1st GBO Meeting

Going Beyond in Oncology

1st European Course for MDs in training

NOVEMBER, 28th 2018 - MILANO

The price of the new oncology: balance between research and routine

Francesco Perrone

oncologist

Istituto Nazionale Tumori

Napoli

Conflicts of interest

- Compensation for advisory board
  - Astra Zeneca, Bayer, Celgene, Incyte, Pierre Fabre, Sandoz
- Grant to NCI Naples for clinical research
  - Astra Zeneca, Baxter, Bayer, Eli Lilly, Merck, Roche

Where is the balance?

- My plan is to show you that there is no balance in the trajectory of the price of new drugs
- I will not necessarily look for balance in my argumentation
- I identify myself with the payer, and the payer obviously says that the price is too high…

Agenda

- **Drug price**
- US vs Europe (& rest_of_the_world)
- Financial toxicity
- The Italian way

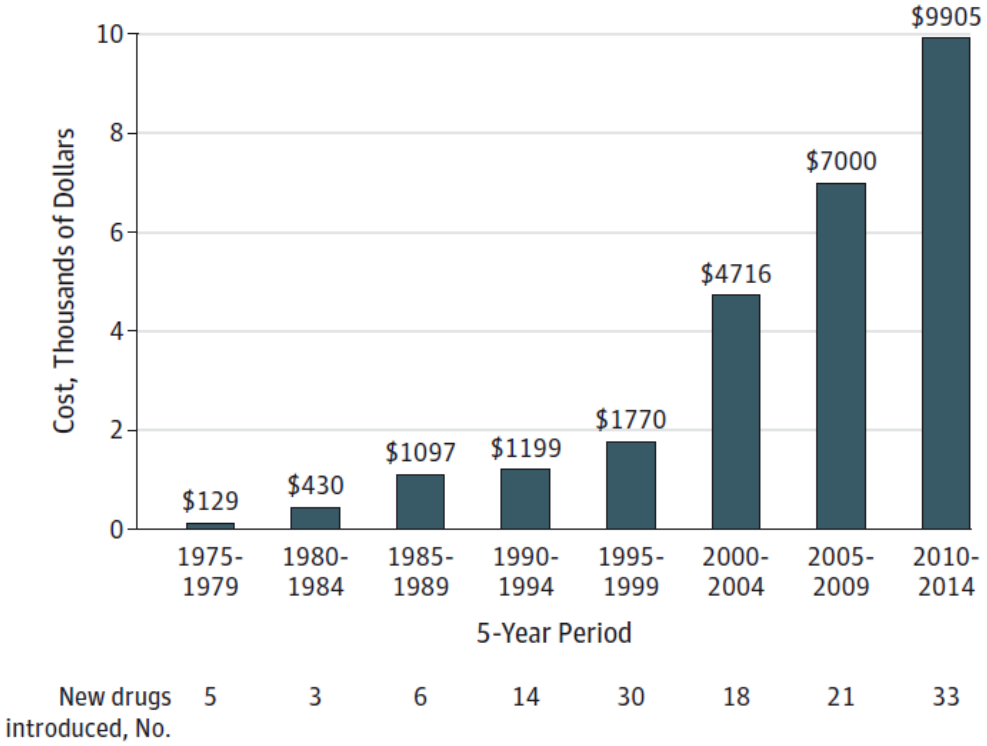
These drugs cost too much.

EDITORIAL

Perspectives on Cost and Value in Cancer Care

Leonard B. Saltz, MD

Figure. Cancer Drugs Hit Market at Ever-Higher Prices



JAMA Oncology Published online October 22, 2015

Approved Products

Resources for You

- Approved Cellular and Gene Therapy Products

IMLYGIC (talimogene laherparepvec)

STN: 125518
Proper Name: talimogene laherparepvec
Tradename: IMLYGIC
Manufacturer: Amgen Inc.
Indication:

- Indicated for the local treatment of unresectable cutaneous, subcutaneous, and nodal lesions in patients with melanoma recurrent after initial surgery.

JAMA Dermatology | Original Investigation

Economic Evaluation of Talimogene Laherparepvec Plus Ipilimumab Combination Therapy vs Ipilimumab Monotherapy in Patients With Advanced Unresectable Melanoma

Abdulaali R. Almutairi, PharmD; Nimer S. Alkhatib, PharmD, MS; Mok Oh, PharmD, MS; Clara Curiel-Lewandrowski, MD; Hani M. Babiker, MD; Lee D. Cranmer, MD, PhD; Ali McBride, PharmD, MS; Ivo Abraham, PhD

JAMA Dermatol. doi:10.1001/jamadermatol.2018.3958
Published online November 21, 2018.

Table 2. Base-Case Analyses (BCA) and Probabilistic Sensitivity Analyses (PSA) Results for Progression-Free Quality-Adjusted Life-Years (QALY) and Objective Response Rate

Variable	BCA/PSA		
	Talimogene Laherparepvec Plus Ipilimumab	Ipilimumab	US Dollars
PFS Life-Year and PFS QALY			**ICER and ICUR**
Cost, $	494 983/501 478	132 950/131 176	NA
ICER PFS life-year gained	1.15/1.18	0.98/0.93	2 129 606/1 481 208
ICUR PFS QALY gained	0.95/0.97	0.79/0.75	2 262 706/1 683 191
ORR			**ICER per Additional Patient Achieving Objective Response**
Follow-up, wk	156	152	NA
Cost, $	474 904/478 274	132 810/131 131	NA
ORR overall	0.39/0.39	0.18/0.18	1 629 019/1 653 062
ORR stage IIIB/IIIC/IVM1a	0.44/0.44	0.19/0.19	1 368 376/1 388 572
ORR stage IVM1b/IVM1c	0.33/0.33	0.16/0.16	2 012 318/2 042 018
ORR $BRAF^{V600E}$ wild type	0.42/0.42	0.10/0.10	1 069 044/1 084 822
ORR $BRAF^{V600E}$ mutant	0.34/0.34	0.32/0.32	17 104 700/17 357 150

Abbreviations: ICER, incremental cost-effectiveness ratio; ICUR, incremental cost-utility ratio; NA, not applicable; ORR, objective response rate; PFS, progression-free survival.

