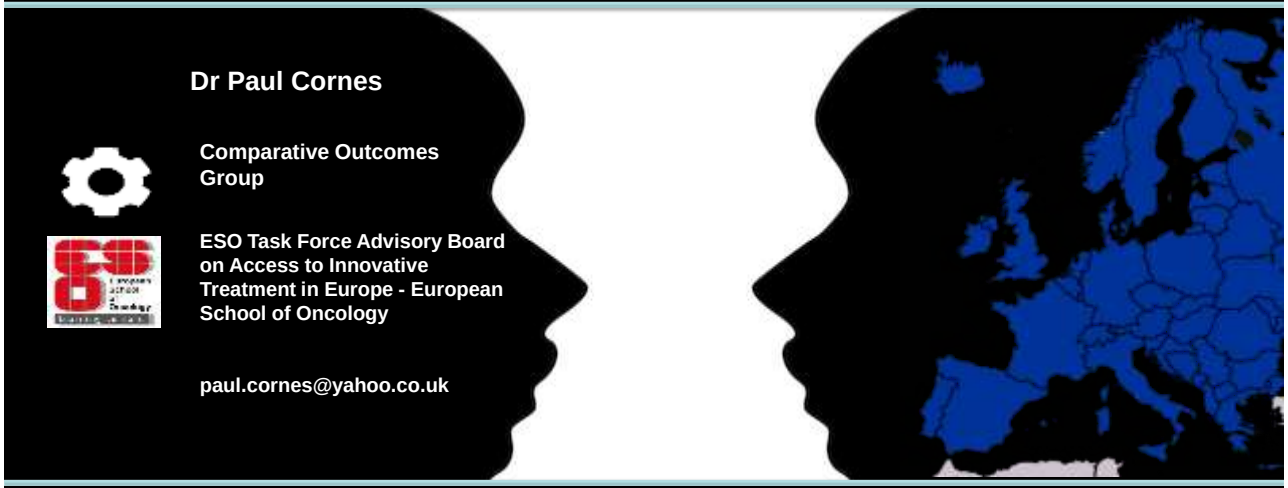
10 years of biosimilars - who benefits?



Dr Paul Cornes

Comparative Outcomes Group

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

paul.cornes@yahoo.co.uk

Dr Paul Cornes
Disclosures March 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**

These slides and their content are the responsibility of Dr Paul Cornes.

Please let me know if there are errors or omissions…

…or you have a better way of explaining it

CME question: After 10 years of European Biosimilars – which statement do you think is correct?

A. There is clear evidence that patient access and outcomes are improved by biosimilars

B. Most of the rich nations of the world have sufficient resource for healthcare

C. Biosimilars are not yet an essential component of European Healthcare

D. Biosimilars are not interchangeable with reference drugs

E. There is no evidence in March 2017 that trastuzumab biosimilars in development can match reference drugs for efficacy in breast cancer

eahp european association of hospital pharmacists

10 years of biosimilars - who benefits?

- The problem of sustainable healthcare
- The value of biosimilars
- Is there a risk to biosimilars?
- The future of biosimilars

eahp european association of hospital pharmacists

Ref: [1] Map Image. CCO License. https://upload.wikimedia.org/wikipedia/commons/7/7a/United_Kingdom_Portugal_Locator.png. Accessed March 13, 2017

10 years of biosimilars - who benefits?

- **The problem of sustainable healthcare**
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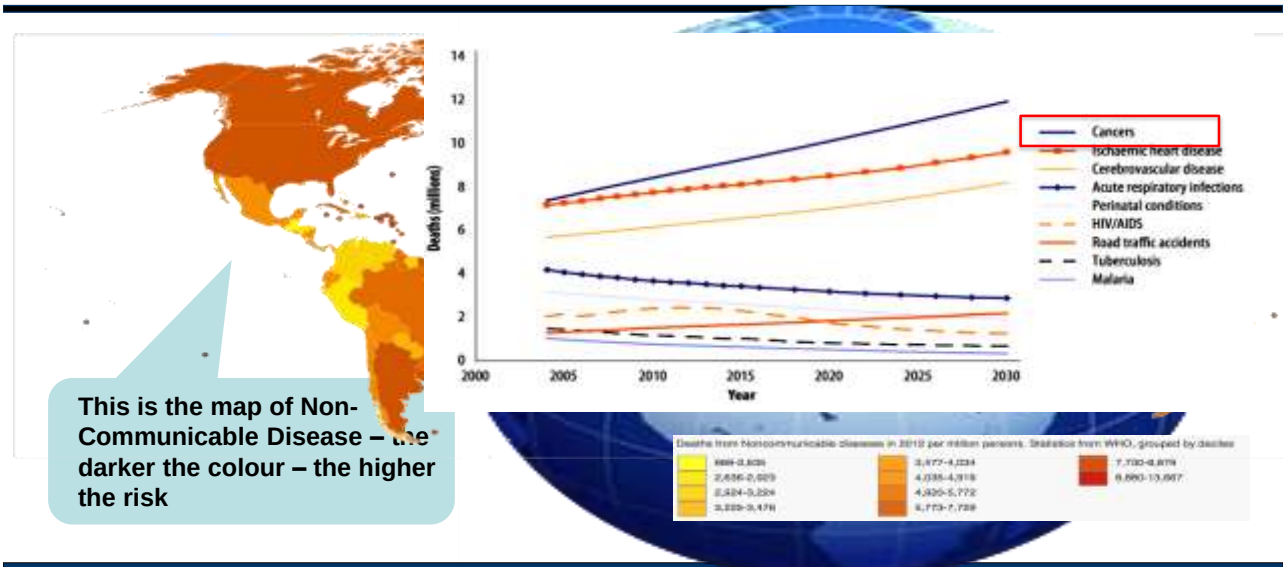
eahp european association of hospital pharmacists

Ref: [1] Map Image. CCO License. https://upload.wikimedia.org/wikipedia/commons/7/7a/United_Kingdom_Portugal_Locator.png. Accessed March 13, 2017

We live in the era of Non-Communicable Disease

Ref [1] https://upload.wikimedia.org/wikipedia/commons/thumb/c/c6/Noncommunicable_diseases_world_map-Deaths_per_million_persons-WHO2012.svg/2000px-Noncommunicable_diseases_world_map-Deaths_per_million_persons-WHO2012.svg.png. Accessed Nov 3, 2016 [2] Non-communicable diseases. The Kings Fund. https://www.kingsfund.org.uk/time-to-think-differently/trends/disease-and-disability/non-communicable-diseases. Accessed Nov 6, 2016

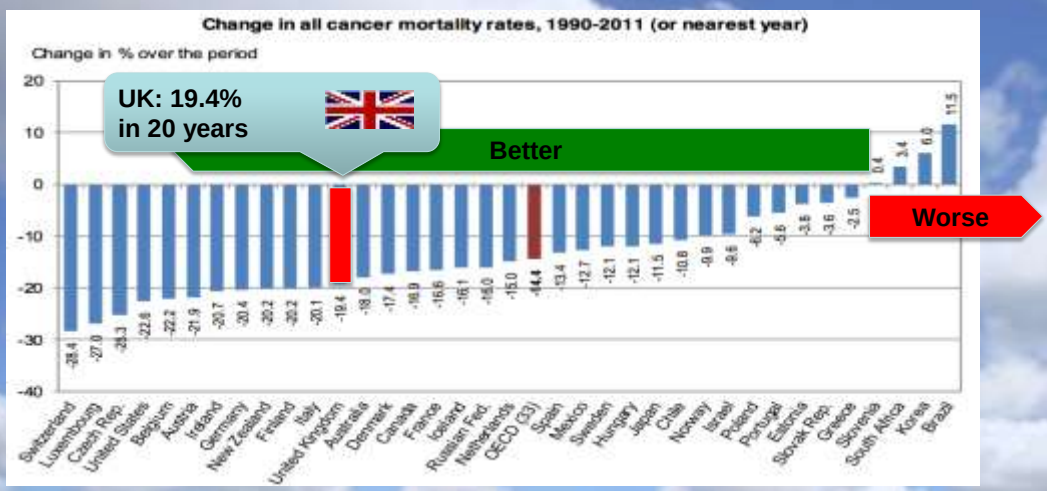
We live in the era of Non-Communicable Disease – with cancer the main threat



Ref [1] https://upload.wikimedia.org/wikipedia/commons/thumb/c/c6/Noncommunicable_diseases_world_map-Deaths_per_million_persons-WHO2012.svg/2000px-Noncommunicable_diseases_world_map-Deaths_per_million_persons-WHO2012.svg.png. Accessed Nov 3, 2016 [2] Non-communicable diseases. The Kings Fund. https://www.kingsfund.org.uk/time-to-think-differently/trends/disease-and-disability/non-communicable-diseases. Accessed Nov 6, 2016

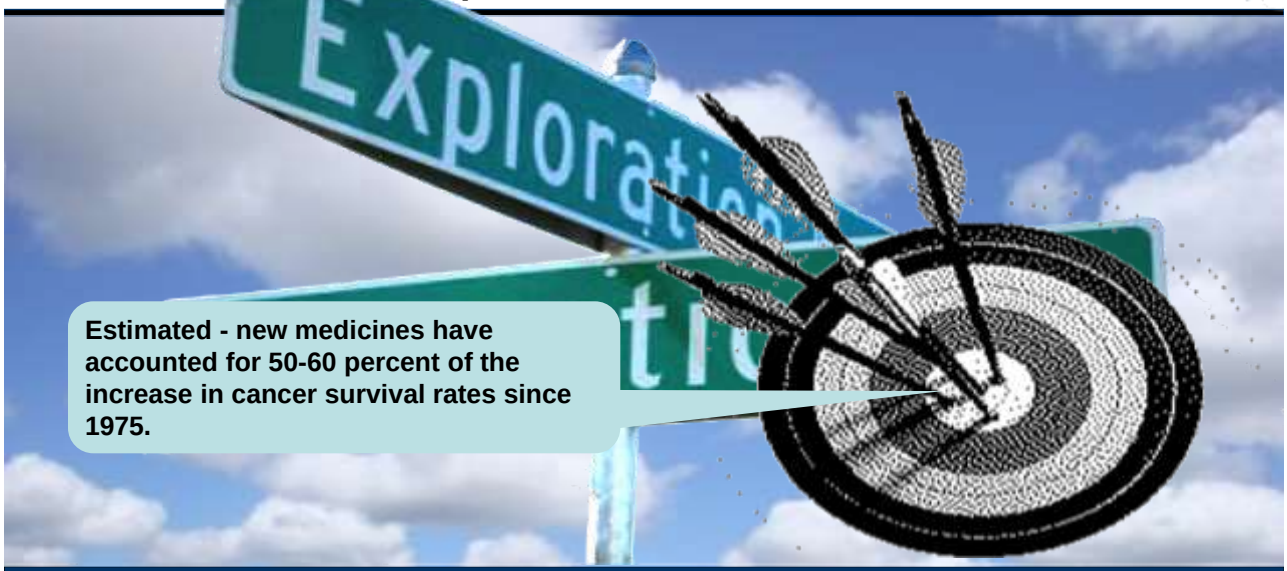
Good news for cancer treatment: worldwide – more people survive cancer

- Reduction in cancer deaths –



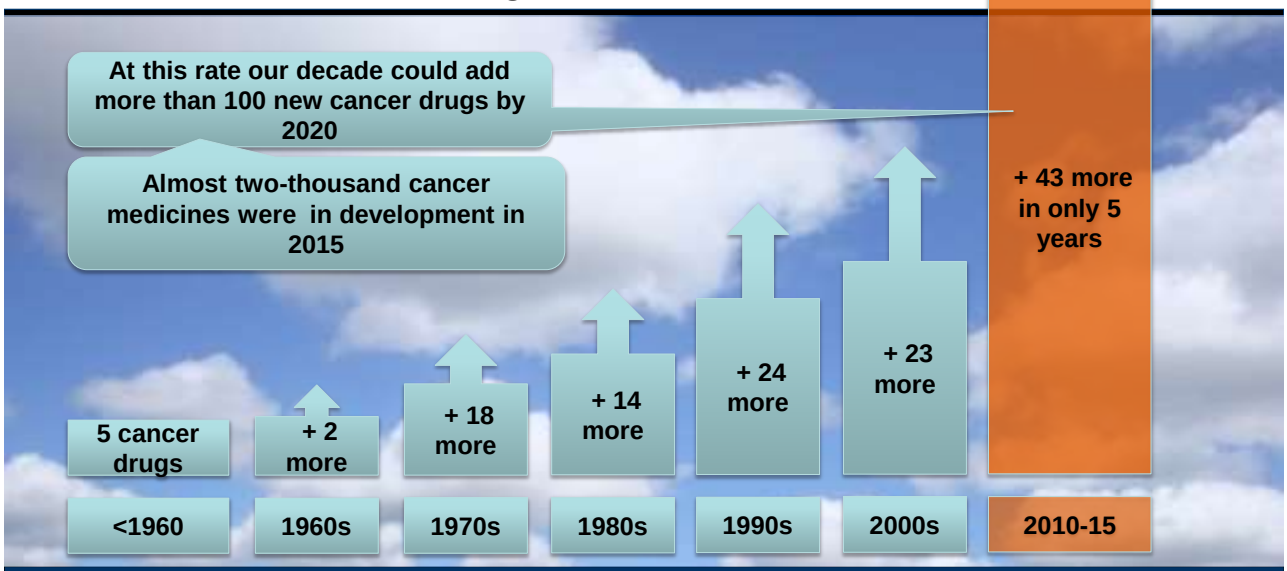
Ref: [1] Cancer Care: Chart Set. www.oecd.org/health/health-systems/cancer-care.htm. Accessed March 21, 2016

Good new[illegible]r cancer treatment: worldwid[illegible]people survive cancer



Lichtenberg Fr. The Expanding Pharmaceutical Arsenal in the War on Cancer. National Bureau of Economic research Working Paper No. 10328. February 2004.

