

Thema:

***Maatschappelijke verantwoordelijkheid van de farmaceutische industrie: beschikbaarheid en betaalbaarheid van de toegang tot zorg***

*Erasmus*

Erasmus School of  
Health Policy  
& Management

# *Farma uitgedaagd. Kunnen wij spreken van fair medicine?'*

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**Najaarsvergadering VGR**

***November 2, 2018***

**Erasmus University Rotterdam**



# DISCLOSURE INFORMATION

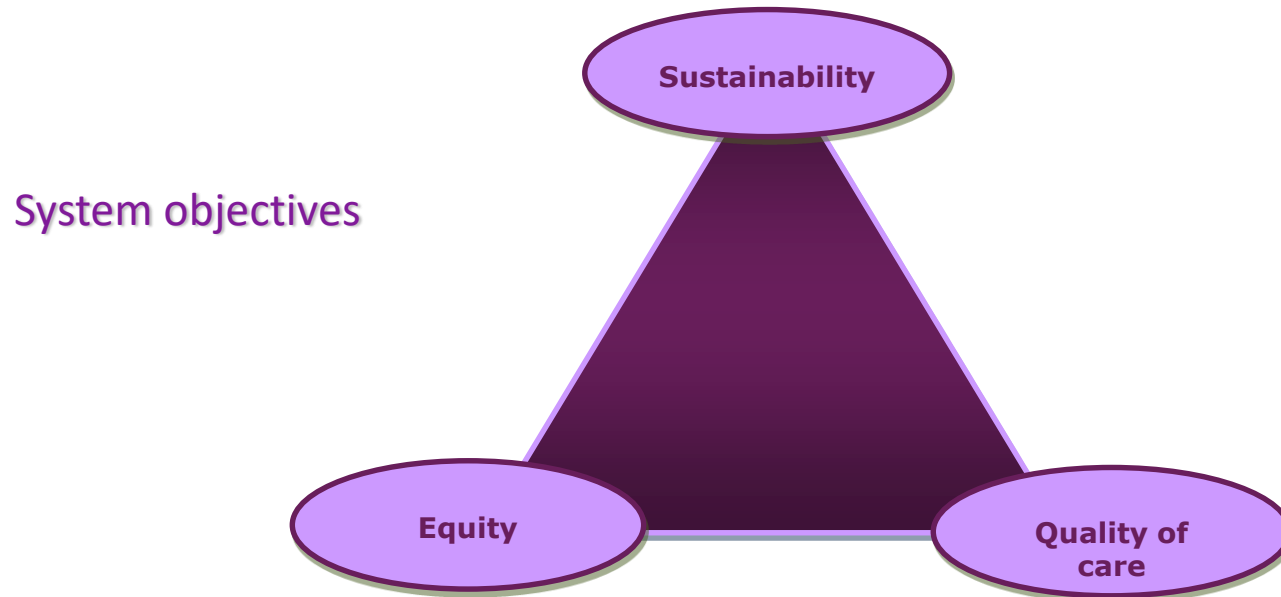
## CARIN UYL-DE GROOT

Institutional financial interests – Unrestricted grants:

Boehringer Ingelheim, Celgene, Janssen-Cilag, Genzyme, Astellas, Sanofi, Roche, Astra Zeneca, Amgen, Gilead, Merck, Bayer, Glycostem Therapeutics



## Policy goals in health care



### Goal:

Ensuring **affordable** and equitable access for (all) patients to **effective** therapies in a sustainable manner

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## Cancer survival in Europe 1999–2007 by country and age: results of EURO CARE-5—a population-based study



Roberta De Angelis, Milena Sant, Michel P Coleman, Silvia Francisci, Paolo Baili, Daniela Pierannunzio, Annalisa Trama, Otto Visser, Hermann Brenner, Eva Ardanaz, Magdalena Bielska-Lasota, Gerda Engholm, Alice Nennecke, Sabine Siesling, Franco Berrino, Riccardo Capocaccia, and the EURO CARE-5 Working Group\*

### Summary

**Background** Cancer survival is a key measure of the effectiveness of health-care systems. EURO CARE—the largest cooperative study of population-based cancer survival in Europe—has shown persistent differences between countries for cancer survival, although in general, cancer survival is improving. Major changes in cancer diagnosis, treatment, and rehabilitation occurred in the early 2000s. EURO CARE-5 assesses their effect in cancer survival in 29 European countries.

**Methods** In this retrospective observational study we analysed data from 107 cancer registries for more than 10 million patients with cancer diagnosed up to 2001 and followed up to 2008. Uniform quality control procedures were applied to all datasets. For patients diagnosed 2000–07, we calculate 5-year relative survival for 46 cancers weighted by age and country. We also calculated country-specific and age-specific survival for ten common cancers, together with survival differences between time periods for 1999–2001, 2002–04, and 2005–07).

**Findings** 5-year relative survival generally increased steadily over time for all European regions. The largest increases from 1999–2001 to 2005–07 were for prostate cancer (73·4% [95% CI 72·9–73·9] vs 81·7% [81·3–82·1]), non-Hodgkin lymphoma (53·8% [53·3–54·4] vs 60·4% [60·0–60·9]), and rectal cancer (52·1% [51·6–52·6] vs 57·6% [57·1–58·1]). Survival in eastern Europe was generally low and below the European mean, particularly for cancers with good or intermediate prognosis. Survival was highest for northern, central, and southern Europe. Survival in the UK and Ireland was intermediate for rectal cancer, breast cancer, prostate cancer, skin melanoma, and non-Hodgkin lymphoma, but low for kidney, stomach, ovarian, colon, and lung cancers. Survival for lung cancer in the UK and Ireland was much lower than for other regions for all periods, although results for lung cancer in some regions (central and eastern Europe) might be affected by overestimation. Survival usually decreased with age, although to different degrees depending on region and cancer type.

