - Sandoz
  - Teva
Why are we here?

Essential medicines and health products

Access to essential medicines as part of the right to health

Access to essential medicines as part of the right to the highest attainable standard of health ("the right to health") is well-founded in international law. The right to health first emerged as a social right in the World Health Organization (WHO) Constitution (1946)* and in the Universal Declaration of Human Rights (1948)*. The binding International Covenant on Economic, Social, and Cultural Rights (ICESCR) of 1966* details the progressive realization of the right to health through four concrete steps, including access to health facilities, goods and services.

The authoritative General Comment 14 (2000)* further applies the principles of accessibility, availability, appropriateness and assured quality to goods and services.
The patterns of global disease are changing

Noncommunicable diseases (NCDs), including heart disease, stroke, cancer, diabetes and chronic lung disease, are collectively responsible for almost 70% of all deaths worldwide.

This is the map of Non-Communicable Disease – the darker the colour – the higher the risk.
We live in the era of Non-Communicable Disease – with cancer the main threat

To manage this we need INNOVATION – in cancer prevention, diagnosis and treatment

This is the map of Non-Communicable Disease – the darker the colour – the higher the risk
Good news for cancer medicine:

Estimated — new medicines have accounted for 50-60 percent of the increase in cancer survival rates since 1975.
Good news for cancer treatment: Innovation in cancer medicines

At this rate our decade could add more than 100 new cancer drugs by 2020

5 cancer drugs

<1960

1960s + 2 more

1970s + 18 more

1980s + 14 more

1990s + 24 more

2000s + 23 more

2010-18

+ 81 more in only 8 years

Future of ALL medicine budgets – issues of affordability?

- Global spending on cancer medicines


- $96 Billion in 2013
- $132 Billion in 2017

2x the rate of general drug spending

Increasing at 12-14% year-on-year

Source: IQVIA MIDAS; IQVIA Institute, Dec 2017
Global Health Challenge for today

World Bank and WHO: Half the world lacks access to essential health services, 100 million still pushed into extreme poverty because of health expenses.

News release
13 DECEMBER 2017 | TOKYO - At least half of the world's population cannot obtain essential health services, according to a new report from the World Bank and WHO.

Our Greatest Challenge for 2018?
Affordable Access to healthcare
Global Health Challenges – access to affordable care is not just a problem for the poorer nations


Our Greatest Challenge for 2018?

Affordable Access to healthcare
Health Economics

- The only medicine that works
- Is one that we can afford to use

For example – novel checkpoint inhibitors all carry list prices more than $12,000 a month.

For example – novel checkpoint inhibitors all carry list prices more than $12,000 a month.

median annual cost of a new cancer drug launched in 2017 exceeded $150,000²

$56,516

The median household income in the United States is $56,516, according to 2015 data from the U.S. Census. But that rises and falls depending on close you are to peak earning age, which is typically around age 49 for men and 40 for women. How does your salary compare? 24 Aug 2017

there are serious gaps in availability of basic chemotherapeutic and biologic medicines in many Central and Eastern European countries.
Access to biologics in Europe: decided by wealth & not need

There is a strong correlation between the wealth of a country and the number of patients on biologics\(^1\)

- Example - Access to biologic medicines for Inflammatory Bowel Disease patients\(^1\)-\(^2\)

CZE: Czech Republic; DEU: Germany; ESP: Spain; FRA: France; HUN: Hungary; LVA: Latvia; POL: Poland; ROM: Romania; SWE: Sweden; SVK: Slovakia

The reality of cancer care now

- “We must confront a stark reality: cancer care is not affordable for most patients, many payers, and nearly all governments. This is a real and immediate issue across the world” ¹

We Have a Problem …

By Ed Silverman

Two years ago, the U.S. Food and Drug Administration took a step that some thought would never occur—it approved the sipuleucel-T (Provenge) vaccine for late-stage prostate cancer. The move came after a protracted episode involving allegations of conflicts of interest among a pair of FDA advisory committee members who recruited the tending a life by 4.1 months is worth the price of Provenge. It has also prompted larger questions about the underlying technology and the need to develop more vaccines. Provenge is made by culturing a patient’s immune cells with a recombinant antigen. The individualized product is then infused back into the patient, activating the immune system to target and attack the cancer. This “immunotherapy” under-
The reality of cancer care now

Only patients in the United States, Germany and United Kingdom have access to more than 40 of the 55 oncology medicines initially launched between 2012 and 2016, due to manufacturers not filing for regulatory approval, delays or denials of approval, or manufacturers awaiting the results of reimbursement negotiations prior to launching the drug in the country.