Good news for cancer treatment: Innovation in cancer drugs



Ref: [1] Cornes P. Pictogram created from data in - Savage P. Development and economic trends in cancer therapeutic drugs: Analysis of modern and historical treatment costs compared to the contemporary GDP per capita. J Clin Oncol 32, 2014 (suppl; abstr e17535) updated to 2014 with data from [2] 2014 New Drug Approvals Hit 18-Year High. Forbes Jan 2, 2015. URL: http://www.forbes.com/sites/bernardmunos/2015/01/02/the-fda-approvals-of-2014/ . Accessed Sept 23, 2015, updated to 2015 with [3] Thomas D. 2015 FDA Approvals: Highest Levels in Over a Decade. Biotech-now.org. 01/08/2016. http://www.biotech-now.org/business-and-investments/2016/01/2015-fda-approvals-highest-levels-in-over-a-decade. Accessed Jan 27, 2016 [4] Medicines under development 2015. Source: 2015 profile: biopharmaceutical research industry. PhRMA 2015. Chimica Oggi - Chemistry Today - 2016;34(1):14

New targeted precision medicines are transforming cancer care

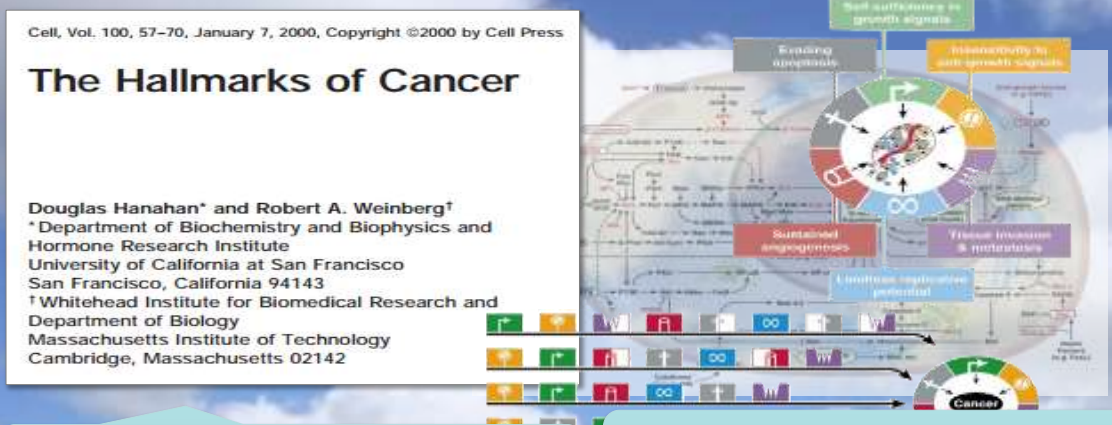
Cancer Disease	Old Model	Old Survival	Personalized Model	Personalized Survival
Acute promyelocytic leukemia	Chemotherapy	19 months	All-*trans* retinoic acid	>58 months
Chronic myeloid leukemia	Chemotherapy	6 years	Imatinib	>22 years
Melanoma	Dacarbazine	<10 months	Vemurafenib	16 months
Medullary thyroid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

Chemotherapy era vs. targeted medicines era

Examples where survival has more than tripled

Ref: [1] European Patients' Rights Day: 10 benefits the EU brings to patients. EC Memo Brussels, 12 May 2014. http://europa.eu/rapid/press-release_MEMO-14-341_en.htm. Accessed June 19, 2015 .

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

Ref [1] Hanahan D, Weinberg RA (January 2000). "The Hallmarks of Cancer". Cell 100 (1): 57–70

The aspirations for personalised medicine are realistic – not just "blue sky" thinking

- Reduction in cancer deaths –

Ref: [1] Cancer Care: Chart Set. www.oecd.org/health/health-systems/cancer-care.htm. Accessed March 21, 2016 [2] Under-80 cancer deaths 'eliminated by 2050' claim. NHS Choices Jan 14, 2015. URL: http://www.nhs.uk/news/2015/01January/Pages/Under-80-cancer-deaths-eliminated-by-2050-claim.aspx . Accessed Sept 27, 2016 [3] Overcoming Cancer in the 21st Century. UCL. 14 JANUARY 2015. URL: http://www.ucl.ac.uk/pharmacy/departments/practice-policy/VF_Embargo.pdf. Accessed Sept 27, 2016

Where were we?

I am sorry to report that you have breast cancer

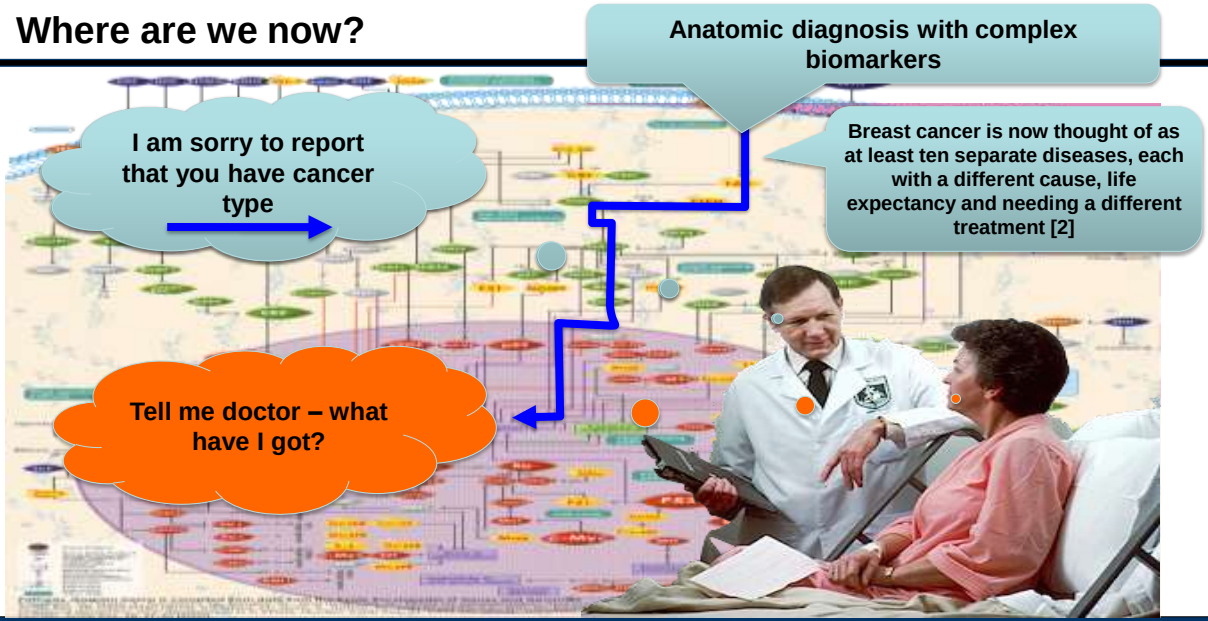
Tell me doctor – what have I got?

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
Unspecified

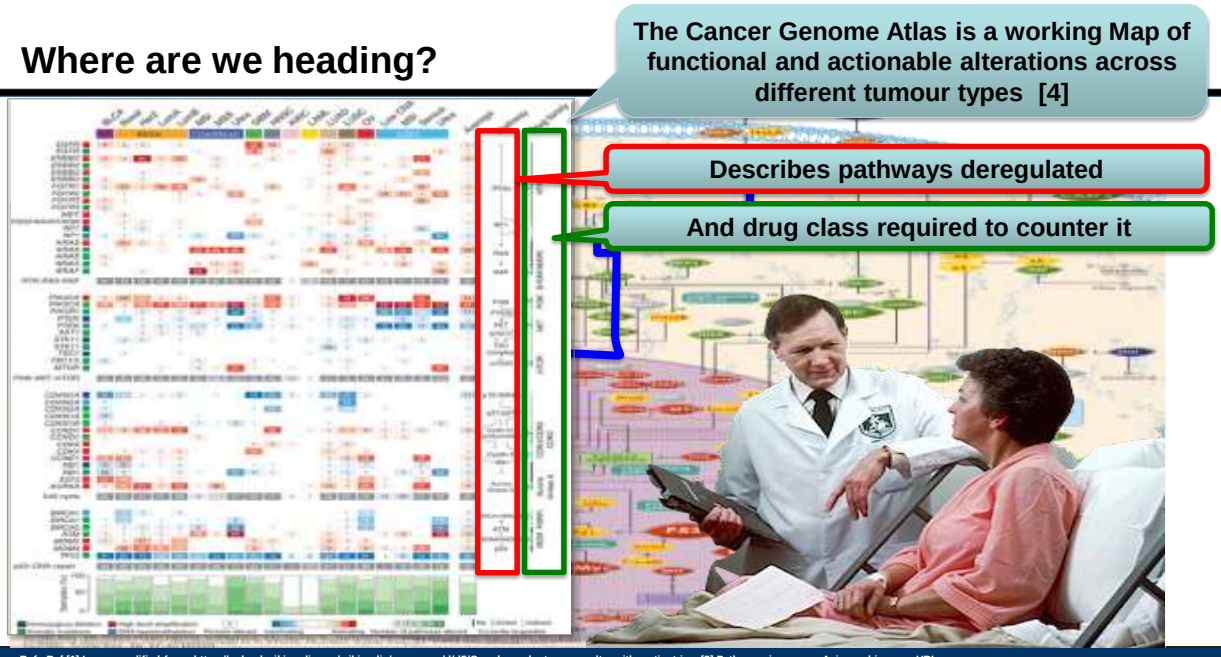
Ref: Ref [1] Image modified from https://upload.wikimedia.org/wikipedia/commons/d/d5/Oncology_doctor_consults_with_patient.jpg [2] Pathways in cancer. Avivasysbio.com. URL: http://www.avivasysbio.com/media/pdf/etc/Aviva_Pathway_Cancer.pdf. Accessed September 15, 2015.

Where are we now?



Ref: Ref [1] Image modified from https://upload.wikimedia.org/wikipedia/commons/d/d5/Oncology_doctor_consults_with_patient.jpg [2] Pathways in cancer. Avivasysbio.com. URL: http://www.avivasysbio.com/media/pdf/etc/Aviva_Pathway_Cancer.pdf. Accessed September 15, 2015. [2] Gallagher J. Tumours shrunk 'dramatically' in 11 days. BBC 10 March 2016. URL = http://www.bbc.co.uk/news/health-35775314. Accessed March 12, 2016

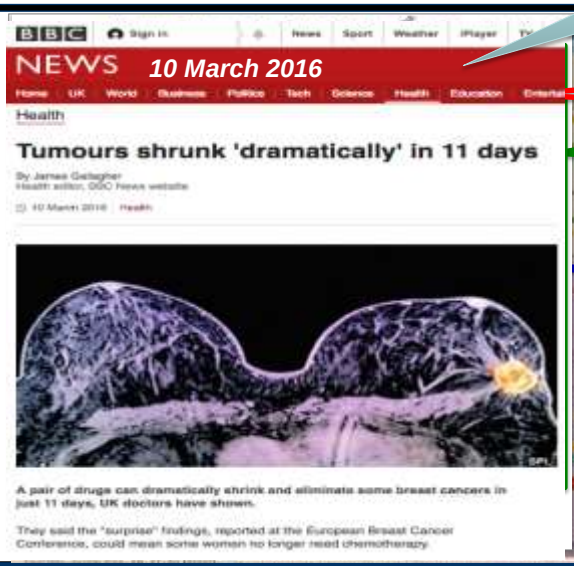
Where are we heading?



Ref: Ref [1] Image modified from https://upload.wikimedia.org/wikipedia/commons/d/d5/Oncology_doctor_consults_with_patient.jpg [2] Pathways in cancer. Avivasysbio.com. URL: http://www.avivasysbio.com/media/pdf/etc/Aviva_Pathway_Cancer.pdf. Accessed September 15, 2015. [3] Sharma, P et al. Immune Checkpoint Targeting in Cancer Therapy: Toward Combination Strategies with Curative Potential. Cell 2015;161(2):205–214 [4] Giovanni Ciriello G et al. Emerging landscape of oncogenic signatures across human cancers. Nature Genetics 2013;45:1127–1133 doi:10.1038/ng.2762

Where are we heading?

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


BBC NEWS 10 March 2016

Health

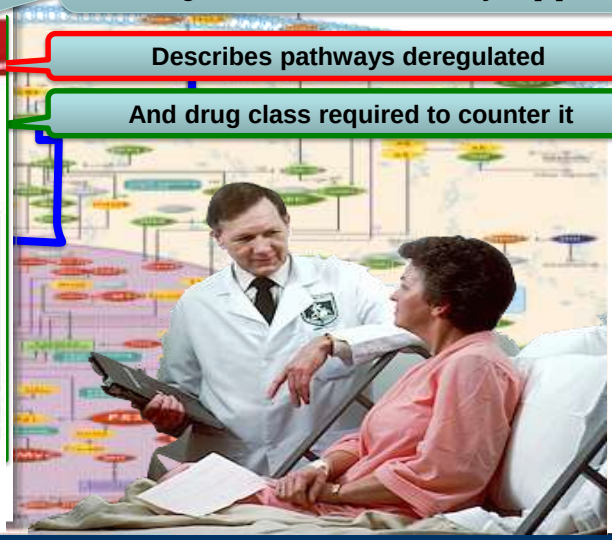
Tumours shrunk 'dramatically' in 11 days

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.

Describes pathways deregulated

And drug class required to counter it



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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 is six times as effective as traditional methods, a landmark study has found.

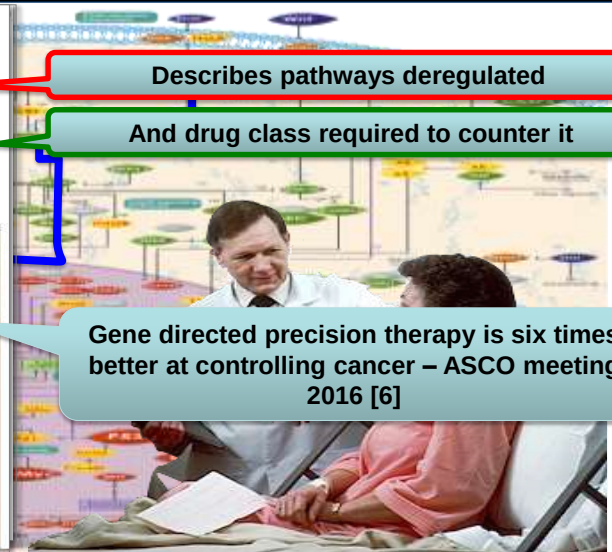
Experts have hailed the so-called 'personalised medicine' as the biggest breakthrough since chemotherapy.

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.