*Lancet Oncol* 2014;15:23–34

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See [Online](#) for an author interview with Roberta de Angelis

\*Members of the EURO CARE-5 Working Group are listed in the appendix

**Centro Nazionale di Epidemiologia, Sorveglianza e Promozione della Salute, Istituto Superiore di Sanità, Rome, Italy** (R De Angelis MSc, S Francisci PhD, D Pierannunzio PhD, R Capocaccia MSc); **Analytical Epidemiology and Health Impact Unit** (M Sant MD, P Baili MSc); **Evaluative Epidemiology Unit** (A Trama MD, F Berrino MD), **Department of Preventive and**

**Findings: 5-year relative survival generally increased steadily over time for all European regions.**

# The good news (2): Many innovative (cancer) drugs



**OPDIVO™**  
(nivolumab)  
INJECTION FOR INTRAVENOUS USE 10 mg/mL



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(lumacaftor/ivacaftor)  
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EXPORT OF PRESCRIPTION MEDICINES

BRINGING CURE...  
BUILDING HOPE

# The bad news (1):

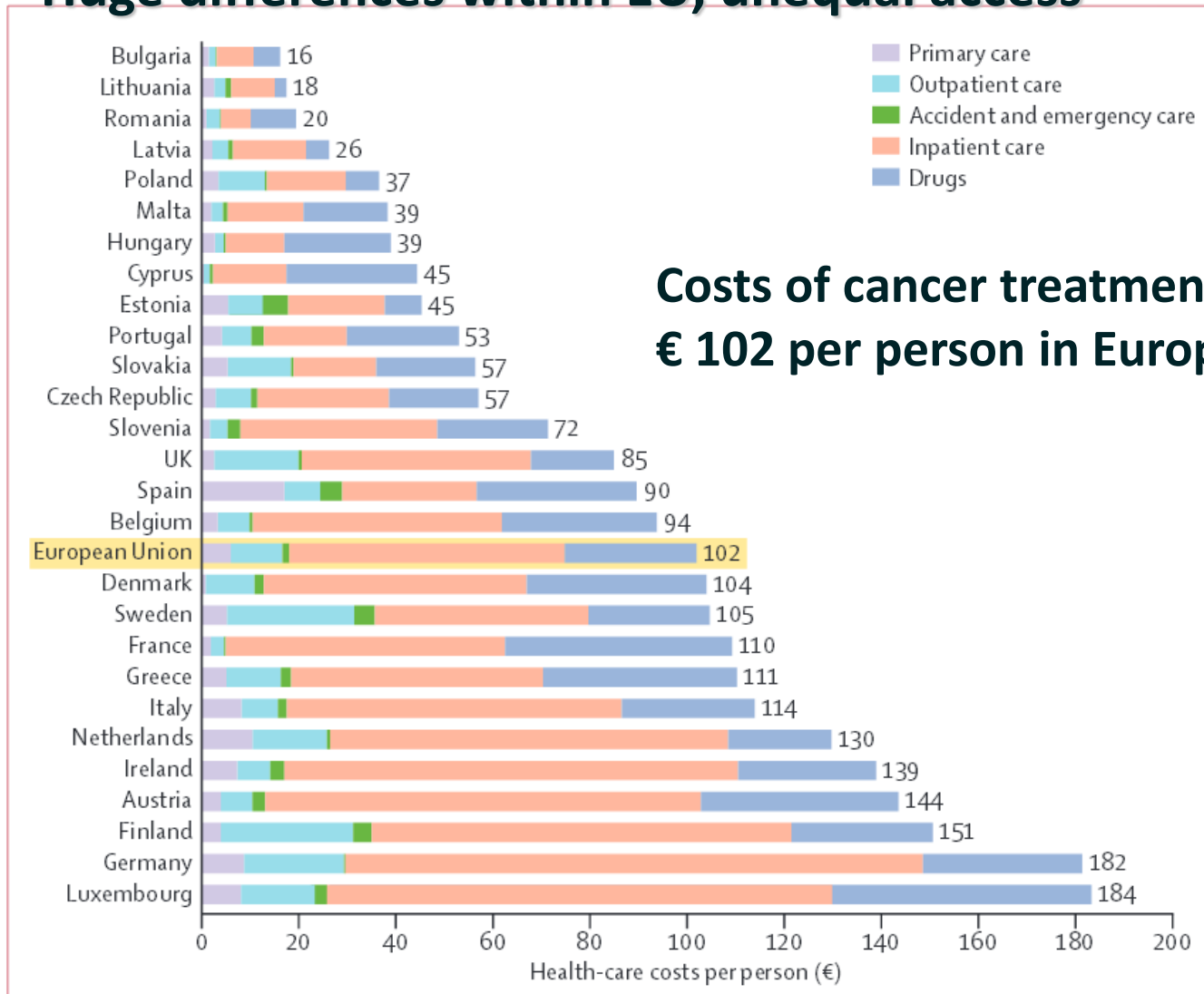
Rise in health expenditures 2000-2015  
as share Gross Domestic Product (GDP)

<b>Country</b>	<b>2000</b>	<b>2005</b>	<b>2010</b>	<b>2015</b>
Austria	9.2	9.6	10.1	10.4
Czech Republic	5.7	6.4	6.9	7.5
Denmark	8.1	9.1	10.4	10.6
France	9.5	10.2	10.7	11.0
Germany	9.8	10.2	11.0	11.1
Ireland	5.9	7.7	10.6	9.4
Netherlands	7.1	9.4	10.4	10.8
Norway	7.7	8.3	8.9	9.9
Poland	5.3	5.8	6.4	6.3
Spain	6.8	7.7	9.0	9.0
United Kingdom	6.3	7.4	8.5	9.8
<b>Average EU</b>	<b>7.3</b>	<b>8.2</b>	<b>8.9</b>	<b>9.0</b>

*Ezra*

# The bad news (2):

## Huge differences within EU, unequal access



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**Figure 1: Health-care costs of cancer per person in European Union countries in 2009, by health-care service category**

Data not adjusted for price differentials.



# Result budget problems

The Netherlands (2014): € 530 million spent on new cancer drugs

Maximum growth budget per year: 1.2%

New cancer drugs 2016	Estimated costs per	ICER	Estimated budget impact
Nivolumab	<b>Opportunity cost</b>		200 mln
Pertuzumab	€ 78.000	€ 150.000	€ 40 mln
Ibrutinib	€ 70.000	Unknown	€ 100 mln
Palbociclib	Unknown	Unknown	€100 mln
CAR-T cells	€300-400.000	Unknown	Unknown

# Affordable (expensive) therapies

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Met dank aan Matthijs Versteegh

institute for  
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Dedicated to improving decision making in  
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3,000 patients