NOVARTIS

Our Work About Us News Investors

Novartis receives first ever FDA approval for a CAR-T cell therapy, Kymriah(TM) (CTL019), for children and young adults with B-cell ALL that is refractory or has relapsed at least twice

AUG 30, 2017

Web Exclusives >

Novartis Sets a Price of $475,000 for CAR T-Cell Therapy

Tony Hagen @oncobiz
Published Online: Wednesday, Aug 30, 2017

News & Events

Home > News & Events > Newsroom > Press Announcements

FDA News Release

FDA approves an oncology drug that targets a key genetic driver of cancer, rather than a specific type of tumor

New drug Vitrakvi targets specific receptor kinase that promotes tumors

SHARE TWEET LINKEDIN PIN IT EMAIL PRINT

For Immediate Release November 26, 2018

Larotrectinib - Vitrakvi

- Initial price for adults: $32,800 for one month
- $393,600 annually
- Initial price for childres (liquid oral): $11,000/month

- Complex strategy of Bayer to allow all patients with NTRK fusion to receive the drug…

The high price of anticancer drugs: origins, implications, barriers, solutions

Nature Reviews Clinical Oncology · March 2017

Vinay Prasad, Kevin De Jesús and Sham Mailankody

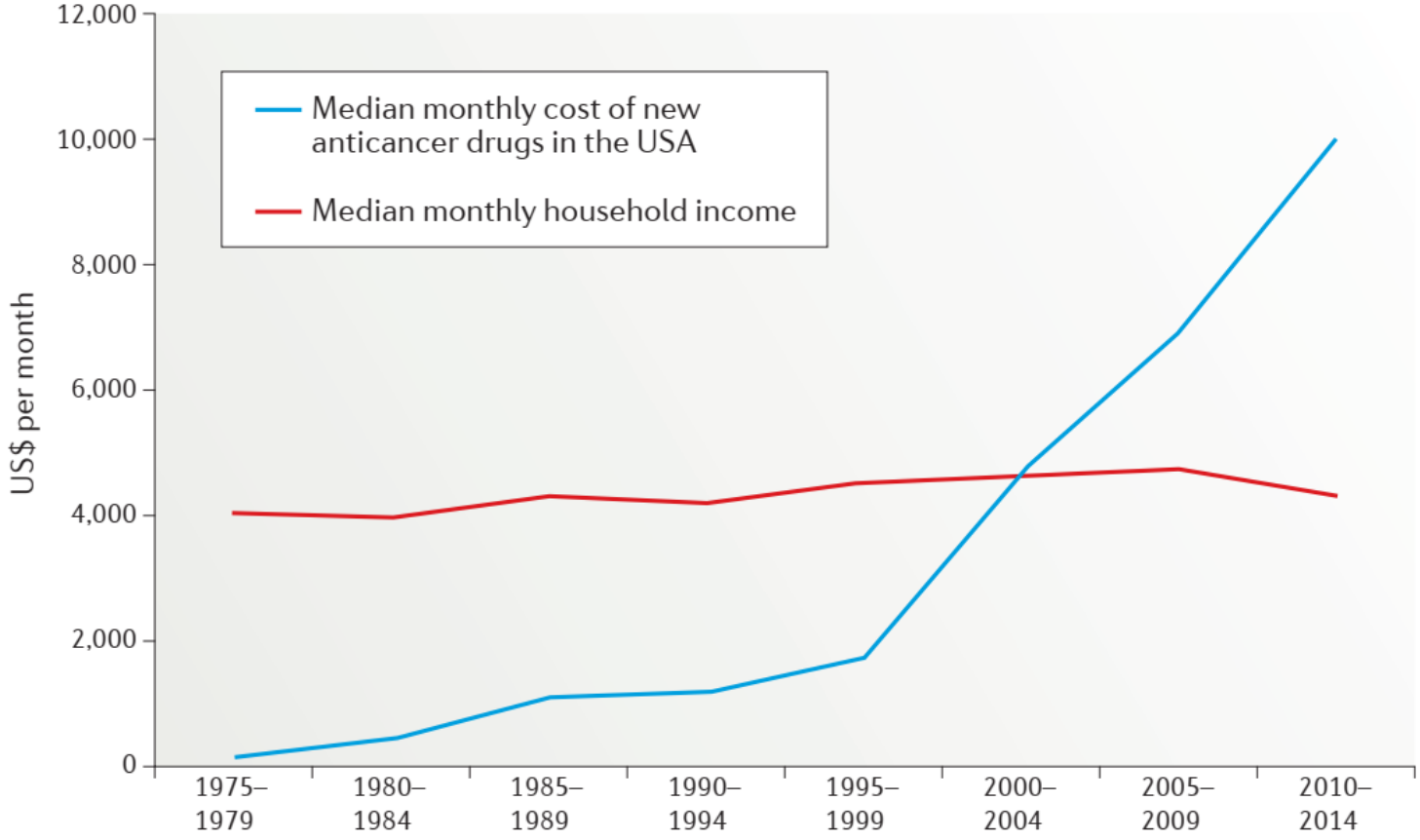


Figure 2 | **Median monthly launch price of a new anticancer drug, compared with median monthly household income from 1975–2014 in the USA.** Data on household incomes were obtained from the 2015 United States Census[130], and drug prices were obtained from Bach & Schnorr[131].

RESEARCH LETTER

Five Years of Cancer Drug Approvals: Innovation, Efficacy, and Costs

Sham Mailankody, MB BS
Vinay Prasad, MD, MPH

Results | From January 1, 2009, to December 31, 2013, the US FDA approved 51 drugs in oncology for 63 indications.

Type of drug	N (%)	Median price/yr
First-in-class	21 (41%)	$ 116.100
Next-in-class	30 (59%)	$ 119.765
		P=0.42

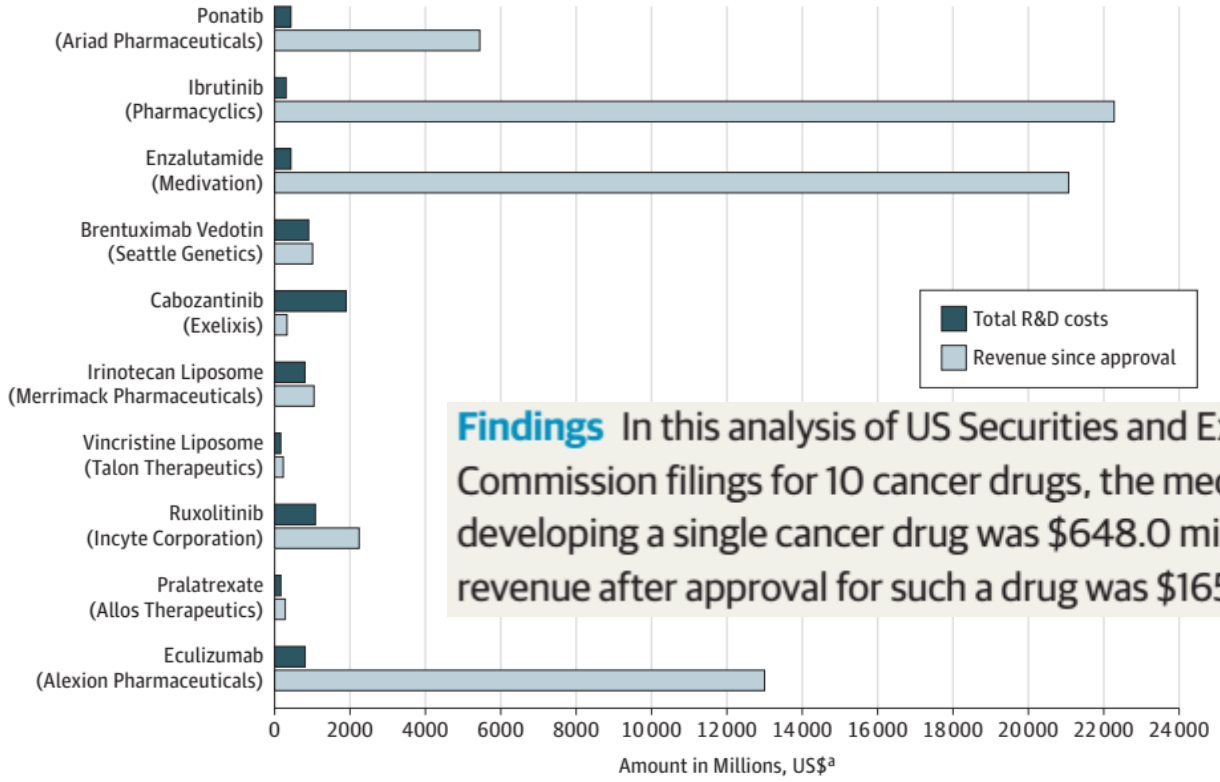
JAMA Oncology July 2015 Volume 1, Number 4

