Dr Paul Cornes
Disclosures August 2017

- Salary received:
  - United Kingdom National Health Service

- Honoraria received:
  - Accord Healthcare
  - Amgen
  - Bernstein
  - British Medical Journal
  - European Generics Association
  - Global Academy of Health Sciences
  - Hospira/Pfizer
  - Janssen
  - Lilly
  - Merck Serono
  - Napp
  - National Cancer Society Malaysia
  - Pharmaceutical Association of Malaysia
  - Roche
  - Sandoz
  - Synsana EEIG
  - Teva
Biosimilars -- Can the dream of affordable cancer care come true?

Dr Paul Cornes

Comparative Outcomes Group

ESO Task Force Advisory Board on Access to Innovative Treatment in Europe - European School of Oncology

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Biosimilars -- Can the dream of affordable cancer care come true?
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If we apply what we already know AND continue our current pattern of year-on-year improvement this is no dream!

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NHS choices Your health, your choices

Health A-Z Live Well Care and support

Under-80 cancer deaths 'eliminated by 2050' claim

Wednesday January 14 2015
We live in the era of Non-Communicable Disease

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

The World’s greatest Health Risk is now Cancer – and that risk is still rising

This is the map of Non-Communicable Disease – the darker the colour – the higher the risk
Good news for cancer treatment: worldwide – more people survive cancer

- Reduction in cancer deaths –


UK: 19.4% in 20 years
Good news for cancer treatment: worldwide—more people survive cancer

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

Almost two-thousand cancer medicines were in development in 2015


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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

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.
The aspirations for personalised medicine are realistic – not just “blue sky” thinking

- Reduction in cancer deaths –

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

Where are we now?

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.

Cancer 2017 is an anatomic diagnosis with complex prognostic & predictive biomarkers.
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?

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

The cancer revolution: Personalised treatment that's 'six times better' than traditional methods at beating the disease

The revolutionary approach tailors treatment to each cancer patient. Experts have hailed the 'personalised medicine' as a huge breakthrough. Research will show how the technique increases chances of survival.

By SOPHIE BORLAND, HEALTH EDITOR IN CHICAGO FOR THE DAILY MAIL

PUBLISHED: 00:12, 4 June 2016 | UPDATED: 01:39, 4 June 2016

A revolutionary approach to cancer which tailors treatment to each patient six times as effective as traditional methods, a landmark study has found. Experts have hailed the so-called 'personalised medicine' as the biggest breakthrough since chemotherapy.

The technique sees a patient's tumour genetically tested as soon as they are diagnosed. This allows doctors to determine whether the cancer is aggressive, whether chemotherapy is necessary and exactly which drugs are needed.

Research involving 13,203 patients, to be unveiled at the world's largest cancer conference next week, will show the technique drastically increases chances of survival and reduces the risk of the disease spreading and returning.

Gene directed precision therapy is six times better at controlling cancer – ASCO meeting 2016 [6]

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

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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? Combination targeted precision therapy

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

Will my health insurance cover that?

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

$10,000 x 3 x 12 = $360,000 a year

We Have a Problem ...  

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 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...
Access to Innovation Has One Key Rule

The only treatment that works is a one that we can afford to give.

On our current spending patterns, healthcare is unsustainable.

Especially for cancer.

Biosimilars – Can the dream of affordable cancer care come true?

- The problem of sustainable healthcare
- The value of biosimilars
- How have European biosimilars performed?
- The future of biosimilars
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There is no new money to fund a wave of investment in innovative medicine

- Since 2008 there has been a massive gap between the value of what is earned and what is being spent

Ref: [1] Matthew Lynn. All the signs point to a new recession – a worse one. The Spectator, 5 March 2016. http://www.spectator.co.uk/2016/03/the-next-recession/
Future demographic trends threaten national finances even further

- Workers paying for healthcare 20-64 years
  - 1950: 7.2:1
  - 1980: 5.1:1
  - 2050: 2.1:1

- Dependency ratio changes predicted 1970-2050:
  - UK = 4.3 to 2.1:1
  - Germany = 4.1 to 1.6:1
  - USA = 5.3 to 2.6:1

Action - What we can do about it

- We need to create a budget to expand access

Ref: [1]
Costs already limit access to healthcare – even in the richest nations of the world

- Many patients did not fill or skipped a prescription, did not visit doctor with medical problem, or did not get recommended care.

Many Europeans may be surprised to see rich nations where >10% of those on below average income fail in 1 or more tests of access to healthcare.

![Graph showing access to healthcare by income level and country](image_url)

Patients in only 6 countries had access to at least half of the 49 new oncology medicines launched 2010–2014

Availability of Oncology Medicines Launched 2010-2014

Patients in only 2 countries had access to reimbursement for at least half of the new oncology medicines launched 2014–2015

Reimbursement status of cancer medicines approved in 2014 and 2015

Innovative Oncology Drugs Not Reimbursed in these countries

The reality of cancer care now – the WISH Forum Report

“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.”


Biologic drugs transform more than just cancer

- Targeted biologic therapies offer more efficacy and less toxicity than past generations of small-molecule medicines—transforming many once hard-to-treat diseases

Biosimilars – Can the dream of affordable cancer care come true?

- The problem of sustainable healthcare
- **The value of biosimilars**
- How have European biosimilars performed?
- The future of biosimilars

The EU notes the potential savings from Biosimilar medicines

- The cumulative potential savings to health systems in the five major European Union (EU) markets and the U.S., as a result of the use of biosimilars,
  - EUR 50 -100 billion in aggregate over the next five years
The EU reports on strategies for sustainable care place biosimilars as a central policy imperative

- Key recommendations include

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 for new and existing medicines, and measures to make drug prices transparent.