Describes pathways deregulated

And drug class required to counter it

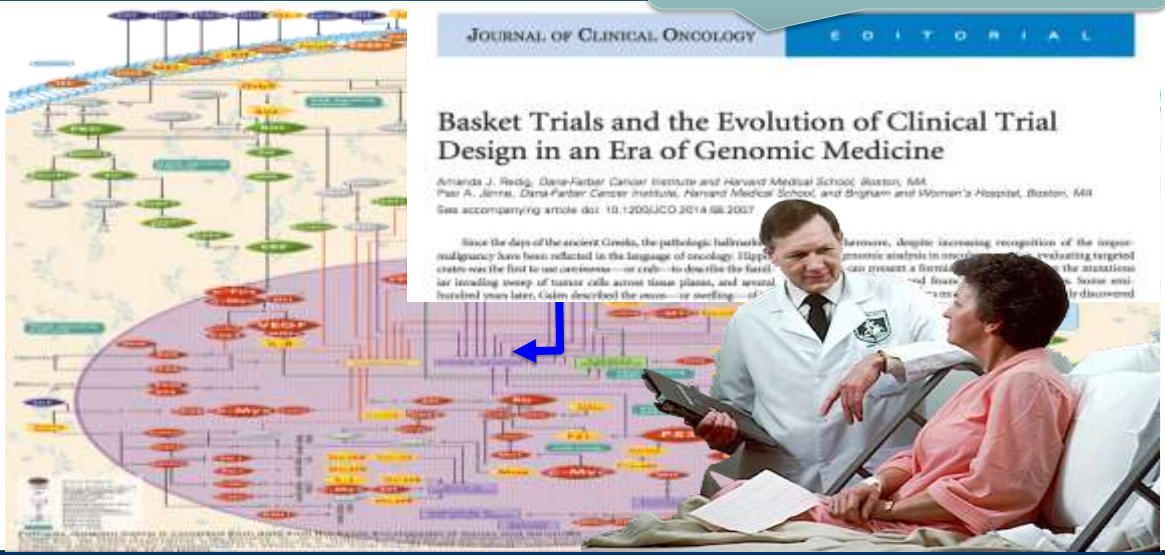


Gene directed precision therapy is six times better at controlling cancer – ASCO meeting 2016 [6]

Ref: Ref [1] Image modified from https://upload.wikimedia.org/wikipedia/commons/d/d5/Oncology_doctor_consults_with_patient.jpg [2] Pathways in cancer. Avivasysbio.com. URL: http://www.avivasysbio.com/media/pdf/etc/Aviva_Pathway_Cancer.pdf. Accessed September 15, 2015. [3] Sharma, P et al. Immune Checkpoint Targeting in Cancer Therapy: Toward Combination Strategies with Curative Potential. Cell 2015;161(2):205–214 [4] Giovanni Ciriello G et al. Emerging landscape of oncogenic signatures across human cancers. Nature Genetics 2013;45:1127–1133 doi:10.1038/ng.2762 [6] Borland S. The cancer revolution: Personalised treatment that's 'six times better' than traditional methods at beating the disease. DailyMail, Published: 00:12, 4 June 2016 | Updated: 01:39, 4 June 2016. http://www.dailymail.co.uk/news/article-3624700/The-cancer-revolution-Personalised-treatment-s-six-times-better-traditional-methods-beating-disease.html#ixzz4AvW44bcO. Accessed June 6, 2016

Where are we heading?

"Basket trials" now mean we will treat cancers by genomic diagnosis, not anatomic site [4]



Ref: Ref [1] Image modified from https://upload.wikimedia.org/wikipedia/commons/d/d5/Oncology_doctor_consults_with_patient.jpg [2] Pathways in cancer. Avivasysbio.com. URL: http://www.avivasysbio.com/media/pdf/etc/Aviva_Pathway_Cancer.pdf. Accessed September 15, 2015. [3] Sharma, P et al. Immune Checkpoint Targeting in Cancer Therapy: Toward Combination Strategies with Curative Potential. Cell 2015;161(2):205–214 [4] Redig, AJ et al. Basket Trials and the Evolution of Clinical Trial Design in an Era of Genomic Medicine. JCO February 9, 2015 JCO.2014.59.8433

Where are we heading?

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Where are we heading?

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

Ref [1] Image modified from https://upload.wikimedia.org/wikipedia/commons/d/d5/Oncology_doctor_consults_with_patient.jpg [2] IMS Health Study: Cancer Drug Innovation Surges As Cost Growth Moderates. URL: http://www.imshealth.com/portal/site/imshealth/menuitem.c76283e8bf81e98f53c753c71ad8c22a/?vgnextoid=19b381d71adc5410VgnVCM10000076192ca2RCRD&vgnextchannel=5ec1e590cb4dc310VgnVCM100000a48d2ca2RCRD Accessed September 15, 2015.

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 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

sending 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-

Ref: [1] Steven Brill. Bitter Pill: Why Medical Bills Are Killing Us. Time April 4, 2013 [2] Silverman E. *Biotechnol Healthc.* 2012;9(4):13-16.

Access to innovation has one key rule

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

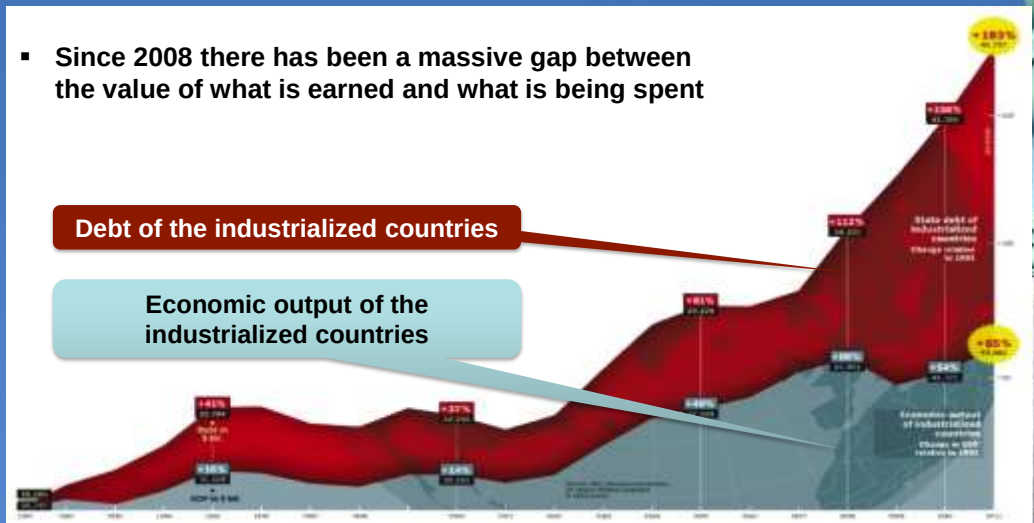
On our current spending patterns – healthcare is unsustainable

Especially for cancer

Ref: European Patients' Rights Day: 10 benefits the EU brings to patients. EC Memo Brussels, 12 May 2014. http://europa.eu/rapid/press-release_MEMO-14-341_en.htm. Accessed June 19, 2015 .

There is no new money to fund a wave of investment in innovative medicine

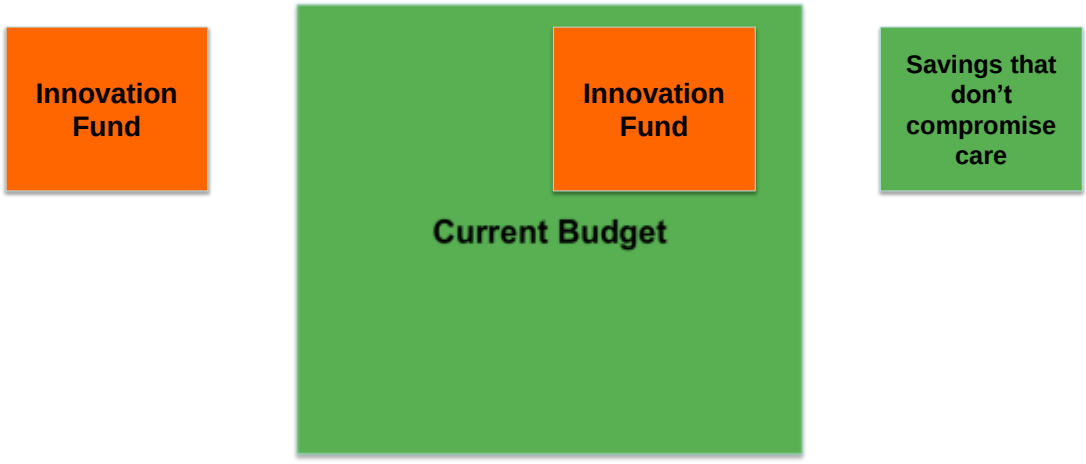
- **Since 2008 there has been a massive gap between the value of what is earned and what is being spent**



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/ [2] Per capita debt in selected countries. Der Spiegl. http://www.spiegel.de/international/world/bild-806772-300815.html. Accessed March 6, 2016

Action - What we can do about it

- We need to create a budget to expand access

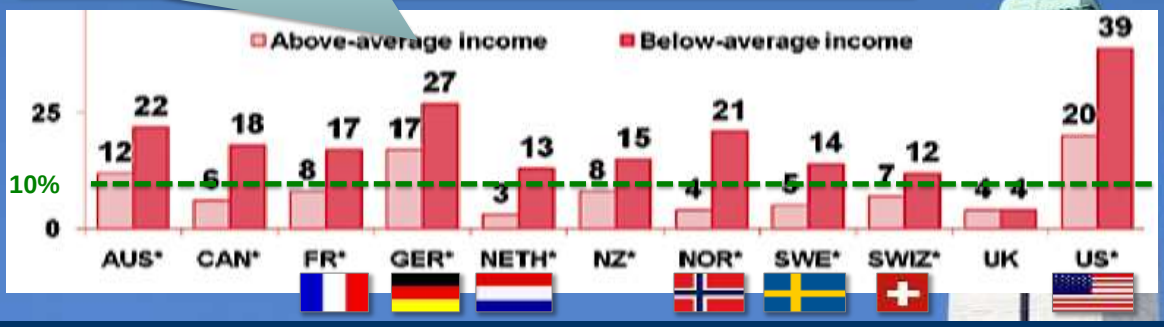


Ref: [1]

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.

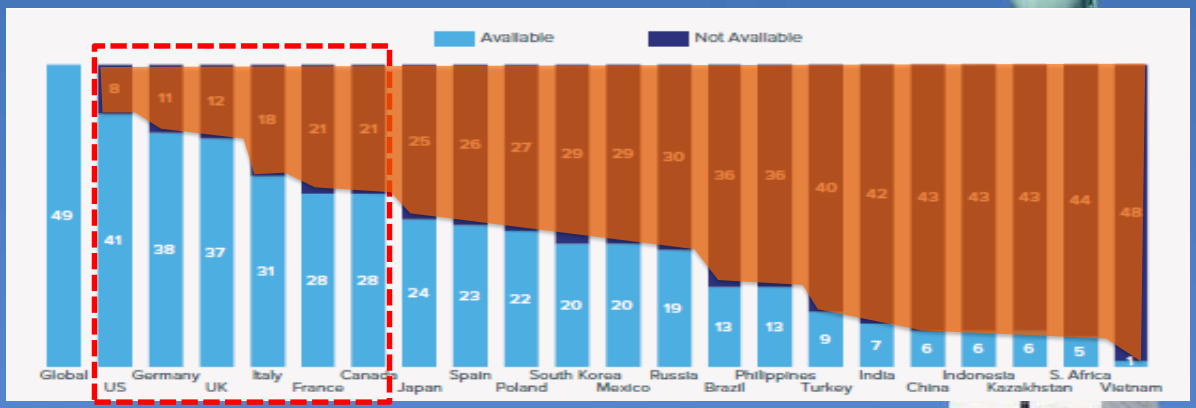
Many Europeans may be surprised to see rich nations where >10% of those on below average income fail in 1 or more tests of access to healthcare



Ref: [1] The Future of Healthcare in Europe: Summary report: Future of Healthcare in Europe conference UCL. https://www.ucl.ac.uk/european-institute/analysis-publications/publications/FHE_FINAL_online.pdf. Accessed March 7, 2016

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

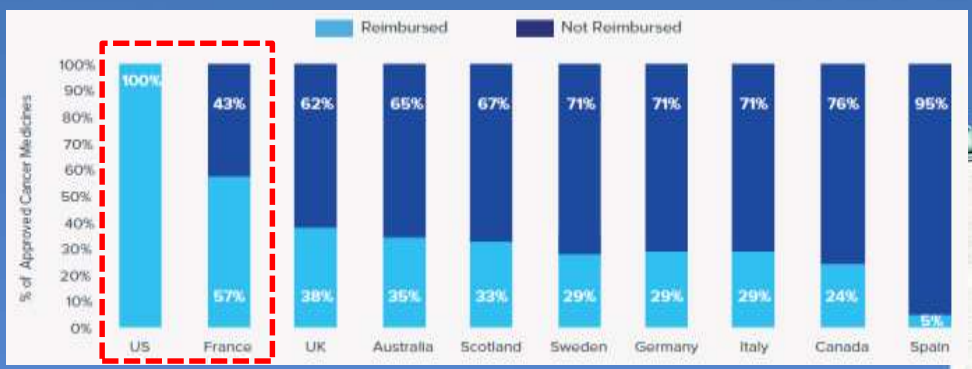
Availability of Oncology Medicines Launched 2010-2014



Ref: [1] IMS Institute for Healthcare Informatics Global Oncology Trend Report 2016

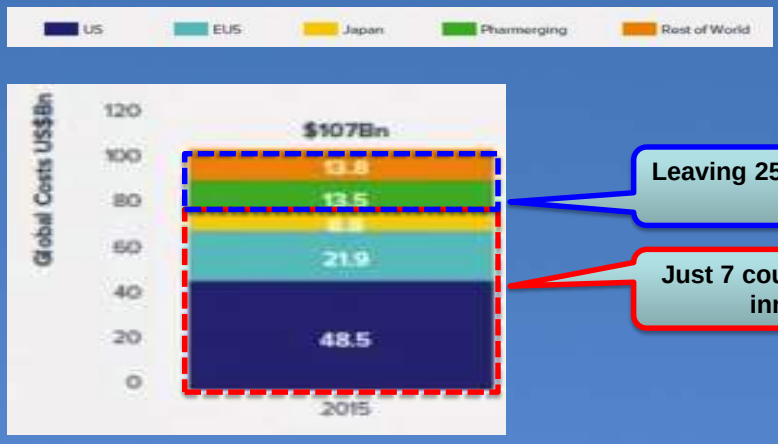
Patients in only 2 countries had access to reimbursement for at least half of the new oncology medicines launched 2014–2015

Reimbursement status of cancer medicines approved in 2014 and 2015



Ref: [1] IMS Institute for Healthcare Informatics Global Oncology Trend Report 2016

The innovative cancer drug market is still only for the richest – 2015 data



Leaving 25% for the other 193 nations of the world

Just 7 countries use 75% of the worlds innovative cancer drugs

Ref: [1] Spotlight on New Oncology Drugs: Access, Costs, and Use. Cancer Network. August 05, 2016 | Practice & Policy. http://www.cancernetwork.com/practice-policy/spotlight-new-oncology-drugs-access-costs-and-use. Accessed Oct 15, 2016

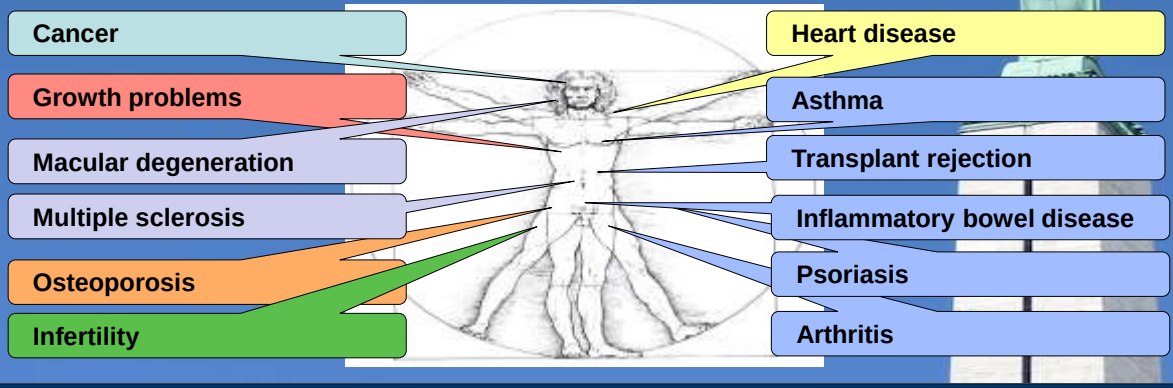
The reality of cancer care now

- ***"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"***

Ref: [1] Thomas R et al. Delivering affordable cancer care a value challenge to health systems. Report of the WISH Delivering Affordable Cancer Care Forum 2015. URL: www.wish.org.qa. Accessed Oct 17, 2016 [2] Image – CCO License - https://upload.wikimedia.org/wikipedia/commons/c/cc/Science_and_Mechanics_Nov_1931_cover.jpg. Accessed Nov 2, 2016

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



Ref: [1] Green M. Targeting Targeted Therapy. N Engl J Med 2004; 350: 2191–2193.