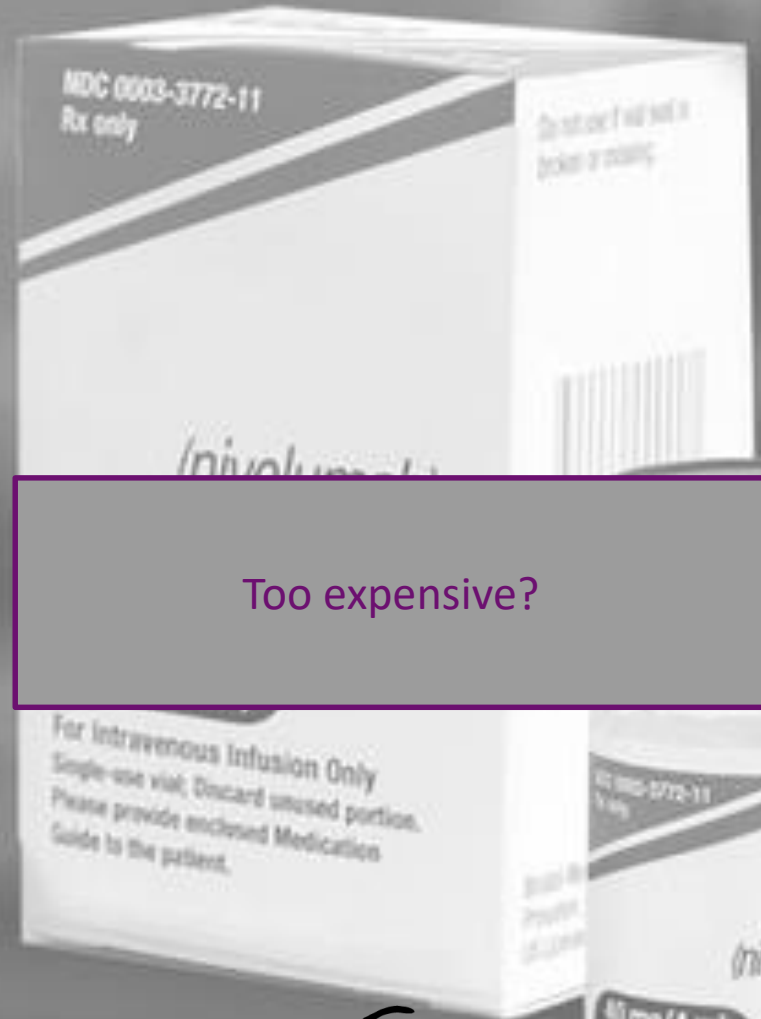
€80,000 per patient

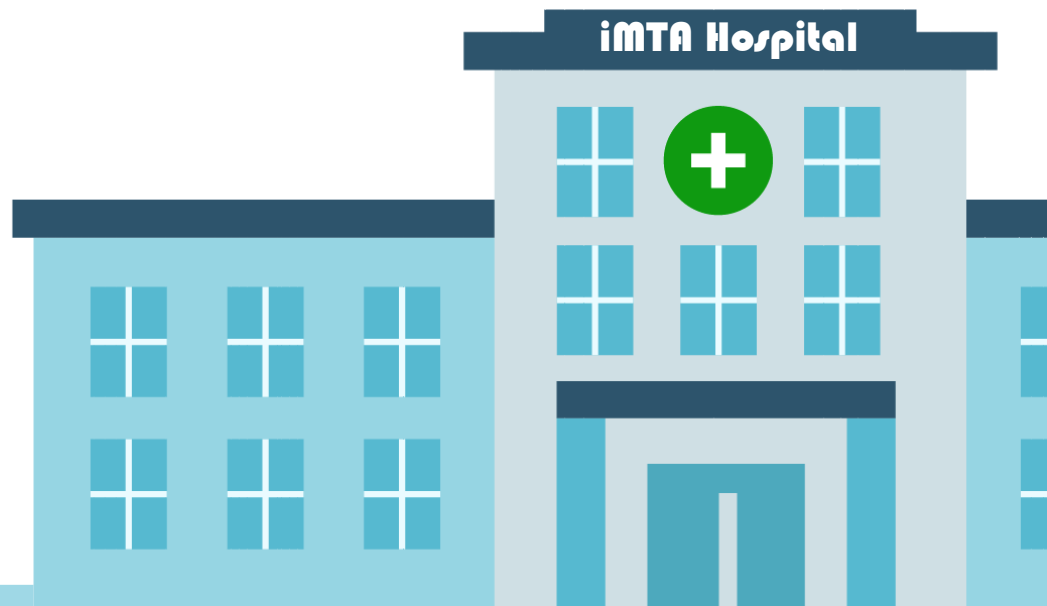


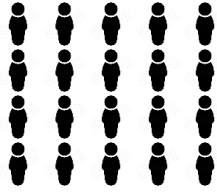
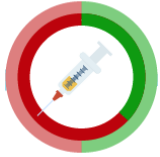
Survival gain of 3 months  
(median)



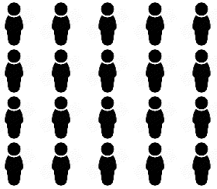
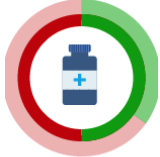
Too expensive?



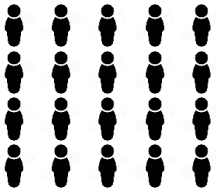




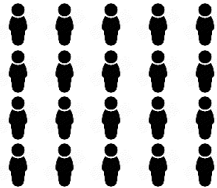
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“The invisible patient”



