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

paul.cornes@yahoo.co.uk

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

Ref: Image: "Innovation“, Creative Commons Zero (CC0), Public Domain. http://maxpixel.freegreatpicture.com/Inspiration-Innovation-Idea-Thought-Imagination-2123970. Accessed May 17, 2017

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

If we apply what we already know AND continue our current pattern of year-on-year improvement this is no dream !

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

paul.cornes@yahoo.co.uk

NHS choices Your health, your choices

Health A-Z | Live Well | Care and support

Under-80 cancer deaths 'eliminated by 2050' claim

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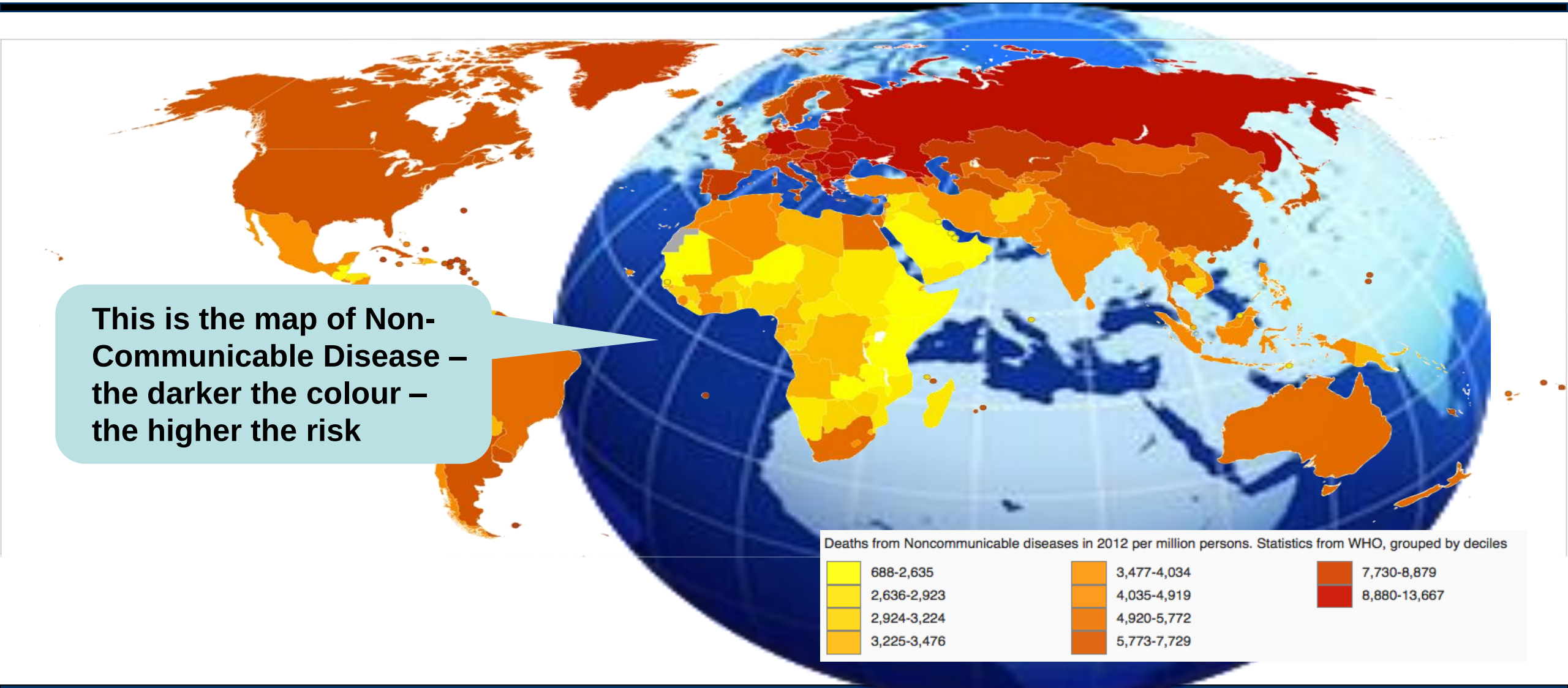
Wednesday January 14 2015

Ref [1] : Image: "Innovation", Creative Commons Zero (CC0), Public Domain. http://maxpixel.freegreatpicture.com/Inspiration-Innovation-Idea-Thought-Imagination-2123970. Accessed May 17, 2017 [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

We live in the era of Non-Communicable Disease

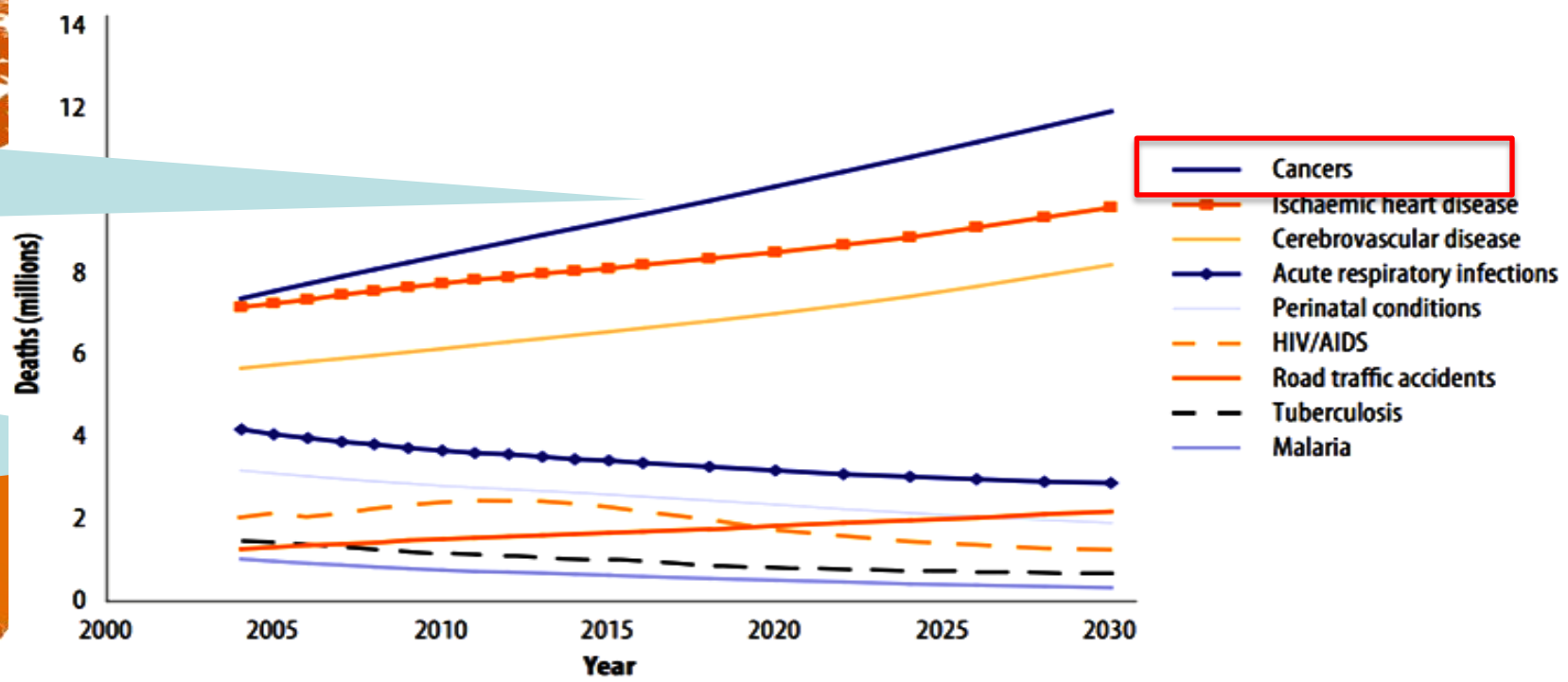


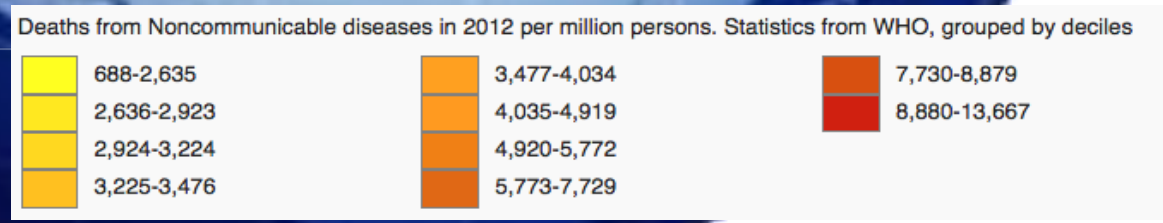
Ref [1] https://upload.wikimedia.org/wikipedia/commons/thumb/c/c6/Noncommunicable_diseases_world_map-Deaths_per_million_persons-WHO2012.svg/2000px-Noncommunicable_diseases_world_map-Deaths_per_million_persons-WHO2012.svg.png. Accessed Nov 3, 2016 [2] Non-communicable diseases. The Kings Fund. https://www.kingsfund.org.uk/time-to-think-differently/trends/disease-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

We live in the era of Non-Communicable Disease

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

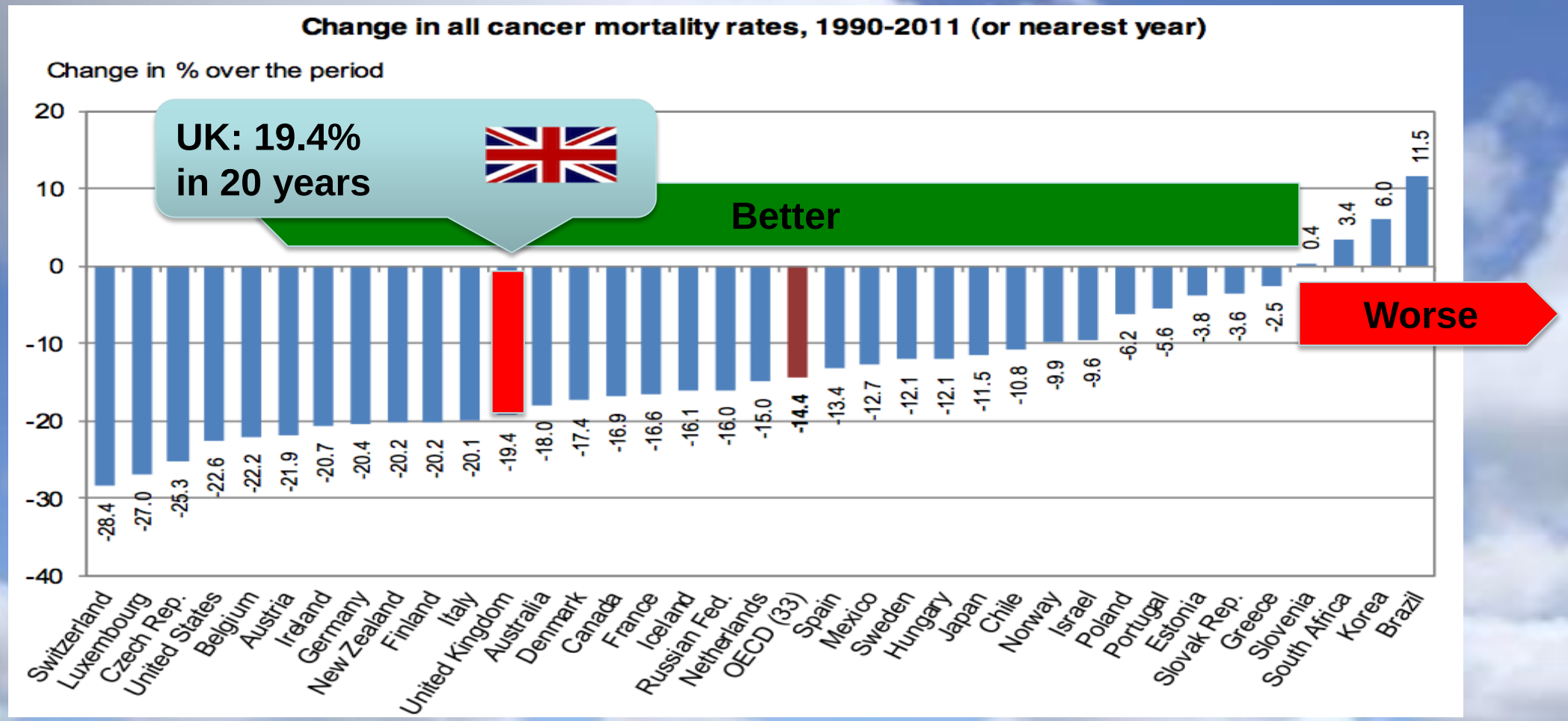




Ref [1] https://upload.wikimedia.org/wikipedia/commons/thumb/c/c6/Noncommunicable_diseases_world_map-Deaths_per_million_persons-WHO2012.svg/2000px-Noncommunicable_diseases_world_map-Deaths_per_million_persons-WHO2012.svg.png. Accessed Nov 3, 2016 [2] Non-communicable diseases. The Kings Fund. https://www.kingsfund.org.uk/time-to-think-differently/trends/disease-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

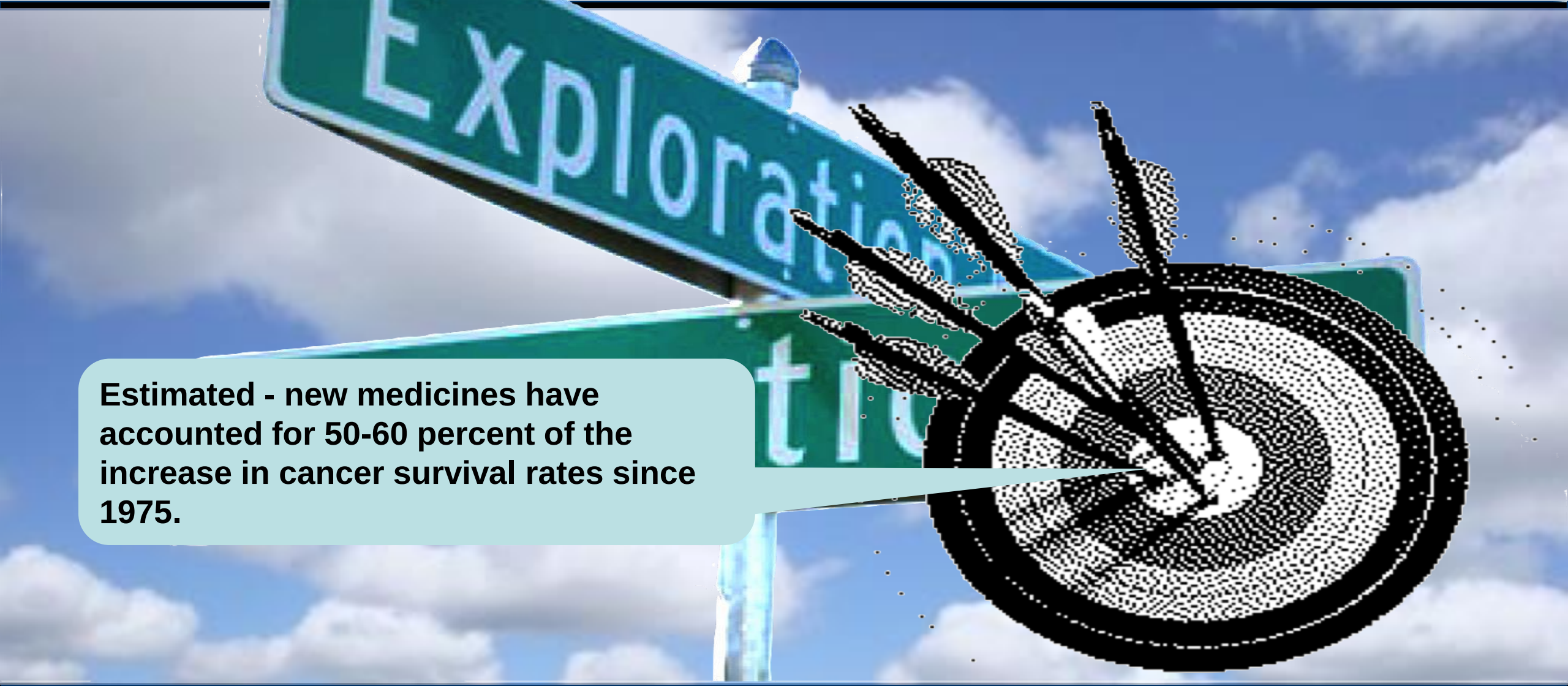
Good news for cancer treatment: worldwide – more people survive cancer