JAMA Internal Medicine | Original Investigation

Research and Development Spending to Bring a Single Cancer Drug to Market and Revenues After Approval

Vinay Prasad, MD, MPH; Sham Mailankody, MBBS

Figure. Comparison of Drug Development Costs With Revenue Earned After Approval



Findings In this analysis of US Securities and Exchange Commission filings for 10 cancer drugs, the median cost of developing a single cancer drug was $648.0 million. The median revenue after approval for such a drug was $1658.4 million.

R&D indicates research and development.

[a] Adjusted to 2017 US dollars.

The high price of anticancer drugs: origins, implications, barriers, solutions

Nature Reviews Clinical Oncology · March 2017

Vinay Prasad, Kevin De Jesús and Sham Mailankody

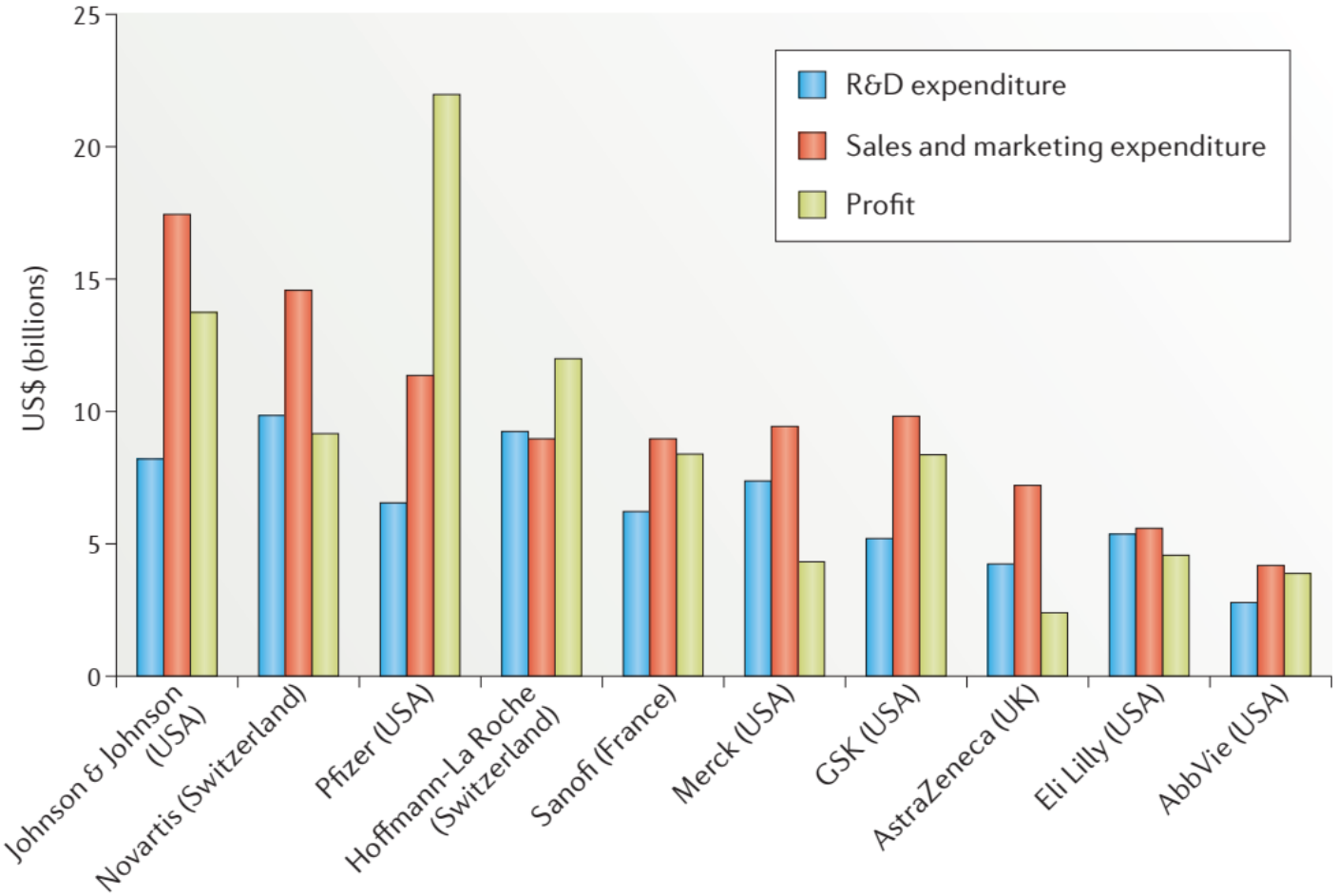
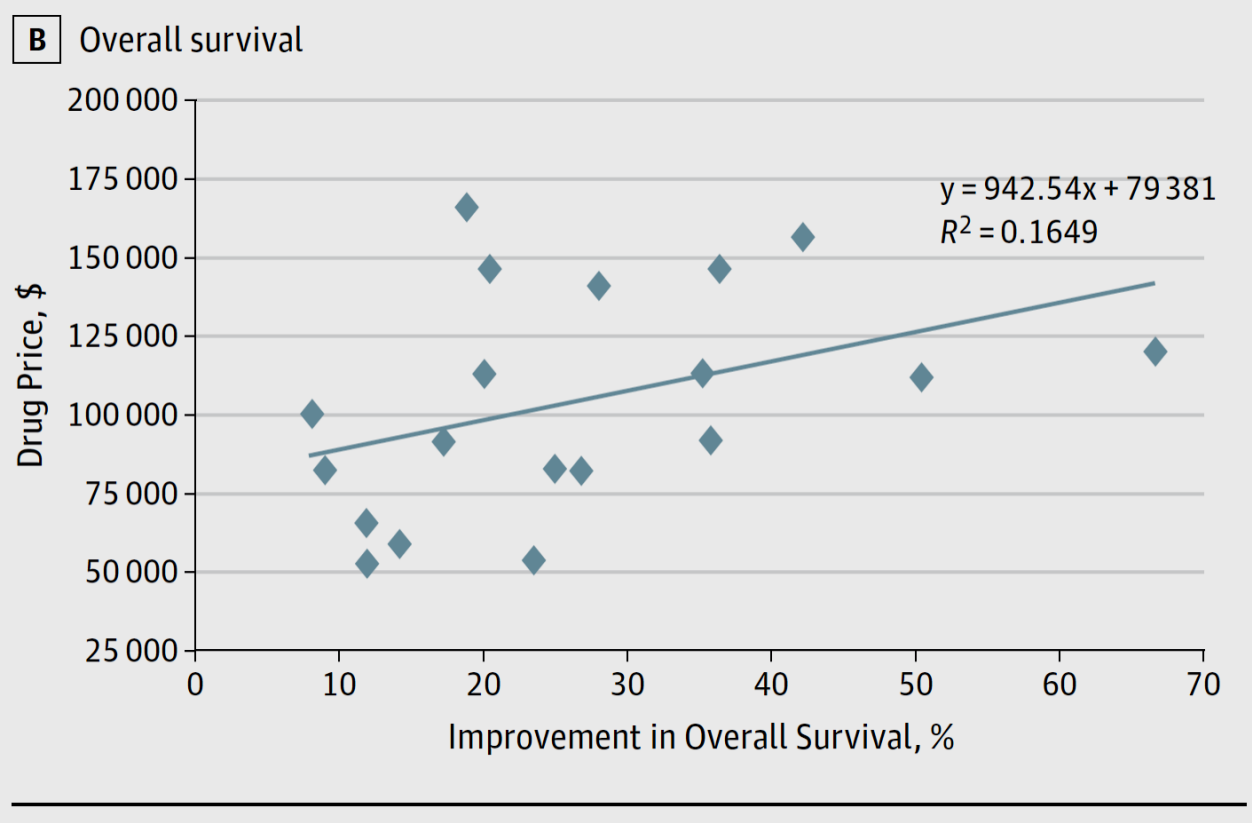