10 years of biosimilars - who benefits?

- The problem of sustainable healthcare
- The value of biosimilars
- Is there a risk to biosimilars?
- The future of biosimilars

eahp
european association of hospital pharmacists

Ref: [1] Map Image. CCO License. https://upload.wikimedia.org/wikipedia/commons/7/7a/United_Kingdom_Portugal_Locator.png. Accessed March 13, 2017

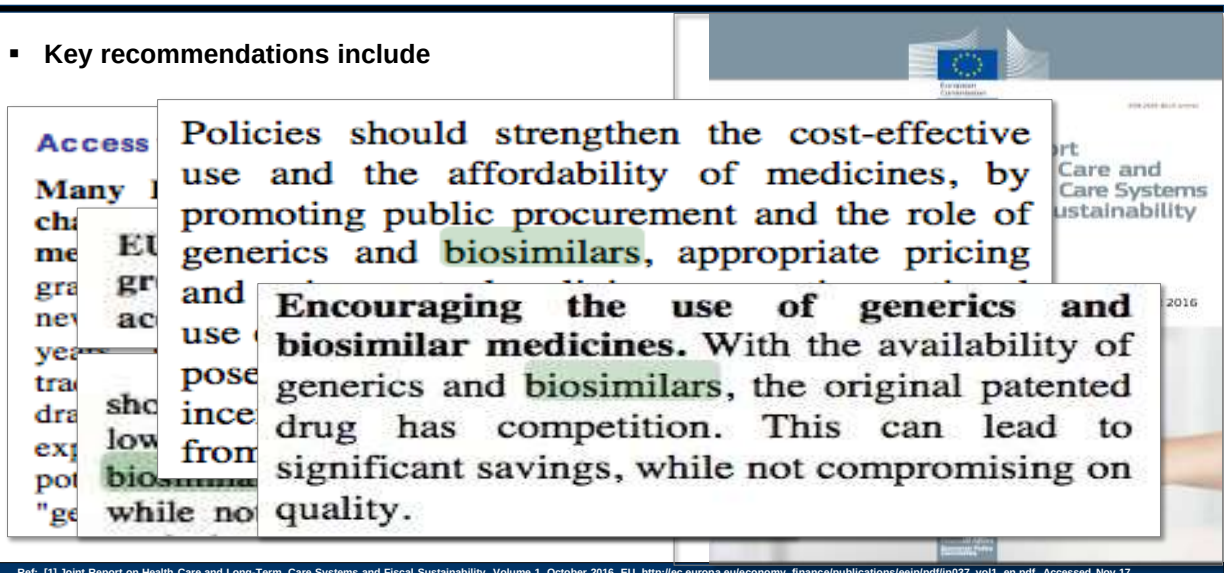
The EU notes the potential savings from Biosimilar medicines

- **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**

Ref: [1] Delivering on the Potential of Biosimilar Medicines The Role of Functioning Competitive Markets. IMS March 2016. www.theimsinstitute.org, accessed April 7, 2016

The EU reports on strategies for sustainable care place biosimilars as a central policy imperative

- **Key recommendations include**



Ref: [1] Joint Report on Health Care and Long-Term Care Systems and Fiscal Sustainability, Volume 1, October 2016. EU. http://ec.europa.eu/economy_finance/publications/eeip/pdf/ip037_vol1_en.pdf. Accessed Nov 17, 2016

The Promise of biosimilar medicines

High cost biologics create a problem	Cost Savings from Biosimilars	That cheaper biologics could resolve
Challenge		**Result**
Effective targeted therapy held back for later stage of disease	→	Effective targeted therapy used earlier in the disease
Treatment reserved for only the most severe cases	→	More patients have access to treatment
Innovative therapies unaffordable	→	Biosimilars free up budget to buy innovative medicines
Budgets for certain therapy areas are inadequate	→	Additional budget can be directed to areas of unmet need

Ref: Adapted from Henry D, Taylor C. Pharmacoeconomics of Cancer Therapies: Considerations With the Introduction of Biosimilars. Seminars in Oncology. 2014;41, Supplement 3:S13–20

Reality

The ~~Promise~~ of biosimilar medicines

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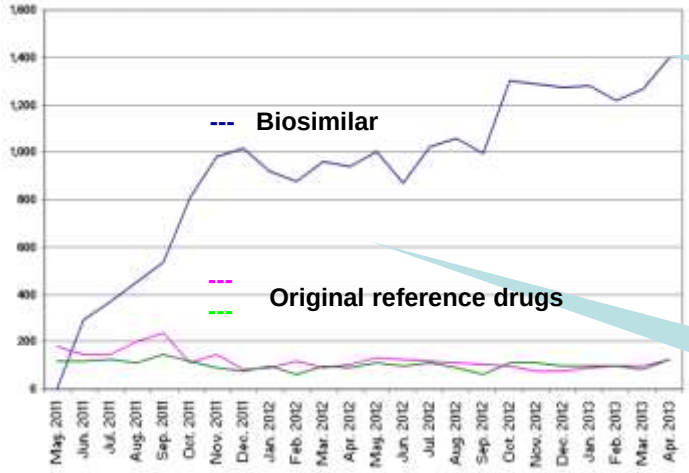
The impact of biosimilar filgrastim in London

- **NHS London – daily volumes of G-CSF prescribed**



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

1. Antony Grosso, London Procurement Programme, 2012, quoted in Gascón P, et al. *Support Care Cancer*. 2013;21:2925-2932; 2. Kashyap Thakrar. Biosimilar G-CSF: Implementation & lessons learnt. Centre for Medicines Optimisation UK. http://centreformedicinesoptimisation.co.uk/files/Kash%20Thakrar%20Biosimiar%20-%20GCSF.pdf. Accessed 10 June 2015.

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

Gascón P, et al. Clinical experience with Zarzio® in Europe: what have we learned? *Support Care Cancer*. 2013;21:2925-2932.

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,"

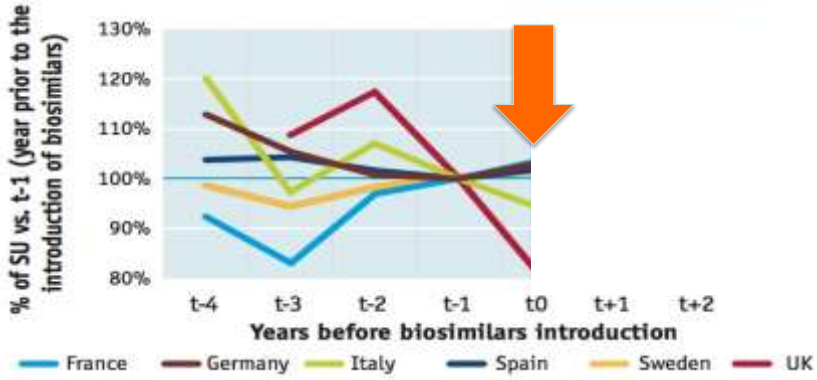
"Previously around one third of women receiving docetaxel-based chemotherapy suffered from neutropeanic fever. We now see it in less than 7 percent."

PHARMAC reports: expanded access 25% & budget savings!

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

Ref: [1] Biosimilar filgrastim. More for less – the biosimilar filgrastim story. PHARMAC Annual Review 2014. URL: http://www.pharmac.health.nz/about/annual-review/2014/biosimilar-filgrastim/. Accessed Jan 27, 2015 [2] Ref: Filgrastim change - A view from the front line. PHARMAC Annual Review 2014. PHARMAC. http://www.pharmac.health.nz/about/annual-review/2014/biosimilar-filgrastim/filgrastim-sidebar/. Accessed Jan 27, 2015

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

IMS Health. Shaping the biosimilars opportunity: A global perspective on the evolving biosimilars landscape. December 2011. http://www.imshealth.com/ims/Global/Content/Home%20Page%20Content/IMS%20News/Biosimilars_Whitepaper.pdf.

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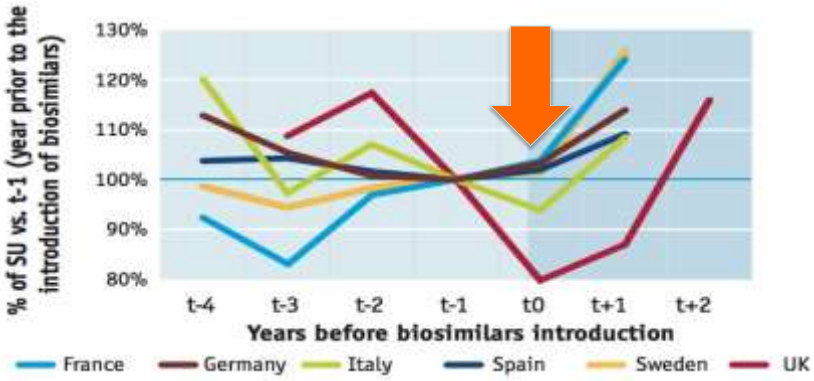


- **Trends in use of white cell growth factors – G-CSF before and after biosimilar introduction in the EU**

IMS Health. Shaping the biosimilars opportunity: A global perspective on the evolving biosimilars landscape. December 2011. http://www.imshealth.com/ims/Global/Content/Home%20Page%20Content/IMS%20News/Biosimilars_Whitepaper.pdf.

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**

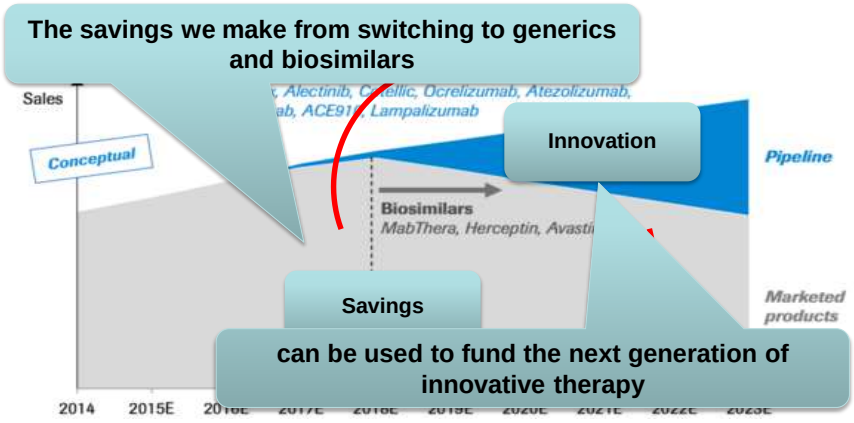
NICE accepted that biosimilar price competition had dramatically reduced the actual contract prices for epoetin

1. NICE technology appraisal guidance [TA142] May 2008. Epoetin alfa, epoetin beta and darbepoetin alfa for cancer treatment-induced anaemia. http://www.nice.org.uk/guidance/ta142. Accessed 10 June 2015;
2. NICE technology appraisal guidance [TA323] November 2014. Erythropoiesis-stimulating agents (epoetin and darbepoetin) for treating anaemia in people with cancer having chemotherapy (including review of TA142). http://www.nice.org.uk/guidance/ta323. Accessed 10 June 2015.