- Reduction in cancer deaths –



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

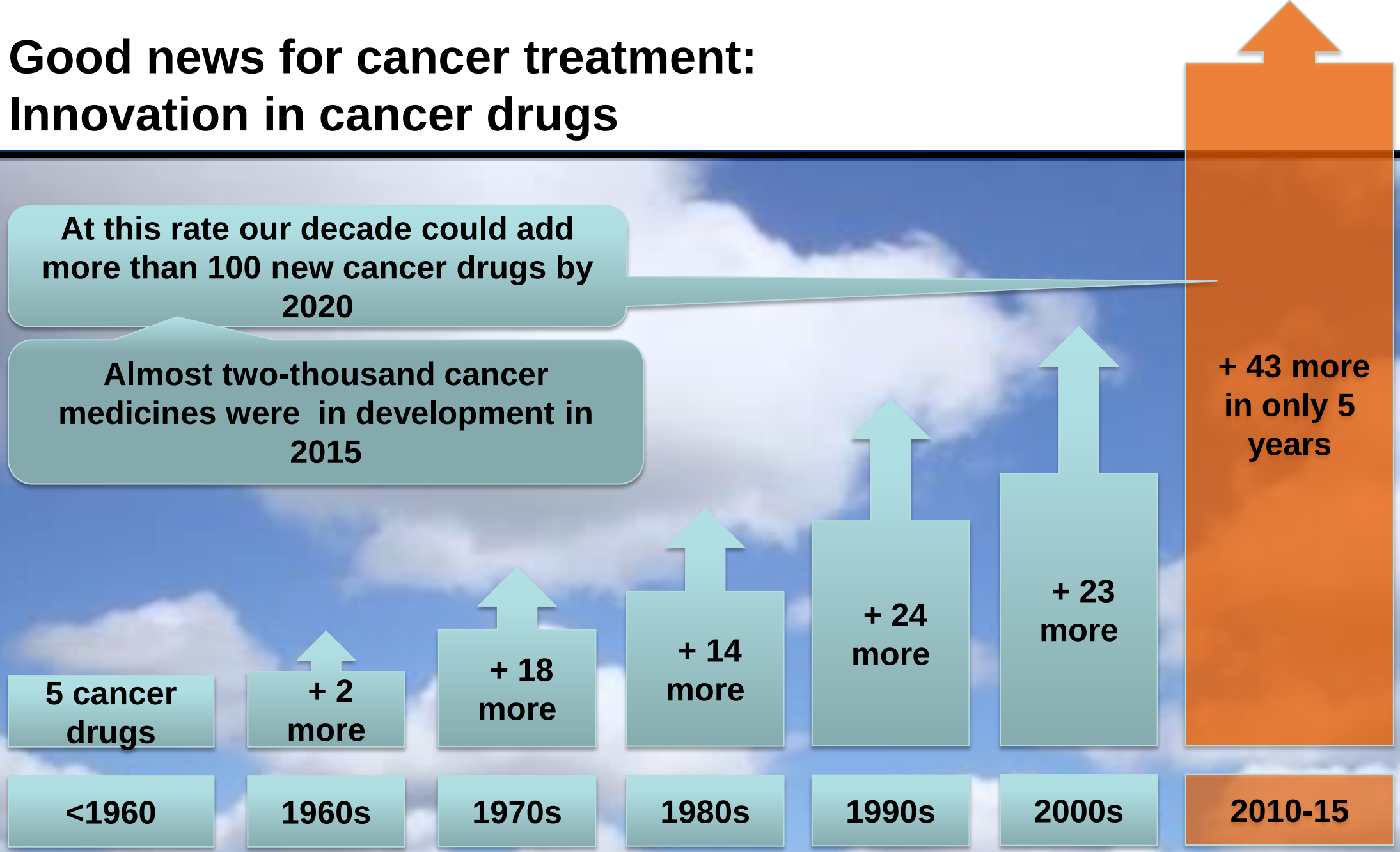
Good nev for cancer treatment: worldwid people survive cancer



Estimated - new medicines have accounted for 50-60 percent of the increase in cancer survival rates since 1975.

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

REVIEWS

Targeted therapy in rare cancers—adopting the orphans

Javier Munoz and Razelle Kurzrock

Abstract | Designation of a rare 'orphan' disease is usually conferred by a prevalence of one in 1,500 to 2,500 individuals. Increasingly, orphan diseases are also being defined by their molecular fingerprints. Rare diseases are uniquely challenging from a therapeutic standpoint; it is critical to modify clinical study design of treatments for orphan disorders as well as for the increasingly smaller molecular subsets within frequently occurring cancers. In spite of the immense challenges associated with developing a treatment for a rare disorder, some of the most groundbreaking therapeutic discoveries have been made in orphan malignancies. This situation may be because a limited number of driver molecular aberrations occur in rare disorders, which can be targeted by agents. Here, we describe drug-class examples of targeted therapies for orphan diseases, with particular emphasis on malignancies or tumour-prone nonmalignant conditions, as well as potential therapeutic strategies that can be adopted to treat these orphan conditions.

Munoz, J. & Kurzrock, R. Nat. Rev. Clin. Oncol. 9, 631–642 (2012); published online 11 September 2012; doi:10.1038/nrclinonc.2012.160

Introduction

Cancer is one of the most common causes of death worldwide.[1] Treatment of metastatic disease has yielded only modest results, and most patients succumb to their disease. To a large extent, these dismal outcomes are probably because cancer consists of hundreds of molecular disease subsets, each requiring its own personalized treatment approach. Therefore, the standard paradigm of classifying patients by histology alone, and treating large unselected groups of patients with the same treatment

rare diseases as "life-threatening or chronically debilitating diseases that are of such low prevalence that special combined efforts are needed to address them."[2] ESMO defines rare tumours as those with an incidence of fewer than six per 100,000 persons per year.[3] The United States Orphan Drug Act defines as orphan diseases as conditions "for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for such disease or condition will [be] recovered

Chemotherapy era vs. targeted medicines era

Examples where survival has more than tripled

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

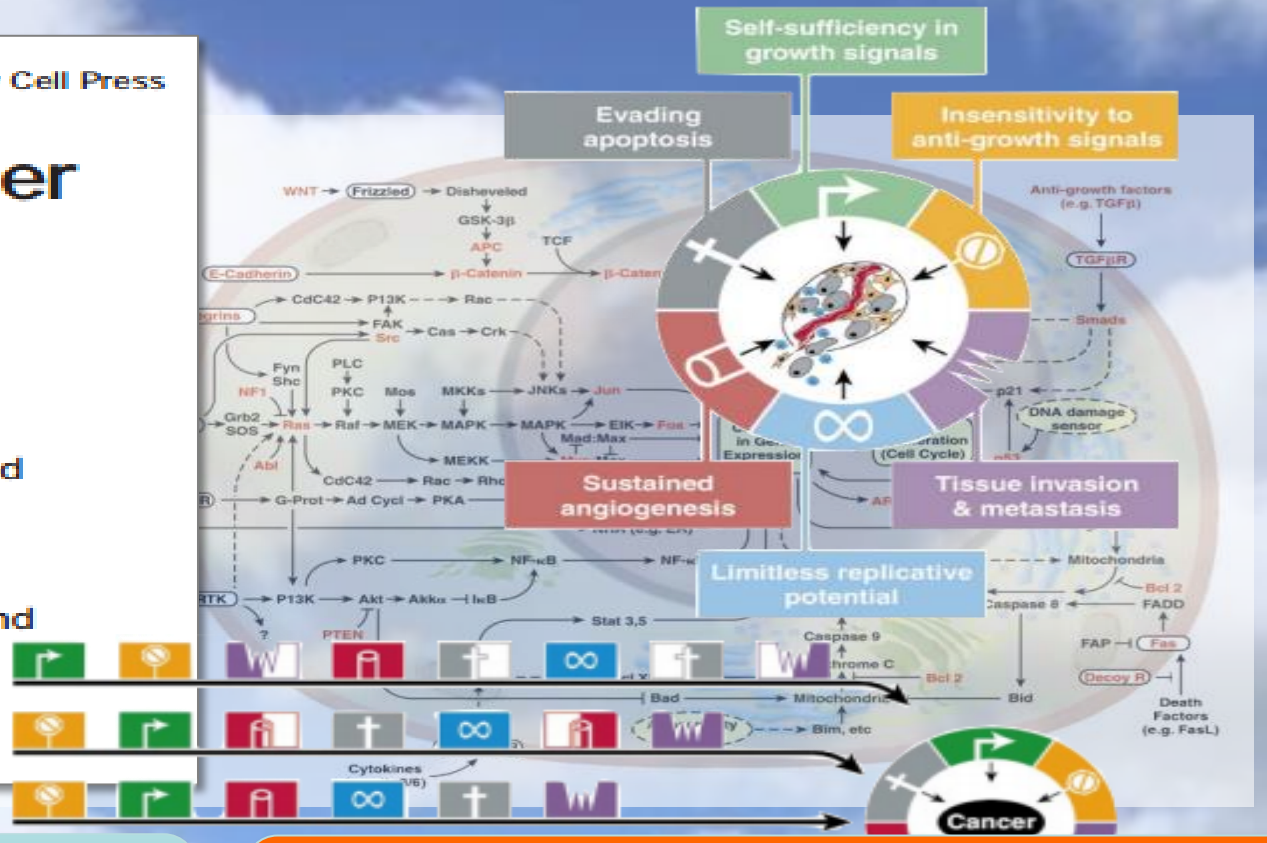
Ref: [1] European Patients' Rights Day: 10 benefits the EU brings to patients. EC Memo Brussels, 12 May 2014. http://europa.eu/rapid/press-release_MEMO-14-341_en.htm. Accessed June 19, 2015 .

The possibility at the millennium, 2000

Cell, Vol. 100, 57–70, January 7, 2000, Copyright ©2000 by Cell Press

The Hallmarks of Cancer

Douglas Hanahan* and Robert A. Weinberg†
*Department of Biochemistry and Biophysics and
Hormone Research Institute
University of California at San Francisco
San Francisco, California 94143
†Whitehead Institute for Biomedical Research and
Department of Biology
Massachusetts Institute of Technology
Cambridge, Massachusetts 02142



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 –

NHS choices Your health, your choices

Health A-Z | Live Well | Care and support

Under-80 cancer deaths 'eliminated by 2050' claim

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Wednesday January 14 2015

“Cancer deaths will be elimin
80 by 2050,” The Independe
the optimistic prediction cont
written by specialists in phar
University College London (U

Embargoed until 00.01 hours
Wednesay 14 January 2015

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Overcoming Cancer in the 2

With increased cancer risk awareness a
effective preventive and curative treat
before late old age could be elimina

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 q…nt – *right, left, unspecified*
Lower-outer q…nt – *right, left, unspecified*
Axillary tail – *rig…*
Overlapping …
Unspecifie…

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?

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

I am sorry to report that you have cancer type

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]

Tell me doctor – what have I got?

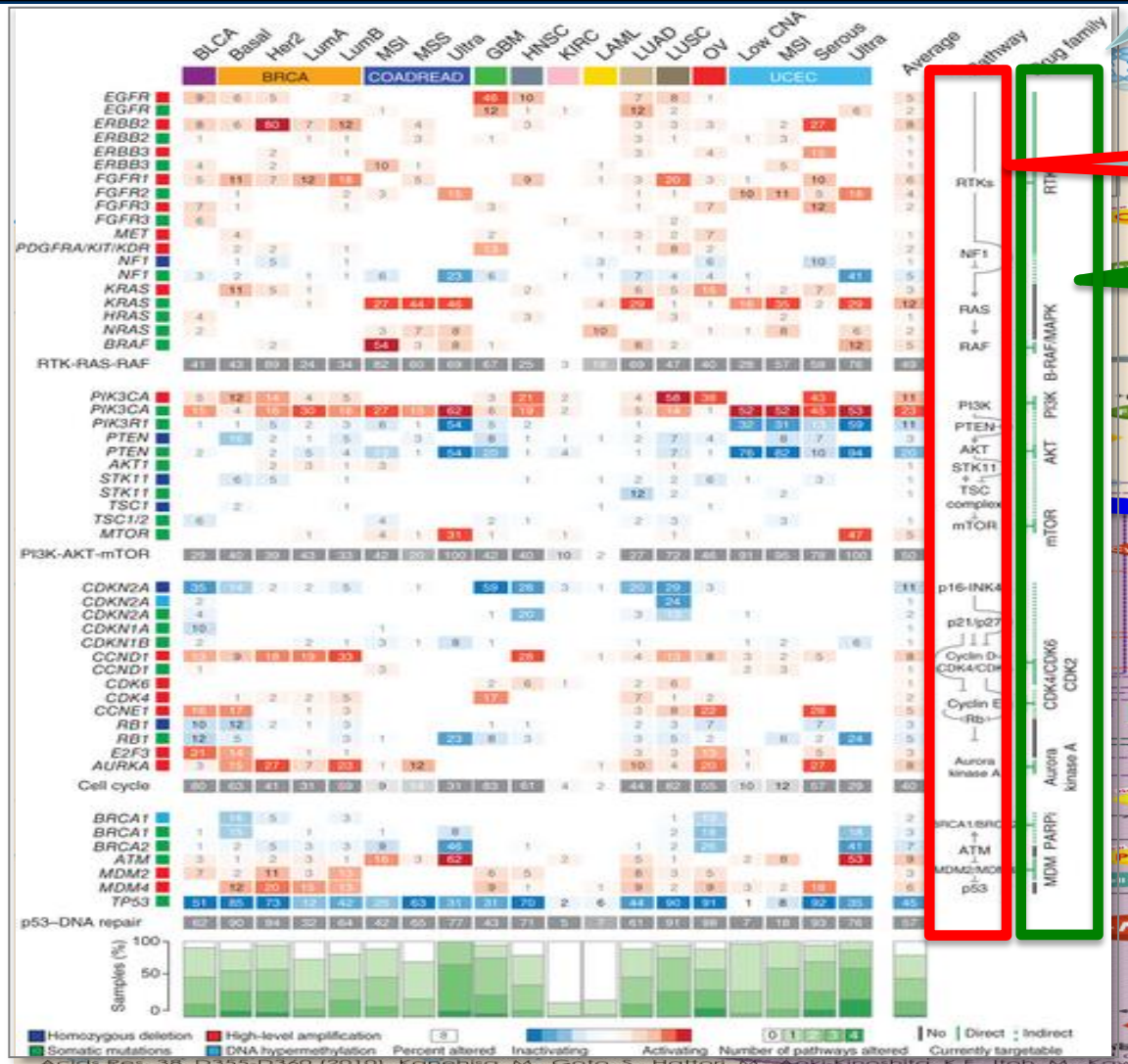
Ref: Ref [1] Image modified from https://upload.wikimedia.org/wikipedia/commons/d/d5/Oncology_doctor_consults_with_patient.jpg [2] Pathways in cancer. Avivasysbio.com. URL: http://www.avivasysbio.com/media/pdf/etc/Aviva_Pathway_Cancer.pdf. Accessed September 15, 2015. [2] Gallagher J. Tumours shrunk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

