

Biosimilars – can we do without them?

Dr Paul Cornes

Thursday 17th March, 2016
EAHP - Vienna



Dr Paul Cornes Disclosures March 2016

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

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

Please let me know if there are errors or omissions

Biosimilars – can we do without them?

Dr Paul Cornes, Oncologist



Comparative Outcomes Group



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Access to Innovative Treatment in
Europe

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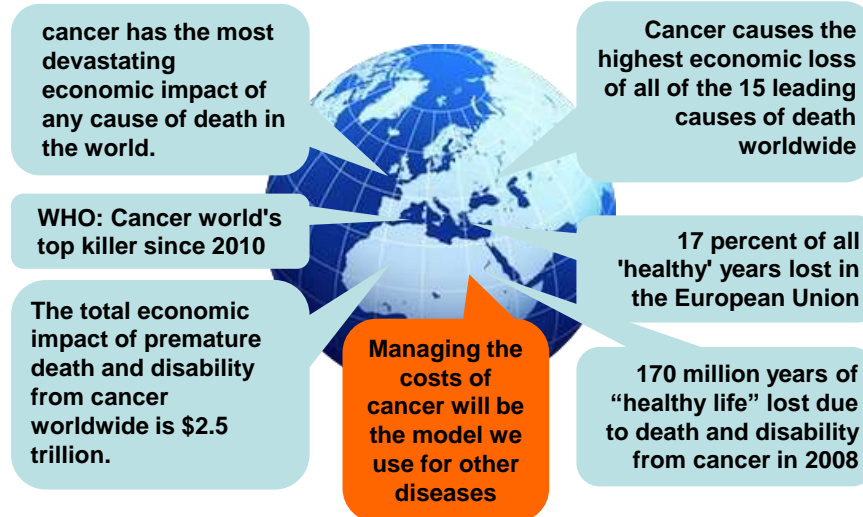


Biosimilars – can we do without them?



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

There is a cost to cancer



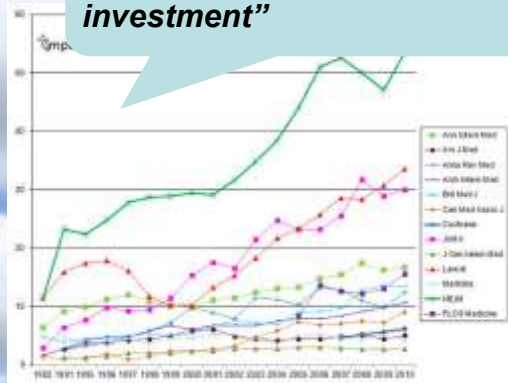
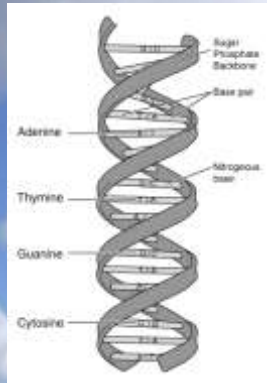
Ref [1] www.usatoday.com/story/health/2008-12-09/cancer, N.Mim [2] <http://www.cancer.org/jci/groups/content/InternationalAffairs/documental/documental/capc-026203.pdf> [3] Smith M. Life-Years Lost to Cancer More than 150 Million. <http://www.medpagetoday.com/HematologyOncology/OtherCancers/35325>, Accessed March 15, 2016. [4] Loppet G. Investing in Cancer Prevention and Control to Reduce Global Economic Burden. <http://am.asco.org/investing-cancer-prevention-and-control-reduce-global-economic-burden>, Accessed March 15, 2016

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



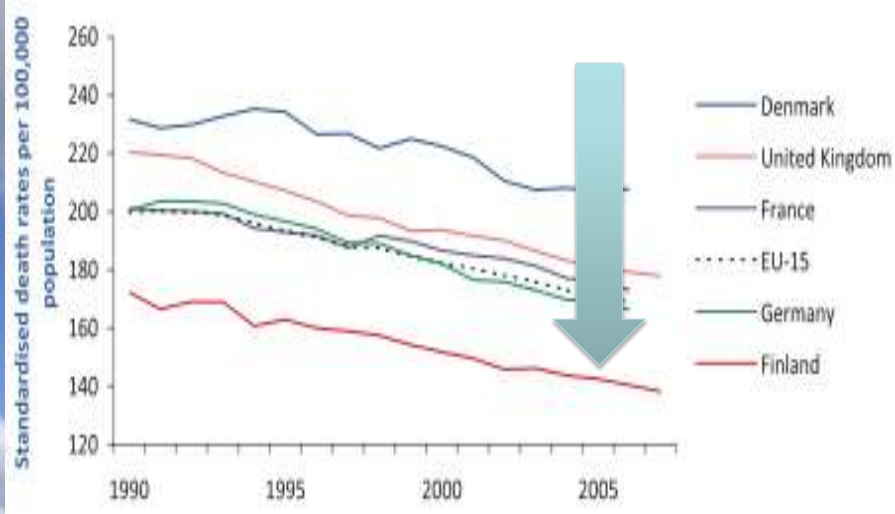
Good news for medicine

- Basic cancer science is paying back on its investment
- One medical paper a minute *“Think about health spending as not consumption but investment”*
Library of Medicine