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 significant savings, while not compromising on quality.
## The Promise of biosimilar medicines

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The impact of biosimilar filgrastim in London

- NHS London – daily volumes of G-CSF prescribed

![Graph showing the impact of biosimilar filgrastim in London.](image)

- 5 times more patients treated within 2 years
- While still saving almost 3 million euros each year
- Biosimilars enabled treatment to be given to patients with lower risk or earlier stage disease

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The impact of biosimilar filgrastim in Sweden

- Savings from Biosimilar G-CSF switch in Southern Health Care region in Sweden (population 1.7 million)

  Five-fold increase in daily G-CSF usage

  But still net savings of €2 million

  This represents a saving of 4%–5% of the total drug budget

New Zealand experience: “More for less – the biosimilar filgrastim story”

- Biosimilar filgrastim introduced to New Zealand in 2012

  Oncologist, Dr Richard Isaacs said… “The impact of this change for patients and hospitals has been dramatic,”

  “Previously around one third of women receiving docetaxel-based chemotherapy suffered from neutropeanic fever. We now see it in less than 7 percent.”

  "The price reduction and expanded patient access that resulted from this competition underscores the importance of biosimilars…” PHARMAC

Biosimilars Bring Treatments into Reimbursement That Might Otherwise Be Unaffordable

- Trends in use of white cell growth factors – G-CSF before and after biosimilar introduction in the EU

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Biosimilars reverse negative funding decisions

- 2008 – NICE Technology Appraisal Guidance No. 142
  • Epoetin alfa, epoetin beta and darbepoetin alfa are **clinically effective** for cancer treatment-induced anaemia
  • But not cost-effective

- 2014 – NICE Technology Appraisal Guidance No. 323
  • Erythropoiesis-stimulating agents (epoetin and darbepoetin) for treating anaemia in people with cancer having chemotherapy **are clinically effective**
  • And are now cost-effective at real contract prices

NICE accepted that biosimilar price competition had dramatically reduced the actual contract prices for epoetin

Biosimilar savings fund access to innovative therapy

- Drug-makers have outlined their plans to adapt to biosimilars - using the savings to allow payers to reinvest in their next generation of treatment innovation

The chart from a presentation at the J.P. Morgan Healthcare Conference demonstrates how biosimilars are expected to affect sales in coming years [1]

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- “All countries can do something, many of them a great deal, to improve the efficiency of their health systems, thereby releasing resources that could be used to cover more people, more services and/or more of the costs”

The WHO top priority is to control drug spending

The commonest treatment we use in medicine is drug treatment

Ten leading causes of inefficiency

Rational Medicine Use

“Medicine use is rational (appropriate, proper, correct) when
• patients receive the appropriate medicines,
• in doses that meet their own individual requirements,
• for an adequate period of time, and
• at the lowest cost both to them and the community.”

Irrational (inappropriate, improper, incorrect) use of medicines
• is when one or more of these conditions are not met.”

We are given clear moral leadership guidance by the WHO
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How have European biosimilars performed - Economics

By definition – biosimilars carry no clinically meaningful differences for patients

The only reason to use a biosimilar is economic: to make healthcare sustainable and increase patient access to effective treatment

In a decade of use – with more than 700 Million patient days exposure – there has never been an indication that an EMA approved biosimilar shows a different risk or benefit profile to the reference drug.

European Approved Biosimilars have never failed to match the reference drug in an extrapolated indication.

Biosimilars are interchangeable.

Confidence is high: “Position Statements” by Medical Societies against Biosimilars have been reversed.
How have European biosimilars performed – Interchangeability: EU National regulators Speak Up

Key Points

Biosimilars are copy versions of an already existing biological medicinal product. They are high-quality products and as efficacious and safe as the original biological medicines.

Because of the high similarity, there is no reason to believe that the body’s immune system would react differently to the biosimilar compared with the original biological upon a switch. This view is supported by the current experience with biosimilars on the market and by literature data.

In our opinion, switching patients from the original to a biosimilar medicine or vice versa can be considered safe.
How have European biosimilars performed – Research: The changing trend of publications about biosimilars: 2004-2015

- Thorsten Daubenfeld, and colleagues analysed the trends in approach to biosimilars in papers published 2004 through 2015

This should not surprise us - following decades of use of the same regulatory processes to manage manufacturing changes in Biologics.

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Expectations of Future Biosimilars: Therapeutic Oncology Drugs

- Biologic drugs are now essential medicines for the world that we must provide to the world at affordable prices

- Crucially The latest WHO essential drugs list for cancer now includes 3 biologics

European Approval of biosimilars of Rituximab

- 2 approved


- Filgrastim
- Trastuzumab
- Rituximab
European Approval of biosimilars of Trastuzumab

- Pending
  - 1 approved by US Oncology Advisory Drugs Committee
  - 3 others submitted to European Regulator

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Combination Precision Cancer therapy needs biosimilar price competition to bring the dream to reality

Without Biosimilars – most health systems cannot afford even Biologic Monotherapy

Biosimilars are now essential to sustain Innovative European healthcare

Biosimilars – physicians knowledge: Biosimilars Forum Survey 2016 – Results

- Do you believe biosimilars will be safe and appropriate for use in naïve and existing patients?


Physicians seem to be split 50:50

What is the opinion of Europe’s Medical Oncologists
Biosimilars -- Can the dream of affordable cancer care come true?

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