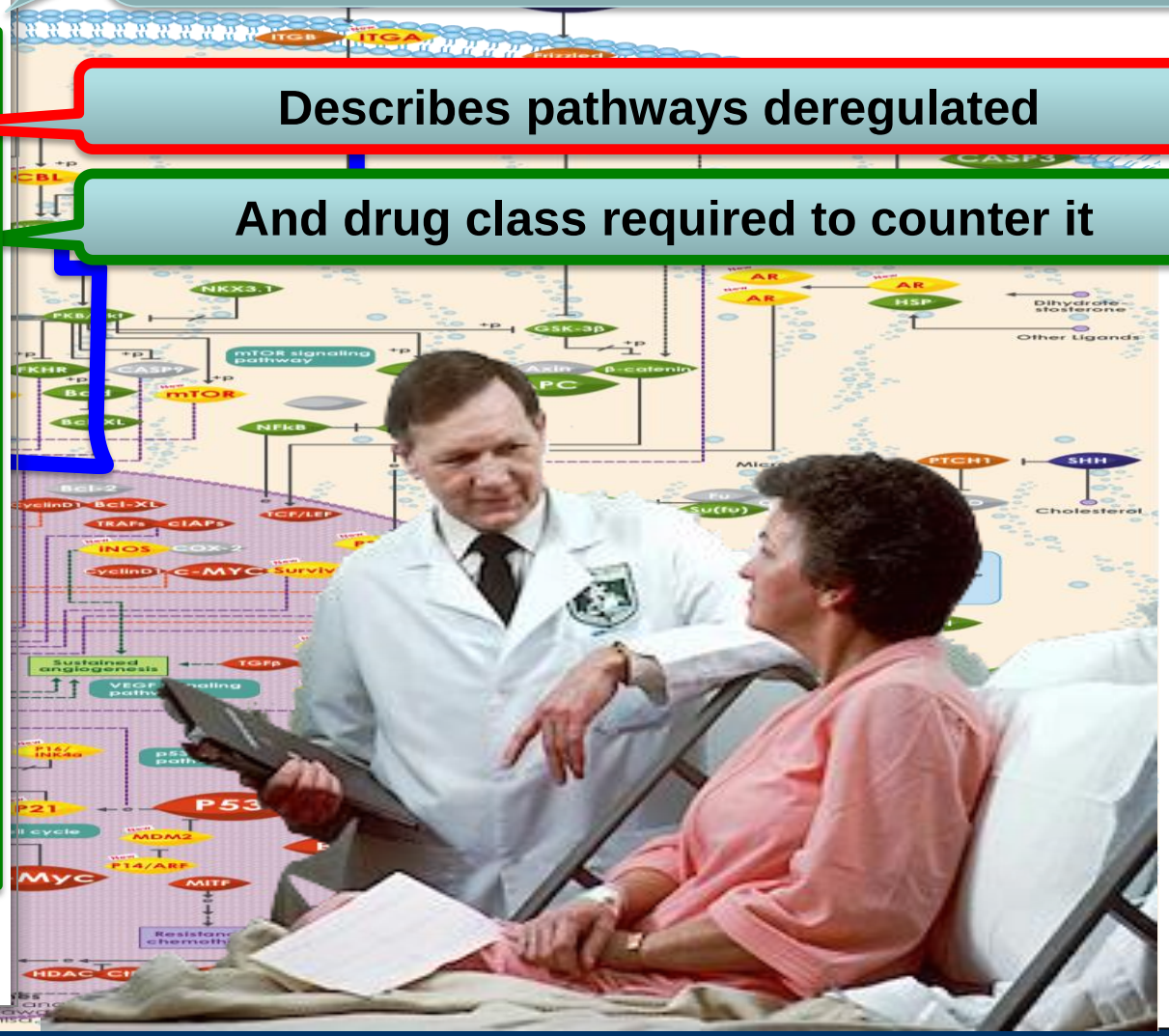
Where are we heading?

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





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Where are we heading?

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NEWS *10 March 2016*

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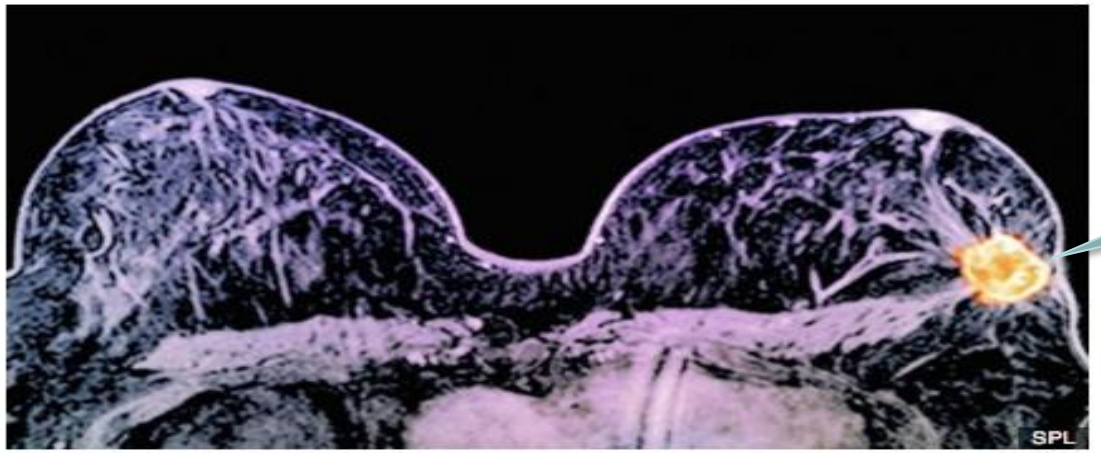
Health

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.

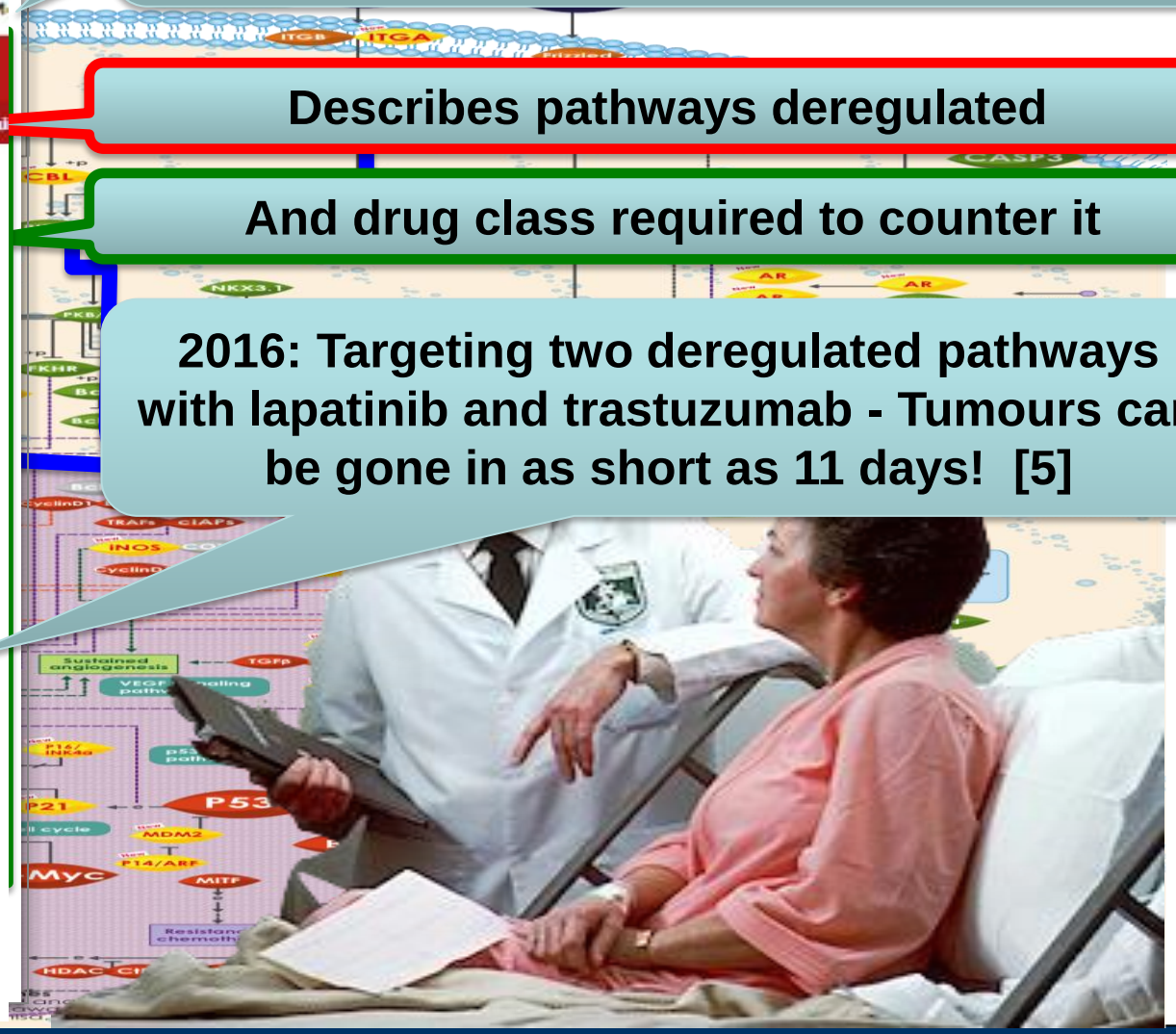
Nucleic Acids Res. 28, 27-30 (2000).

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

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



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?

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.

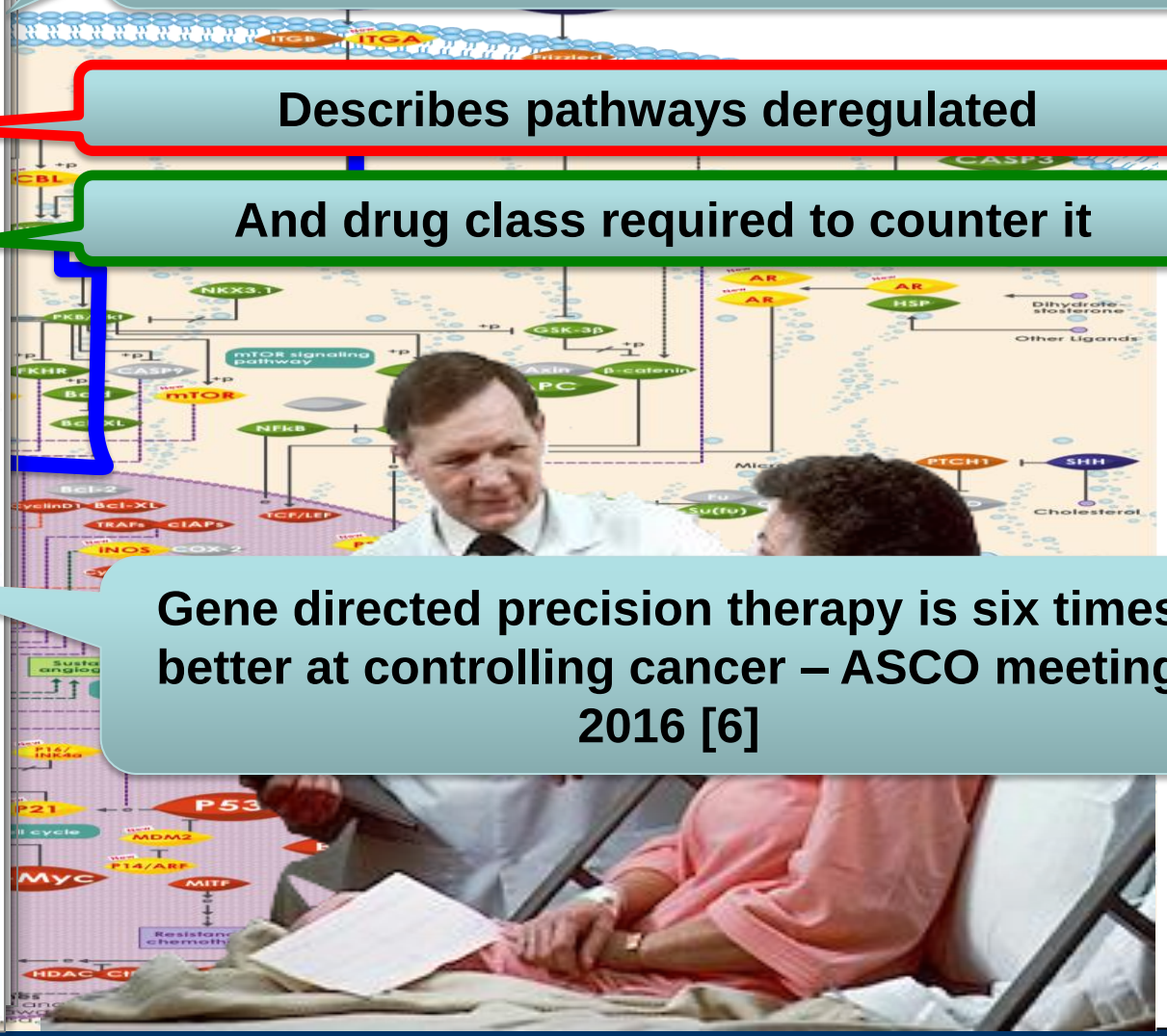
The technique sees a patient's tumour genetically tested as soon as they are diagnosed. This allows doctors to determine whether the cancer is aggressive, whether chemotherapy is necessary and exactly which drugs are needed.

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.

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

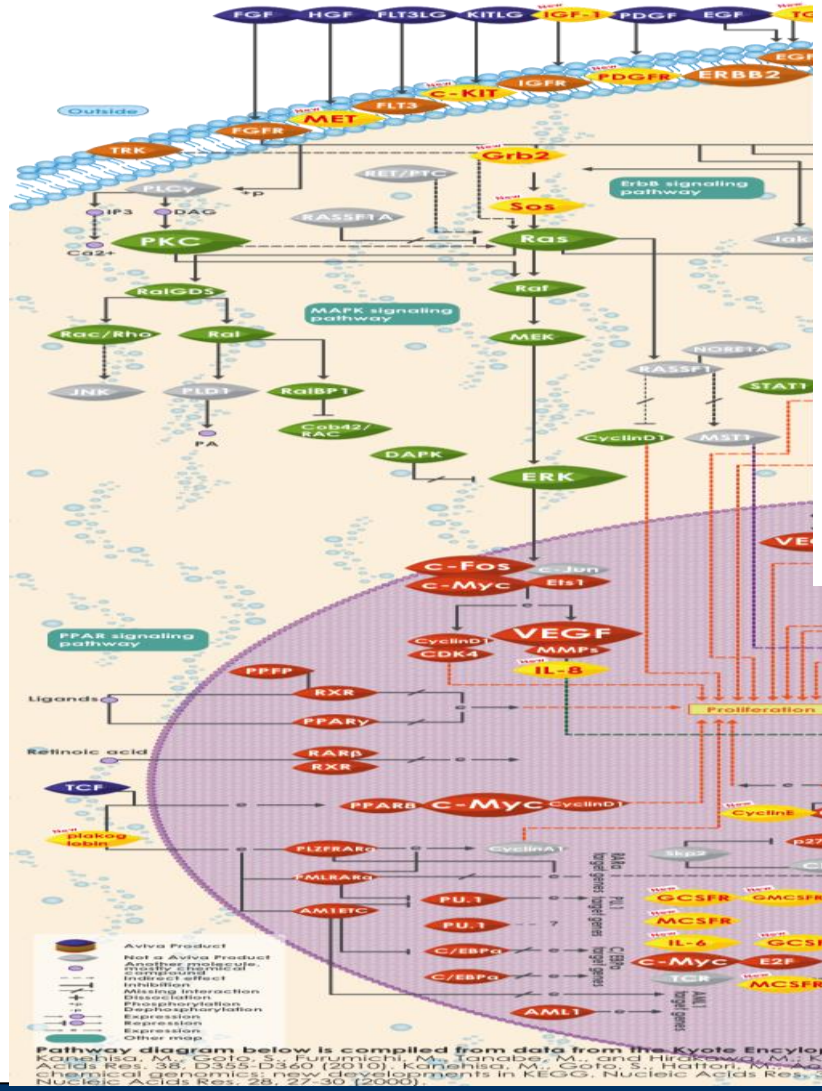


Gene directed precision therapy is six times better at controlling cancer – ASCO meeting 2016 [6]

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#ixzz4AnW443cO. Accessed June 6, 2016

Where are we heading?