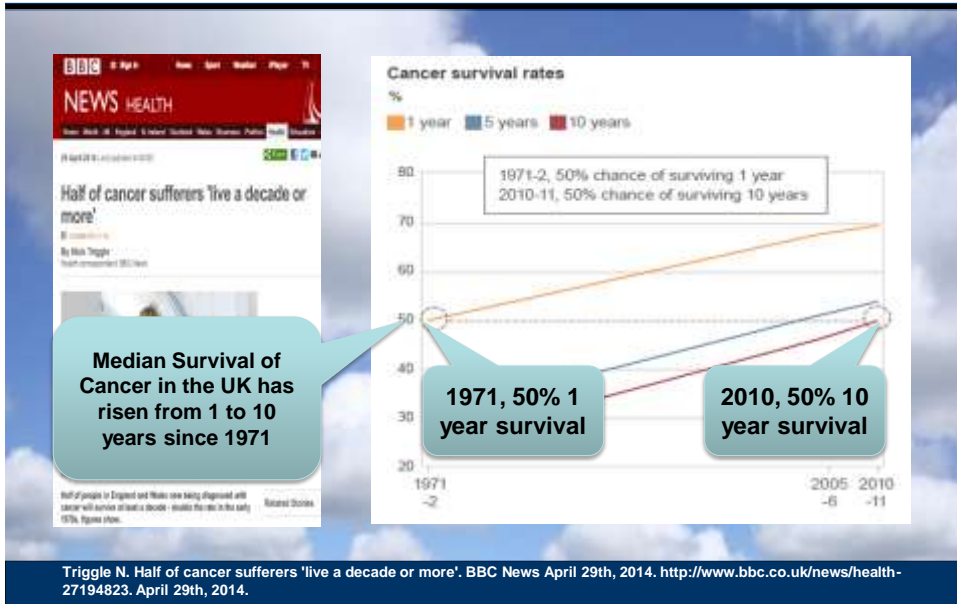
MEDLINE Citation Counts by Year of Publication. Available at http://www.nlm.nih.gov/bsd/medline_cit_counts_yr_pub.html, accessed 2012 Sept 11. Template:2010 - Impact factor of selected medical journals.jpg/credit

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

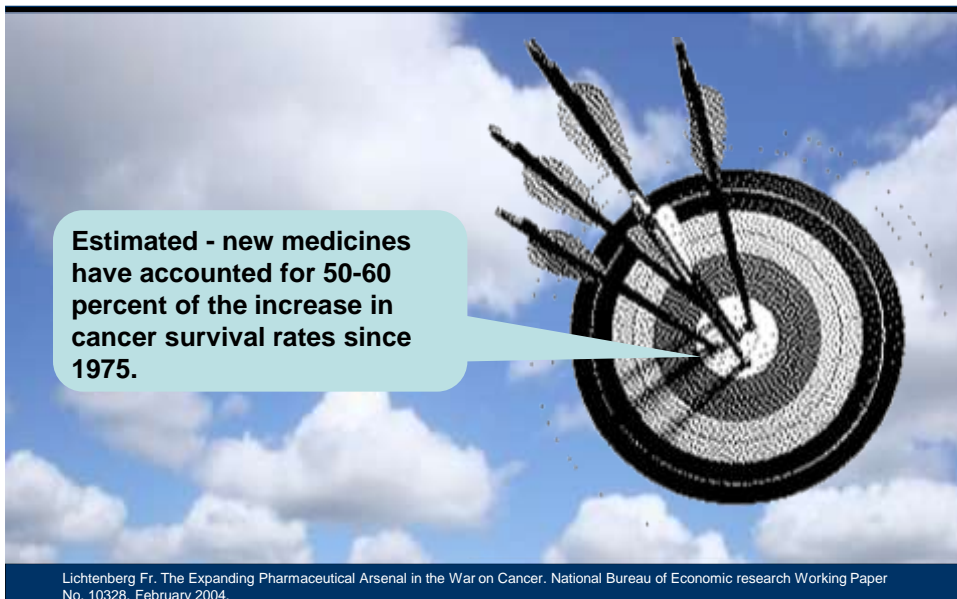


Ref: [1] WHO Health for all database [2] [2] Health and Social Care Information Centre. NHS Outcomes Framework. Nov 2014. www.hscic.gov.uk/catalogue/PUB15930/nhs-out-fram-ind-nov-14-comm.pdf. Accessed Jan 9, 2016