Biosimilar savings fund access to innovative therapy

- **Roche has outlined its plan to adapt to biosimilars - using the savings to allow payers to reinvest in their next generation of innovation**

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



Ref: [1] Lorenzetti L. Biosimilars Are Coming After Big Pharma's Bottom Line. Fortune. Jan 12, 2016, 2:02 PM EST. URL: http://fortune.com/2016/01/12/biosimilars-big-pharma/. Accessed Jan 25, 2016

Reality
The ~~Promise~~ of biosimilar medicines

Challenge		Result
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Cost Savings from Biosimilars

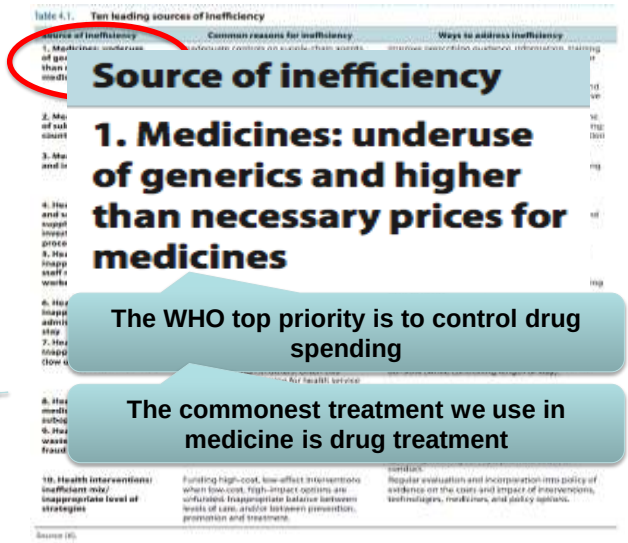
Physicians need biosimilars to sustain healthcare innovation

Ref: Adapted from Henry D, Taylor C. Pharmacoeconomics of Cancer Therapies: Considerations With the Introduction of Biosimilars. Seminars in Oncology. 2014;41, Supplement 3:S13–20

WHO – World Health Report 2010: *"More health for the money"*

- ***"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"***

Ten leading causes of inefficiency



Ref WHO. World health report 2010.Chapter 4: More health for the money. URL: www.who.int/whr/2010/10_chap04_en.pdf. Accessed OCT 29, 2014

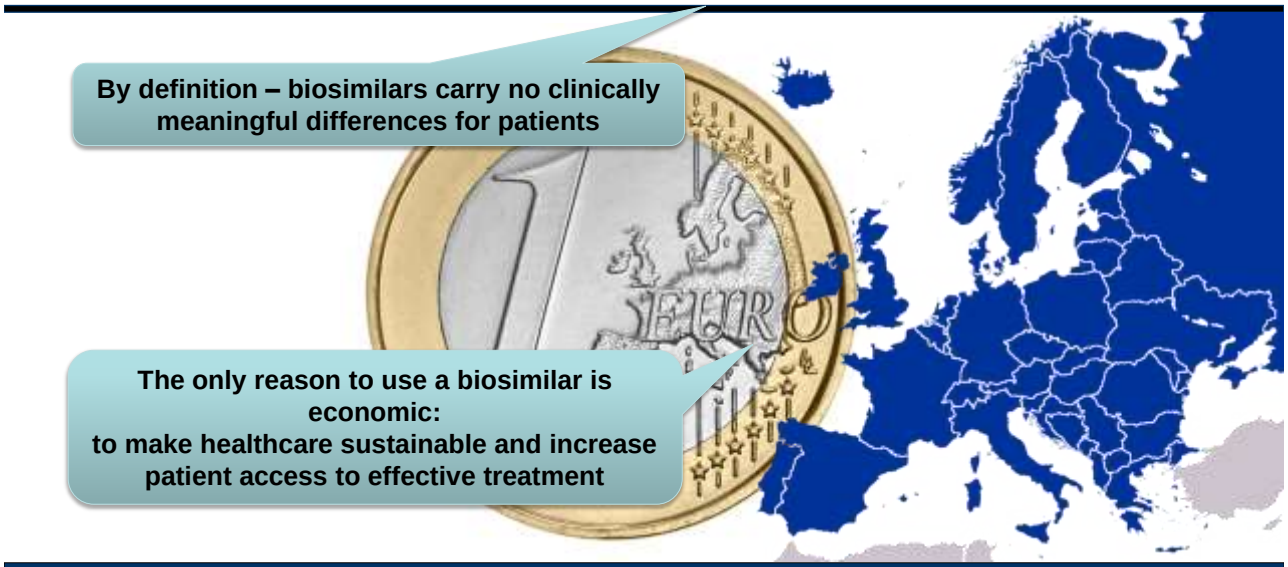
10 years of biosimilars - who benefits?

- **The problem of sustainable healthcare**
- **The value of biosimilars**
- **Is there a risk to biosimilars?**
- **The future of biosimilars**

eahp european association of hospital pharmacists

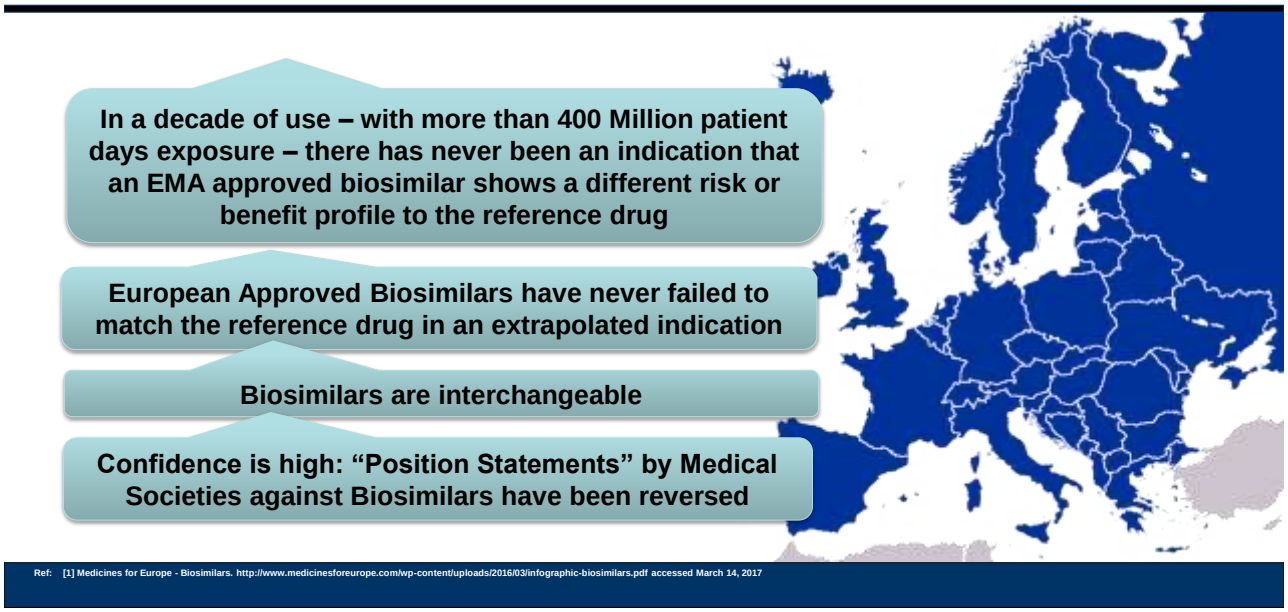
Ref: [1] Map Image. CCO License. https://upload.wikimedia.org/wikipedia/commons/7/7a/United_Kingdom_Portugal_Locator.png. Accessed March 13, 2017

Is there a risk despite the financial benefits of Biosimilars?



Ref: [1] Document Title: What is a Biosimilar Medicine? Clinical and Scientific Policy and Strategy Team, NHS England. https://www.england.nhs.uk/wp-content/uploads/2015/09/biosimilar-guide.pdf. Accessed Nov 15, 2016

Is there a risk despite the financial benefits of Biosimilars?

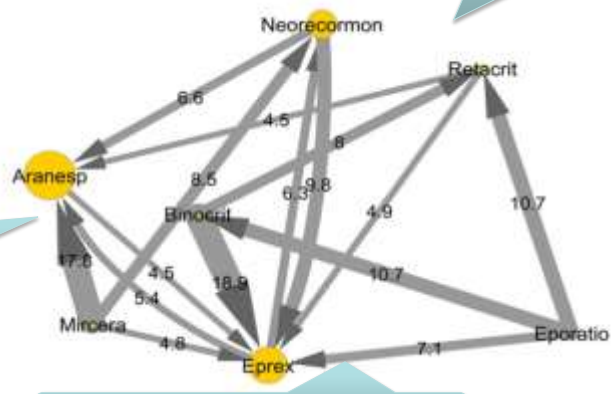


Ref: [1] Medicines for Europe - Biosimilars. http://www.medicinesforeurope.com/wp-content/uploads/2016/03/infographic-biosimilars.pdf accessed March 14, 2017

Interchange of biologics is frequent: Often between originator drugs!

- **Switching patterns of erythropoiesis-stimulating agents (ESAs) over one year**
  - The size of each node indicates the number of users;
  - the size of each arrow indicates the proportion of users (minimum 4 %) who switched between one product and another;

49,491 patients on ESAs in 4 regions of Italy



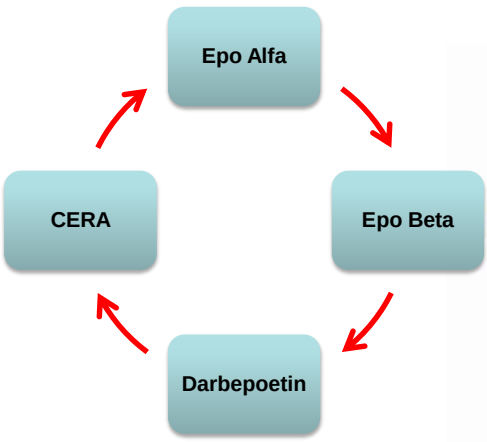
Most switching occurs between reference epoetin-alfa and epoetin-beta reference drugs

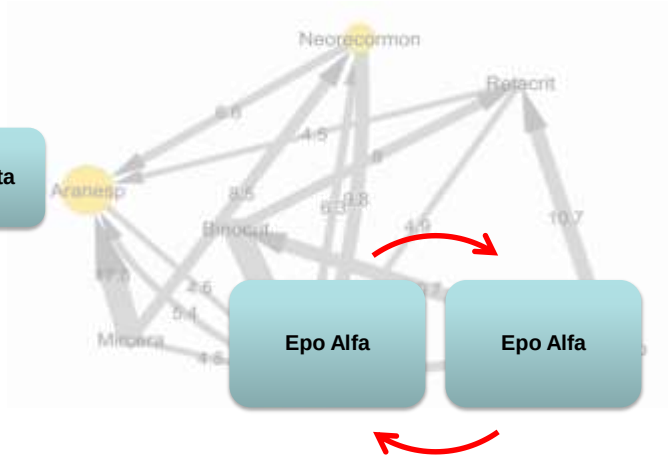
In practice – Physicians have regarded the 4 different reference drugs in the epoetin class as "Interchangeable"

4006 switchers (17.0 %)

Reff: Agenzia Italiana del Farmaco (AIFA). Position paper sui farmaci biosimilari (28/05/2013). Available from: http://www.agenziafarmaco.gov.it/sites/default/files/AIFA_POSITION_PAPER_FARMACI_BIOSIMILARI.pdf.

Is switching to a biosimilar more of a risk than switching to another originator drug ?





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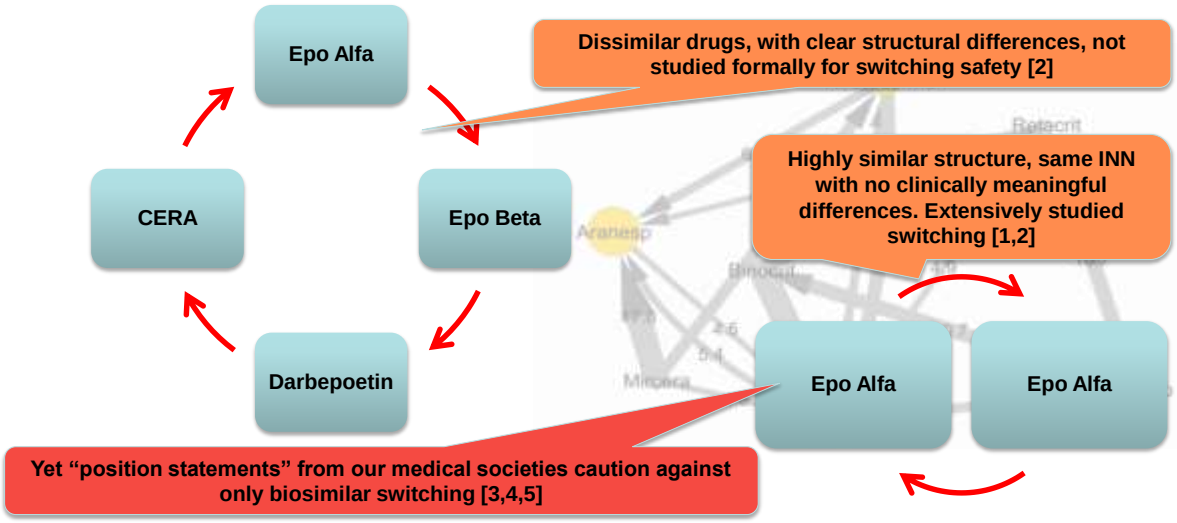


Ref: [1]Ebbers HC, Muerzberg M, Schellekens H. The safety of switching between therapeutic proteins. Expert Opin Biol Ther. 2012 Nov;12(1):1473-85. doi: 10.1517/14712598.2012.711308. Epub 2012 Jul 31. [2] Carmen D'Amore et al. Switching Between Epoetins: A Practice in Support of Biosimilar Use. BioDrugs. Published online Jan 4, 2016. DOI 10.1007/s40259-015-0155-0 [3] Bouchet JL et al. Position statements regarding usage of biosimilars of Epoetins. Position paper of the Société de néphrologie. Nephrol Ther. 2009 Feb;5(1):61-6. [4] Covic A, et al.Biosimilars and biopharmaceuticals: what the nephrologists need to know--a position paper by the ERA-EDTA Council. Nephrol Dial Transplant. 2008 Dec;23(12):3731-7. [5] Shaldon S. Biosimilars and biopharmaceuticals: what the nephrologist needs to know--a position paper by the ERA-EDTA Council. Nephrol Dial Transplant. 2009 May;24(5):1700-1

Replacing one biologic with another is not necessarily an issue

Approval 28 Oct 1982
Formulation Revision 02 Dec 1982
Manufacturing Change or Addition
27 Oct 1987, 10 May 1993, 25 April 1996, 28 Jan 1998, 10 Jan 2003, 10 Nov 2003, 29 Mar 2012, 07 Nov 2012, 09 Jan 2013, 10 May 2013, 30 May 2013, 31 May 2013, 15 Aug 2013, 18 Mar 2014, 20 Jun 2014, 23 Sep 2014, 30 Oct 2014

Approval 25 Jun 1991
Formulation Revision 02 Dec 1982
Manufacturing Change or Addition
13 Jun 1996, 18 Oct 1999, 19 Jun 2002, 25 Jun 2010,

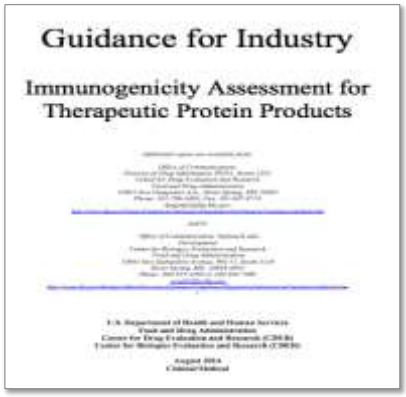
Escherichia coli
No data on manufacturing changes found in the public domain

Patients have been switched between human insulin products for more than 20 years. These in turn have been subject to multiple manufacturing changes

Source Drugs @FDA,

Can switching to a biosimilar be harmful? Theory

- For switching to be a problem – there would have to be a "carry over" effect from one drug to another
  - The only mechanism that we can imagine causing this would be immunogenicity leading to anti-drug antibody formation
- For switching to be a problem, the two drugs would need to have a different immune profile
  - For this reason, regulators set strict guidance on immunogenicity before a biologic can be approved [2]