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



Pathway diagram below is compiled from data from the Kyoto Encyclopedia of Genes and Genomes

Kanehisa, M., Goto, S., Furumichi, M., Tanabe, M., and Hirakawa, M.; KEGG for representation and analysis of molecular networks involving diseases and drugs. Nucleic Acids Res. 38, D355-D360 (2010). Kanehisa, M., Goto, S., Hattori, M., Aoki-Kinoshita, K.F., Itoh, M., Kawashima, S., Katayama, T., Araki, M., and Hirakawa, M.; From genomics to chemical genomics: new developments in KEGG. Nucleic Acids Res. 34, D354-D357 (2006). Kanehisa, M. and Goto, S.; KEGG: Kyoto Encyclopedia of Genes and Genomes. Nucleic Acids Res. 28, 27-30 (2000).

JOURNAL OF CLINICAL ONCOLOGY | EDITORIAL

Basket Trials and the Evolution of Clinical Trial Design in an Era of Genomic Medicine

Amanda J. Redig, *Dana-Farber Cancer Institute and Harvard Medical School, Boston, MA*
Pasi A. Jänne, *Dana-Farber Cancer Institute, Harvard Medical School, and Brigham and Women's Hospital, Boston, MA*

See accompanying article doi: 10.1200/JCO.2014.58.2007

Since the days of the ancient Greeks, the pathologic hallmarks
hermore, despite increasing recognition of the impor-
malignancy have been reflected in the language of oncology. Hippo
genomic analysis in oncol
evaluating targeted
crates was the first to use *carcinoma*—or crab—to describe the famil-
can present a formi
n the mutations
iar invading sweep of tumor cells across tissue planes, and several
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hundred years later, Galen described the *oncos*—or swelling—of
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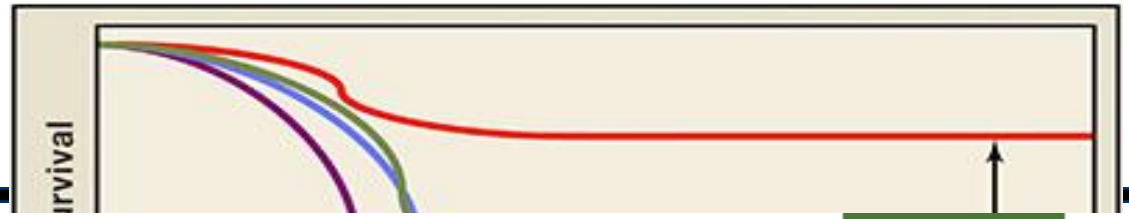
ly discovered

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?



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

How should we treat it?

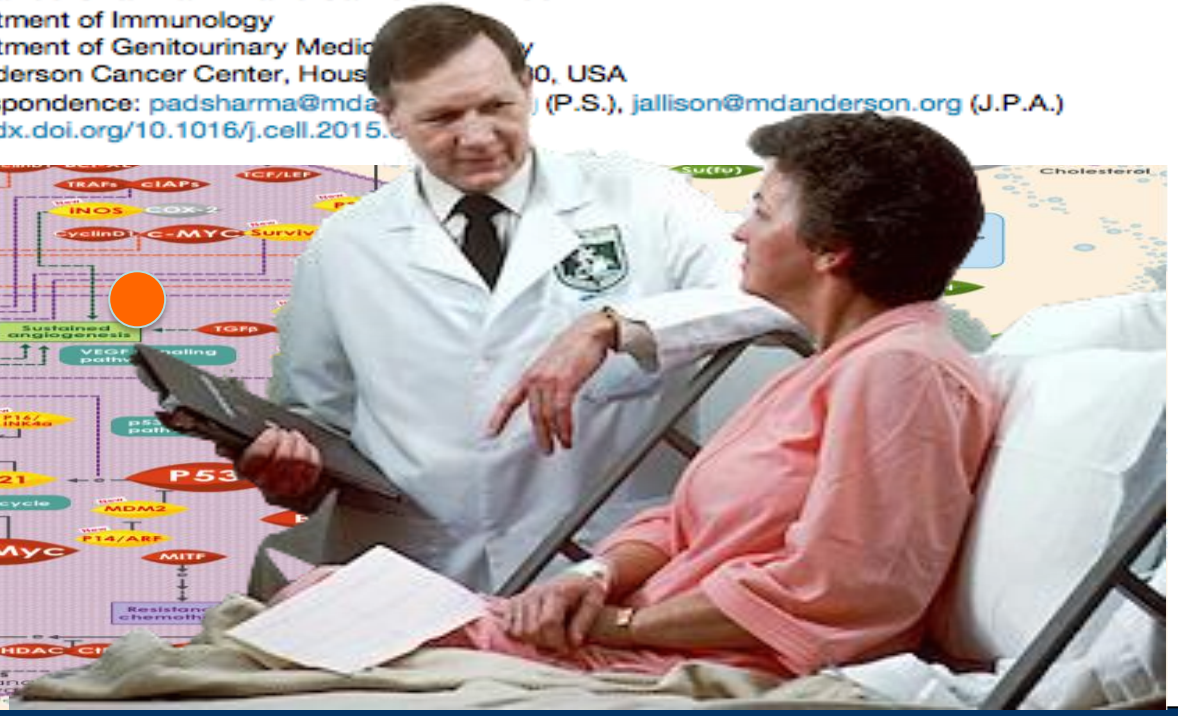
Leading Edge

Review

Cell

Immune Checkpoint Targeting in Cancer Therapy: Toward Combination Strategies with Curative Potential

Padmanee Sharma[1,2,*] and James P. Allison[1,*]
[1]Department of Immunology
[2]Department of Genitourinary Medic
MD Anderson Cancer Center, Hous 0, USA
*Correspondence: padsharma@mda (P.S.), jallison@mdanderson.org (J.P.A.)
http://dx.doi.org/10.1016/j.cell.2015.



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

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

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 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

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: Image: "Innovation“, Creative Commons Zero (CC0), Public Domain. http://maxpixel.freegreatpicture.com/Inspiration-Innovation-Idea-Thought-Imagination-2123970. Accessed May 17, 2017

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

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

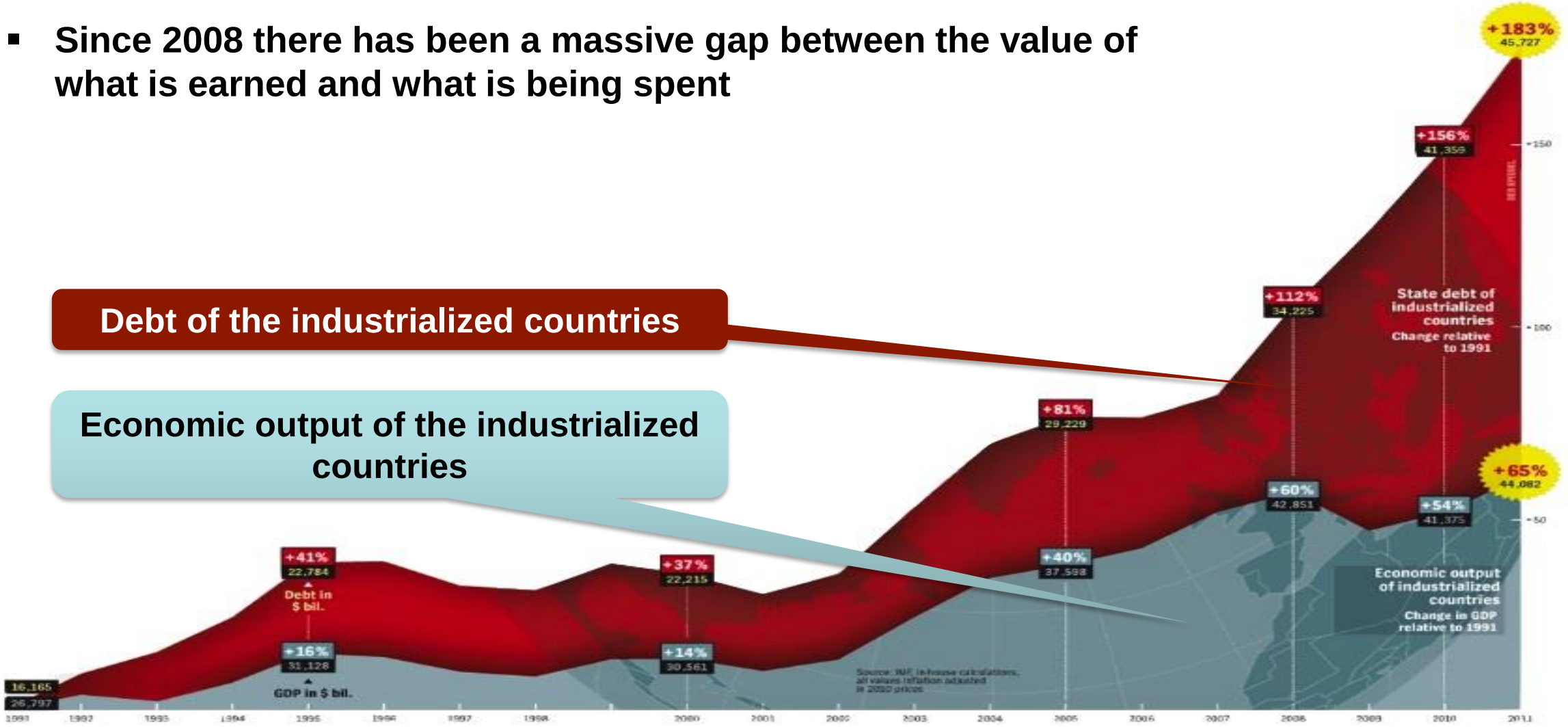
Biosimilars –
Can the dream of affordable cancer care come true?

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

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

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

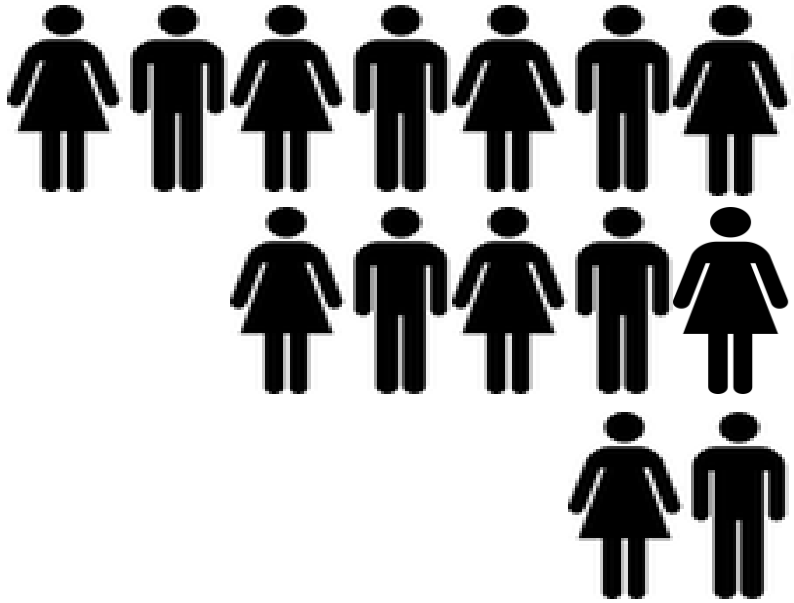
- **Since 2008 there has been a massive gap between the value of what is earned and what is being spent**



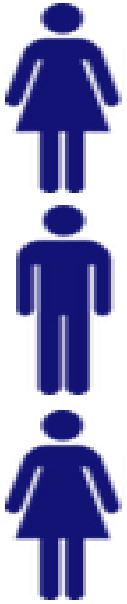
Ref: [1] Matthew Lynn. All the signs point to a new recession – a worse one. The Spectator, 5 March 2016. http://www.spectator.co.uk/2016/03/the-next-recession/ [2] Per capita debt in selected countries. Der Spiegl. http://www.spiegel.de/international/world/bild-806772-300815.html. Accessed March 6, 2016

Future demographic trends threaten national finances even further

- **Workers paying for healthcare 20-64 years**



Population >65years

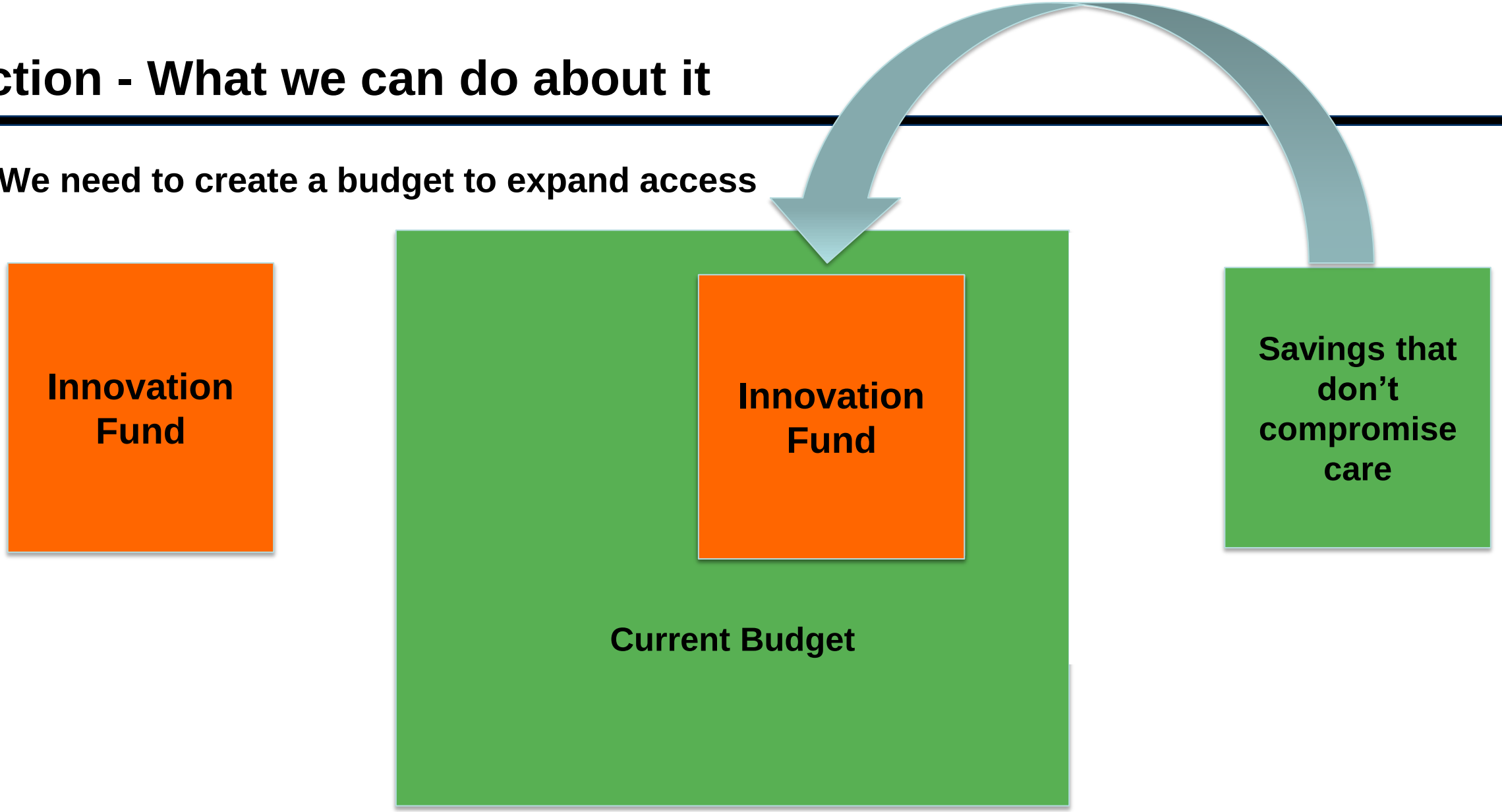


- **1950**
  - 7.2:1
- **1980**
  - 5.1:1
- **2050**
  - 2.1:1
- **Dependency ratio changes predicted 1970-2050:**
  - **UK = 4.3 to 2.1:1**
  - **Germany = 4.1 to 1.6:1**
  - **USA = 5.3 to 2.6:1**