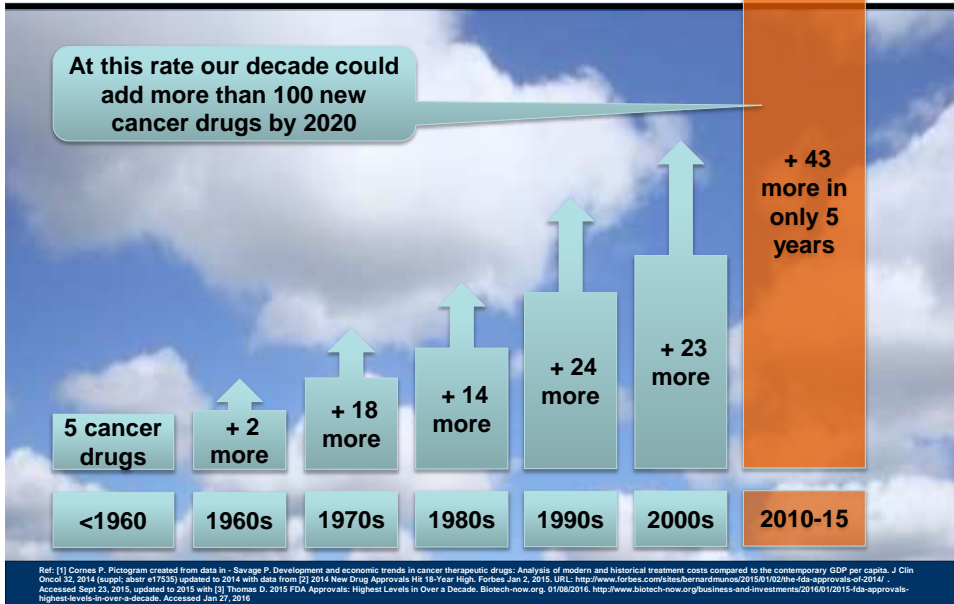
Good news for cancer treatment: Cancer survival is improving