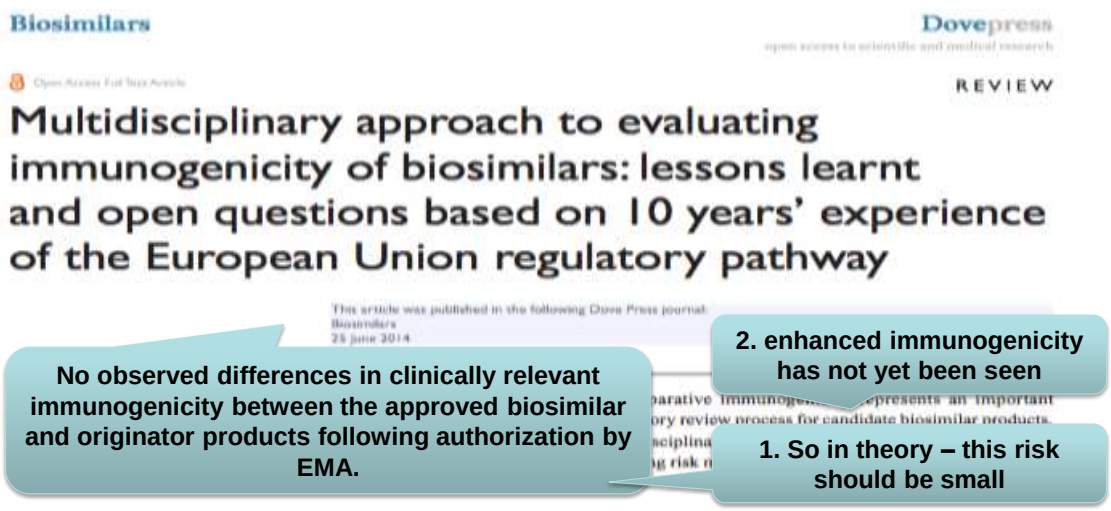

Guidance for Industry

Immunogenicity Assessment for Therapeutic Protein Products

1. So in theory – this risk should be small

Ref: [1] Yanai H et al. Levels of drug and antidrug antibodies are associated with outcome of interventions after loss of response to infliximab or adalimumab. Clin Gastroenterol Hepatol. 2015 Mar;13(3):522-530.e2. doi: 10.1016/j.cgh.2014.07.029. Epub 2014 Jul 25. [2]Guidance for Industry Immunogenicity Assessment for Therapeutic Protein Products. U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER). August 2014. URL:

Can switching to a biosimilar be harmful? Theory – Anti-drug immunity


Biosimilars

Dovepress

REVIEW

Multidisciplinary approach to evaluating immunogenicity of biosimilars: lessons learnt and open questions based on 10 years' experience of the European Union regulatory pathway

This article was published in the following Dove Press journal:
Biosimilars
25 June 2014

No observed differences in clinically relevant immunogenicity between the approved biosimilar and originator products following authorization by EMA.

2. enhanced immunogenicity has not yet been seen

1. So in theory – this risk should be small

Ref: [1] European Medicines Agency. Similar biological medicinal products containing biotechnology-derived proteins as active substance: non-clinical and clinical issues, CHMP/BMWP/42832/2005 rev1, Draft Revision, June 3, 2013. Available from: http://www.ema.europa.eu/ema/index.jsp?curl=pages/includes/document/document_detail.jsp?webContentId=WC500144124&mid=WC0b01ac058009a3dc.2. Accessed Jan 11, 2016

Can switching to a biosimilar be harmful? Practice

- In practice, with 10 years of experience of biosimilars in Europe, no problems have been identified.
  - Over that time, patient exposure to biosimilars has been measured in millions

3. And in practice – this risk has not been seen

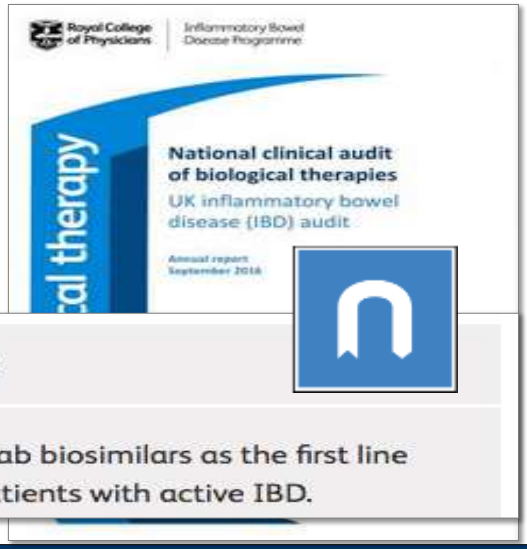
2. enhanced immunogenicity has not yet been seen

1. So in theory – this risk should be small

Ref: [1] Ebbers HC et al. The safety of switching between therapeutic proteins. Expert Opin Biol Ther 2012;12(11):1473-85

Reversing negative "Position Statements" – UK British Society of Gastroenterology

- Between 1 March 2015 and 29 February 2016, 138 (87%) of the 159 eligible adult trusts / health boards and 19 (76%) of the 25 IBD specialist paediatric sites in the UK participated in this audit or the Personalised Anti-TNF Therapy in Crohn's disease study
- 2722 adult and 278 paediatric patients entered to the audit.



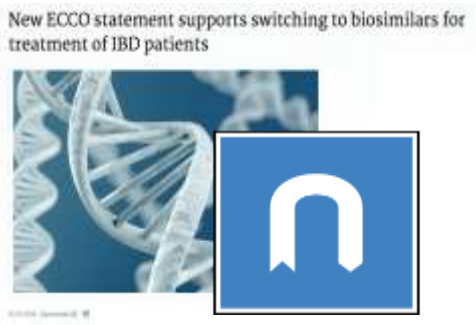
Key recommendations

- Clinicians should use infliximab biosimilars as the first line anti-TNFα for appropriate patients with active IBD.

Ref: [1] On behalf of the IBD programme steering group.National clinical audit of biological therapies. UK inflammatory bowel disease (IBD) audit. Annual report September 2016. 22 September 2016. URL: https://www.rcplondon.ac.uk/projects/outputs/national-clinical-audit-biological-therapies-annual-report-2016. Accessed Sept 26, 2016

Reversing negative "Position Statements" – European Crohn's and Colitis Organization (ECCO)

- **December 2016 - Updated position statement on biosimilars**

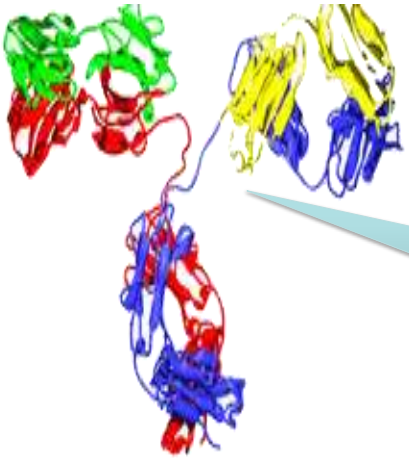


- ***"Switching from the originator to a biosimilar in patients with IBD is acceptable following appropriate discussion between physicians, nurses, pharmacists, and patients, and according to national recommendation"***
- ***"When a biosimilar product is registered in the European Union, it is considered to be as efficacious as the reference product when used in accordance with the information provided in the Summary of Product Characteristics"***

Ref: [1] New ECCO statement supports switching to biosimilars for treatment of IBD patients. Pharmaletter Dec 12, 2016. http://www.thepharmaletter.com/article/new-ecco-statement-supports-switching-to-biosimilars-for-treatment-of-ibd-patients. Accessed Dec 12, 2016

The greatest challenge in switching has been Infliximab in Rheumatoid Disease

- **Infliximab is the most important 2nd generation drug to learn from**



- **Rheumatoid disease is an immune disease of anti-antibody formation**
- **Infliximab is the drug with the highest rate of ADAb in the class: 20-40% of patients exposed with Rheumatoid**

"Rheumatoid factor" is an Anti-Antibody Complex [2]

To date – 4 systematic reviews confirm safety and efficacy

Ref: [1] Antibody Image. CCO License, Wikimedia. https://upload.wikimedia.org/wikipedia/commons/thumb/a/a9/Antibody_IgG2.png/220px-Antibody_IgG2.png. Accessed Jan 4, 2017 [2] Song YW, Kang EH. Autoantibodies in rheumatoid arthritis: rheumatoid factors and anticitrullinated protein antibodies. QJM: An International Journal of Medicine. 2010;103(3):139-146. doi:10.1093/qjmed/hcp165.

1: Infliximab Biosimilars – Safety & Efficacy: Systematic review September 2015

- By September 15, 2015 there were 15 English-language reports that confirmed equivalence in the safety, efficacy, or pharmacokinetic profiles of biosimilar and reference TNF-α inhibitors -
  - 8 randomized controlled trials (RCTs), 4 abstracts describing trial extensions, 2 retrospective case series and 1 cross-sectional study

The risk of bias was generally low for all trials

Treatment-emergent adverse events and serious adverse events were comparable

Biosimilars showed similar efficacy with American College of Rheumatology Remission Criteria (ACR20) responses

Ref: [1] Chingcuanco F, Segal J, Kim SC, Alexander GC. Safety, Efficacy, and Pharmacokinetic Bioequivalence of Biosimilar Tumor Necrosis Factor-Alpha Inhibitors Compared with Their Reference Biologics: A Systematic Review. Value in Health, Volume 19, Issue 3, May 2016, Page A226

2: Infliximab Biosimilars – Safety & Efficacy: Systematic review August 2016

- A systematic review of 19 efficacy & switching studies with anti-TNF biosimilars shows
  - Ten trials assessed immunogenicity
- Results
  - no clinically significant differences in efficacy
  - No clinically significant loss of effect from switching [1]


Annals of Internal Medicine REVIEW

Bioequivalence of Biosimilar Tumor Necrosis Factor-α Inhibitors Compared With Their Reference Biologics

A Systematic Review

Francine Chingcuanco, MHS; Jodi B. Segal, MD, MPH; Seoyoung C. Kim, MD, ScD, MSCE; and G. Caleb Alexander, MD

Ref: [1] Chingcuanco, F et al. Bioequivalence of Biosimilar Tumor Necrosis Factor- Inhibitors Compared With Their Reference Biologics. A Systematic Review. Ann Intern Med. doi:10.7326/M16-0428. Published at www.annals.org on 2 August 2016.

3: Infliximab Biosimilars – Switching Studies Only: Systematic review November 2016

- **Moots et al: AJR 2016: Systematic review of switching studies of infliximab (INF), etanercept (ETN), adalimumab (ADA), or rituximab (RTX) switched between originator biologics and biosimilars.**


Switching to Biosimilars in Rheumatology: Evidence-Based Practice

- **Switching data was available for 12 studies in rheumatic diseases with 2104 patients**
  - Switch — Number of studies
  - INF/CT-P13 — 4
  - INF/SB2 — 1
  - INF/unidentified biosimilar — 2
  - ETN/SB4 — 2
  - ETN/GP2015 — 1
  - ADA/SB5 — 1
  - RTX/CT-P10 — 1

The INF/CT-P13 studies showed efficacy and safety of INF and CT-P13 to be similar in switch and maintenance groups, and similar pre- and post-switch

Immunogenicity was assessed in 3 studies and did not change post-switch.

Ref: [1] Moots RJ, et al. Switching to Biosimilars in Rheumatology: Evidence-Based Practice [abstract]. Arthritis Rheumatol. 2016; 68 (suppl 10). http://acrabstracts.org/abstract/switching-to-biosimilars-in-rheumatology-evidence-based-practice/. Accessed November 23, 2016.

4: February 2017


FEBRUARY 2017


Journal of Autoimmunity

Efficacy, safety and pharmacokinetics of biosimilars of anti-tumor necrosis factor-α agents in rheumatic diseases; A systematic review and meta-analysis

Yuga Komaki, M.D. [a], Akihiro Yamada, M.D., Ph.D. [a], Fukiko Komaki, M.D. [a], Praneeth Kudaravalli, M.D. [b], Dejan Micic, M.D. [c], Akio Ido, M.D., Ph.D. [d], Atsushi Sakuraba, M.D., Ph.D. [a]

- **Further metanalysis anti-TNF-a Biosimilars vs Reference drugs:**
  - **infliximab,**
  - **adalimumab**
  - **etanercept**
- **Nine studies reporting outcomes in 3291 patients with rheumatoid arthritis (RA) and ankylosing spondylitis (AS) were identified**
  - (5 infliximab, 2 adalimumab, and 2 etanercept)
- **Conclusion: "*biosimilars of anti-TNF-a agents had an overall comparable efficacy and safety profile compared to their reference agents in RA and AS*"**

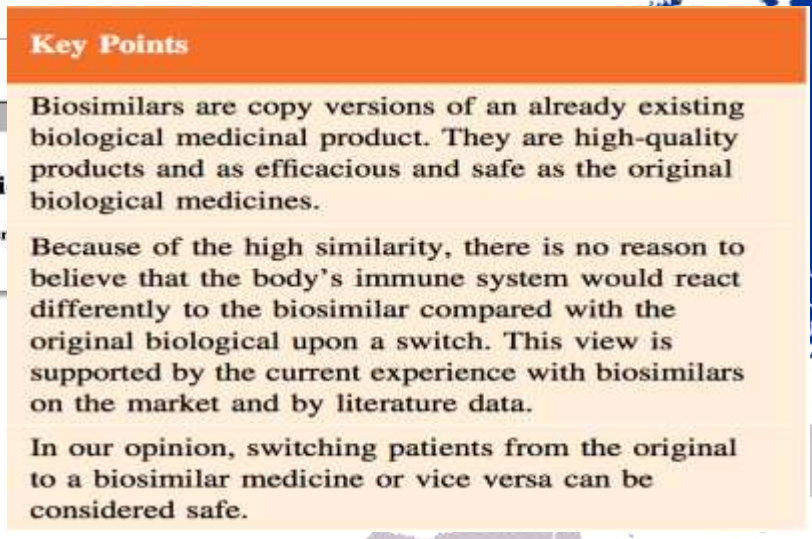
Ref: [1] Y. Komaki, et al., Efficacy, safety and pharmacokinetics of biosimilars of anti-tumor necrosis factor-a agents in rheumatic diseases; A systematic review and meta-analysis, Journal of Autoimmunity (2017), http://dx.doi.org/10.1016/j.jaut.2017.02.003

Interchangeability – EU National regulators Speak Up


BioDrugs
DOI 10.1007/s40259-017-0210-0
CURRENT OPINION

Interchangeability of Bi

Pekka Kurki[1] · Leon van Aerts[2] · Eler
Venke Skibeli[5] · Martina Weise[6]


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.