Ref: [1] The Economist-Old Age Dependency Ratios-May 2009. http://www.economist.com/node/13611235. Accessed nov 7, 2016 [2] The Economist-Old Age Dependency Ratios-May 2009. http://www.economist.com/node/13611235. Accessed nov 7, 2016 [2] The Economist-Falling short. The trouble with pensions. Economist Jun 12th 2008, 13:09. http://www.economist.com/node/11529345. Accessed nov 7, 2016

Action - What we can do about it

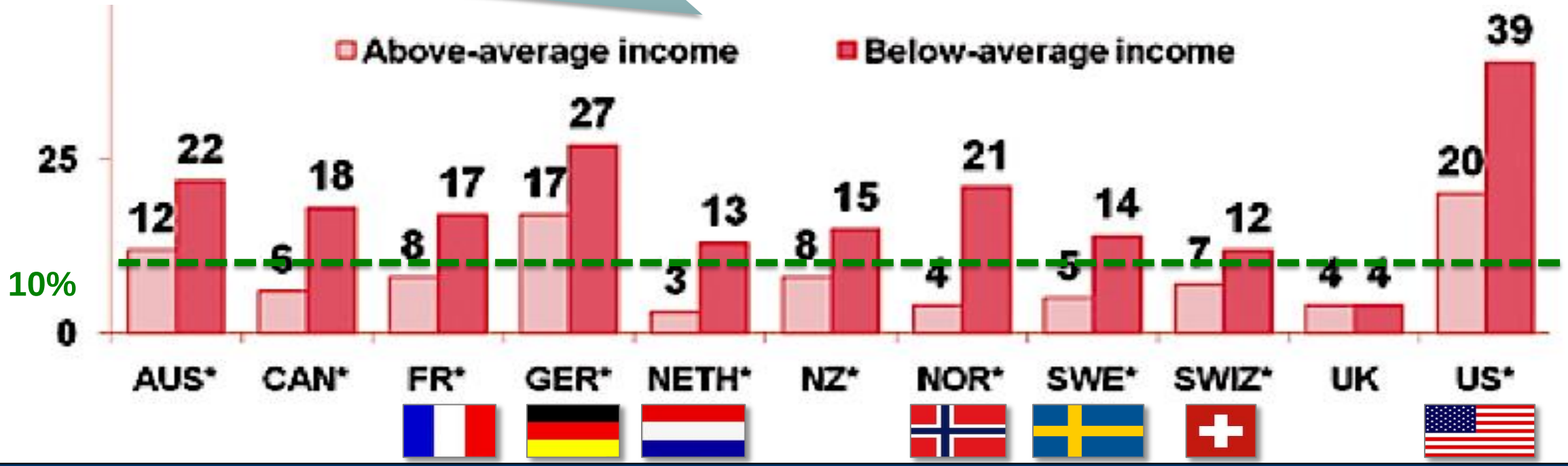
- We need to create a budget to expand access



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.**

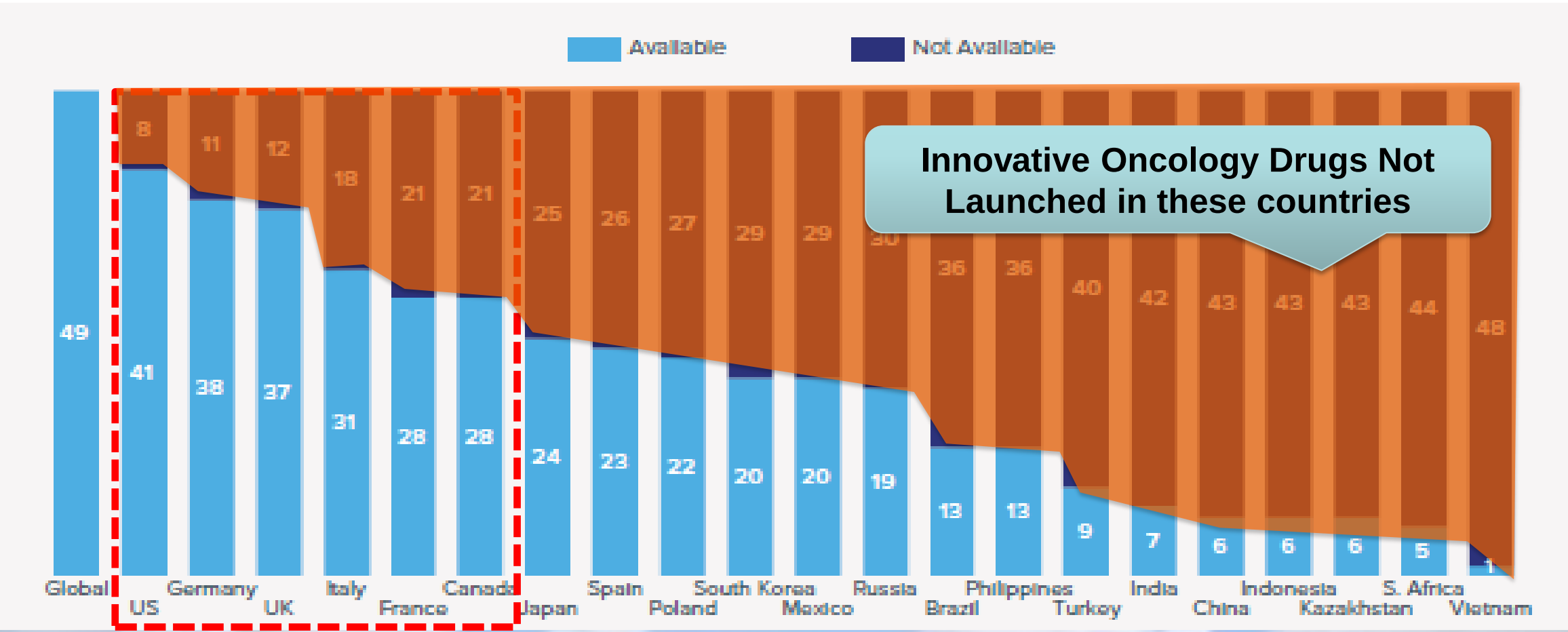
Many Europeans may be surprised to see rich nations where >10% of those on below average income fail in 1 or more tests of access to healthcare



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

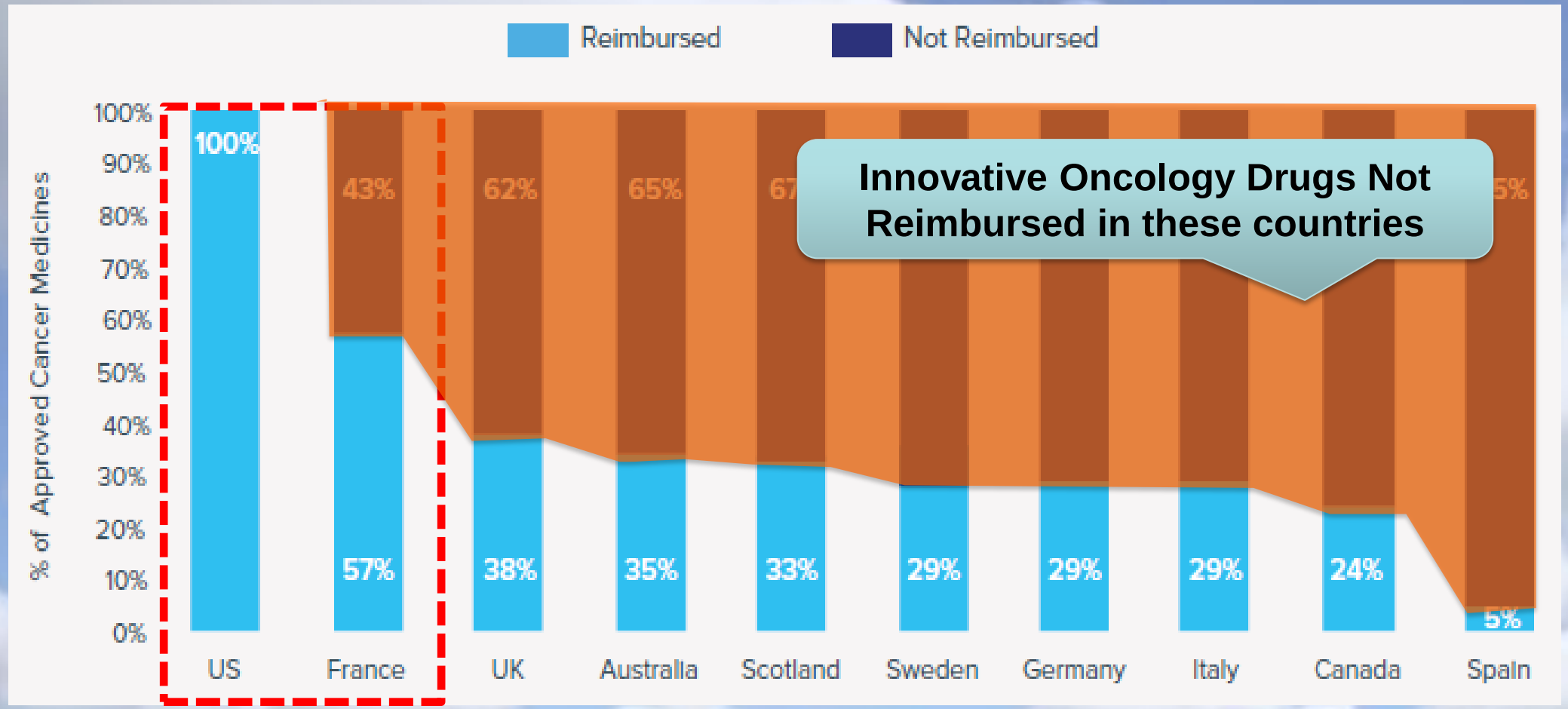
Availability of Oncology Medicines Launched 2010-2014



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

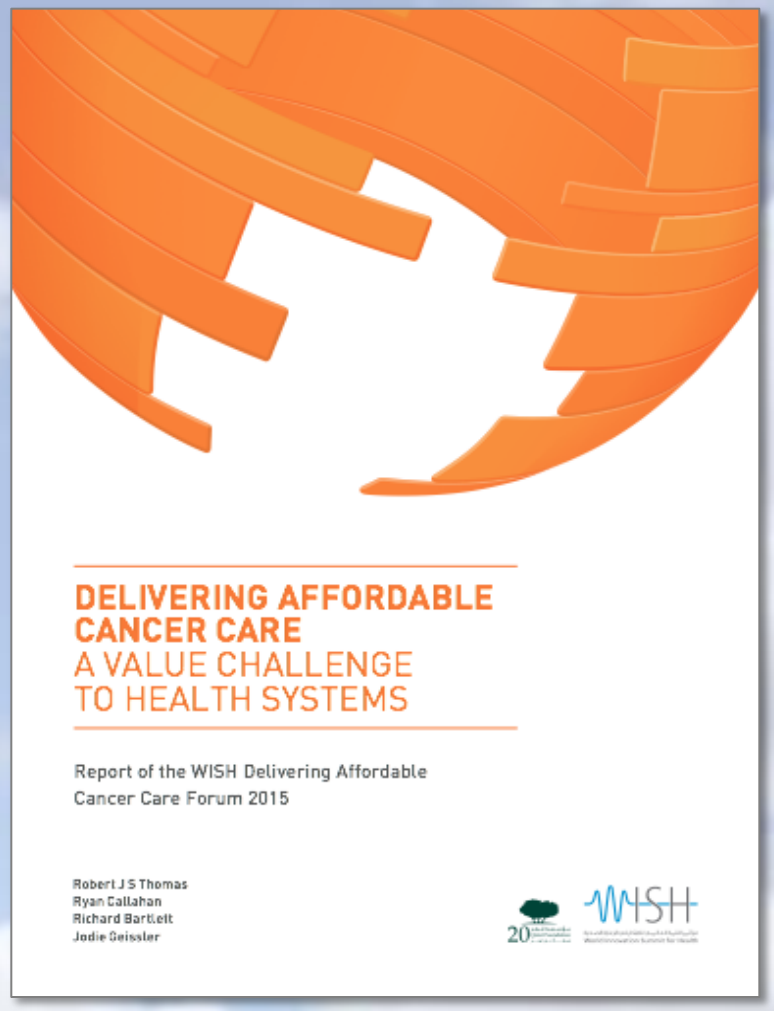
Reimbursement status of cancer medicines approved in 2014 and 2015



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

The 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 ”



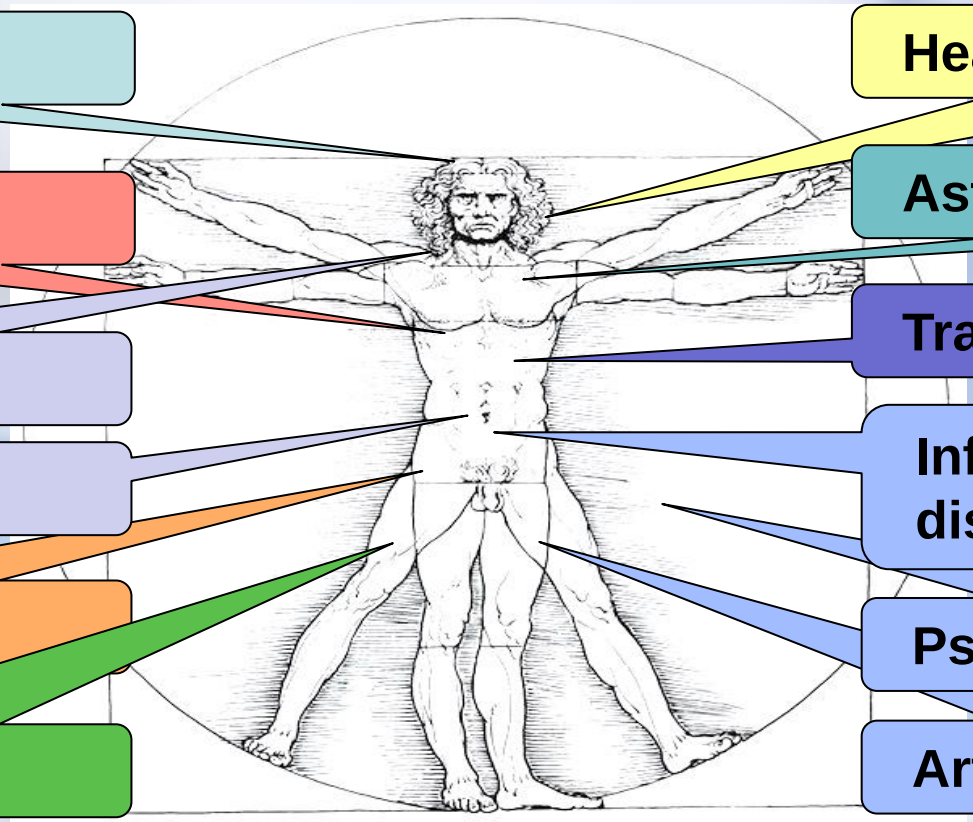
WISH
مؤتمر القمة العالمي للابتكار في الرعاية الصحية
World Innovation Summit for Health

World Innovation Summit for Health
A Healthier World Through Global Collaboration

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: http://www.wish-qatar.org/app/media/1425. Accessed Aug 27, 2017 [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.