The Payers’ perspective: Medical strategies and metrics will have to change

- Pre-EBM - Evidence Based Medicine
  - Focus on a novel mechanism of action?
  - Response = CR, PR, SD, PD

- EBM - Evidence Based Medicine
  - Focus on efficacy OS, QoL

- VBM - Value Based Medicine
  - Focus on effectiveness and “value” to stakeholders Cost/QALY
The Evolution of Medical Decision Making:

▪ We have to learn to provide

▪ The most effective treatments

▪ In the most cost-effective way

VBM
“Is this worth doing compared with other things we could do with the same resource?”
Important Similarities Between Physicians and Economists

1. Realistic approach to life’s problems
2. Reliance on quantitative information
3. Often must make difficult choices in the face of uncertainty
4. Good decisions require comparing benefits and risks (costs)

Important Similarities & Differences Between Physicians and Economists

1. Realistic approach to life’s problems
2. Reliance on quantitative information
3. Often must make difficult choices in the face of uncertainty
4. Good decisions require comparing benefits and risks (costs)

Physicians are usually concerned with an individual patient or small numbers of patients.

Economists are usually concerned with large aggregations:
- organisations, industries, governments,
- society as a whole

So – why the Economic Focus on GI cancers?
What’s the cost of GI cancer in Europe?

- Main cancer diagnoses among men and women in EU countries, 2018

More diagnoses than Breast Cancer

Respiratory Cancers

Haematological Malignancies

Gastrointestinal Malignancies

651,102 Europeans diagnosed in 2018

What’s the cost of GI cancer in Europe?

- European cancer mortality, 2015

More deaths than Breast Cancer

More deaths than Lung Cancer

Gastrointestinal Malignancies

349,508 Europeans died in 2015

What's the cost of GI cancer in Europe?

Gastrointestinal Malignancies

651,102 Europeans diagnosed in 2018

349,508 Europeans died in 2015

What’s the cost of GI cancer in Europe?

- **The Economic perspective**

  **“Direct Costs”**
  - Medical Care
    - Including Patient Co-Payments

  **“Indirect Costs”**
  - Morbidity
  - Mortality

  This affects families as well as patients

Gastrointestinal Malignancies

- 651,102 Europeans diagnosed in 2018
- 349,508 Europeans died in 2015

What’s the Direct Cost of GI cancer in Europe?

- The Economic perspective – NHS England Data

Gastrointestinal Malignancies

Direct Costs

Colorectal Cancer costs more over a decade than Breast, Prostate or Lung Cancer

Colorectal (2010 £)

<table>
<thead>
<tr>
<th>18-64</th>
<th>£65</th>
</tr>
</thead>
<tbody>
<tr>
<td>201</td>
<td>435</td>
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<tr>
<td>1023</td>
<td>1760</td>
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<td>5014</td>
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<td>1688</td>
<td>2630</td>
</tr>
<tr>
<td>1370</td>
<td>2236</td>
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Total (9 Years) 38 098

Breast (2010 £)

<table>
<thead>
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<tbody>
<tr>
<td>165</td>
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<td>2630</td>
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<tr>
<td>1370</td>
<td>2236</td>
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</table>

Total (9 Years) 26 304

Prostate (2010 £)

<table>
<thead>
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Total (9 Years) 18 056

Lung (2010 £)

<table>
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<tr>
<td>344</td>
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<tr>
<td>310</td>
<td>542</td>
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<td>2671</td>
<td>3365</td>
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</tbody>
</table>

Total (9 Years) 25 847

Europeans diagnosed in 2018 (651,102)

Europeans died in 2015 (349,508)

What’s the **Direct Cost** of GI cancer in the USA?

