Biosimilars – can we do without them?

Dr Paul Cornes

Thursday 17th March, 2016
EAHP - Vienna
Salary received:
- United Kingdom National Health Service

Honoraria received:
- Accord Healthcare
- Amgen
- Bernstein
- British Medical Journal
- European Generics Association
- Hospira
- Janssen
- Lilly
- Merck Serono
- Napp
- Pharmaceutical Association of Malaysia
- Pfizer
- Roche
- Sandoz
- Teva

These slides and their content were created by Dr Paul Cornes.

Please let me know if there are errors or omissions.
Biosimilars – can we do without them?

Dr Paul Cornes, Oncologist

Comparative Outcomes Group

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

European School of Oncology
Piazza Indipendenza, 2
6500 Bellinzona - Switzerland

paul.cornes@yahoo.co.uk
Biosimilars – can we do without them?

Biosimilars – I can’t imagine the world of medicine without them
There is a cost to cancer

- Cancer has the most devastating economic impact of any cause of death in the world.
- Cancer causes the highest economic loss of all of the 15 leading causes of death worldwide.
- WHO: Cancer world's top killer since 2010.
- The total economic impact of premature death and disability from cancer worldwide is $2.5 trillion.
- 17 percent of all 'healthy' years lost in the European Union.
- 170 million years of “healthy life” lost due to death and disability from cancer in 2008.
- Managing the costs of cancer will be the model we use for other diseases.

There is a cost to cancer
There is a cost to cancer care

“Think about health spending as not consumption but investment”

Spending is not a negative – it is a positive good

We are treating the world's most important disease – its greatest killer
Good news for medicine

- Basic cancer science is paying back on its investment
- One medical paper a minute is added to the PubMed US National Library of Medicine

“Think about health spending as not consumption but investment”
Good news for cancer treatment: worldwide – more people survive cancer

Good news for cancer treatment: Cancer survival is improving

Median Survival of Cancer in the UK has risen from 1 to 10 years since 1971

1971, 50% 1 year survival
2010, 50% 10 year survival
Cancer survival is improving

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 drugs

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

- 5 cancer drugs
- More drugs in:
  - <1960
  - 1960s
  - 1970s
  - 1980s
  - 1990s
  - 2000s
  - 2010-15

Good news for medical treatment: Innovation for all medicines is rising

Number of Commercial Investigational New Drugs by year at the US FDA

Exploration Dr
Innovation Dr
1984 Nobel Prize for Medicine awarded jointly to Jerne, Köhler and Milstein

"for the discovery of the principle for production of monoclonal antibodies".

3 decades later
3 decades of Innovation:
1984 to 2016 Monoclonal antibody development

- Head and Neck Cancer
- Breast Cancer
- Bowel Cancer
- Leukaemia
- Lymphoma
- Ovary cancer
- Secondary bone cancer
- Melanoma skin cancer
- Macular Degeneration
- Multiple sclerosis
- Asthma
- Heart disease
- Transplant rejection
- Inflammatory bowel disease
- Psoriasis
- Arthritis

3 decades later

Monoclonals in cancer - lymphoma

- **Rituximab**
  - Halves lymphoma relapse
Monoclonals in breast cancer

- **Trastuzumab**
  - Halves the chance of relapse
  - Reduces death by 33%

Romond EH, et al. NEJM. 2005;353:1673-1684
MAbs: 71% reduction in disability in multiple sclerosis

MAbs: Controlling rheumatoid arthritis

Thermal imaging of hand and elbow joints before......

..and after Mab therapy

MAbs - halves hospitalizations, surgeries, and procedures in fistulizing Crohn’s disease

MAbs for psoriasis

New targeted precision medicines are transforming cancer care

<table>
<thead>
<tr>
<th>Cancer Disease</th>
<th>Old Model</th>
<th>Old Survival</th>
<th>Personalized Model</th>
<th>Personalized Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute promyelocytic leukemia</td>
<td>Chemotherapy</td>
<td>19 months</td>
<td>All-trans retinoic acid</td>
<td>&gt;58 months</td>
</tr>
<tr>
<td>Chronic myeloid leukemia</td>
<td>Chemotherapy</td>
<td>6 years</td>
<td>Imatinib</td>
<td>&gt;22 years</td>
</tr>
<tr>
<td>Melanoma</td>
<td>Dacarbazine</td>
<td>&lt;10 months</td>
<td>Vemurafenib</td>
<td>16 months</td>
</tr>
<tr>
<td>Medullary thyroid cancer</td>
<td>Chemotherapy</td>
<td>36 months</td>
<td>Vandetanib</td>
<td>Not reached</td>
</tr>
<tr>
<td>Gastrointestinal stromal tumour</td>
<td>Chemotherapy</td>
<td>12-18 months</td>
<td>Imatinib</td>
<td>Close to 5 years</td>
</tr>
<tr>
<td>Relapsed Hodgkin lymphoma</td>
<td>Chemotherapy</td>
<td>1.2 years</td>
<td>Brentuximab vedotin</td>
<td>22.4 months</td>
</tr>
</tbody>
</table>

Chemotherapy era vs. targeted medicines era

Examples where survival has more than tripled

Good news for cancer treatment

Drugs in development,

900 drugs in development are for cancer

Source: Medco, R&D Directions

*Top ten therapeutic areas for the world’s big pharmaceutical firms, includes drugs in Phase I, II, III or awaiting FDA approval

Biosimilars – can we do without them?