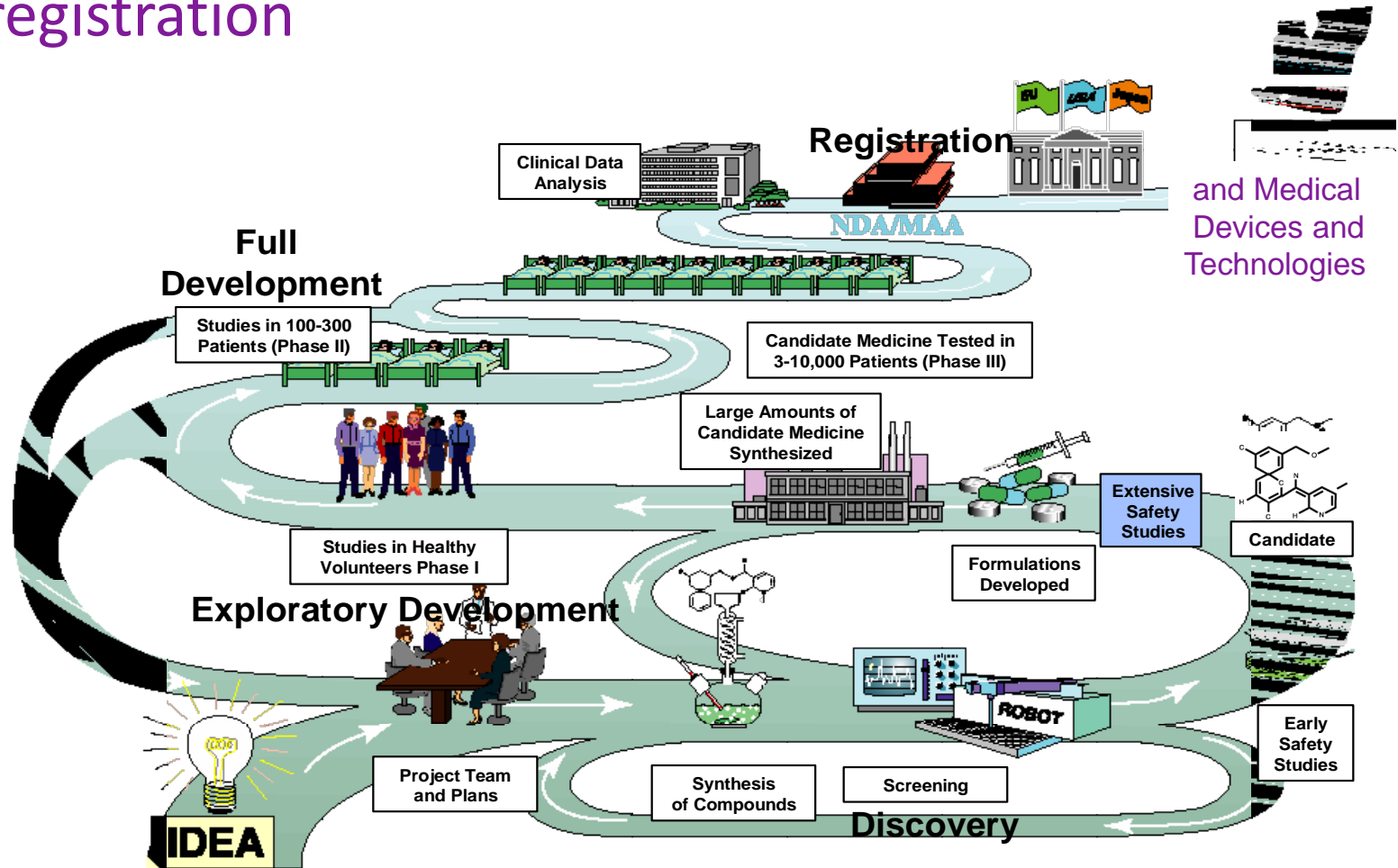
# Opportunity costs

What we give to patient A, we cannot give to patient B.

Given a **limited health care budget** (or a limited willing to pay a higher premium) it is **unethical** not to make a societal decision.

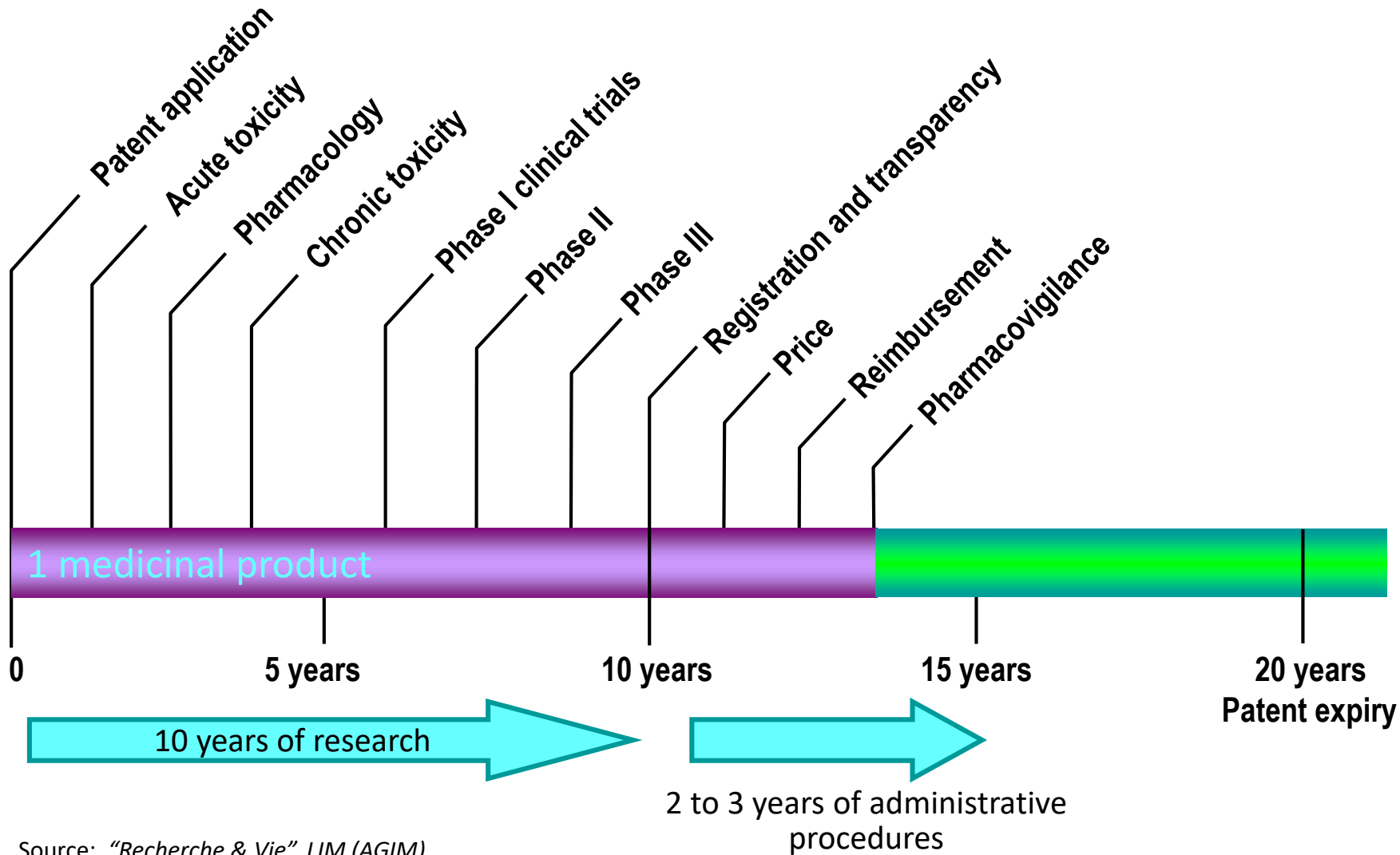
# Why is it expensive?