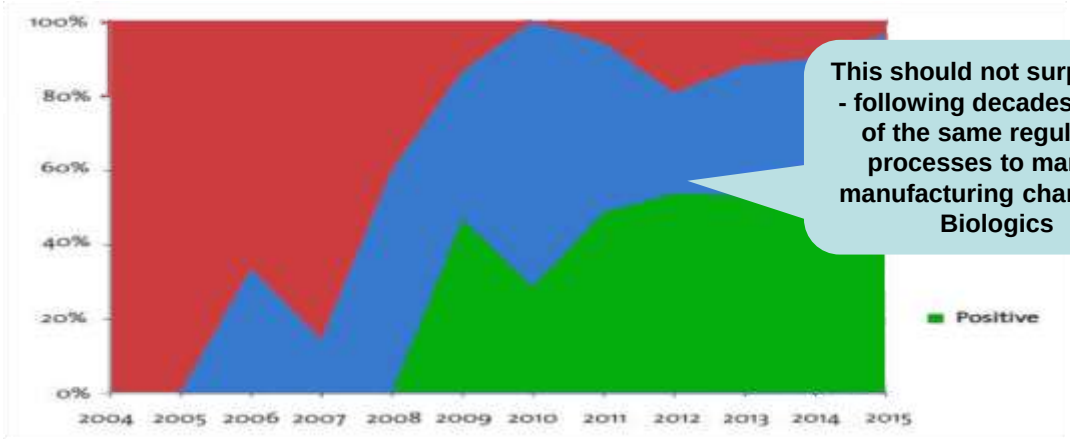
In our opinion, switching patients from the original to a biosimilar medicine or vice versa can be considered safe.

- **Finland**
- **Germany**
- **Netherlands**
- **Norway**

Ref: [1] Pekka Kurki, Leon van Aerts, Elena Wolff-Holz, Thijs Giezen, Venke Skibeli, Martina Weise. Interchangeability of Biosimilars: A European Perspective. BioDrugs DOI 10.1007/s40259-017-0210-0. accessed March 14, 2017

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**



Ref: [1] Image adapted from - Thorsten Daubenfeld, Jonas Dassow, Maximilian Keßler and Jonas Schulze. Understanding the market dynamics of biosimilars. J Business Chemistry. 2016;13(1). http://www.businesschemistry.org/article/?article=218. Accessed May 25, 2016

10 years of biosimilars - who benefits?

- The problem of sustainable healthcare
- The value of biosimilars
- Is there a risk to biosimilars?
- The future of biosimilars

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Ref: [1] Map Image. CCO License. https://upload.wikimedia.org/wikipedia/commons/7/7a/United_Kingdom_Portugal_Locator.png. Accessed March 13, 2017

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

Ref: [1] 19th WHO Essential Medicines List, 2015. WHO. http://www.who.int/medicines/publications/essentialmedicines/en/. Accessed March 17, 2016

Expectations of Future Biosimilars: Therapeutic Oncology Drugs

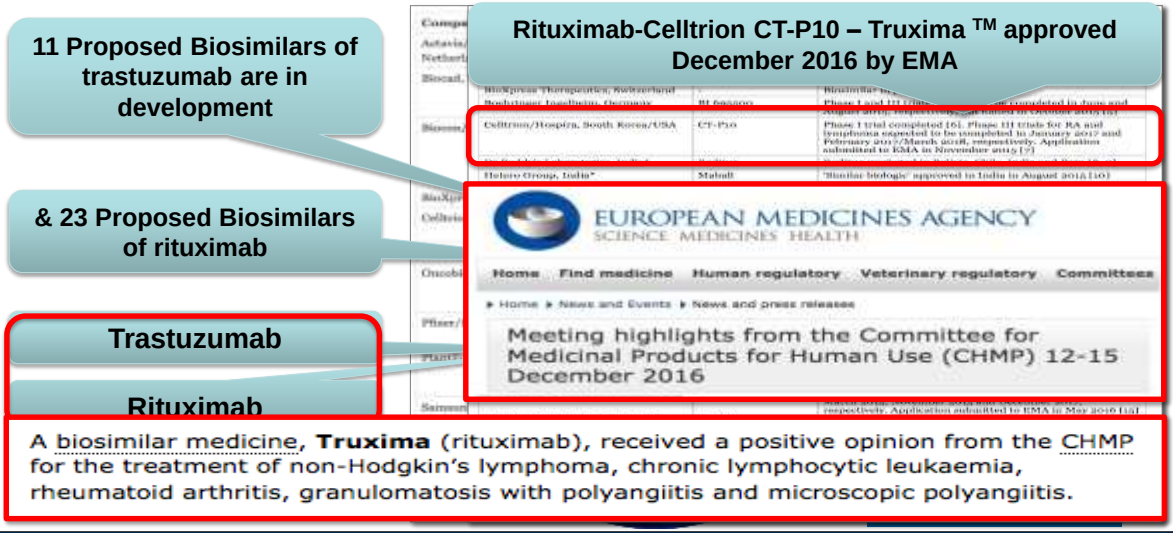
11 Proposed Biosimilars of trastuzumab are in development

& 23 Proposed Biosimilars of rituximab

Trastuzumab

Rituximab

Rituximab-Celltrion CT-P10 – Truxima ™ approved December 2016 by EMA



Ref: [1] Biosimilars of trastuzumab. Posted 19/09/2014, Last update: 12 August 2016, GaBI. http://www.gabionline.net/Biosimilars/General/Biosimilars-of-trastuzumab. Accessed Nov 8, 2016 [2] Meeting highlights from the Committee for Medicinal Products for Human Use (CHMP) 12-15 December 2016. http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2016/12/news_detail_002665.jsp&mid=WC0b01ac058004d5c1. Accessed Dec 23, 2016

Expectations of Future Biosimilars: Therapeutic Oncology Drugs: Trastuzumab

11 Proposed Biosimilars of trastuzumab are in development

3 RCTs of proposed biosimilars of trastuzumab have reported clinical outcomes to date December 9, 2016

A 4th study has reported headline results only

ABP-980

BCD-022

Myl 1410

CT-P6

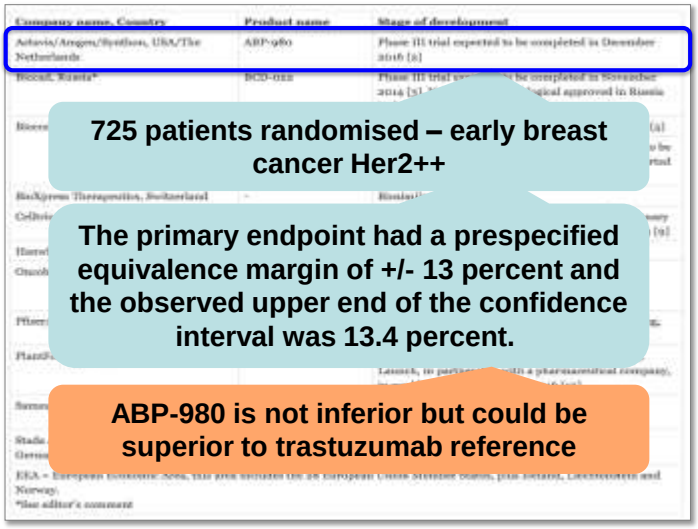
[illegible], USA/The Netherlands	ABP-980	Phase III trial expected to be completed in December 2016 [2]
[illegible]	BCD-022	Phase III trial expected to be completed in November 2014 [3]. Non-originator biological approved in Russia in January 2016 [4]
Biocon/Mylan, India*	CanMab	'Similar biologic' launched in India in October 2013 [5]
	Hercules (Myl-1401O)	Phase III trial in metastatic breast cancer expected to be completed in December 2016 [6]. Positive data reported [illegible] [7]
BioXpress Therapeutics, Switzerland	-	Biosimilar in pipeline
[illegible] Korea	Herzuma (CT-P6)	Marketed in South Korea following approval in January 2014 [8]. Phase III trial started in EEA in April 2014 [9]
Hanwha Chemical, South Korea	HD201	Phase I study in Europe as of 2015
Oncobiologics/Viropro, USA	-	Biosimilar in development; One of six monoclonal antibody biosimilars for which the companies are collaborating [10]
Pfizer/Hospira, USA	PF-05280014	Phase I study completed [11]. Phase III study ongoing, expected to be completed March 2018 [12]
PlantForm, Canada	-	Clinical trials in humans expected to begin in 2014. Launch, in partnership with a pharmaceutical company, in world markets expected in 2016 [13]
Samsung Bioepis, South Korea	SB3	Phase III trial in early breast cancer expected to be completed in May 2016 [6]
Stada Arzneimittel/Gedeon Richter, Germany/Hungary	-	Collaborating on biosimilars of trastuzumab and infliximab [14]

EEA = European Economic Area, this area includes the 28 European Union Member States, plus Iceland, Liechtenstein and Norway.
*the editor's comment

Ref: [1] Biosimilars of trastuzumab. Posted 19/09/2014, Last update: 12 August 2016, GaBI. http://www.gabionline.net/Biosimilars/General/Biosimilars-of-trastuzumab. Accessed Nov 8, 2016 [2] Meeting highlights from the Committee for Medicinal Products for Human Use (CHMP) 12-15 December 2016. http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2016/12/news_detail_002665.jsp&mid=WC0b01ac058004d5c1. Accessed Dec 23, 2016

Expectations of Future Biosimilars: Therapeutic Oncology Drugs: Trastuzumab

- **Amgen ABP-980**
- **Phase III trial in Early Breast Cancer expected to be completed in December 2016**
- **ClinicalTrials.gov Identifier:**
- **NCT01901146**



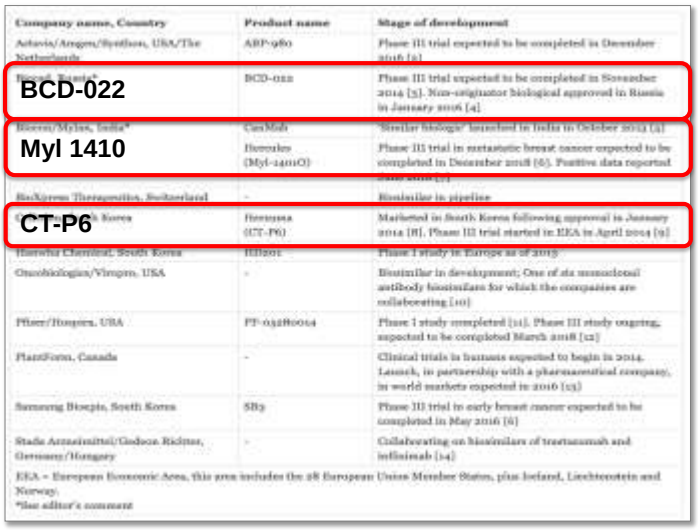
Ref: [1] Biosimilars of trastuzumab. Posted 19/09/2014, Last update: 12 August 2016, GaBI. http://www.gabionline.net/Biosimilars/General/Biosimilars-of-trastuzumab. Accessed Nov 8, 2016 [2] Amgen And Allergan Announce Top-Line Results From Phase 3 Study Evaluating ABP 980. Amgen. http://www.amgen.com/media/news-releases/2016/07/amgen-and-allergan-announce-top-line-results-from-phase-3-study-evaluating-abp-980-compared-with-trastuzumab-in-patients-with-human-epidermal-growth-factor-receptor-2-positive-early-breast-cancer/. Accessed Nov 15, 2016

Expectations of Future Biosimilars: Therapeutic Oncology Drugs: Trastuzumab

3 RCTs of proposed biosimilars of trastuzumab in Metastatic Disease have reported clinical outcomes to date Dec 9, 2016

2 RCTs have met their targets for Clinical Equivalence of the Primary Endpoint

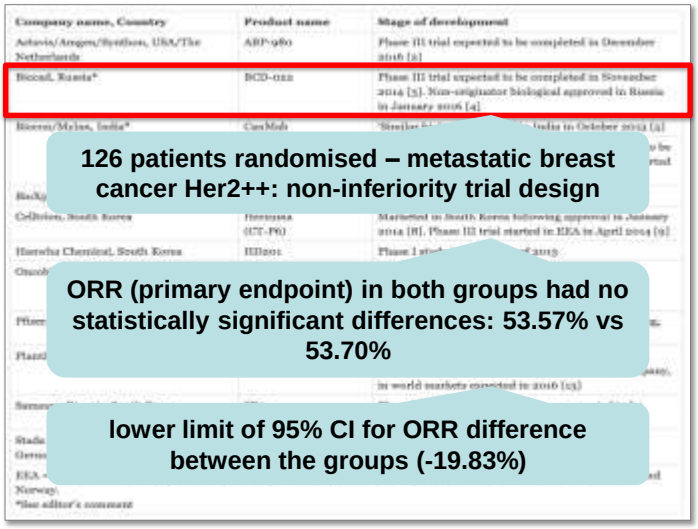
1 RCT met a Non-Inferiority Target



Ref: [1] Biosimilars of trastuzumab. Posted 19/09/2014, Last update: 12 August 2016, GaBI. http://www.gabionline.net/Biosimilars/General/Biosimilars-of-trastuzumab. Accessed Nov 8, 2016 [2] Meeting highlights from the Committee for Medicinal Products for Human Use (CHMP) 12-15 December 2016. http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2016/12/news_detail_002665.jsp&mid=WC0b01ac058004d5c1. Accessed Dec 23, 2016

Expectations of Future Biosimilars: Therapeutic Oncology Drugs: Trastuzumab

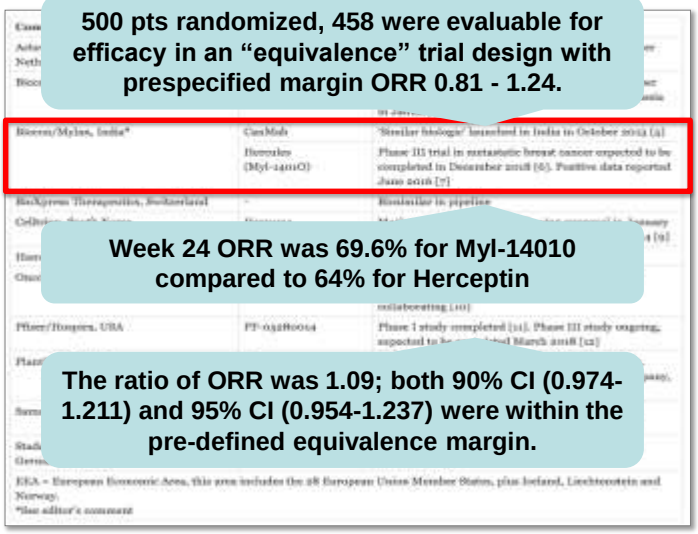
- **Biocad BCD-022**
- **Non-originator biological approved in Russia in January 2016 [2]**
- **Trial: NCT01764022**
- **Launched in at least Russia, Vietnam, Sri-Lanka**



Ref: [1] Biosimilars of trastuzumab. Posted 19/09/2014, Last update: 12 August 2016, GaBI. http://www.gabionline.net/Biosimilars/General/Biosimilars-of-trastuzumab. Accessed Nov 8, 2016 [2] GaBI Online - Generics and Biosimilars Initiative. Trastuzumab non-originator biological approved in Russia [www.gabionline.net]. Mol, Belgium: Pro Pharma Communications International; [cited 2016 Apr 8]. Available from: www.gabionline.net/Biosimilars/News/Trastuzumab-non-originator-biological-approved-in-Russia