Biologics – I can’t imagine the world of medicine without precision targeted therapies
The possibility at the millennium, 2000

The complexity of 200 different cancers may be explained by a few unregulated pathways.

And so the diversity of cancer might be treated by a limited panel of concurrent targeted precision therapies.

Where are we now?

I am sorry to report that you have breast cancer

Tell me doctor – what have I got?

Anatomic diagnosis

Malignant Neoplasm of Female Breast
ICD-10-CM (Category C50)
Nipple and areola – right, left, unspecified
Central portion – right, left, unspecified
Upper-inner quadrant – right, left, unspecified
Lower-inner quadrant – right, left, unspecified
Upper-outer quadrant – right, left, unspecified
Lower-outer quadrant – right, left, unspecified
Axillary tail – right, left, unspecified
Overlapping – right, left, unspecified
Unspecified – right, left, unspecified


I am sorry to report that you have breast cancer.

Tell me doctor – what have I got?

Breast cancer is now thought of as at least ten separate diseases, each with a different cause, life expectancy and needing a different treatment [2]
Where are we heading?

The Cancer Genome Atlas is a working Map of functional and actionable alterations across different tumour types [4]

Describes pathways deregulated

And drug class required to counter it

Where are we heading?

2016: Targeting two deregulated pathways with lapatinib and trastuzumab - Tumours can be gone in as short as 11 days! [5]

Describes pathways deregulated

And drug class required to counter it

Tumours shrunk 'dramatically' in 11 days

By James Gallagher
Health editor, BBC News website

© 10 March 2016 | Health

A pair of drugs can dramatically shrink and eliminate some breast cancers in just 11 days, UK doctors have shown.

They said the "surprise" findings, reported at the European Breast Cancer Conference, could mean some women no longer need chemotherapy.

Where are we heading?" Basket trials” now mean we will treat cancers by genomic diagnosis, not anatomic site [4]
Where are we heading?

With 3 key steps deregulated – we need 3 concurrent cancer therapies

How should we treat it?

Where are we heading?

With 3 key steps deregulated – we need 3 concurrent cancer therapies

the average cost per month for a branded oncology drug in the U.S. is now approximately $10,000 [2]

$10,000 \times 3 \times 12 = $360,000 a year

Will my health insurance cover that?


[2] IMS Health Study: Cancer Drug Innovation Surges As Cost Growth Moderates. URL:
http://www.imshealth.com/portal/site/imshealth/menuitem.c76283e8bf81e98f53c753c71ad8c22a/?vgnextoid=19b381d71adc5410VgnVCM100000076192ca2RCRD&vgnextchannel=5ec1e590cb4dc310Vg
2015 was another record year for drug innovation

8 cancer drugs approved in 2015 had a six-figure price [1]

The median wage in the US per person is $26,695 [2]

<table>
<thead>
<tr>
<th>DRUG NAME</th>
<th>INDICATION</th>
<th>ANNUAL PRICE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kanuma</td>
<td>LAL deficiency</td>
<td>$310,000</td>
</tr>
<tr>
<td>Strepsiq</td>
<td>Juvenile-onset hypophosphatasia</td>
<td>$285,000</td>
</tr>
<tr>
<td>Orkambi</td>
<td>Cystic fibrosis</td>
<td>$259,000</td>
</tr>
<tr>
<td>Utravi</td>
<td>Pulmonary arterial hypertension</td>
<td>$160,000–170,000</td>
</tr>
<tr>
<td>Tagrisso</td>
<td>Lung cancer</td>
<td>$153,000</td>
</tr>
<tr>
<td>Alecensa</td>
<td>ALK-positive lung cancer</td>
<td>$150,000a</td>
</tr>
<tr>
<td>Empliciti</td>
<td>Multiple myeloma</td>
<td>$140,000b</td>
</tr>
<tr>
<td>Portrazza</td>
<td>Lung cancer</td>
<td>$137,000a</td>
</tr>
<tr>
<td>Farydak</td>
<td>Multiple myeloma</td>
<td>$119,000a</td>
</tr>
<tr>
<td>Ibrance</td>
<td>Metastatic breast cancer</td>
<td>$118,200</td>
</tr>
<tr>
<td>Ninlaro</td>
<td>Multiple myeloma</td>
<td>$113,000a</td>
</tr>
<tr>
<td>Darzalex</td>
<td>Multiple myeloma</td>
<td>$110,000</td>
</tr>
</tbody>
</table>

*a Based on announced monthly or four-week pricing. b For first year of treatment.