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

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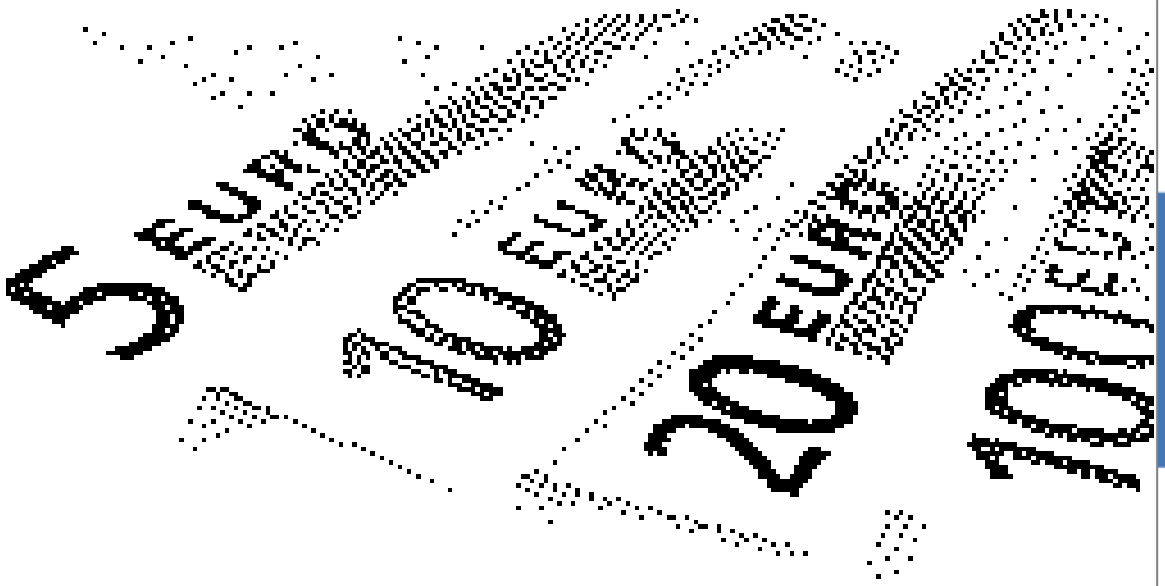
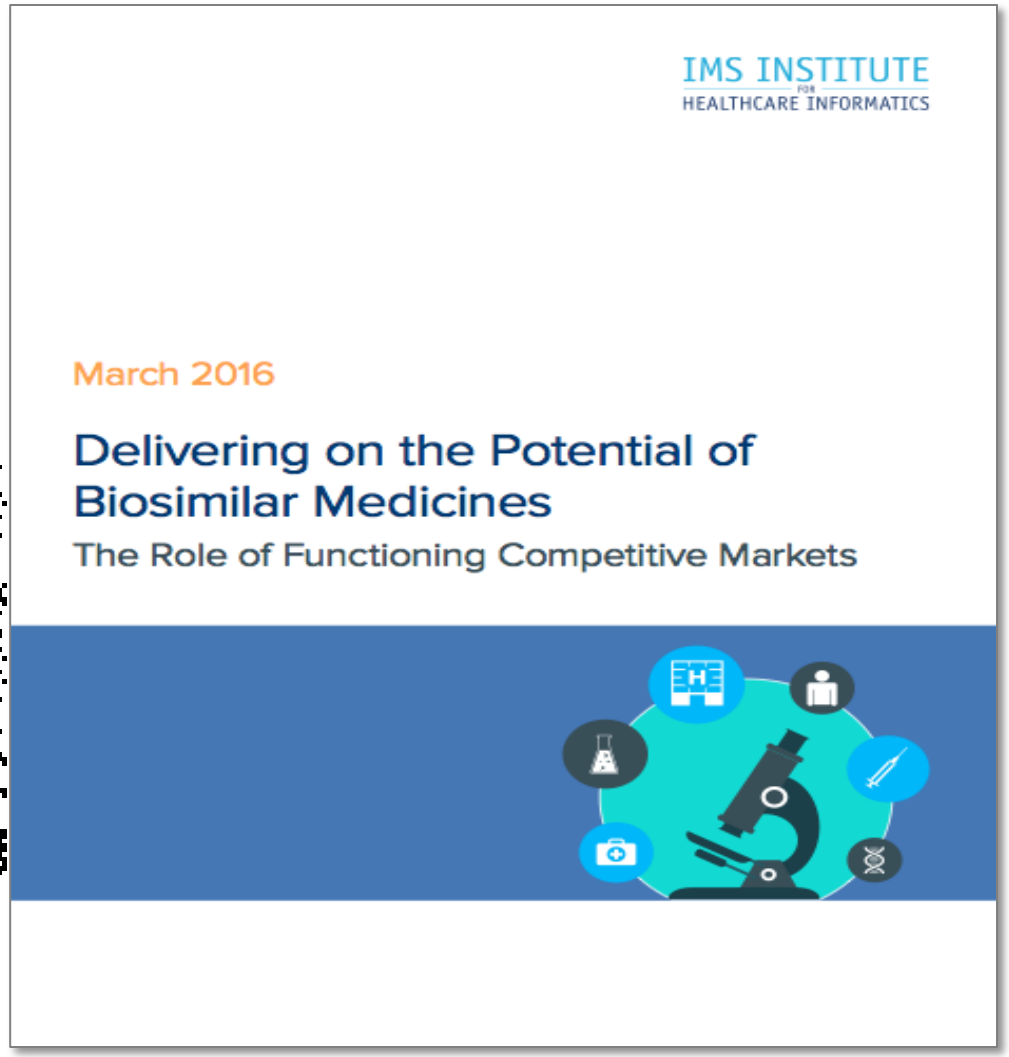
Ref: [1] Map Image. CCO License. https://upload.wikimedia.org/wikipedia/commons/7/7a/United_Kingdom_Portugal_Locator.png. Accessed March 13, 2017

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**

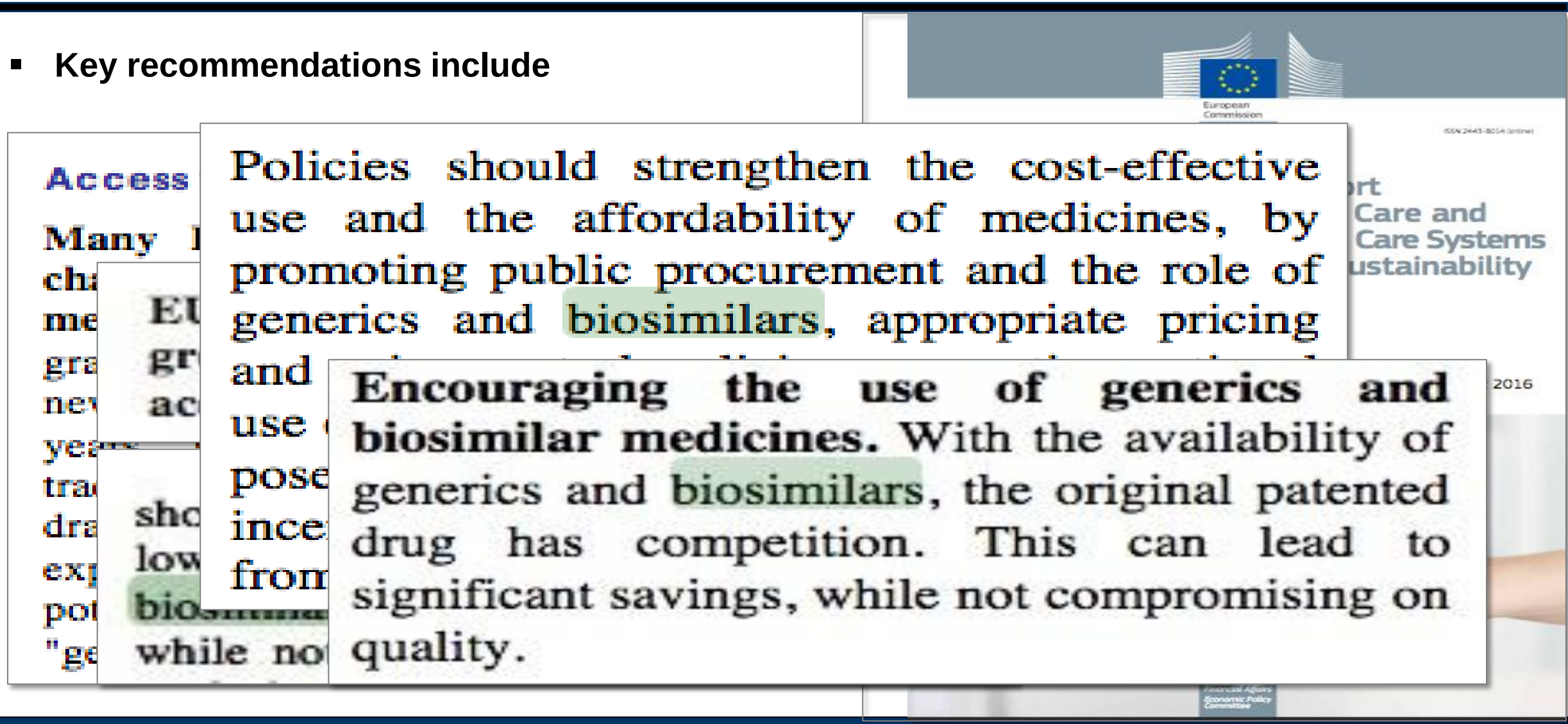




Ref: [1] Delivering on the Potential of Biosimilar Medicines The Role of Functioning Competitive Markets. IMS March 2016. www.theimsinstitute.org, accessed April 7, 2016

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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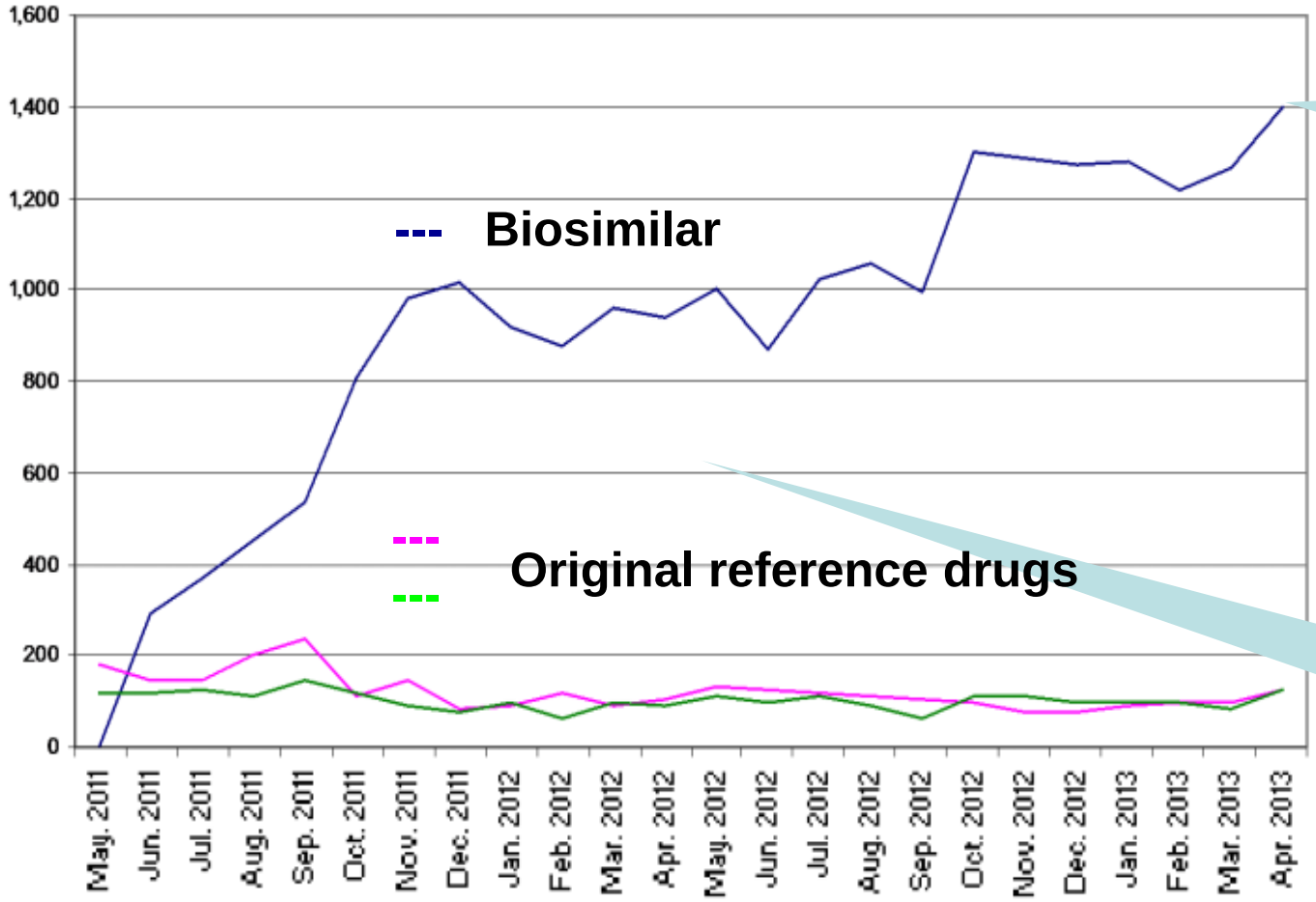
The impact of biosimilar filgrastim in London

- **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,”

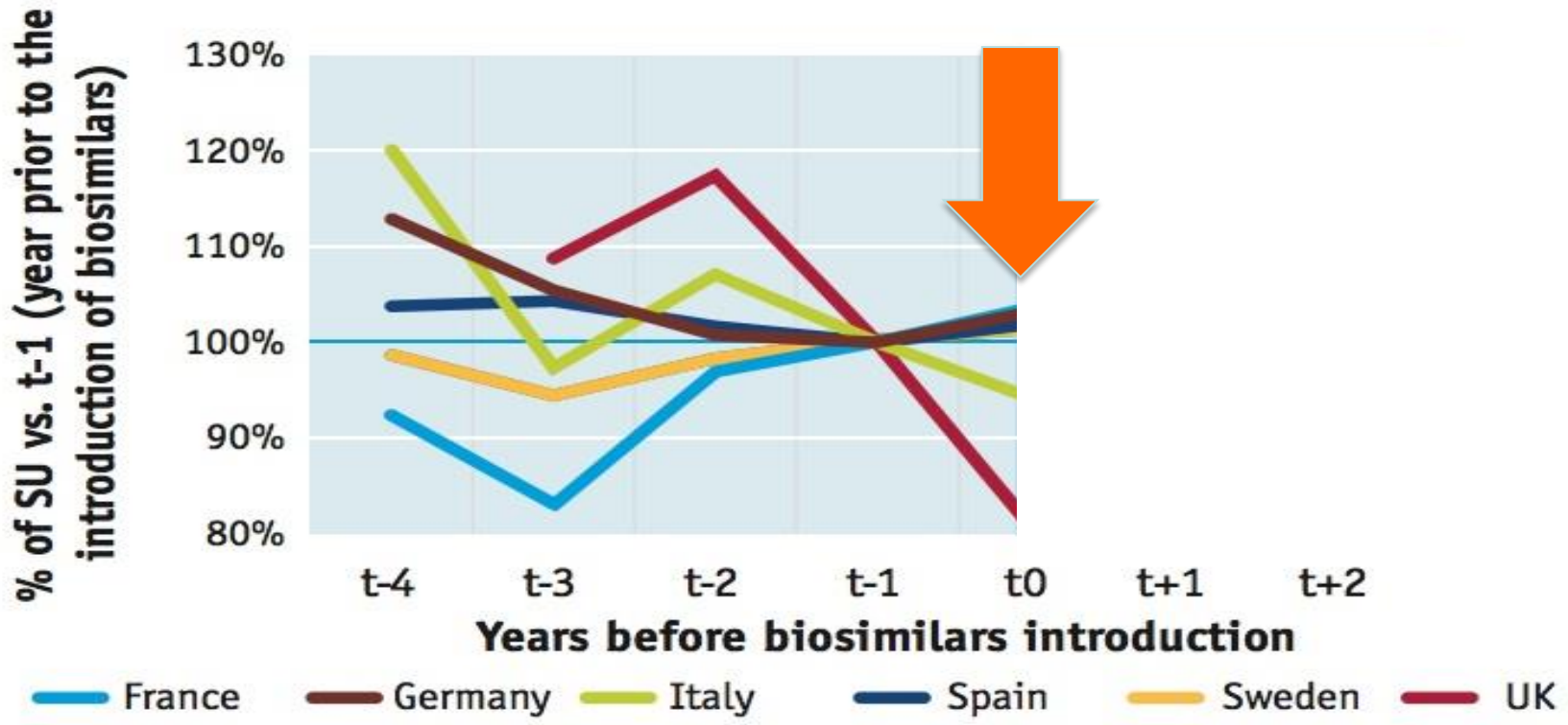
“Previously around one third of women receiving docetaxel-based chemotherapy suffered from neutropeanic fever. We now see it in less than 7 percent.”