Figure 3 | **Annual profits, and annual expenditure on research and development (R&D) and marketing for the 10 largest pharmaceutical companies in 2013** (REF 48).

Five Years of Cancer Drug Approvals: Innovation, Efficacy, and Costs

Sham Mailankody, MB BS
Vinay Prasad, MD, MPH



OS: $R^2 = 0.165$

JAMA Oncology July 2015 Volume 1, Number 4

The high price of anticancer drugs does not reflect therapeutic benefit in Italy

Trotta F, Mayer F, Barone-Adesi F, Esposito I, Da Cas R, Traversa G, Perrone F, Martini N, Addis A.

Submitted

53 anticancer drugs (67 labels)
reimbursed by AIFA (2011-2016)

OS available for 16 drugs (17 labels)
PFS available in 25 drugs (29 labels)

Correlation of negotiated price with

OS_change: R^2=0.029, P=0.51
PFS_change: R^2=0.004, P=0.74

Agenda

- Drug price
- **US vs Europe (& rest_of_the_world)**
- Financial toxicity
- The Italian way

The high price of anticancer drugs: origins, implications, barriers, solutions

Nature Reviews Clinical Oncology · March 2017

Vinay Prasad, Kevin De Jesús and Sham Mailankody

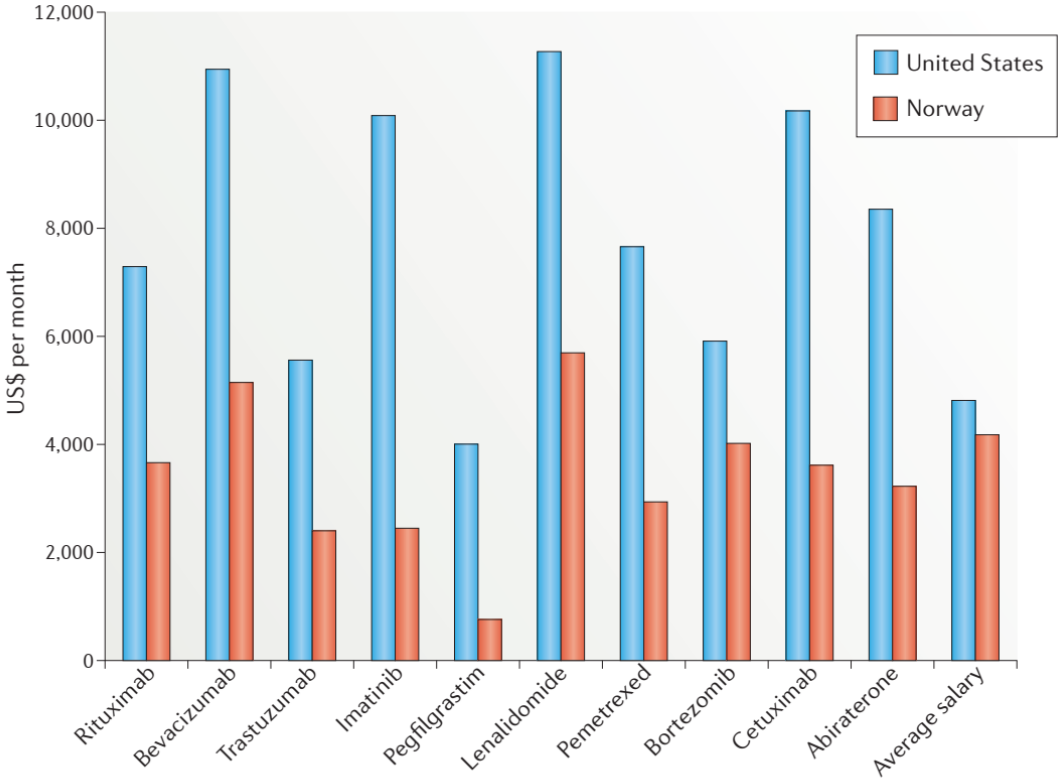


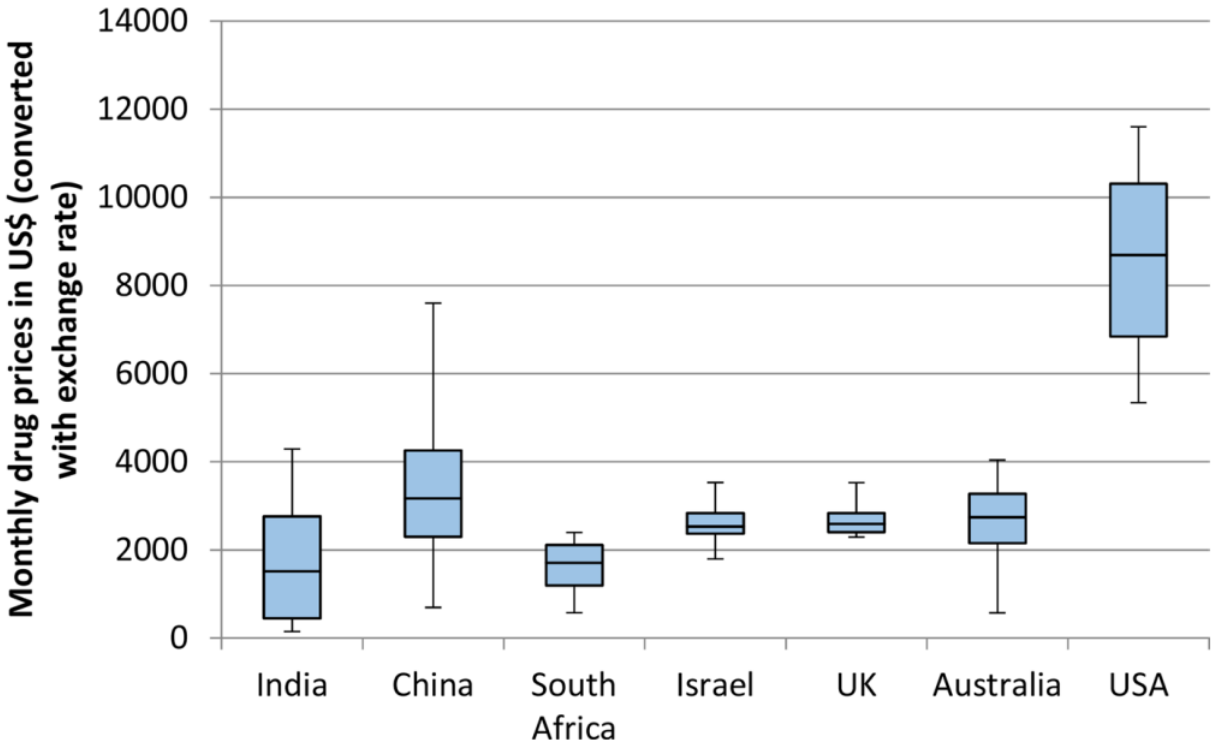
Figure 1 | **Cost of one month of treatment with the top 10 bestselling anticancer drugs in the USA[10] and Norway[127].** Drug prices are calculated for an adult weighing 70 kg, with a body surface area of 1.7 m^2. For drugs reimbursed through the Medicare part B programme, we obtained the average sales price (ASP) from the Centers for Medicare and Medicaid services[128]; for drugs reimbursed through Medicare part D, we obtained the 'full cost of the drug' (REF. 129).