- **The Economic perspective – USA Data**


<table>
<thead>
<tr>
<th>Malignancy</th>
<th>Initial</th>
<th>Continuing</th>
<th>End-of-Life</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pancreatic</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Esophageal</td>
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<tr>
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<td></td>
<td></td>
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<tr>
<td>Ovarian</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

3 of the top 5 US cancers by annual direct costs are Gastrointestinal

European Data shows very different performance between Health Systems

- Colorectal cancer (CRC) mortality rates vs spend in 7 European countries


Spend in EUROPE varies 20 fold without clear evidence of benefit
European Data shows very different performance between Health Systems

- Colorectal cancer (CRC) mortality rates vs spend in 7 European countries

North America Data shows very different performance between Health Systems

- First Line Metastatic Colorectal cancer (CRC) treatment costs compared

  - British Columbia: Monthly Cost $6,195 USD
  - Western Washington State: Monthly Cost $12,345; P < .01

Spend in North America varies 2 - fold without clear evidence of benefit

“Variation” is a *trigger word* for Health Economists

Variation suggests 3 lines of investigation

- Unnecessary duplication of tests and services
- Avoidable adverse events
- Low-value care: ineffective, inappropriate, not cost-effective
- Discarded inputs (e.g. unused medicines)
- Overpriced input (e.g. generic vs brand medicines)
- High cost inputs used unnecessarily (e.g. physician instead of nurse, inpatient instead of outpatient care)
- Administrative waste
- Fraud, abuse and corruption

Health systems typically look at Direct Costs of care as a ”Patient Pathway”

1. Public awareness and primary prevention
2. Diagnosis and staging
3. Treatment
4. Follow-up / Surveillance
5. End of Life

Step 1: Prevention and Early Diagnosis

- Treatment Cost = £3559 / €3969

- Stage I
  93.2% 5 year OS

- Stage IV
  8.8% 5 year OS

- 10 Year Pathway Cost, all Colorectal Cancer = £38,098 / €42,473

VALUE OF EARLY DIAGNOSIS:
1/10th the cost to diagnose and treat as stage I


Step 3: Primary Treatment

IDEA-Study: SHORTER NON-INFERIOR
3y DFS rate NSD for CAPOX regimens:
5,071 patients randomised
95% CI: 0.85–1.06

CAPOX Available as an all-generic regimen since 2013

Using CAPOX saves $4080 USD / €3590 over FOLFOX

Patients prefer oral Capecitabine over IV regimens

VALUE OF PRIMARY TREATMENT:
Less Hospital Resource / Less cost / Patient Preferred

Step 3B: Post Primary Treatment

1. Public awareness and primary prevention
2. Diagnosis and staging
3. Treatment
4. Follow-up / Surveillance
5. End of Life

Further lines of treatment? Further lines of treatment? Further lines of treatment?

Step 3B: Post Primary Treatment – 2017 Guideline Options Include...

1. Public awareness and primary prevention

2. Diagnosis and staging

3. Treatment

4. Follow-up / Surveillance

5. End of Life

### Targeted Therapies
- Bevacizumab
- Ramucirumab
- Ziv-aflibercept
- Cetuximab
- Panitumumab
- Regorafenib
- Vemurafenib

### Immunotherapies
- Ipilimumab
- Nivolumab
- Pembrolizumab
Step 3B: Post Primary Treatment

1. Public awareness and primary prevention
2. Diagnosis and staging

- **Targeted Therapies**
  - **Bevacizumab**
    - Total incremental cost (2015 US$): 60,551
    - ICER (US$/QALY): 571,240
  - **Vemurafenib**

Step 3C: Post Primary Treatment


2017 Vogel identified at least 5 treatment options beyond 2nd line with evidence for effect.

Many more therapies had ACTIVITY with PFS or DFS gains – but how useful are SURROGATE OUTCOMES to predict CLINICAL BENEFIT.
Form many potential lines of therapy – Can we select effective treatments?