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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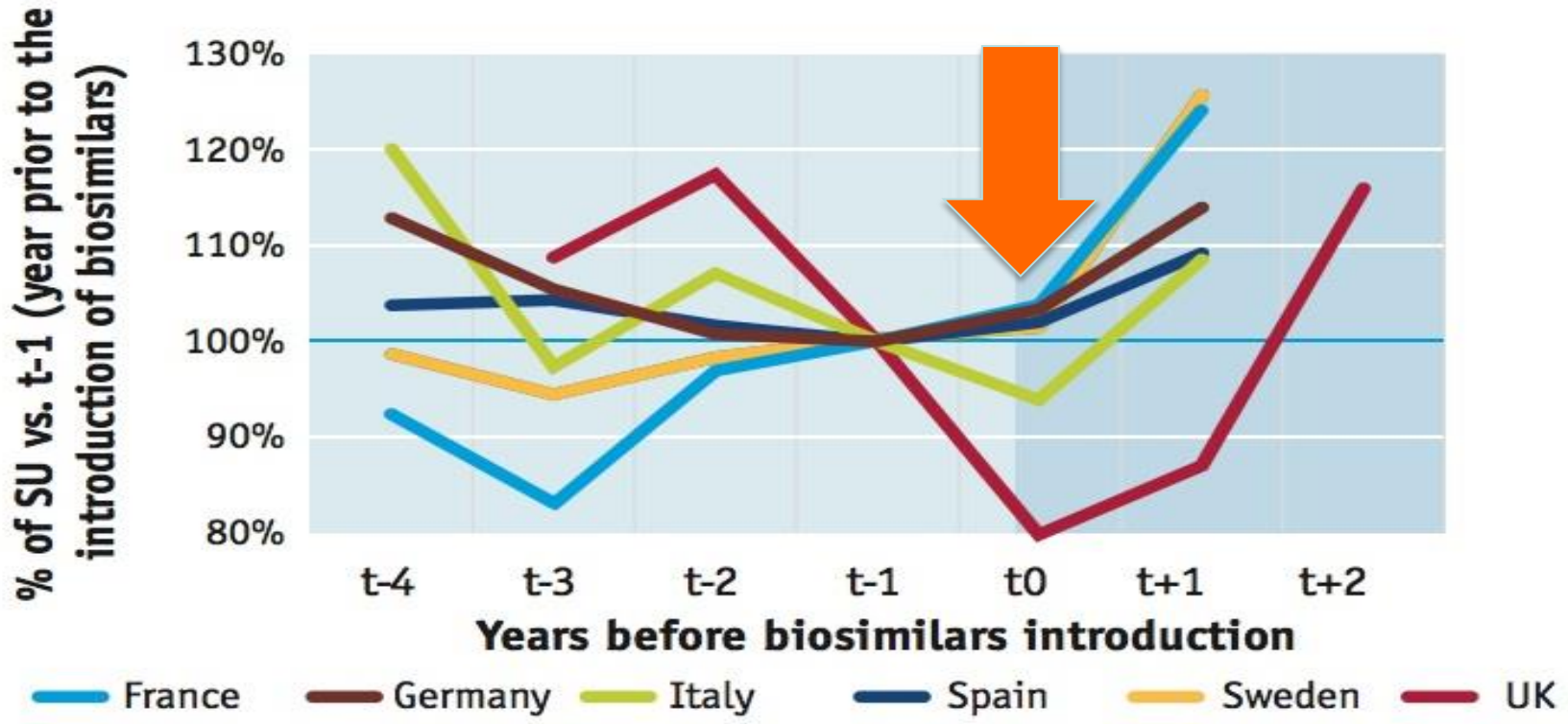

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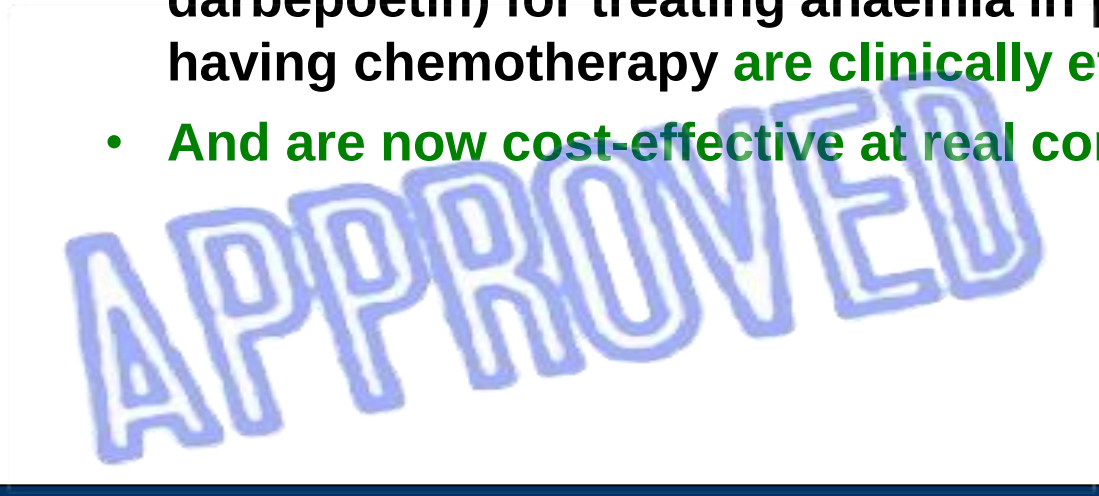
Biosimilars reverse negative funding decisions

- **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**



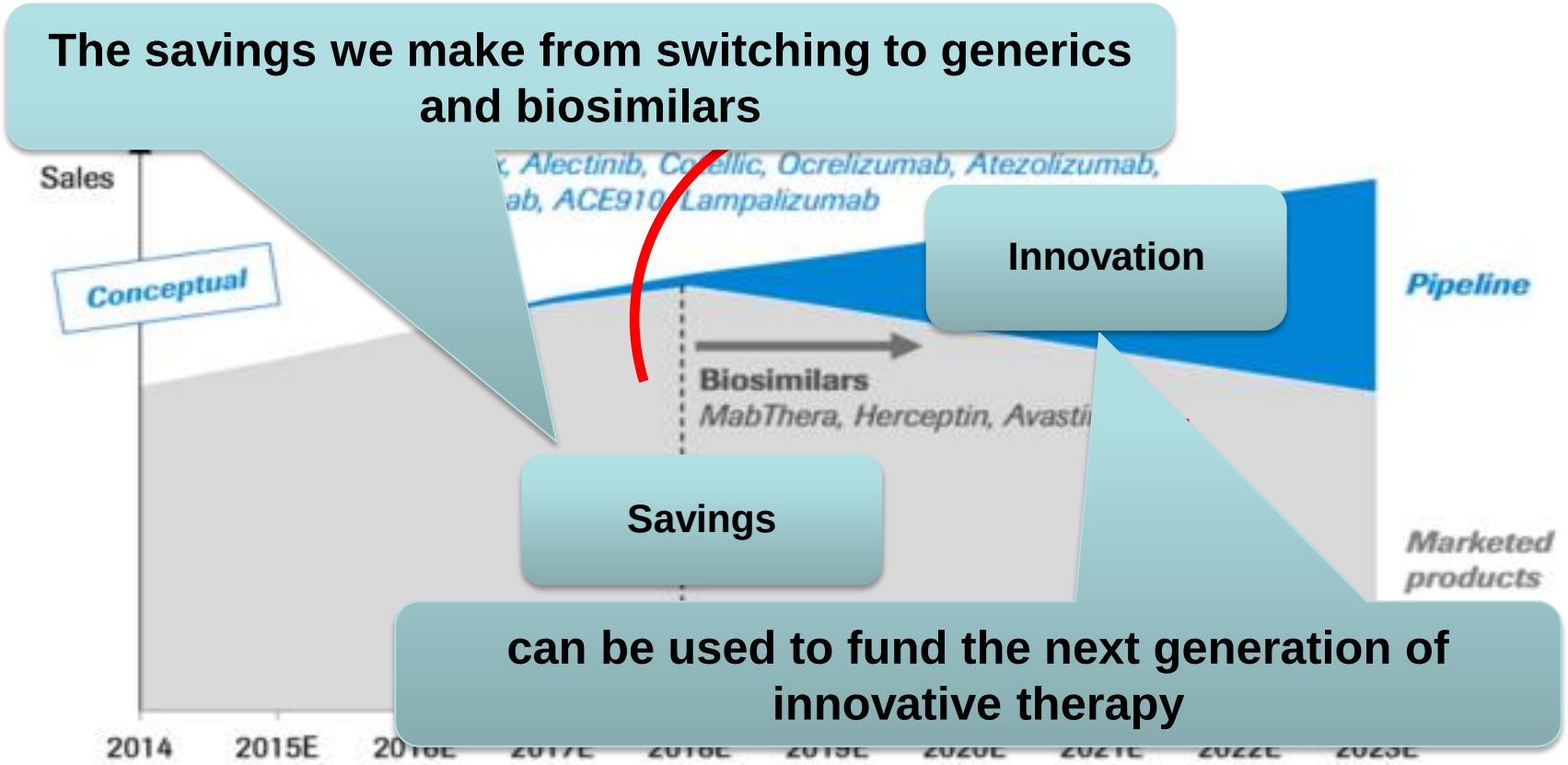
NICE accepted that biosimilar price competition had dramatically reduced the actual contract prices for epoetin

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

- **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]



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

Cost Savings from Biosimilars

Physicians need biosimilars to sustain healthcare innovation

Challenge		Result
Effective targeted therapy held back for later stage of disease	→	Effective targeted therapy used earlier in the disease
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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

Table 4.1. **Ten leading sources of inefficiency**

Source of inefficiency	Common reasons for inefficiency	Ways to address inefficiency
1. Medicines: underuse		
10. **Health interventions: inefficient mix/ inappropriate level of strategies**	Funding high-cost, low-effect interventions when low-cost, high-impact options are unfunded. Inappropriate balance between levels of care, and/or between prevention, promotion and treatment.	conduct. Regular evaluation and incorporation into policy of evidence on the costs and impact of interventions, technologies, medicines, and policy options.

Source [6].

Source of inefficiency

1. Medicines: underuse of generics and higher than necessary prices for medicines

The WHO top priority is to control drug spending

The commonest treatment we use in medicine is drug treatment

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

Rational Medicine Use

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 .

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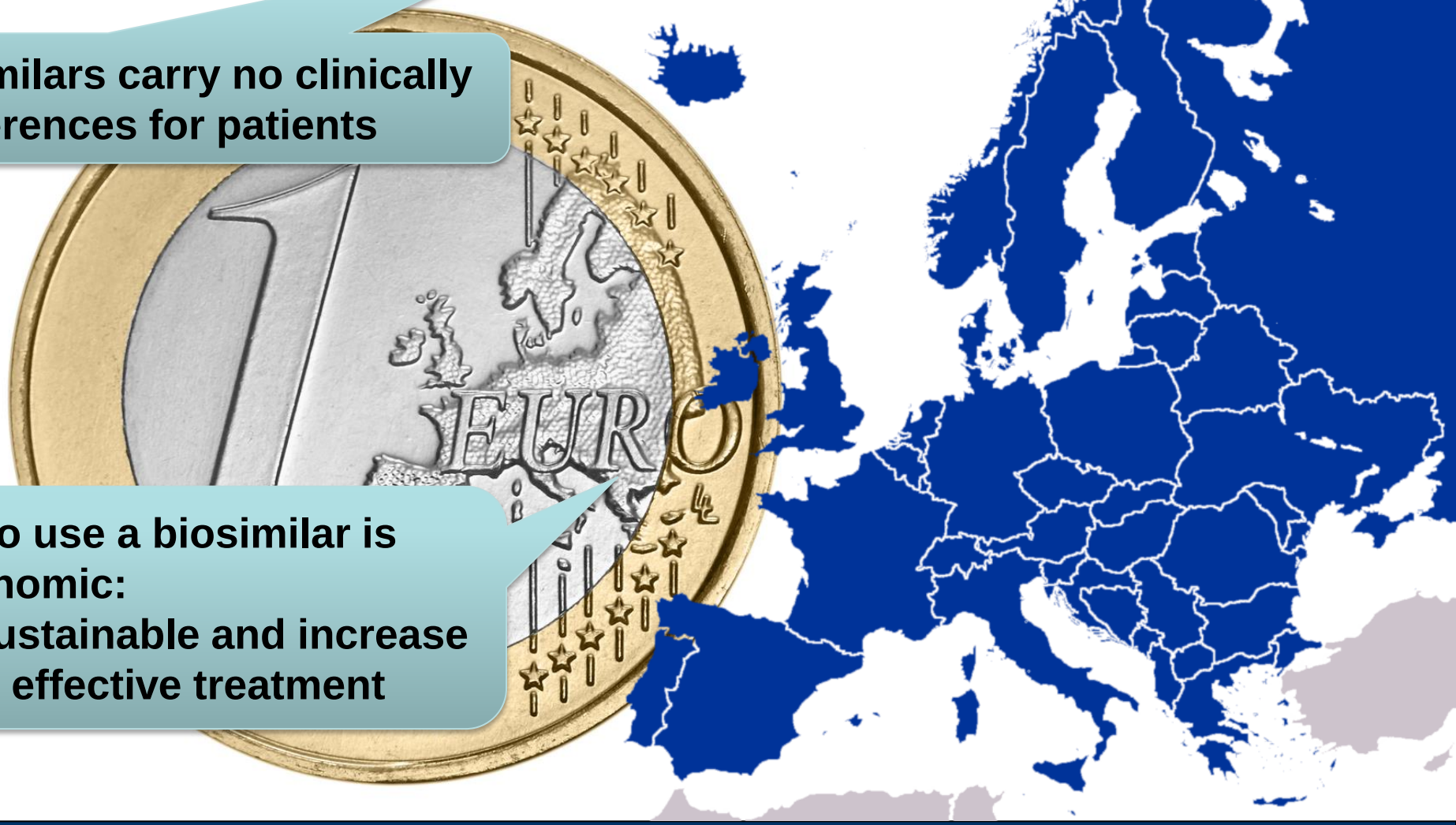
Ref: [1] Map Image. CCO License. https://upload.wikimedia.org/wikipedia/commons/7/7a/United_Kingdom_Portugal_Locator.png. Accessed March 13, 2017

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

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

How have European biosimilars performed - Outcomes

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

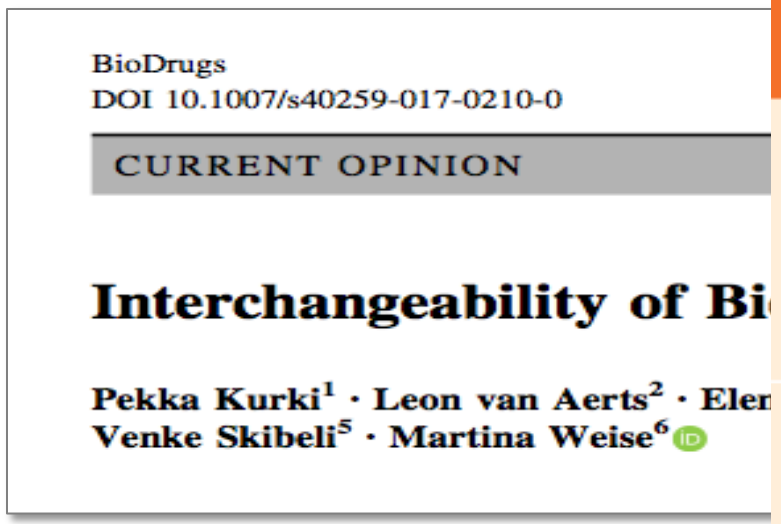
European Approved Biosimilars have never failed to match the reference drug in an extrapolated indication

Biosimilars are interchangeable

Confidence is high: “Position Statements” by Medical Societies against Biosimilars have been reversed

Ref: [1] Medicines for Europe - Biosimilars. http://www.medicinesforeurope.com/wp-content/uploads/2016/03/infographic-biosimilars.pdf accessed March 14, 2017 [2] Medicines for Europe information based on EMA Post-authorisation Safety Update Reports (PSURs) reported by Adrian van den Hoven. Biosimilar medicines clinical use: an experience based-EU perspective. FDA Presentation 13 July 2017, Washington D.C. ,USA. http://www.medicinesforeurope.com/docs/20170713%20-%20Biosimilar%20Medicines%20Group,%20EU%20experience-AVH-US%20FDA%20Adcom.pdf. Accessed Aug 31, 2017 [3] Biosimilars in the EU - Information guide for healthcare professionals. Prepared jointly by the European Medicines Agency and the European Commission. http://www.ema.europa.eu/docs/en_GB/document_library/Leaflet/2017/05/WC500226648.pdf. Accessed Aug 31, 2017

How have European biosimilars performed – Interchangeability: EU National regulators Speak Up



- Finland
- Germany
- Netherlands
- Norway

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.