www.impactjournals.com/oncotarget/ Oncotarget, 2017, Vol. 8, (No. 42), pp: 71548-71555

Research Paper

A global comparison of the cost of patented cancer drugs in relation to global differences in wealth

Daniel A. Goldstein[1,2], Jonathon Clark[1], Yifan Tu[3], Jie Zhang[4], Fenqi Fang[4], Robert Goldstein[5], Salomon M. Stemmer[1,6,*] and Eli Rosenbaum[1,*]



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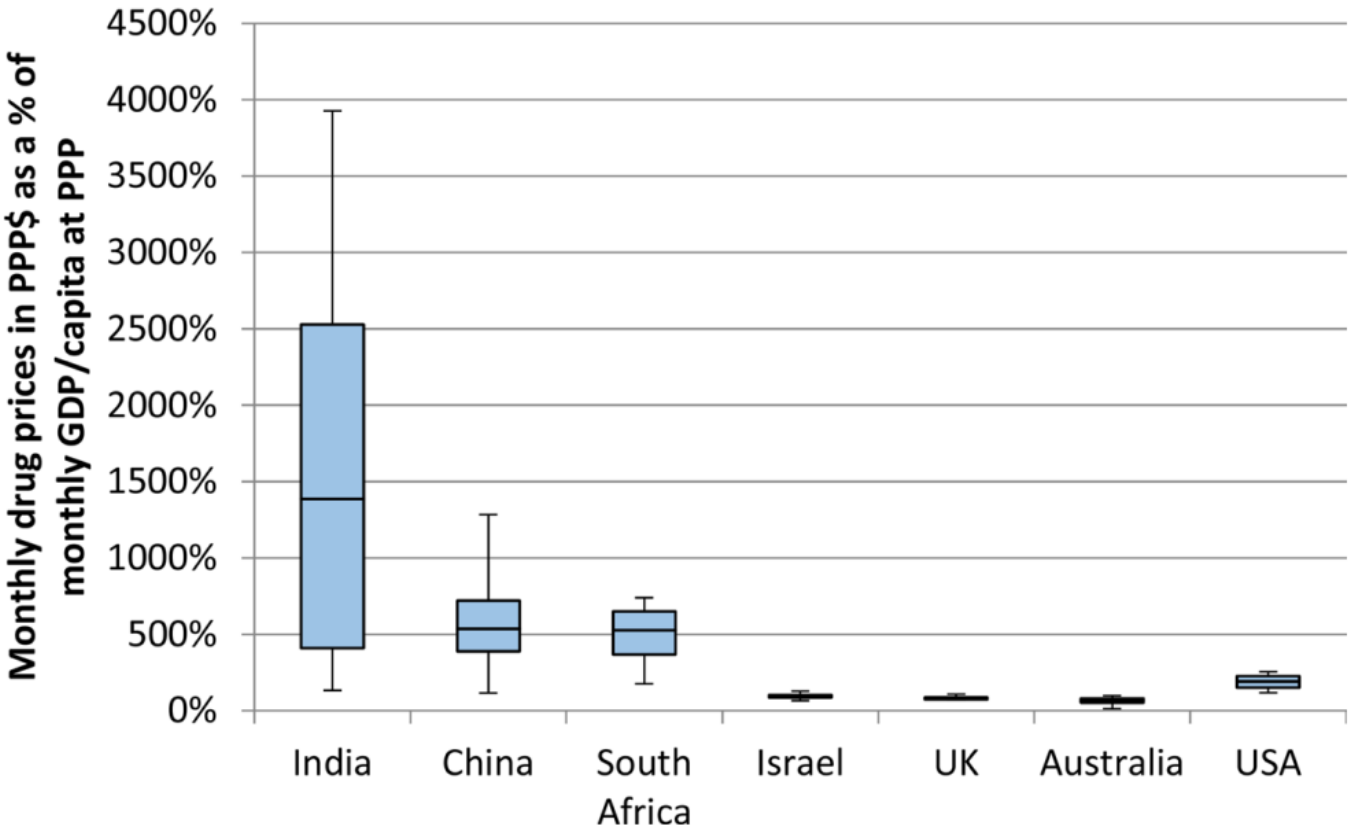


Cancer drugs in 16 European countries, Australia, and New Zealand: a cross-country price comparison study