Development phase: a long and winding road to registration





# Development phase From discovery to patient

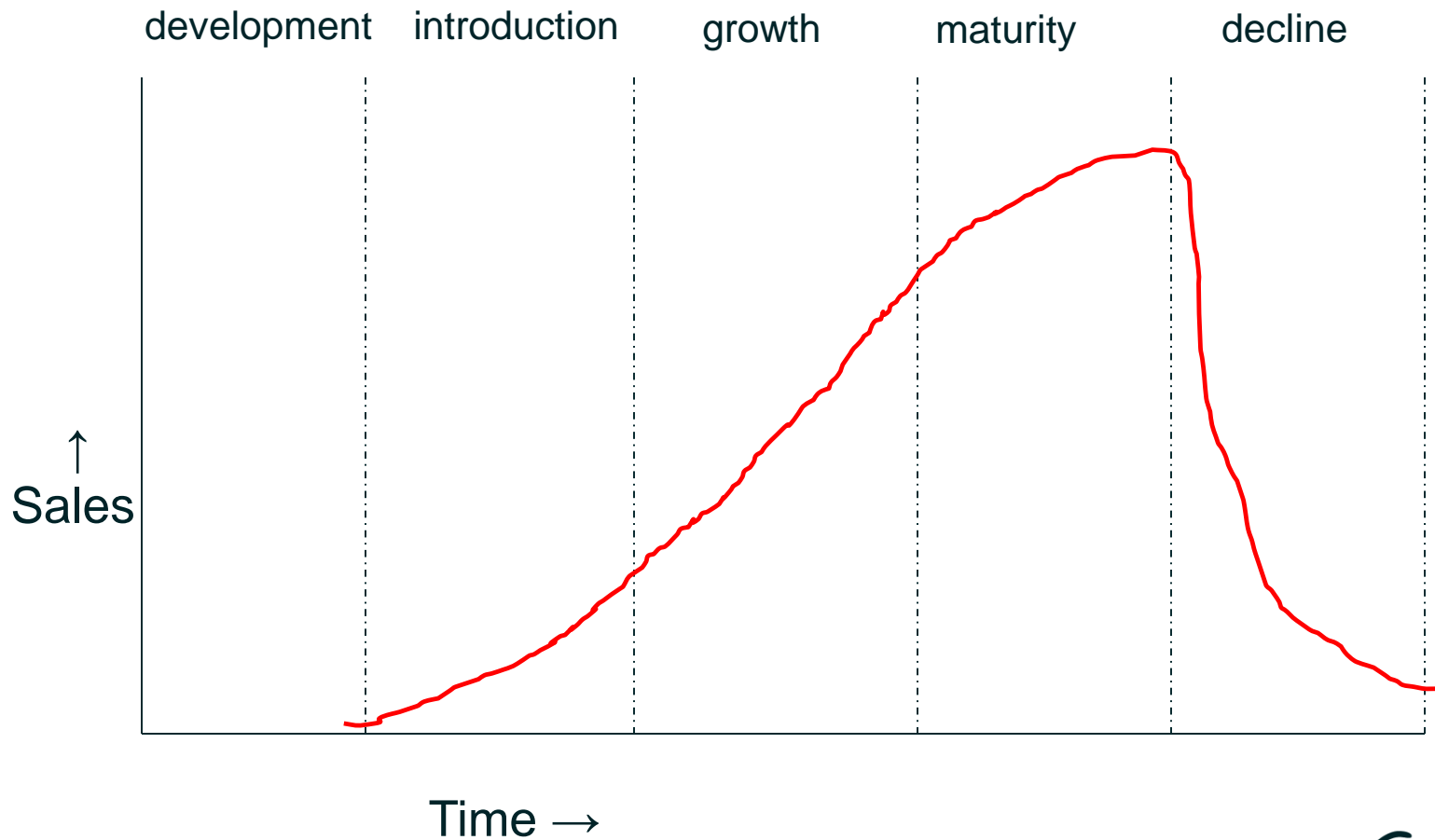


# Costs of development new drug

## Cost factors:

- R&D (including failures)
  - Manufacturing
  - Marketing and promotion
- 
- Estimation: 300 million -2.6 billion dollars