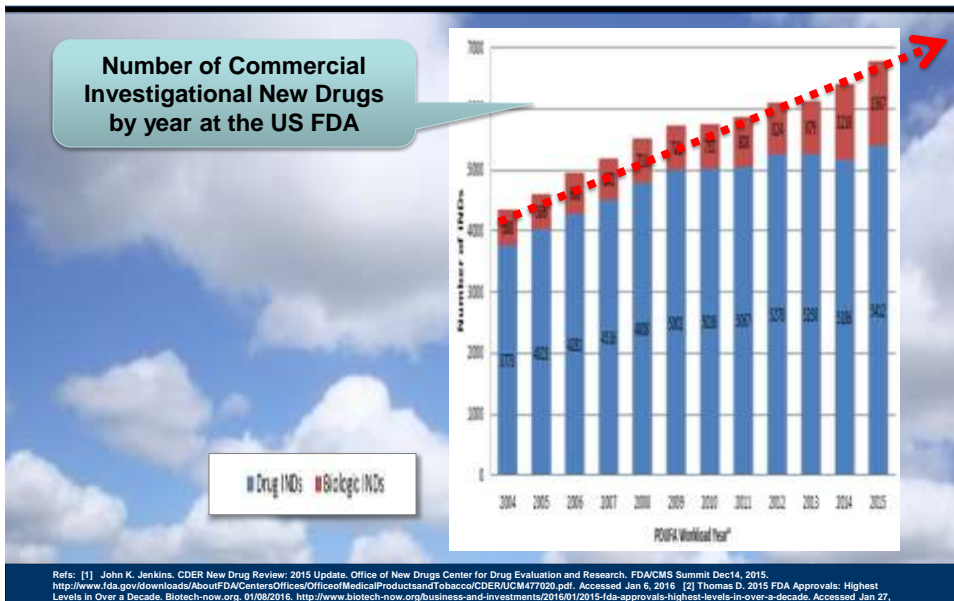
Cancer survival is improving



Good news for cancer treatment: Innovation in cancer drugs



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





Innovation - 1984

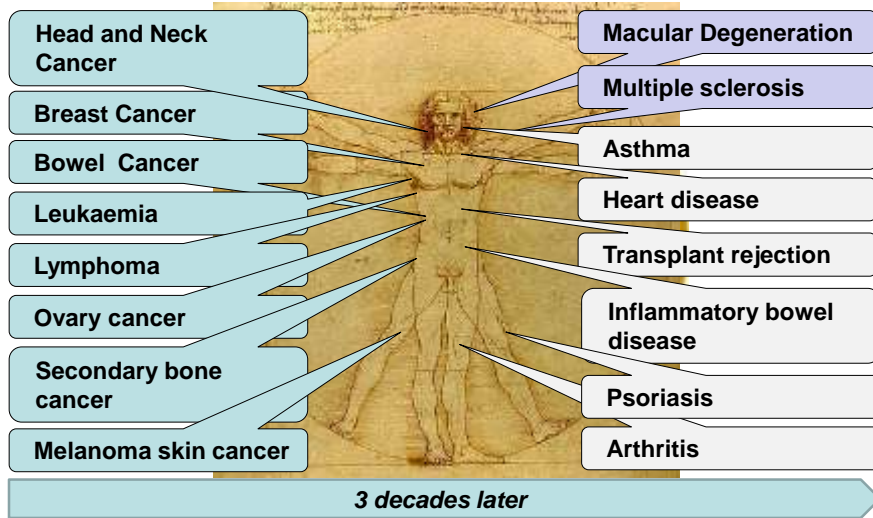
1984 Nobel Prize for Medicine

awarded jointly to Jerne, Köhler and Milstein

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

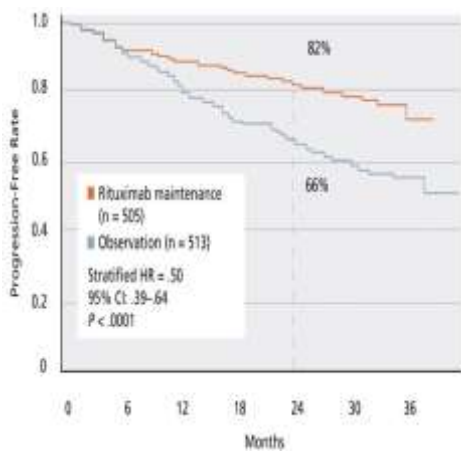
3 decades later

3 decades of Innovation: 1984 to 2016 Monoclonal antibody development



http://en.wikipedia.org/wiki/File:Da_Vinci_Vitruve_Luc_Viatour.jpg

Monoclonals in cancer - lymphoma

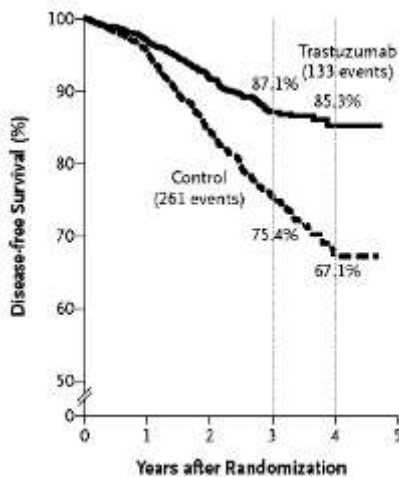


- Rituximab
 - Halves lymphoma relapse



http://www.jncn.org/content/8/Suppl_6/S-1/F3.large.jpg

Monoclonals in breast cancer

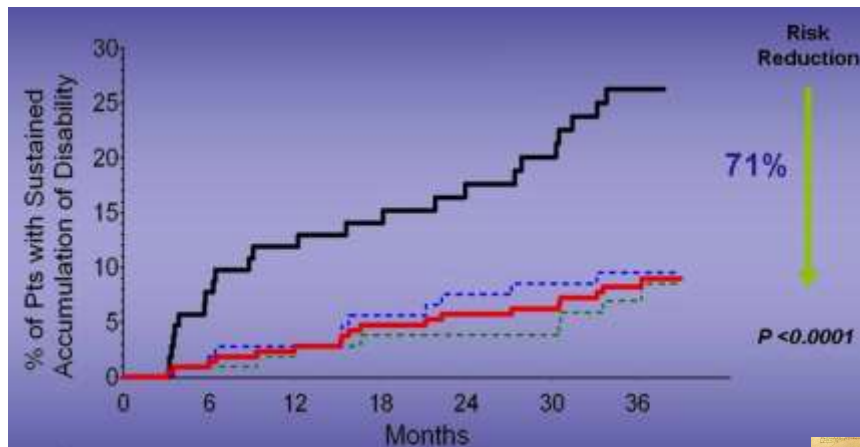


- Trastuzumab
 - Halves the chance of relapse
 - Reduces death by 33%



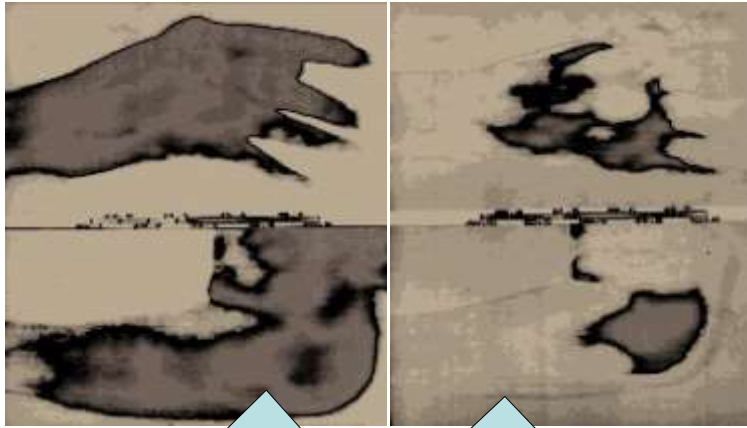
Romond EH, et al. NEJM. 2005;353:1673-1684

MAbs: 71% reduction in disability in multiple sclerosis



Ref: data - Campath-H1 vs interferon from <http://users.ox.ac.uk/~path0116/tig/new1/mstrialfig.jpg>. Accessed Jan 27, 2016

MAbs: Controlling rheumatoid arthritis



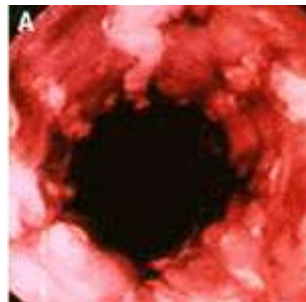
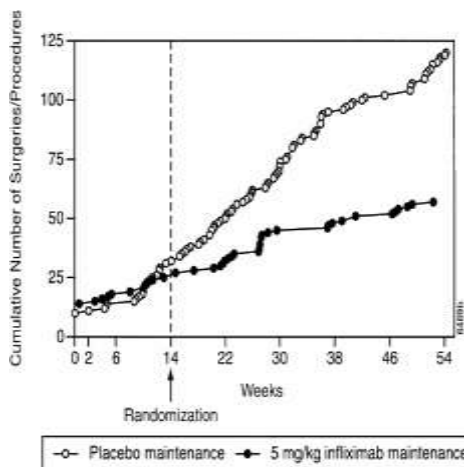
Thermal imaging of hand and elbow joints before.....