Sabine Vogler, Agnes Vitry, Zaheer-Ud-Din Babar

Lancet Oncol 2016; 17: 39–47

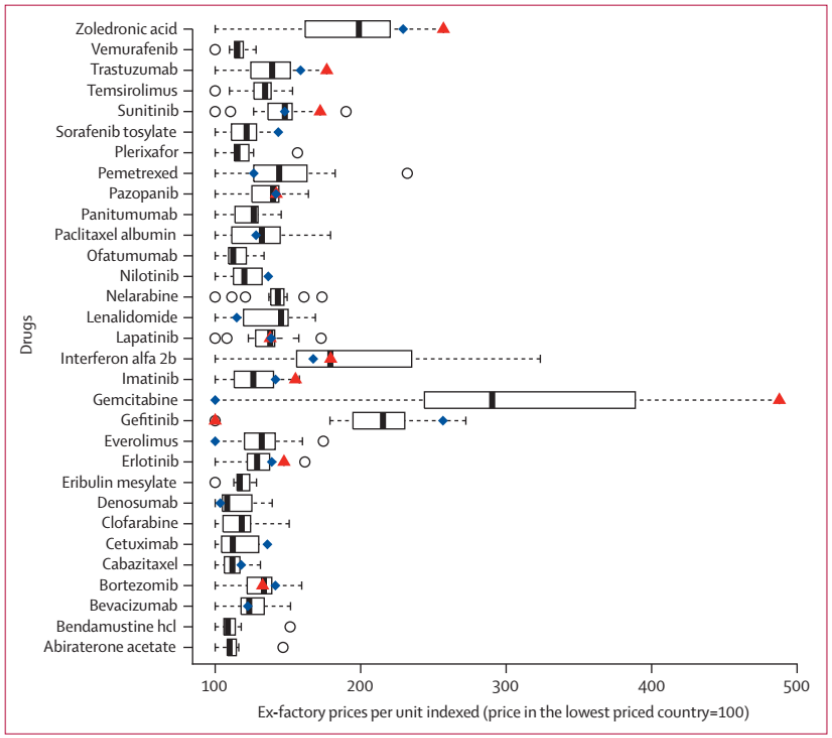


Figure: **Boxplot of drug prices (ex-factory price per unit) indexed (price in the lowest priced country=100), as of June 2013, in 16 European countries, Australia, and New Zealand**
The box displays the interquartile range (IQR); the bottom and top of the box are the 25th and 75th percentiles (the 1st and 3rd quartiles, respectively), and the band near the middle of the box is the median. The dashed lines describe the bottom and top whiskers. The small circles indicate extreme datapoints (commonly referred to as outliers). The blue diamond shows the datapoint for Australia, and the red triangle for New Zealand. The appendix shows boxplots without gemcitabine and without gemcitabine and interferon alfa 2b (for better readability).

[..] However, the surveyed prices do not include discounts negotiated by funding organisations because these **discounts are confidential**.

Because pricing authorities can also only use these official undiscounted prices when they set prices through the common policy of external price referencing, they risk **overpaying**.

European Journal of Cancer (2014) **50**, 3089–3097

An exploratory analysis of the factors leading to delays in cancer drug reimbursement in the European Union: The trastuzumab case

Felipe Ades [a], Chistelle Senterre [b], Dimitrios Zardavas [e], Evandro de Azambuja [a], Razvan Popescu [c], Florence Parent [d], Martine Piccart [a,*]