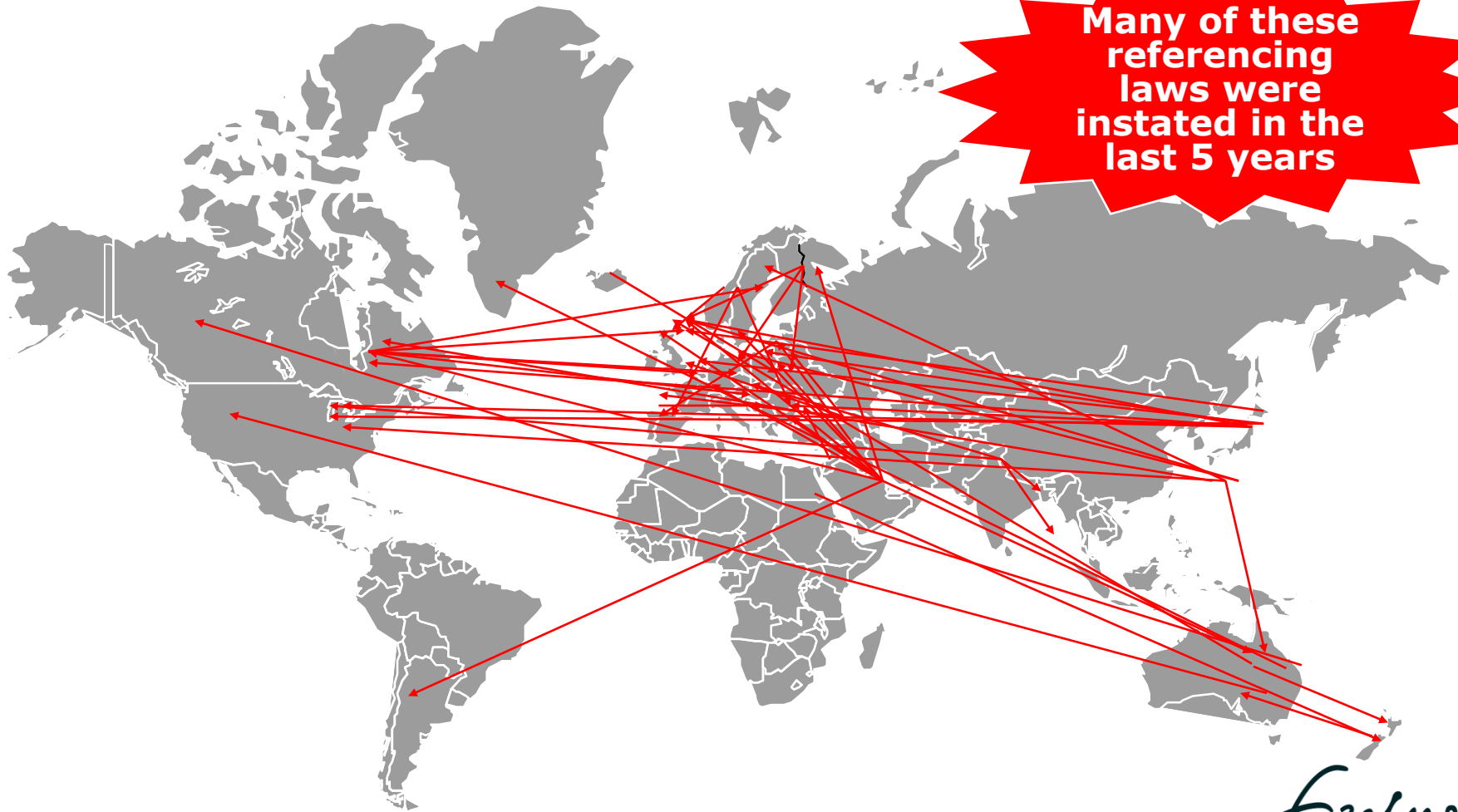
# Life cycle of a technology



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International price referencing is a common global tool for bench-marking pharmaceutical prices

Many of these referencing laws were instated in the last 5 years



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# Worldwide total revenues of leading pharmaceutical companies in 2014 (in billion dollars)

Company	Total revenue (\$)	R&D costs (\$)	Sales and Marketing costs (\$)	Other activities costs*	Profit (\$)	Profit Margin (%)
1. Johnson & Johnson	71.3	8.2	17.5	31.8	13.8	19
2. Novartis	58.8	9.9	14.6	25.1	9.2	16
3. Pfizer	51.6	6.6	11.1	11.6	22.3	13
4. Amgen	47.2	5.2	10.1	11.9	15.8	14
5. AstraZeneca	41.4	5.3	9.9	17.7	8.5	11
6. Merck	39.1	4.7	9.1	15.3	10.0	10
7. GSK	41.4	5.3	9.9	17.7	8.5	21
8. AstraZeneca	25.7	4.3	7.3	11.5	2.6	10
9. Eli Lilly	23.1	5.5	5.7	7.2	4.7	20
10. AbbVie	18.8	2.9	4.3	7.5	4.1	22
<b>Total Top 10 global companies</b>	<b>429.4</b>	<b>65.8</b>	<b>98.3</b>	<b>175.5</b>	<b>89.8</b>	<b>20.9</b>
<b>Percentage of total revenue – profit</b>		<b>(19%)</b>	<b>(29%)</b>	<b>(52%)</b>		

Pharma highest profit: 20%, followed by banks 10%

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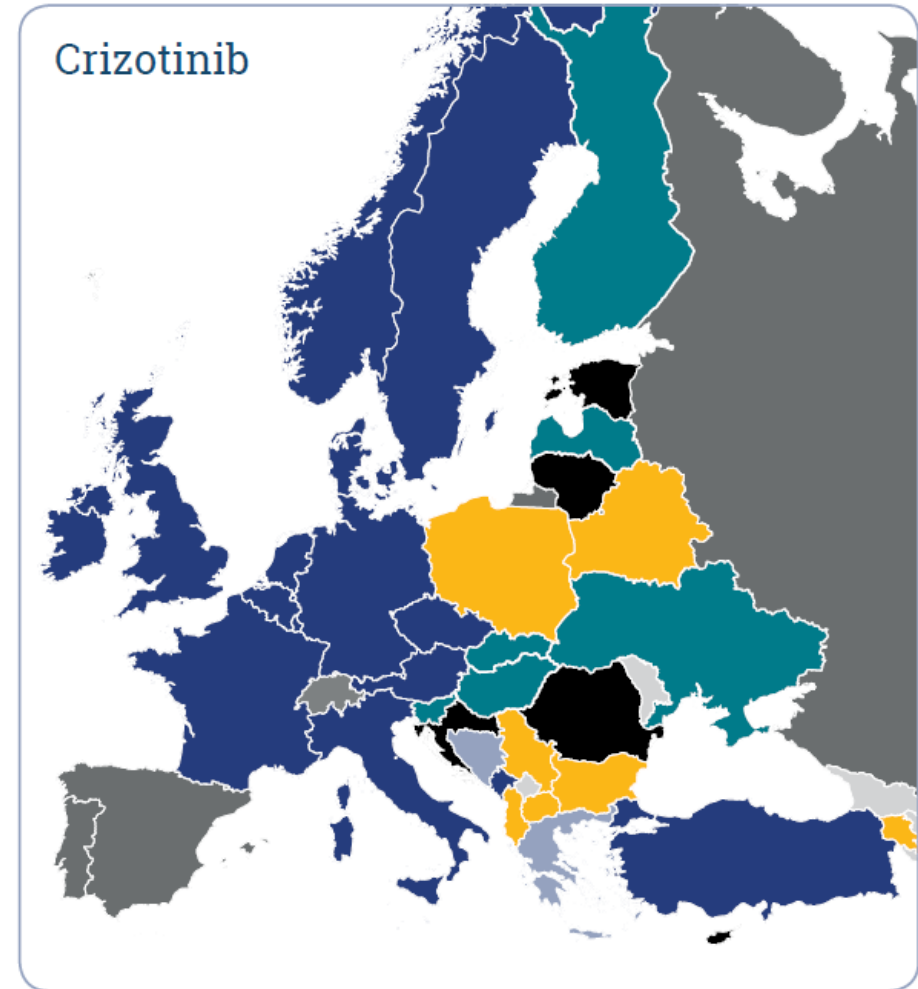
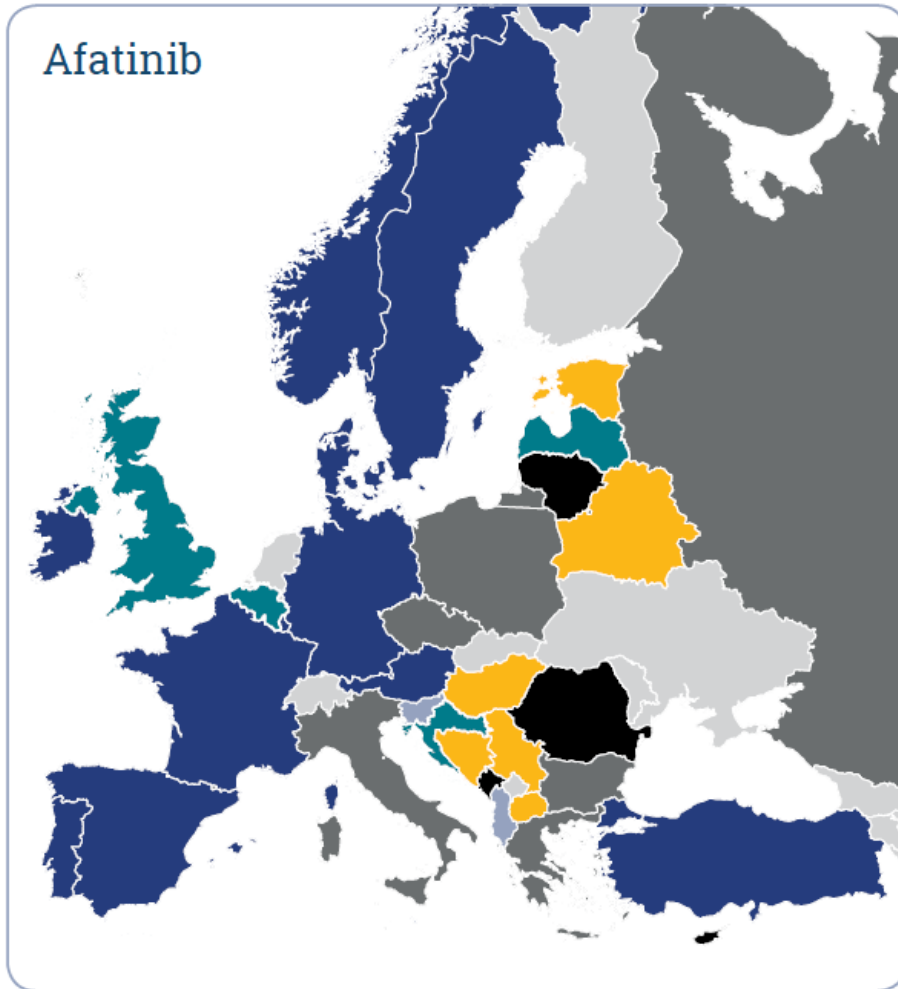
\*Other activities' costs = Total revenue – R&D costs – Sales and marketing costs. Overhead costs are included in R&D, sales and marketing and other activities.