..and after Mab therapy



Ref: [1] Image from - <http://users.ox.ac.uk/~path0116/tig/new1/thefg.gif>. Accessed jan 27, 2016

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



Infliximab

Ref [1] Lichtenstein GR. Infliximab maintenance treatment reduces hospitalizations, surgeries, and procedures in fistulizing Crohn's disease. *Gastroenterology*, Volume 128, Issue 4, Pages 862-869, April 2005. http://en.wikipedia.org/wiki/File:CD_colitis.jpg

MABs for psoriasis



Ref: [1] Sylvia Marecki & Peter Kirkpatrick. Etaluzumab. Nature Reviews Drug Discovery 2004;3:473-474 . URL: http://www.epgpatientdirect.org/send_article.cfm?page355/title/Biologicals

New targeted precision medicines are transforming cancer care

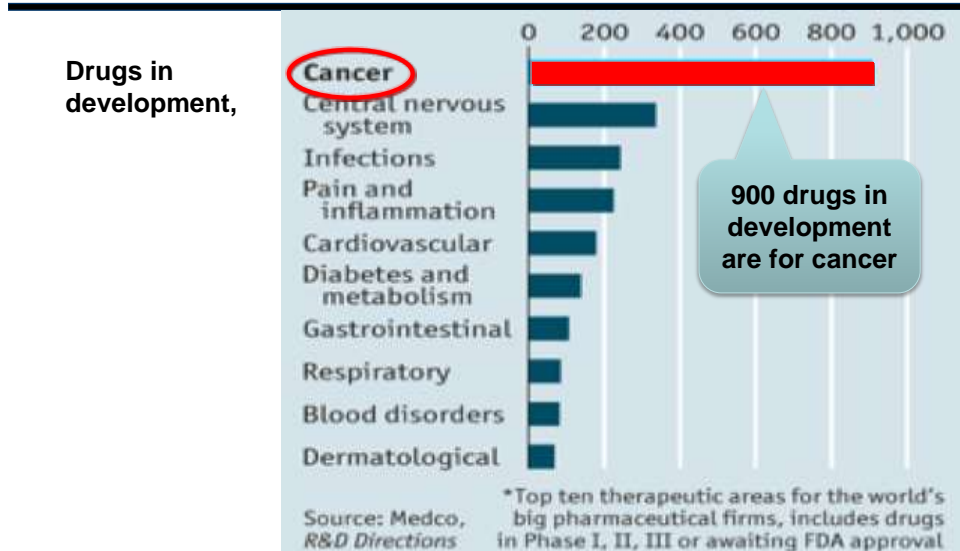
Cancer Disease	Old Model	Old Survival	Personalized Model	Personalized Survival
Acute promyelocytic leukemia	Chemotherapy	19 months	All-trans retinoic acid	>58 months
Chronic myeloid leukemia	Chemotherapy	6 years	Imatinib	>22 years
Melanoma	Dacarbazine	<10 months	Vemurafenib	16 months
Medullary thyroid 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

[1] Munoz and Kurzrock. *Nat Rev Clin Oncol*. 2012;9(11):631-42.
 [2] The Value of Medical Innovation. <http://valueofinnovation.org/a-world-free-from-cancer/#ref3> [Accessed May 2015].

Good news for cancer treatment



The costly war on cancer. The Economist. 2011 May 26. <http://www.economist.com/node/18743951>

Biologics
~~Biosimilars~~ – can we do
 without them?



**Biologics – I can't imagine the world of
 medicine without precision targeted therapies**

The possibility at the millennium, 2000

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

Where are we now?

I am sorry to report that you have breast cancer

Tell me doctor – what have I got?

Anatomic diagnosis

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

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/etcf/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]

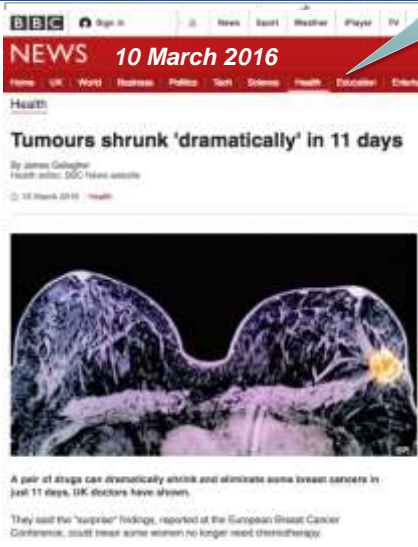
Describes pathways deregulated

And drug class required to counter it

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/etcf/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

Where are we heading?

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



Describes pathways deregulated

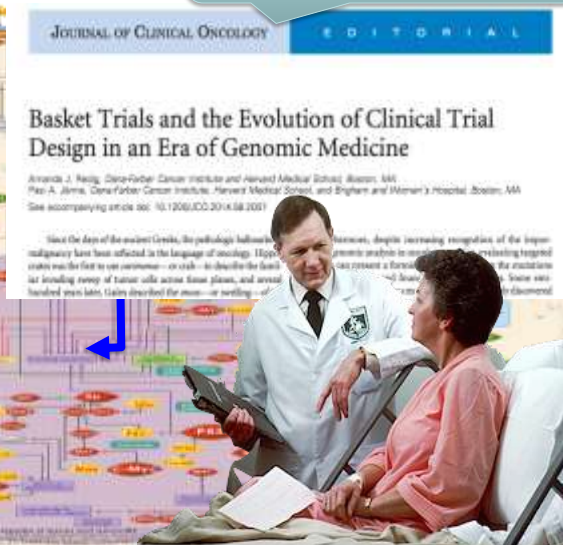
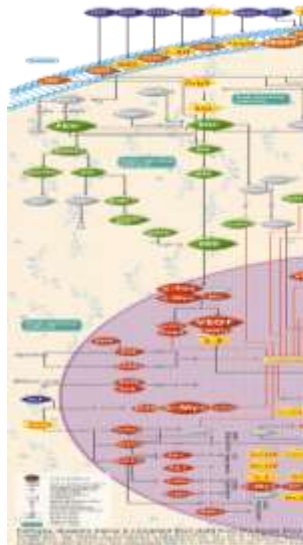
And drug class required to counter it



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 Cirriello G et al. Emerging landscape of

Where are we heading?