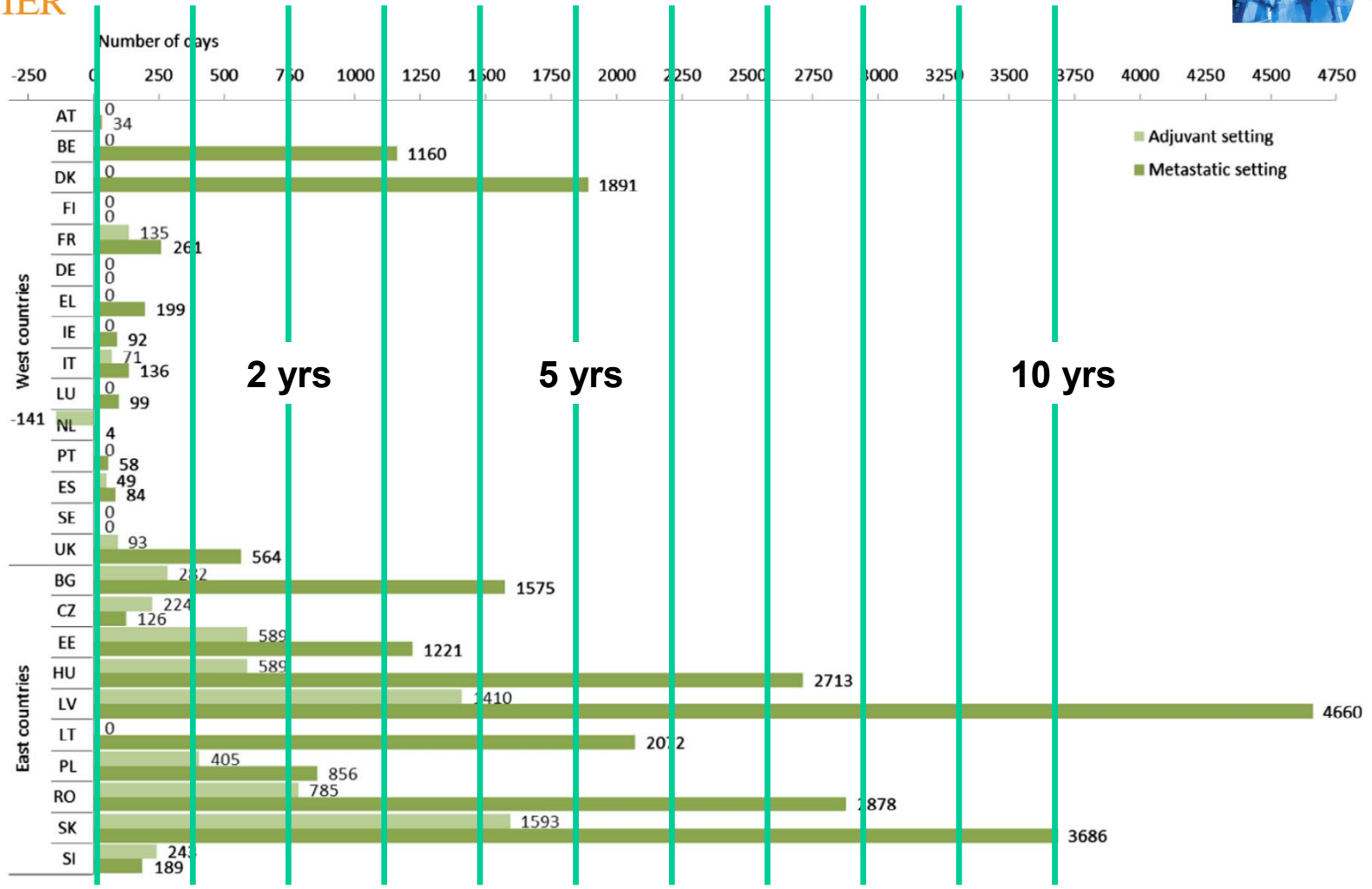


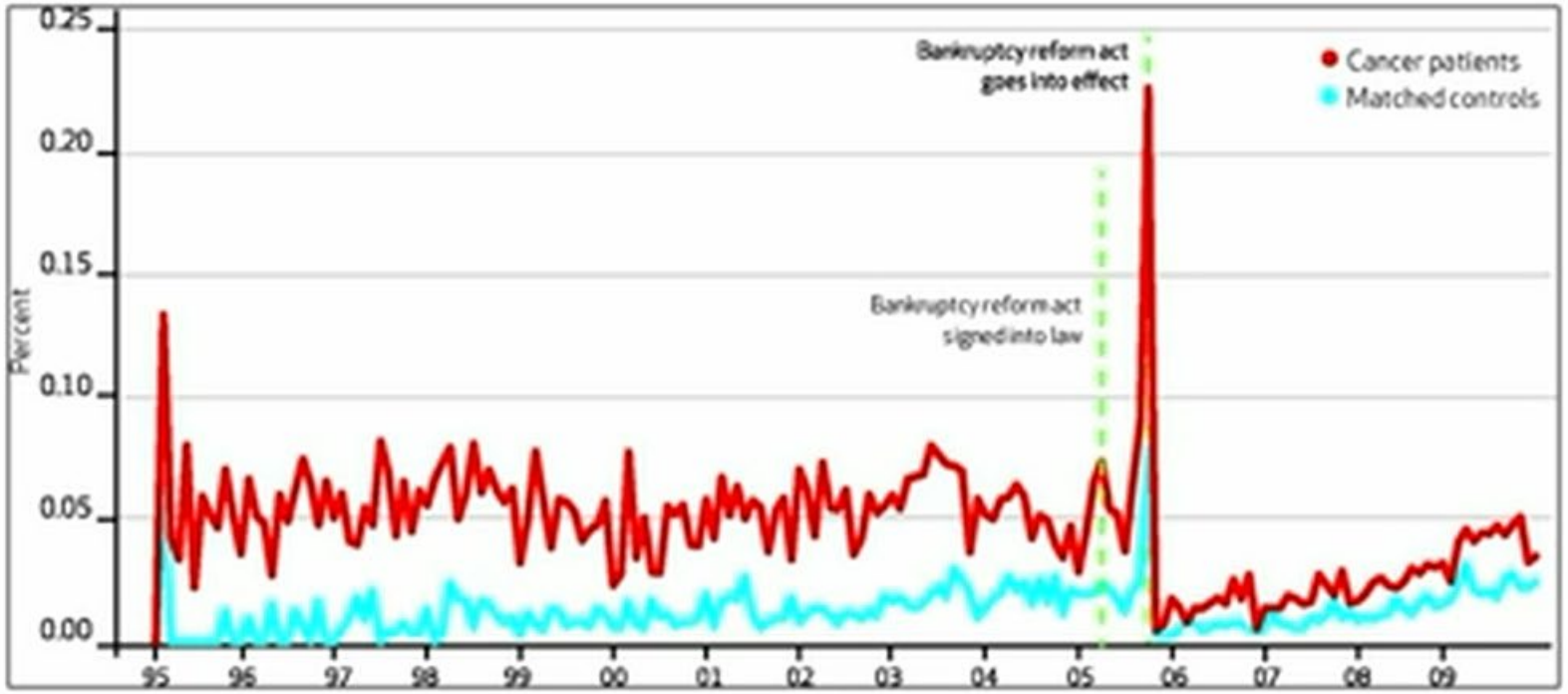
Fig. 1. Time periods for trastuzumab approval/reimbursement in the adjuvant and metastatic settings across European Union (EU) countries.

Agenda

- Drug price
- US vs Europe (& rest_of_the_world)
- **Financial toxicity**
- The Italian way

Cancer and Bankruptcy

- Linked SEER and bankruptcy data in Washington State, 1995 - 2009
- Cancer patients 2.65X more likely to file for bankruptcy



Ramsey et al. Health Aff 2013

Published Ahead of Print on January 25, 2016 as 10.1200/JCO.2015.64.6620
The latest version is at http://jco.ascopubs.org/cgi/doi/10.1200/JCO.2015.64.6620

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Financial Insolvency as a Risk Factor for Early Mortality Among Patients With Cancer

Scott D. Ramsey, Aasthaa Bansal, Catherine R. Fedorenko, David K. Blough, Karen A. Overstreet, Veena Shankaran, and Polly Newcomb

Table 3. Bankruptcy Impact on All-Cause Mortality in the Propensity Score Matched Sample

Cancer Type	No. at Risk	No. of Deaths	HR	95% CI	*P*
Overall	17,021	2,026	1.79	1.64 to 1.96	< .001
Breast	3,788	280	1.48	1.15 to 1.91	.003
Lung	958	350	1.55	1.22 to 1.98	< .001
Melanoma	1,197	51	1.50	0.83 to 2.72	.179
Thyroid	952	23	1.71	0.69 to 4.27	.249
Prostate	2,365	214	2.07	1.56 to 2.74	< .001
Leukemia/lymphoma	1,792	254	1.22	0.93 to 1.61	.146
Uterine	739	42	1.09	0.55 to 2.16	.795
Colorectal	1,430	217	2.47	1.85 to 3.31	< .001
Other	3,800	595	1.49	1.25 to 1.78	< .001

Abbreviation: HR, hazard ratio.

Annals of Oncology Advance Access published October 26, 2016

The association of financial difficulties with clinical outcomes in cancer patients: secondary analysis of 16 academic prospective clinical trials conducted in Italy†

F. Perrone[1*], C. Jommi[2], M. Di Maio[1,‡], A. Gimigliano[1], C. Gridelli[3], S. Pignata[4], F. Ciardiello[5], F. Nuzzo[6], A. de Matteis[6], L. Del Mastro[7], J. Bryce[1], G. Daniele[1], A. Morabito[8], M. C. Piccirillo[1], G. Rocco[9], L. Guizzaro[10,11] & C. Gallo[11]

EORTC C30 Q 28

1995-2012

During the last week, has your physical condition or medical treatment caused you financial difficulties?

Not at all	A little	Quite a bit	Very much
1	2	3	4

26% of 3670 patients with financial problems at baseline

OR of **worse QOL** response
1.35 (95%CI 1.08-1.70)
P=0.009

22.5% of patients develop financial toxicity during treatment

HR of **death**
1.20 (95%CI 1.05-1.37)
P=0.007

FINANCIAL TOXICITY

1576 P_PR Winkler et al. 1577 P Flaum et al.

- After Italian data on 3670 trial patients (ESMO 2016, Annals of Oncology 2016 Dec;27(12):2224-2229), further evidence reported this year on the fact that financial toxicity exists also outside US, in countries where a consolidated public health system exists
- UK: 141 GI-cancer trial patients , question #28 of the EORTC QLQ-C30, 20% developed FT, prevalently the younger ones and those with a worse index of multiple deprivation
- D: Extensive analysis of existing instruments and survey with 247 patients (CRC/NET). Economic deterioration due to disease-related out-of-pocket costs (around 200 euros monthly, 80.6% of patients) and cancer-related income loss (around 800 euros monthly in 37.2% of patients)
- OVERALL, strong need for country/system specific instruments, deeper understanding of the problem, identification of causes and targets for improving individual support.