## Poor image

- Profitability far above average other manufacturing industries (20 vs 10%)
- Innovation is flagging
- Little sensitivity to equity considerations: poorer countries and weaker citizens should have same access to drugs as richer countries and better-off citizens
- More is spend on marketing than on R&D
- Safety issues
- Sometimes illegal activities and unlawful agreements

# Availability of 2 cancer drugs

Source: ECL report, October 2018



# Systems are not sustainable so:

## How to reduce spending?

- Shift from expensive to cheap technologies
- Make patients or the insurance pay a larger part
- Reduce the prices of drugs
- Reduce the total use of drugs
  
- Focus on reduction of prices
- However, also issue of unequal access across Europe

The logo for Erasmus University, featuring the word "Erasmus" in a stylized, cursive script.



## Value based pricing

Incremental cost-effectiveness ratios: Cost per QALY  
Thresholds

- NICE: £ 30.000, US: US\$ 50-100.000
- WHO threshold: depend on WHO region and Gross Domestic Product (GDP)

Still budget impact problem.

Pay for performance (P4)

- Reimbursement dependent on treatment success

Volume-price arrangements

- sales < Y price P1; sales > Y lower price P2

A stylized, handwritten-style logo for Erasmus, featuring a large, flowing 'E' followed by the word 'Erasmus' in a cursive script.

# Rationale for adapting the business model of (cancer) drug pricing

## Issues:

1. A free market does not work for innovative cancer drugs
  - *Informational imbalance*
  - *Failure of competition*
2. Current cancer drug prices not justified by Research and Development (R&D)
3. Country specific solutions did not solve the problem
  - EUNeHTA
4. Restricted access to innovative drugs

The Erasmus logo, featuring the word "Erasmus" in a stylized, cursive script.

## New pricing model innovative (cancer) drugs:

<https://www.youtube.com/watch?v=znTgYPRWyrA>

News and Views | 7 May 2018

### Sustainability and affordability of cancer drugs: a novel pricing model

Carin A. Uyl-de Groot & Bob Löwenberg

*Nature Reviews Clinical Oncology* **15**, 405–406



# The algorithm

$$\text{Fair Cost of New Medicine} = \left[ \frac{\text{R\&D costs}}{\text{nr. of patients} \times \text{years of patent left}} + \text{production costs per patient per year} \right] \times (1 + \text{profit margin})$$

Carin A. Uyl-de Groot and Bob Löwenberg, Sustainability and affordability of cancer drugs: a novel pricing model. *Nature Reviews*, July 2018. [\[link\]](#)

# Some assumptions examples in algorithm

## Costs R&D

- Enzalutamide: US\$473.3 million
- Ruxolitinib: US\$1,097.8 million
- Maximum reported: US\$2.588 billion, including abandoned drugs

## Number remaining patent years

- Average all drugs: appr. 10 years
- Enzalutamide: 13 years
- Ruxolitinib: 12.2 years