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



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

Where are we heading?



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

How should we treat it?

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, Poonamnee, et al. Immune Checkpoint Targeting in Cancer Therapy: Toward Combination Strategies with Curative Potential.

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]

$\$10,000 \times 3 \times 12 = \$360,000$ 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.c76283e8bf81e98f53c753c71ad8c22a7vgnnextoid=19b381471ad65410VgnVCM10000076192ca2RCRD&vgnnextchannel=Sec1e590cb4dc310VgnVCM1000004842c3b929D>. Accessed September 15, 2016.

2015 was another record year for drug innovation

STICKER SHOCK
New drugs for cancer and rare diseases came with hefty list prices

DRUG NAME	INDICATION	ANNUAL PRICE
Karuma	LAL deficiency	\$310,000
Strensiq	Juvenile-onset hypophosphatasia	\$285,000
Orkambi	Cystic fibrosis	\$259,000
Uptravi	Pulmonary arterial hypertension	\$160,000-170,000
Tagrisso	Lung cancer	\$153,000 ^a
Alecensa	ALK-positive lung cancer	\$150,000 ^a
Empliciti	Multiple myeloma	\$140,000 ^b
Portrazza	Lung cancer	\$137,000 ^a
Farydak	Multiple myeloma	\$119,000 ^a
Ibrance	Metastatic breast cancer	\$118,200
Ninlaro	Multiple myeloma	\$113,000 ^a
Darzalex	Multiple myeloma	\$110,000

^a Based on announced monthly or four-week pricing. ^b For first year of treatment.
NOTE: Blue indicates a cancer drug; yellow indicates a rare drug treatment.
SOURCES: Companies, patient groups

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

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

Ref: [1] Lisa M. Jarvis. The Year in New Drugs. Chemical and Engineering News, 2016;94(5):12-17. URL: <http://cen.acs.org/articles/94/05/Year-New-Drugs.html>. Accessed Feb 5, 2016 [2] How much do Americans earn? What is the average US income. MyBudget 360. URL: www.mybudget360.com/how-much-do-americans-earn-what-is-the-average-... Accessed Feb 5, 2016

Where are we heading?



CAN WE AFFORD THE WAR ON CANCER?

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

BY ED SILVERMAN

Two years ago, the U.S. Food and Drug Administration took a step that some thought would never occur — it approved the sipuleucel-T (Provenge) vaccine for late-stage prostate cancer. The move came after a protracted episode involving allegations of conflicts of interest among a pair of FDA advisory committee members who estimated the

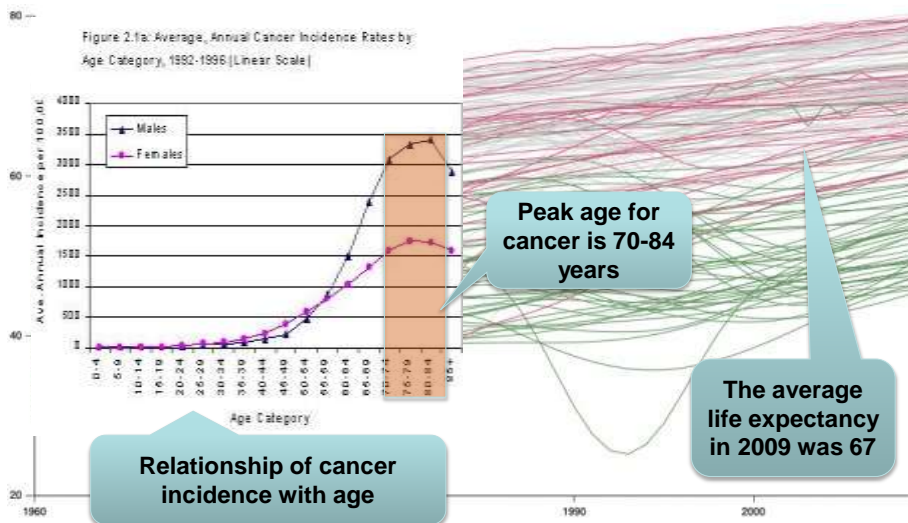
tending a life by 4.1 months is worth the price of Provenge. It has also prompted larger questions about the underlying technology and the need to develop more vaccines.

Provenge is made by culturing a patient's immune cells with a recombinant antigen. The individualized product is then infused back into the patient, activating the immune system to target and attack the cancer. This "immunotherapy" under-



Ref: Silverman E. *Biotechnol Healthc.* 2012;9(4):13-16.