- Does the ESMO *Magnitude of Benefit Scale* direct our choices to cost-effective care?

Form many potential lines of therapy – Can we select effective treatments?

- Does the ESMO Magnitude of Benefit Scale direct decisions to cost-effective care?

Principles - ESMO Scale for Assessing Value of Cancer Drugs

1. Cure takes precedence over deferral of death. ✓
2. Direct endpoints, such as overall survival and quality of life, take precedence over surrogates such as progression-free survival (PFS) and response rate (RR). ✓
3. Disease-free survival in curative disease is a more valid surrogate than PFS and RR in noncurative disease. ✓
4. Cost is not taken into account. ✗

Form many potential lines of therapy – Can we select effective treatments?

NCCN Panel members score each measure using a standardized scale from “1” to “5” with “1” being the least and “5” the most favorable.

Cost-effectiveness is not shown

ECONOMISTS Never Say “Cheap” or “Expensive”

Treatments are either COST-EFFECTIVE or NOT COST-EFFECTIVE

a high cost regimen may be highly effective – and so good value

The EU reports on strategies for sustainable care

- Key recommendations include

  Access to affordable medicines

  Many EU Member States face a challenge to import generic medicines. Public health grapples with how to use new and often expensive medicines. PATents and pharmaceutical spending are soaring. At the same time, the long-term fiscal sustainability of many health care systems is being threatened. A number of countries are struggling to pay for new and expensive medicines. This can compromise patient care and lead to significant savings, while not compromising on quality.

  Policies should strengthen the cost-effective use and the affordability of medicines, by promoting public procurement and the role of generics and biosimilars, appropriate pricing and price-competition.

  Encouraging the use of generics and biosimilar medicines. With the availability of generics and biosimilars, the original patented drug has competition. This can lead to price reduction. The greater the number of biosimilars in the market, the lower the price. This can lead to significant savings, while not compromising on quality.
Brand Competition for treatment options in the 2017 Guidelines

1 Option to save coming soon

1. Public awareness and primary prevention
2. Diagnosis and staging
3. Treatment
4. Follow-up / Surveillance
5. End of Life

### Targeted Therapies
- Bevacizumab patent expires 2010
- Ramucirumab
- Ziv-aflibercept
- Cetuximab patent expired 2016
- Panitumumab
- Regorafenib
- Vemurafenib

### Immunotherapies
- Bevacizumab Biosimilars Approved – for potential launch 2020
- Cetuximab No Biosimilars Approved – despite expired patent

Brand Competition for treatment options in the 2017 Guidelines 1 Option to save coming soon

1. Public awareness and primary prevention
2. Diagnosis and staging
3. Treatment
4. Follow-up / Surveillance
5. End of Life

What is Needed and What is the Role of Biosimilars?

📅 Thursday, 4 July  🕒 09:00 - 09:20

Speaker(s)

Josep Tabernero, Vall d’Hebron University Hospital
Vall d’Hebron University Hospital

Bevacizumab Biosimilars Approved – for potential launch 2020

Cetuximab No Biosimilars Approved – despite expired patent
“Variation” is a trigger word for Health Economists – With 2 clear areas for future work in colorectal cancer

Example: Colorectal Cancer

Deciding the Value of Innovation?

2 years from launch only 3 nations had 70% or more of innovative cancer medicines available (2017) 


Health Systems are adopting “Value Based Medicine”

2 years from launch only 3 nations had 70% or more of innovative cancer medicines available (2017) ¹

All 3 use the same metric: *The cost to gain one extra year of good quality life.*
Health Systems are adopting “Value Based Medicine”


All 3 use the same metric: The cost to gain one extra year of good quality life.
Cancer Care is becoming UNAFFORDABLE – the treatment advances we hear of at ESMO may be implemented in just a few wealthy nations.

GI Cancers Matter – the Human Cost and Financial Cost is significant -- Europe shows 20x variation in costs for no benefit & 9% OS difference without cost.

PATHWAY ANALYSIS shows that we have had successes – as well as failures.

GUIDELINE TOOLS from ESMO and NCCN are helpful – but are not yet VALUE-BASED.