## Profit margin depend on clinical benefit (MCBS score)

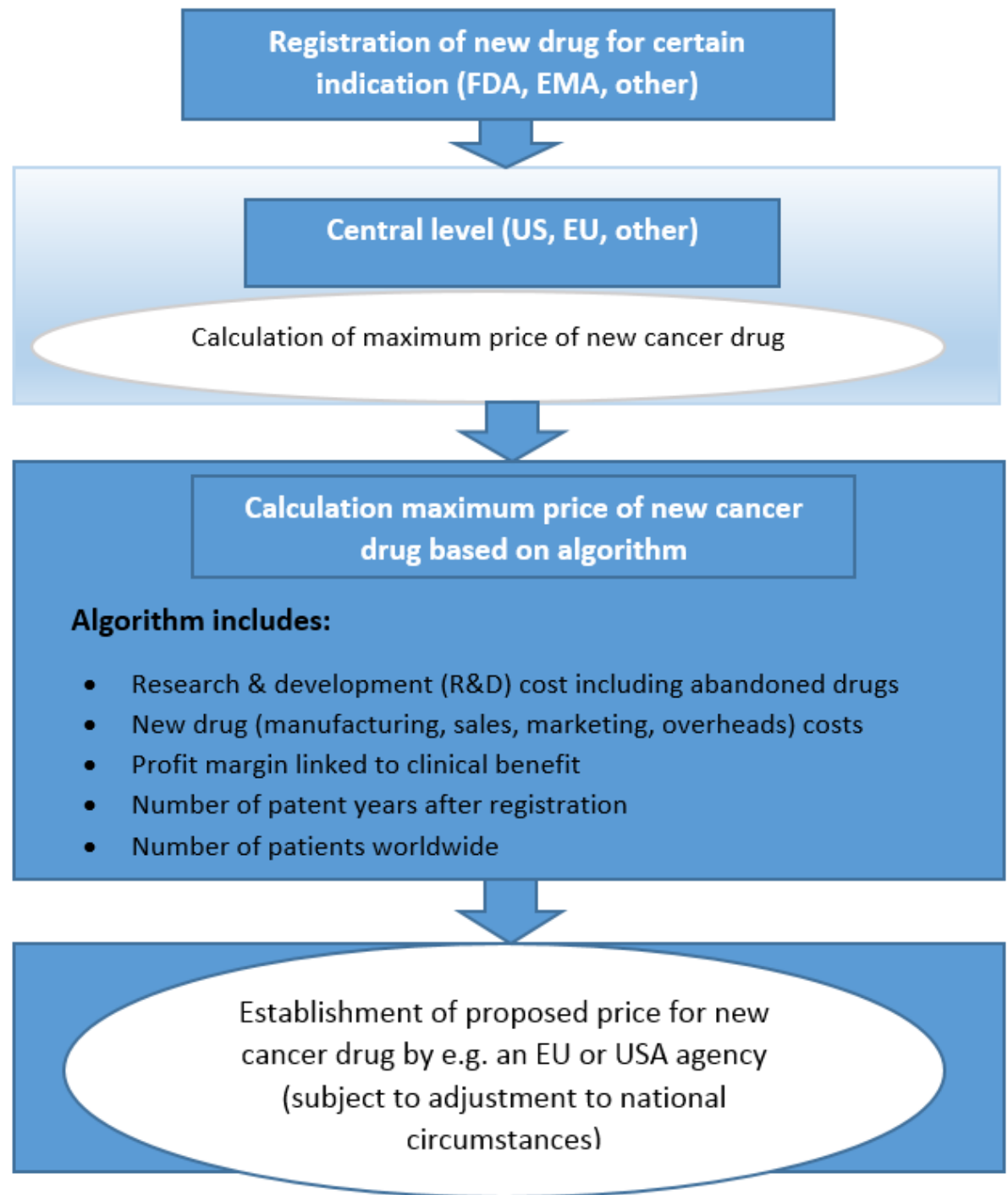
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# Table 1 Calculation of cost price of average treatment of one patient with a new drug

	Estimation number of patients	Costs R&D* (US\$)	Costs Drug (US\$)	Costs without profit (US\$)	Profit margin 20% (US\$)	Profit margin 30% (US\$)	Profit margin 40% (US\$)
Base case 1	100,000	2,558	650	3,208	3,850	4,170	4,491
Base case 2	10,000	25,580	650	26,230	31,476	34,099	36,722
Enzalutamide	140,000	260	1,950	2,210	2,652	2,873	3,094
Enzalutamide	300,000	121	1,950	2,071	2,486	2,693	2,900
Ruxolitinib	7,600	11,840	1,430	13,270	15,924	17,251	18,578
Ruxolitinib	76,000	1,184	1,430	2,614	3,137	3,398	3,660

*copying*

# Outline adapted business model of (cancer) drug pricing



## Ongoing debate and progress

Meetings with the European Parliament

- Resolution: transparency R&D costs, discounts (2017)
- White paper access to medicines (October 2018)

Dutch Ministry of Health: BeNeLuxAI

ESMO: access to medicine hot topic

EHA: task force fair prices

Patient organizations: e.g. Inspire2Live

Pharmaceutical companies (improving access/uptake)

Collaboration with other organizations:

- Fair Medicine
- TheSocialMedwork



# Joint pricing between countries

- Netherlands
- BeNeLuxAI
- And next.....

	Number of inhabitants (in millions)	Perc. Europe (cumulative)	Western Europe
NL	17	2%	4%
BeNELux	29	4%	7%
BeNELuxA	38	5%	9%
BeNeLuxAI	42	6%	10%
UK	66	15%	16%
Italy and Spain	107	29%	25%
Western Europe	421	57%	100%

# Example: niraparib (Zejula)

For the maintenance treatment of ovarian, fallopian tube, or primary peritoneal cancer.

$$\text{Fair Cost} = \left[ \frac{\text{R\&D costs}}{\text{nr. of patients} \times \text{yrs of patent}} + \text{production} \right] \times (1 + \text{profit margin})$$

## Input:

- R&D costs of Tesaro from 2010 to 2017 = €1,882,000,000
- Estimated number of patients = 50,000  
[Source: Globocan 2012. Assumption: 30% eligible patients worldwide]
- Years of patent left = 11.5 years
- Production cost (per patient, per year) = [€5 (per caps) X 3 (caps. per day) X 365]  
= € 5,475
- Profit margin factor = 40%

## Fair price vs. actual price

**Fair price** of niraparib (Zejula) per patient per year = **€14,547**

**Price** of niraparib (Zejula) per patient per year **in The Netherlands** = **€ 126,469**

## Actual revenue vs. calculated revenue with fair price

- **Net sales 2017 (extrapolated) = \$145,333,333**
- **With fair price based on all eligible** = 50,000 patients x €14,547 = **€ 727,338,043 = \$ 833,859,609**

# Measures needed at different levels (national, European), but barriers and limitations

Access issue is broader than discussion about drug prices

Change health systems/legislation: will take years

Patient's right to health – right to have access to optimal quality of cancer care

Collaboration between all stakeholders, including pharmaceutical companies

Encourage joint negotiations

**Role for lawyers?**

# Health systems: Right to health – right to have access to optimal care



## Take home message

- Faster access to new (cancer) therapies
- Better access to new (cancer) therapies
- Lower prices for new (cancer) therapies

It is not a utopia.



**THANK YOU**