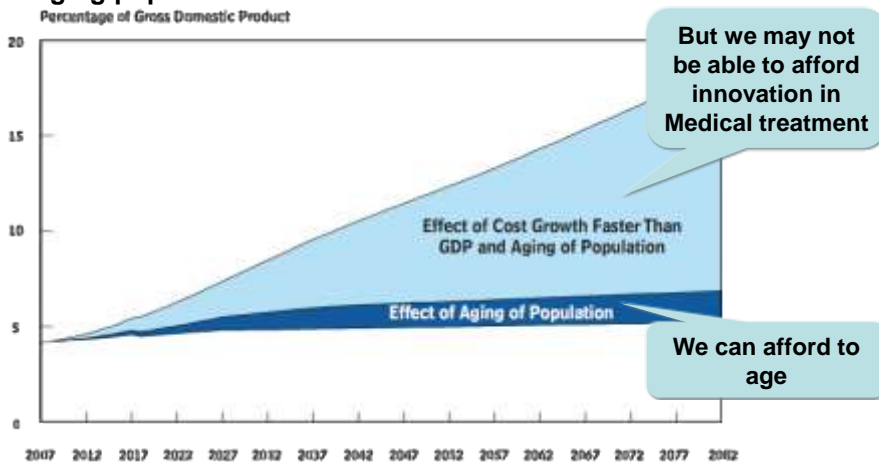
But we have a problem: more cancer to treat



<http://lowingdata.com/2011/10/13/life-expectancy-changes/>
 Myasoedova E. Is the incidence of rheumatoid arthritis rising?: results from Olmsted County, Minnesota, 1955-2007. Arthritis Rheum. 2010 Jun;62(6):1576-82. doi: 10.1002/art.27426

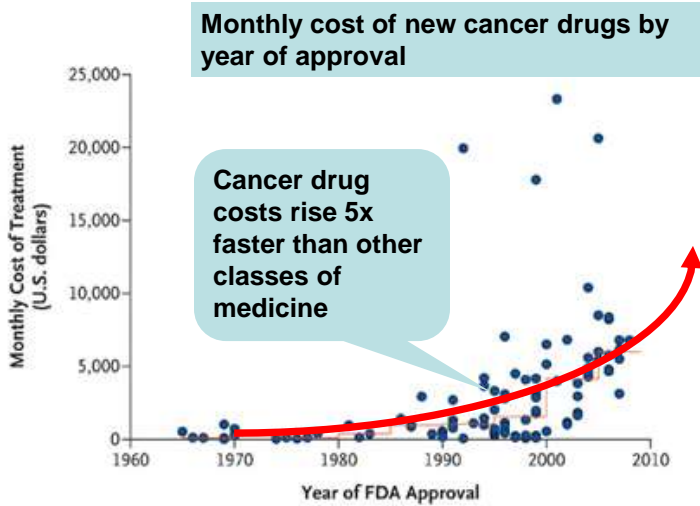
Planning for the Future: What Will Happen to Costs?

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



US Congressional Budget Office. The Long-Term Outlook for Health Care Spending. CBO publication/41646, November 13, 2007. <http://www.cbo.gov/sites/default/files/11-13-ll-health.pdf>. Accessed 10 June 2015

But we have a problem: treatment costs are rising



[1] Bach P. Limits on Medicare's ability to control rising spending on cancer drugs. NEJM. 2009 Feb 7. [2] Beasley D. Analysis: Drug costs become bigger issue in cancer care. Reuters Fri Jun 15, 2012 12:20am EDT. URL: <http://www.reuters.com/article/2012/06/15/us-cancer-cost-idUSBRE8E05B20120615>. Accessed Jan 27, 2015 [3] Kantarjian H. High cost of cancer drugs goes beyond the price. Modern Healthcare. April 4, 2015. <http://www.modernhealthcare.com/article/20150404/MAGAZINE/304049978>. Accessed Sept 26, 2015





What are policy-makers trying to do?

Health Care

Will Health Costs Bankrupt America?

02.23.11, 06:00 PM EST

Forbes Magazine dated March 14, 2011

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

A forbes.com conversation with Robert Langreth, Avik Roy, David Whelan, Matthew Herper--and our audience.

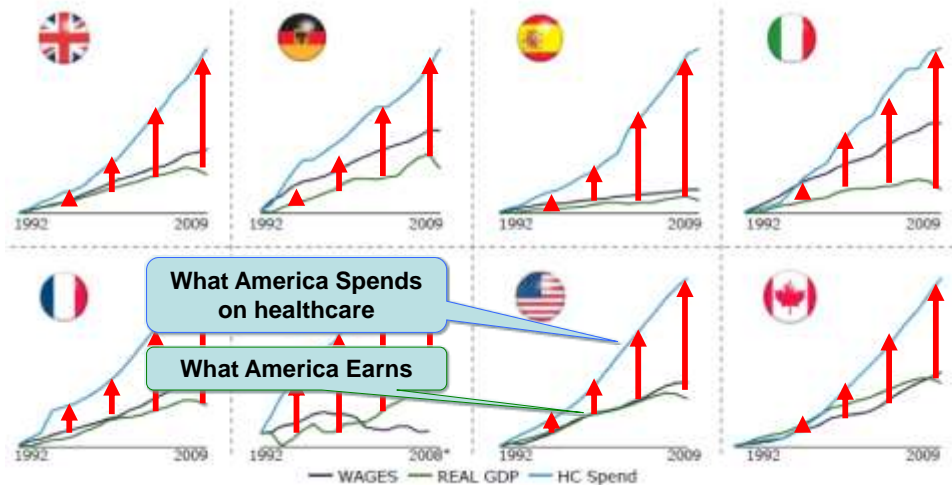
What kept going up even in the depths of the worst recession since the 1930s? Health spending. It rose 4% in 2009 to an alltime record of 17.6% of gross domestic product. We are far above every other nation in health spending but don't have the longevity to show for it. Health costs are by far the biggest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