NOTE: Blue indicates a cancer drug; yellow indicates a rare drug treatment.

SOURCES: Companies, patient groups


Where are we heading?

CAN WE AFFORD THE WAR ON CANCER?

Immunotherapy vaccines could extend survival in a handful of cancers. But personalizing treatment, payers argue, is not sustainable. Where should the line be drawn?

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 reviewed 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” underscores the move toward personalized.
But we have a problem: more cancer to treat

Positional graphic:

- **Relationship of cancer incidence with age**
- **Peak age for cancer is 70-84 years**
- **The average life expectancy in 2009 was 67**

---

Planning for the Future:
What Will Happen to Costs?

What is the driver for increased spending:
Aging populations or medical treatment?

Effect of Cost Growth Faster Than GDP and Aging of Population
Effect of Aging of Population

But we may not be able to afford innovation in Medical treatment

We can afford to age

But we have a problem: treatment costs are rising

Monthly cost of new cancer drugs by year of approval

Cancer drug costs rise 5x faster than other classes of medicine

WALL ST. IN PANIC AS STOCKS CRASH

Attempt Made to Kill Italy’s Crown Prince

Hollywood Fire Destroys Films Worth Millions

Fear 52 Perished in Lake Michigan. Ferry is Missing

Piece of Plane Like Diteman’s Is Found at Sea

High Duty Group Gave $700,000 to Coolidge Drive

Carnegie Charge of Paid Athletes Houses Colleges

Hoover’s Train Halted by Auto Placed on Rails

Warburg Sought to Keep Sea Trip Secret, Aid Says

Sommers Named as Head of New Exchange Bank
What are policy-makers trying to do?

Health Care
Will Health Costs Bankrupt America?
02.23.11, 06:00 PM EST
Forbes Magazine dated March 14, 2011

What kept going up even in the depths of the worst recession since the 1930s? Health spending.


What kept going up even in the depths of the worst recession since the 1930s? Health spending. It rose 4% in 2009 to an alltime record of 17.6% of gross domestic product. We are far above every other nation in health spending but don’t have the longevity to show for it. Health costs are by far the biggest threat to the nation’s fiscal health in the long run.

Health care costs are increasing at an annual rate of 7% a year, which if sustained will bankrupt Medicare in nine years and increase the nation’s overall annual health care tab to $4 trillion in 10 years.

Medical Cost Inflation puts health services at jeopardy

What America Spends on healthcare

What America Earns

We live in difficult times

- To maintain essential services, such as health and education
- The world has borrowed money and created significant debt

Even when our current financial crisis is over we will have to repay debt leaving little spare for increased spending

Yet we need an “innovation fund” to enable our patients to access better care

The threat to health from debt is real

for every 1% decrease in government healthcare spending, maternal mortality rises 10.6% each year in the EU

Regression coefficient [R] 0.0177, P = 0.0021, 95% confidence interval [95% CI] 0.0065–0.0289

The Evolution of Medical Decision Making:

- **Pre-EBM - Evidence Based Medicine**
  - Focus on a novel mechanism of action? **Tumour control, PFS**

- **EBM - Evidence Based Medicine**
  - Focus on efficacy **OS & QOL**

- **VBM - Value Based Medicine**
  - Focus on effectiveness and “value” to stakeholders

**EBM** “Does this intervention make you live significantly longer or live better?”

**VBM** “Is this worth doing compared with other things we could do with the same resource?”

DEFINITION of 'Blockbuster Drug'

a drug that generates annual sales of at least $1 billion

by 2018, biologics worth $68 billion in annual sales will lose patent protection

Even with only 20% discount, this should give the world a $14 Billion health innovation fund

30% gets us $21 Billion

40% pays back $28 Billion

VBM “Is this worth doing compared with other things we could do with the same resource?”
The WHO has made it very clear

- **The leading cause of inefficiency in healthcare is underuse of generics and paying more than necessary for medicines** [1]

- **A Biosimilar is similar in terms of quality, safety, and efficacy to an already licensed reference biotherapeutic product** [2]

- **To use a more expensive version of a drug is “irrational, inappropriate, improper, incorrect”** [3]

“The only drug that works is a drug that we can afford to give”

There are 196 countries in the world

Just 7 countries in the world buy 75% of all biologic drugs

The unmet need for cheaper biologics is significant
“The only drug that works is a drug that we can afford to give.”

We have a common interest between patients, physicians, pharmacists, pharma’ and payers in the success of biosimilars.

There are 196 countries in the world.

Just 7 countries in the world buy 75% of all biologic drugs.

The unmet need for cheaper biologics is significant.

Biosimilars offer a reward to world health that will be substantial.
Biosimilars – why are they so important?

Biosimilars – I can’t imagine the world of medicine without them
Biosimilars – I can’t imagine the world of medicine without them