Expectations of Future Biosimilars: Therapeutic Oncology Drugs: Trastuzumab

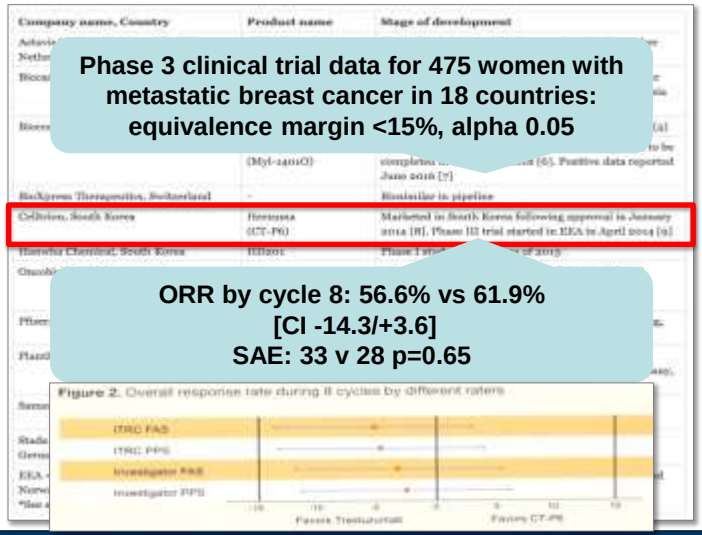
- **Mylan Myl-1401O**
- **"HERiTAge" study - Phase III trial in metastatic breast cancer expected to be completed in December 2018 [2]. Positive data reported June 2016 at ASCO [3,4]**
- **The same drug was launched as CanMab™ in India as an Intended Copy Biologic in 2013**



Ref: [1] Biosimilars of trastuzumab. Posted 19/09/2014, Last update: 12 August 2016, GaBI. http://www.gabionline.net/Biosimilars/General/Biosimilars-of-trastuzumab. Accessed Nov 8, 2016 [2] GaBI Online - Generics and Biosimilars Initiative. Pivotal clinical trials for trastuzumab biosimilars [www.gabionline.net]. Mol, Belgium: Pro Pharma Communications International; [cited 2016 Aug 12]. Available from: www.gabionline.net/Biosimilars/Reports/Pivotal-clinical-trials-for-trastuzumab-biosimilars [3] GaBI Online - Generics and Biosimilars Initiative. Mylan presents comparability data for trastuzumab biosimilar [www.gabionline.net]. Mol, Belgium: Pro Pharma Communications International; [cited 2016 Aug 12]. Available from: www.gabionline.net/Biosimilars/Research/Mylan-presents-comparability-data-for-trastuzumab-biosimilar [4] Rugo HS, Barve A, Waller CF, et al. Heritage: A phase III safety and efficacy trial of the proposed trastuzumab biosimilar Myl-14010 versus Herceptin. Paper presented at: 2016 Annual Meeting of the American Society of Clinical Oncology; June 3-7, 2016; Chicago, IL. Abstract LBA503.

Expectations of Future Biosimilars: Therapeutic Oncology Drugs: Trastuzumab

- **Celltrion CTP6**
- **Approved in Korea 2014 as Herzuma**
- **2014: started an EU trial of adjuvant breast cancer: 532 patients. Due 2019**
- **ClinicalTrials.gov Identifier: NCT02162667**



Ref: [1] Biosimilars of trastuzumab. Posted 19/09/2014, Last update: 12 August 2016, GaBI. http://www.gabionline.net/Biosimilars/General/Biosimilars-of-trastuzumab. Accessed Nov 8, 2016 [2] Im Y-H, Odarchenko P, Grecea D, et al. Double-blind, randomized, parallel group, phase III study to demonstrate equivalent efficacy and comparable safety of CT-P6 and trastuzumab, both in combination with paclitaxel, in patients with metastatic breast cancer (MBC) as first-line treatment. Proc Am Soc Clin Oncol. 2013;13(suppl):629

3 RCTs of proposed biosimilars of trastuzumab have reported Clinical Outcomes

- **All 3 are trials in advanced or metastatic HER2++ Breast Cancer**
  - **1043 patients randomised in total**
  - **The most recent reports with any numeric clinical data were used for each trial that could be accessed Dec 9, 2016**

Drug	CR or PR absent	CR or PR present	SAE absent	SAE present
BCD-022	26	30	59	6
Herceptin	25	29	55	6
Myl 1410	70	160	136	94
Herceptin	82	146	139	89
CT-P6	88	143	211	33
Herceptin	105	139	203	28

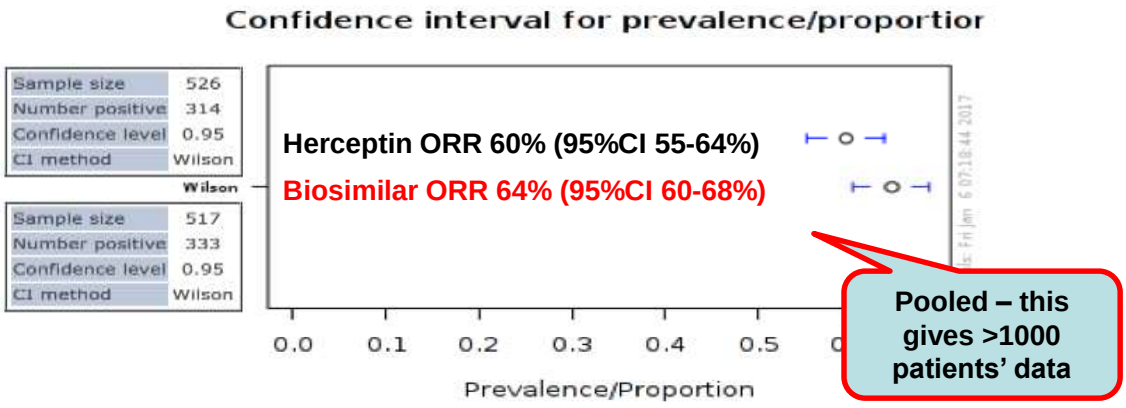
All 3 trials reported Clinical Response rates at 24-25 weeks

Pooled – this gives >1000 patients' data

Ref: [1] Cornes P. Biosimilars in Oncology: Will They Meet Expectations? ESOP Society Programme at ECCO 2017, Jan 27, 2017. Amsterdam, The Netherlands

3 RCTs of proposed biosimilars of trastuzumab have reported Clinical Outcomes

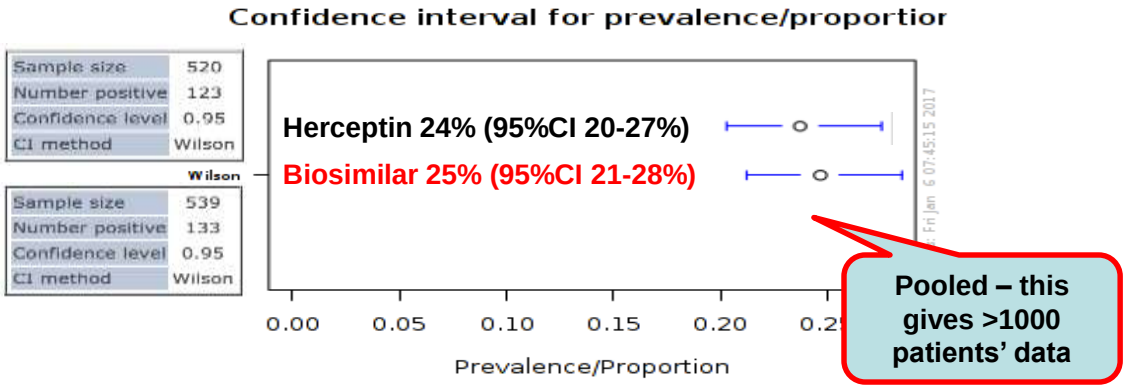
- **1043 patients analysed for Primary Outcome,**
  - **ORR at 24-25 weeks**



Ref: [1] Cornes P. Biosimilars in Oncology: Will They Meet Expectations? ESOP Society Programme at ECCO 2017, Jan 27, 2017. Amsterdam, The Netherlands
[2] 95% Confidence Intervals calculated to 2 decimal places with Epitools, Jan 5, 2017

3 RCTs of proposed biosimilars of trastuzumab have reported Clinical Outcomes

- **1049 patients analysed for SAE**



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10 years of biosimilars - who benefits?

- The problem of sustainable healthcare
- The value of biosimilars
- Is there a risk to biosimilars?
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Ref: [1] Map Image. CCO License. https://upload.wikimedia.org/wikipedia/commons/7/7a/United_Kingdom_Portugal_Locator.png. Accessed March 13, 2017

Rational Medicine Use

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World Health Organization

- "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."
    - (WHO World Medicines Report, 2011).

We are given clear moral leadership guidance by the WHO

Ref: WHO World Medicines Report, 2011 .

Conclusion: After 10 years of European Biosimilars

A. There is clear evidence that patient access and outcomes are improved by biosimilars
B. Most of the rich nations of the world have sufficient resource for healthcare
C. Biosimilars are not yet an essential component of European Healthcare
D. Biosimilars are not interchangeable with reference drugs
E. There is no evidence in March 2017 that trastuzumab biosimilars in development can match reference drugs for efficacy in breast

YES - New Zealand, UK, Sweden – wherever Biosimilars have been adopted into practice

NO - only 7 nations use 75% of the worlds's targeted therapy

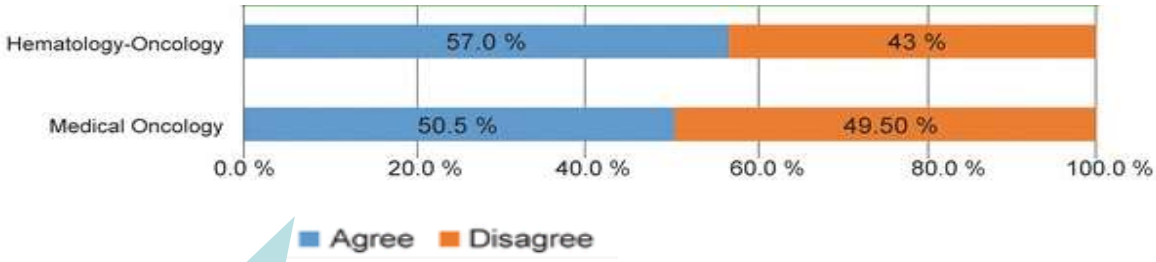
NO - EU 2016 Sustainable Care Report - PRIORITY !

NO - National Regulators Paper confirm Biosimilars are "linterchangeable" Kurki, 2017

NO - You have just seen it !

A Final Problem? Physicians knowledge: Biosimilars Forum Survey 2016 – Results

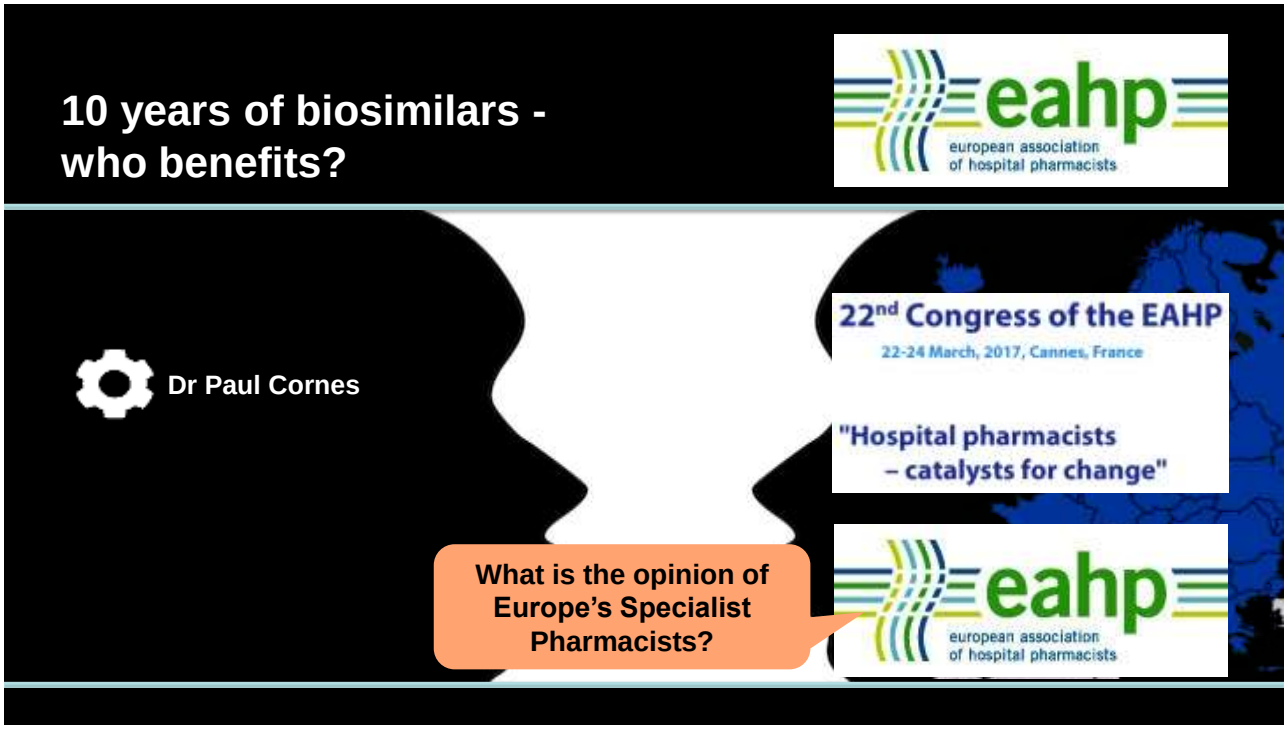
- Do you believe biosimilars will be safe and appropriate for use in naïve and existing patients?



Physicians seem to be split 50:50

What is the opinion of Europe's Specialist Pharmacists?

Ref: [1] Cohen, H., Beydoun, D., Chien, D. et al. Adv Ther (2017) 33: 2160. doi:10.1007/s12325-016-0431-5



CME question: After 10 years of European Biosimilars – which statement do you think is correct?

A. There is clear evidence that patient access and outcomes are improved by biosimilars

B. Most of the rich nations of the world have sufficient resource for healthcare

C. Biosimilars are not yet an essential component of European Healthcare

D. Biosimilars are not interchangeable with reference drugs

E. There is no evidence in March 2017 that trastuzumab biosimilars in development can match reference drugs for efficacy in breast cancer

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