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



Langreth R. Will Health Costs Bankrupt America?. Forbes. <http://www.forbes.com/forbes/2011/0314/health-care-recession-expenditure-bankrupt-america.html>. Callahan D. Health care costs and medical technology. http://www.thehastingscenter.org/uploadedFiles/Publications/Briefing_Book/health%20care%20costs%20chapter.pdf. Accessed May 7th, 2014

Medical Cost Inflation puts health services at jeopardy



What America Spends on healthcare

What America Earns

Walsh K. Biosimilars' utilization and the role payers do play in driving uptake in Europe: an industry perspective. Biosimilar Medicines 11th EGA International Symposium, April 2013. Accessed 5th March, 2014

We live in difficult times

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



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

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

The threat to health from debt is real

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

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

Ref: [1] Front Cover, TIME 13th October, 2008 [2] 2010 National Debt among EU nations - from The European debt crisis. CNN Money. URL = http://money.cnn.com/news/storysupplement/economy/euro_debt/images/map.jpg. Accessed July 5, 2010 [3] Maruthappu M, Ng KYB, Williams C, Atun R, Agrawal P, Zeltner T. The association between government healthcare spending and maternal mortality in the European Union, 1981-2010: a retrospective study. BJOG 2014; DOI:

The Evolution of Medical Decision Making:



- Pre-EBM - Evidence Based Medicine
 - Focus on a novel mechanism of action? **Tumour control, PFS**
- EBM - Evidence Based Medicine
 - Focus on efficacy **OS & QOL**
- VBM - Value Based Medicine
 - Focus on effectiveness and “value” to stakeholders

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

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

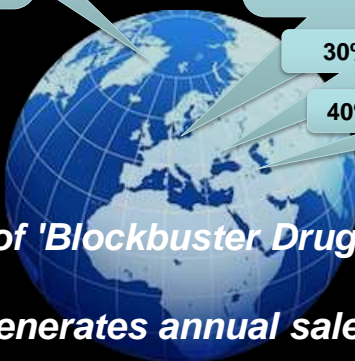
Huber B et al. Oncology Drug Development and Value-based Medicine. <http://www.quintiles.com/library/white-papers/oncology-drug-development-and-value-based-medicine.pdf>. Accessed June 27, 2014

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

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

30% gets us \$21 Billion

40% pays back \$28 Billion



DEFINITION of 'Blockbuster Drug'

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

VBM “Is this worth doing compared with other things we could do
What could we do with 28 free “blockbuster drugs” for the world?”

The WHO has made it very clear



- **Biologic drugs are now essential medicines for the world that we must provide to the world at affordable prices**
- **The latest WHO essential drugs list for cancer now includes 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

The WHO has made it very clear



- ***The leading cause of inefficiency in healthcare is underuse of generics and paying more than necessary for medicines [1]***
- ***A Biosimilar is similar in terms of quality, safety, and efficacy to an already licensed reference biotherapeutic product [2]***

Ref: [1] WHO. World health report 2010. Chapter 4. More health for the money. www.who.int/whr/2010/10_chap04_en.pdf. Accessed 10 June 2015. [2] World Health Organization. Expert Committee on Biological Standardization. Guidelines on Evaluation of Similar Biotechnological Products (SBPs). 23 October 2009. http://www.who.int/biologicals/areas/biological_therapeutics/BIOETHERAPEUTICS_FOR_WEB_22APRIL2010.pdf. Accessed 10 June 2015. [3] WHO World Medicines Report, 2011

The WHO has made it very clear



- *The leading cause of inefficiency in healthcare is underuse of generics and paying more than necessary for medicines [1]*
- *A Biosimilar is similar in terms of **quality, safety, and efficacy** to an already licensed reference biotherapeutic product [2]*

Quality, Safety and Efficacy are the 3 critical attributes of any drug

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

Ref: [1] WHO World health report 2010 Chapter 4. More health for the money. www.who.int/whr/2010/chap04_en.pdf. Accessed 10 June 2015. [2] World Health Organization. Expert Committee on Biological Standardization. Guidelines on Evaluation of Similar Biotherapeutic Products (SBPs). 23 October 2009. http://www.who.int/biologicals/areas/biological_therapeutics/BIOTHERAPEUTICS_FOR_WEB_22APRIL2010.pdf. Accessed 10 June 2015. [3] WHO World Medicines Report, 2011

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



There are 196 countries in the world

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

The unmet need for cheaper biologics is significant

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



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

There are 196 countries in the world

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

The unmet need for cheaper biologics is significant

Biosimilars offer a reward to world health that will be substantial

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



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

- Our immediate target is clear
- Together – we must work to research, develop, trial, approve biosimilars to fulfill the WHO essential medicines directive



Filgrastim

Trastuzumab

Rituximab

The Selection and Use of Essential Medicines

World Health Organization

Biosimilars – why are they so important?



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



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