MUNICH 2018 ESMO congress

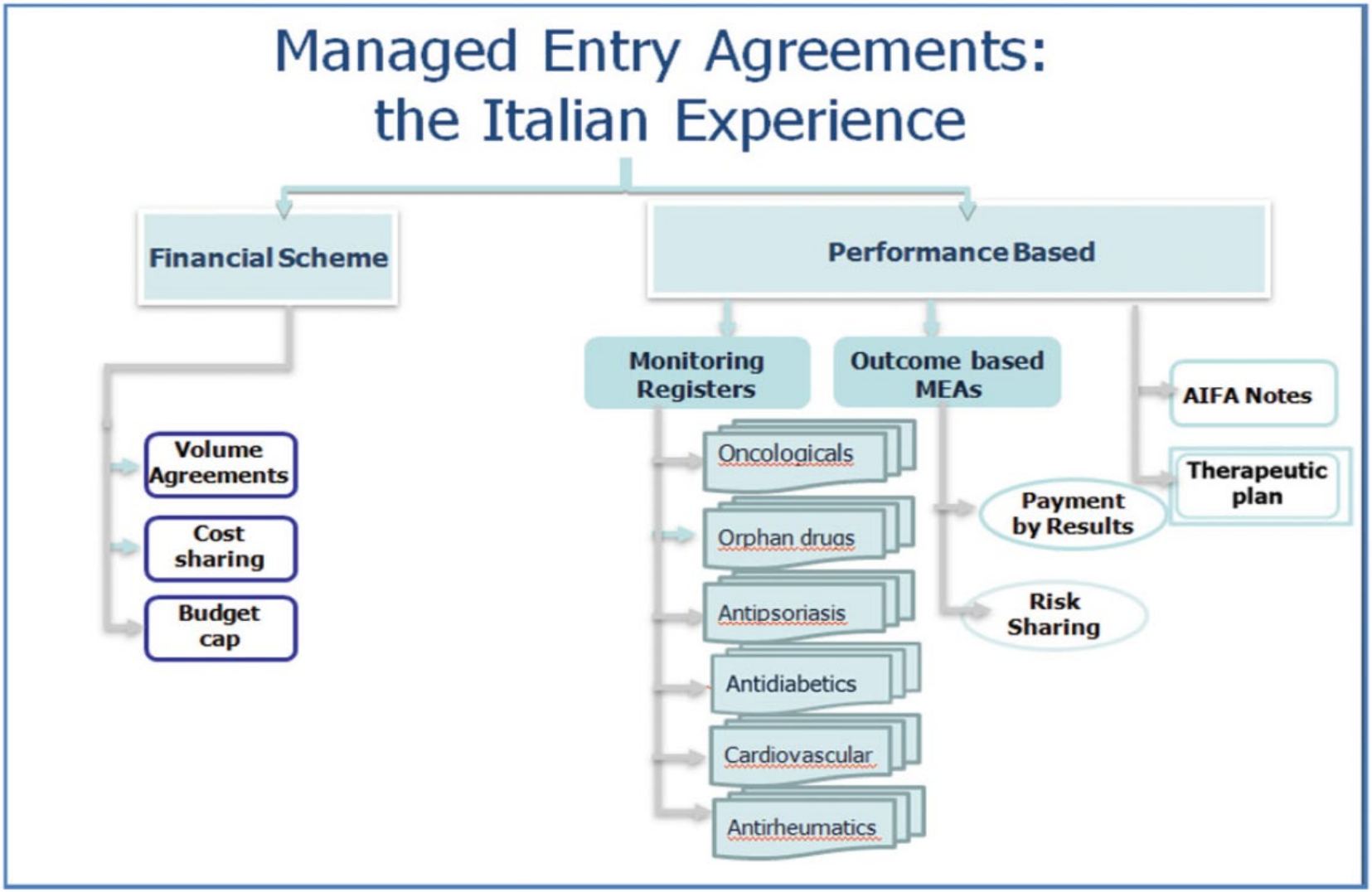
Agenda

- Drug price
- US vs Europe (& rest_of_the_world)
- Financial toxicity
- **The Italian way**

International Journal of Technology Assessment in Health Care, 31:4 (2015), 210–213.

doi:10.1017/S0266462315000446

MONITORING REGISTRIES AT ITALIAN MEDICINES AGENCY: FOSTERING ACCESS, GUARANTEEING SUSTAINABILITY



Cancer's cost conundrum

The price trajectory of oncology drugs is unsustainable — but fixes are in the works.

BY ELIE DOLGIN

STRATEGIES OF CONT

The best data on this sort of scheme come from AIFA, the Italian Medicines Agency, which introduced performance-based reimbursement for 25 cancer drugs in 2006. Two independent analyses[5,6] of the scheme suggest that it introduced extra layers of administration for little financial benefit.

Some pharmaceutical companies are also beginning to offer this kind of guarantee on a voluntary basis. Novartis of Basel, Switzerland, for example, has said that people who receive tisagenlecleucel (sold as Kymriah), the company's $475,000 therapy for leukaemia (available only in the United States, at present), can get a full refund if they show no improvement in the first 30 days after treatment.

Agenzia Italiana del Farmaco
AIFA

OGGETTO: Criteri per la classificazione dei farmaci innovativi e dei farmaci oncologici innovativi ai sensi dell'articolo 1, comma 402 della legge 11 dicembre 2016, n. 232.

Roma, 31 marzo 2017

	Innovatività Riconosciuta		Innovatività Condizionata	Innovatività Non riconosciuta	
Bisogno terapeutico	Massimo	Importante	Moderato	Scarso	Assente
Valore terapeutico aggiunto*	Massimo	Importante	Moderato	Scarso	Assente
Qualità delle prove (GRADE)	Alta		Moderata	Bassa	Molto bassa
Impatto economico	**Fondo farmaci innovativi (oncologici)** Benefici economici Inserimento PTOR		Inserimento PTOR		

* Per i farmaci oncologici il gold standard è la **sopravvivenza globale** e la sua mancanza dovrà essere adeguatamente giustificata. Potranno eventualmente essere considerati PFS, DFS, durata della risposta completa o altri esiti surrogati di cui sia riconosciuto il valore predittivo di beneficio clinico. Si terrà conto anche del relativo profilo di tossicità.

oncoinfo
Istantanee di oncologia medica

DAI CONGRESSI

AIOM al Governo: confermate il Fondo per i farmaci oncologici innovativi

IN **AIOM** · **CONGRESSI** · **IN PRIMO PIANO** – 16 NOVEMBRE 2018

In Italia l'impatto dei farmaci oncologici sulla spesa farmaceutica totale rimane inferiore a quello degli altri Paesi: rappresenta infatti il 13% contro il 17,3% del Regno Unito e il 17% della Germania. Ma dal XX Congresso Nazionale dell'Associazione Italiana di Oncologia Medica (AIOM), in corso a Roma, arriva l'allarme per la tenuta del sistema.

"Fino a quest'anno, il Fondo per i farmaci oncologici innovativi, istituito nel 2016 e pari a 500 milioni di euro, è stato sufficiente per coprire i livelli di spesa", afferma **Stefania Gori, Presidente nazionale AIOM e Direttore del Dipartimento oncologico dell'IRCCS Ospedale Sacro Cuore Don Calabria di Negrar.** "Quest'anno non sarà così. Le stime indicano che, nel 2018, le uscite per queste terapie sforeranno la capienza massima del Fondo, raggiungendo una cifra compresa tra 590 e 610 milioni di euro, con un eccesso tra 90 e 110 milioni rispetto al tetto stabilito. Prima dell'istituzione di questa fonte di risorse dedicate, si temeva che il nostro sistema sanitario non riuscisse a reggere le conseguenze economiche dovute all'arrivo dei nuovi trattamenti, con il rischio di un imminente default del nostro Sistema Sanitario. Ipotesi che non si è verificata. In questi anni, non sono stati negati i nuovi farmaci anticancro e la migliore assistenza è stata garantita a tutti i malati, obiettivo raggiunto grazie alla

Conclusion

- No balance, in my view, in the matter of drug price
- The pace of price increase is, on average, much faster than that of therapeutic progress
- US (more transparently) and European countries (less transparently and with some delay) are suffering for sustaining new drugs and negative direct/indirect effects of financial crisis on patients' outcome are bing reported
- Negotiation (at the level of a single EU member state) is not enough to reach value-based pricing
- Global cooperation (all the stakeholders, everywhere) is absolutely needed

Thank you for your attention