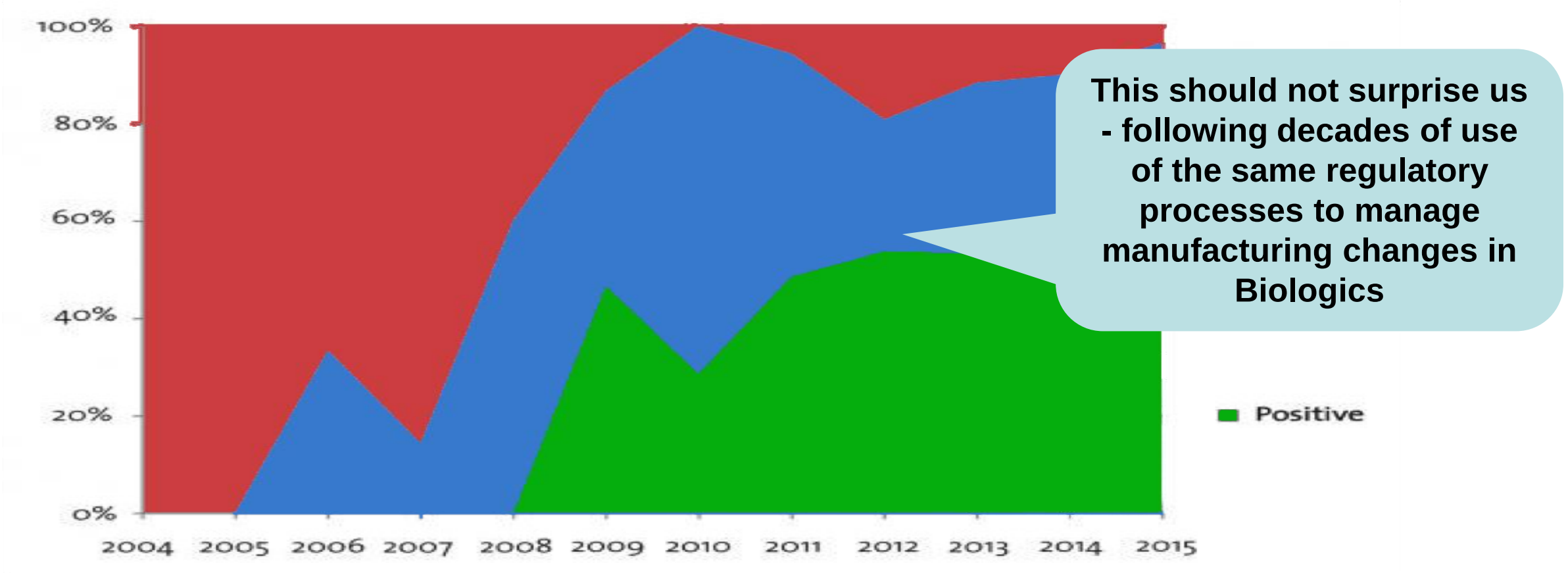
Because of the high similarity, there is no reason to believe that the body's immune system would react differently to the biosimilar compared with the original biological upon a switch. This view is supported by the current experience with biosimilars on the market and by literature data.

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

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

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

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

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Expectations of Future Biosimilars: Therapeutic Oncology Drugs

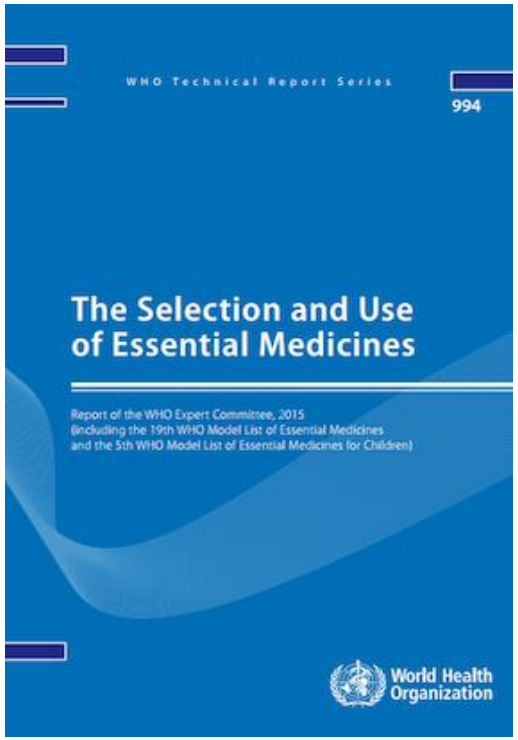
- **Biologic drugs are now essential medicines for the world that we must provide to the world at affordable prices**

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

Filgrastim ✓

Trastuzumab

Rituximab



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

European Approval of biosimilars of Rituximab

- **2 approved**

Filgrastim ✓

Trastuzumab

Rituximab ✓

GaBi Online
Generics and Biosimilars Initiative

GENERICS AND BIOSIMILARS INITIATIVE
Building trust in cost-effective treatments

EMA approval for rituximab biosimilar Truxima

Posted 20/01/2017

The European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) announced on 16 December 2016 that it had recommended granting of marketing authorization for a rituximab biosimilar.

EMA approval for etanercept and rituximab biosimilars

Posted 28/04/2017

The European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) announced on 21 April 2017 that it had recommended granting marketing authorization for the etanercept biosimilar Erelzi and for the rituximab biosimilars Rixathon and Riximyo.

Ref: [1] 19th WHO Essential Medicines List, 2015. WHO. http://www.who.int/medicines/publications/essentialmedicines/en/. Accessed March 17, 2016 [2] EMA approval for rituximab biosimilar Truxima. GaBI Posted 20/01/2017. http://www.gabionline.net/Biosimilars/News/EMA-approval-for-rituximab-biosimilar-Truxima. Accessed August 28, 2017 [3] EMA approval for etanercept and rituximab biosimilars. GaBI Posted 28/04/2017 . http://www.gabionline.net/Biosimilars/News/EMA-approval-for-etanercept-and-rituximab-biosimilars. http://www.gabionline.net/Biosimilars/News/EMA-approval-for-etanercept-and-rituximab-biosimilars. Accessed August 28, 2017

European Approval of biosimilars of Trastuzumab

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

Filgrastim ✓

Trastuzumab ?

Rituximab ✓

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Generics and Biosimilars Initiative

GENERICS AND BIOSIMILARS INITIATIVE
Building trust in cost-effective treatments

EMA accepts application for trastuzumab biosimilar

Posted 07/10/2016

Samsung Bioepis, which is a joint venture between South Korean electronics giant Samsung and biotechnology company Biogen, announced on 3 October 2016 that its

Amgen submits trastuzumab biosimilar to EMA

Posted 24/03/2017

Biotech giant Amgen announced during a conference presentation that it had filed for marketing approval for its trastuzumab biosimilar (ABP 980) in the European Union (EU).

Celltrion submits trastuzumab biosimilar application to EMA

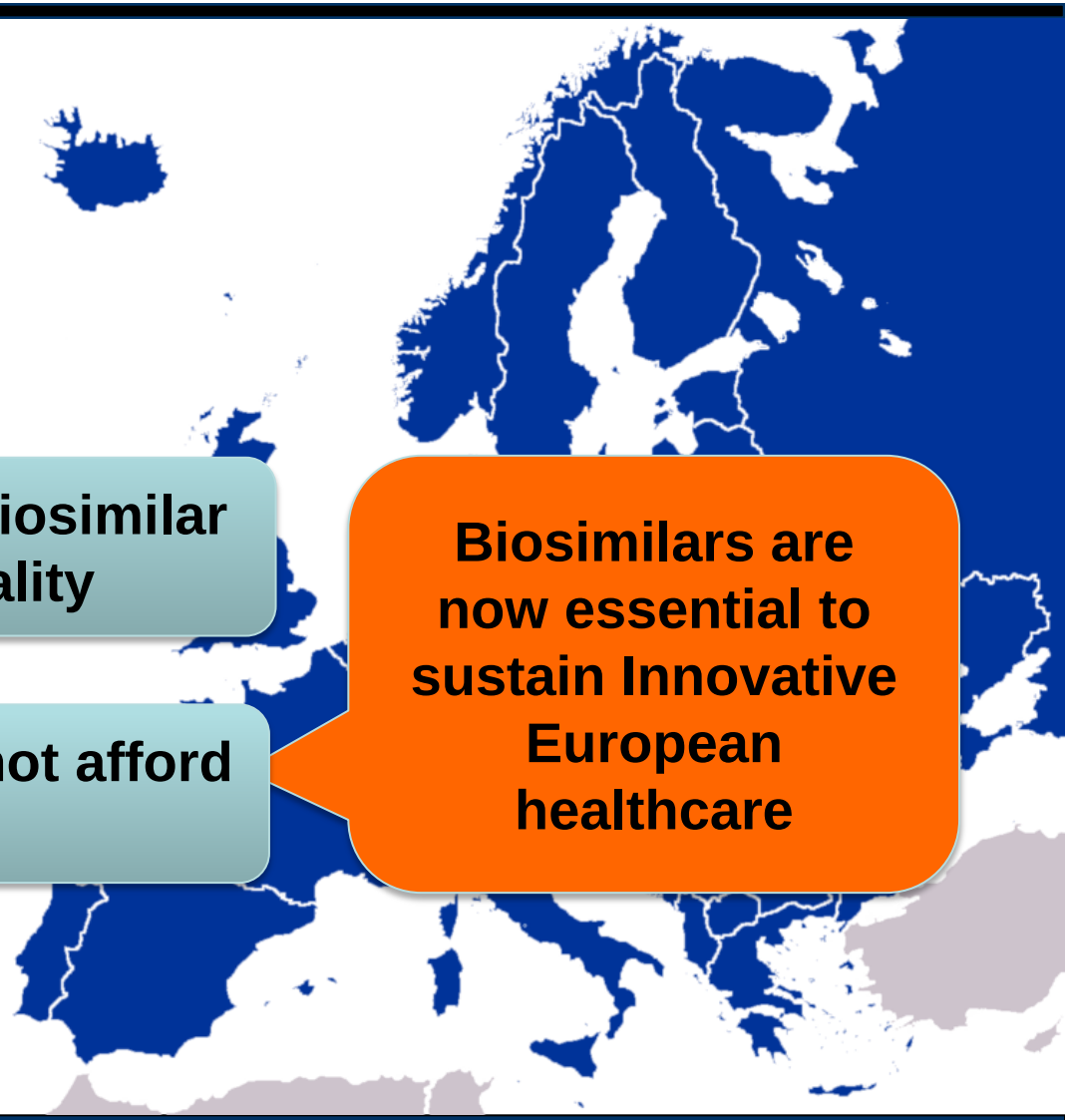
Posted 18/11/2016

South Korean biotechnology company Celltrion has, according to The Korea Herald, submitted another biosimilar application to the European Medicines Agency (EMA).

Ref: [1] 19th WHO Essential Medicines List, 2015. WHO. http://www.who.int/medicines/publications/essentialmedicines/en/. Accessed March 17, 2016 [2] EMA approval for rituximab biosimilar Truxima. GaBI Posted 20/01/2017. http://www.gabionline.net/Biosimilars/News/EMA-approval-for-rituximab-biosimilar-Truxima. Accessed August 28, 2017 [3] EMA approval for etanercept and rituximab biosimilars. GaBI Posted 28/04/2017 . http://www.gabionline.net/Biosimilars/News/EMA-approval-for-etanercept-and-rituximab-biosimilars. http://www.gabionline.net/Biosimilars/News/EMA-approval-for-etanercept-and-rituximab-biosimilars. Accessed August 28, 2017

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



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

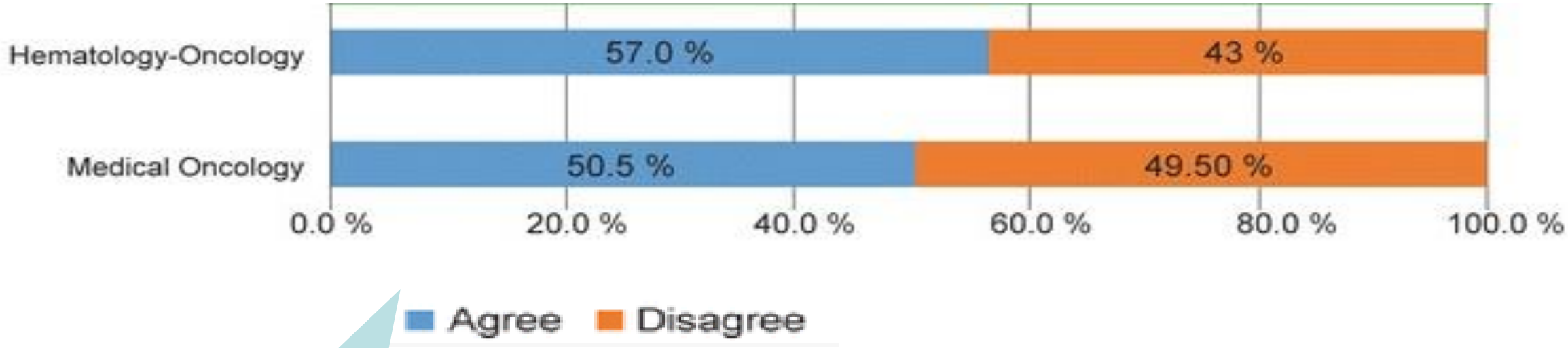
Without Biosimilars – most health systems cannot afford even Biologic Monotherapy

Biosimilars are now essential to sustain Innovative European healthcare

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

Biosimilars – physicians knowledge: Biosimilars Forum Survey 2016 – Results

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



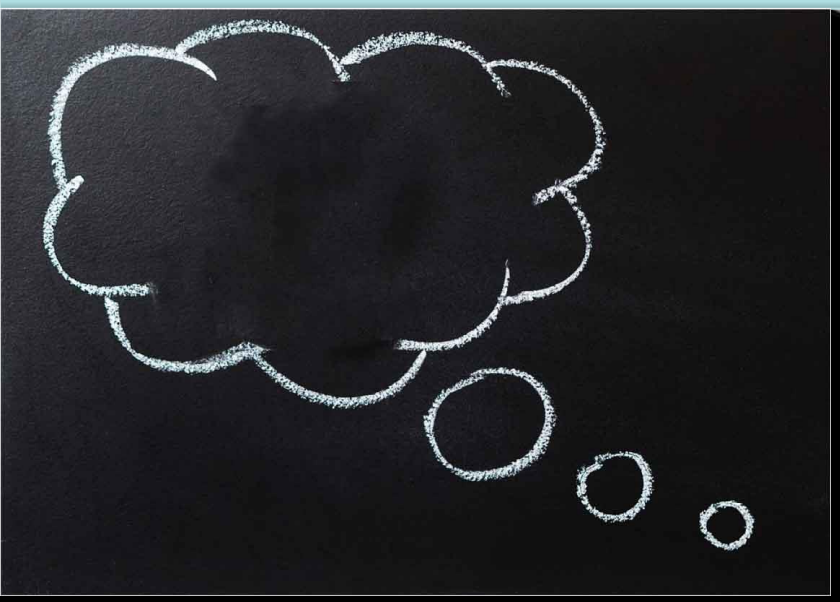
Physicians seem to be split 50:50

What is the opinion of Europe's Medical Oncologists

ESMO
GOOD SCIENCE
BETTER MEDICINE
BEST PRACTICE

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

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



What is the opinion of Europe's Medical Oncologists

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