Erasmus School of
Health Policy
& Management

Patient Access to Newly Registered Anticancer Agents

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Cancer Drug Development Forum

CDDF webinar

Erasmus University Rotterdam

Hot topic for (social)media

AD.NL

Kankermedicijnen hier maanden later op de markt dan in de VS: lange wachttijd dodelijk

Door: NU.nl
Beeld: Pro Shots

(ingezonden 18 september 2020)

Vragen van het lid Ellemeet (GroenLinks) aan de minister voor Medische Zorg over de toelatingsprocedure van medicijnen voor kankerpatiënten

1. Bent u bekend met het bericht 'Kankermedicijnen hier maanden later op de markt dan in de VS: lange wachttijd dodelijk'? [1]
2. Deelt u de mening dat kankerpatiënten sneller toegang tot levensreddende medicijnen zouden moeten hebben?
3. Kunt u aangeven waarom de toelatingsprocedure van het Europees Geneesmiddelen Agentschap (EMA) zo veel trager is dan van de Food and Drug Administration (FDA)?
4. Wat kunt u in Europees verband doen om de toelatingsprocedures van de EMA te versnellen?
5. Hoe komt het dat na toelating van de EMA het gemiddeld nog 128 duurt voordat medicijnen worden toegelaten op de Nederlandse markt?
6. Kunt u aangeven waarom het in Duitsland maar zeventien dagen duurt voordat een medicijn op de markt komt (nadat deze is toegelaten door de EMA)?
7. Bent u bereid te leren van de procedures die andere Europese lidstaten hanteren om de snelheid en transparantie van de Nederlandse procedure te verbeteren?
8. Hoe kan het dat in Oostenrijk en België medicijnen zo veel sneller beschikbaar komen, terwijl Nederland met deze landen samenwerkt om medicijnen snel beschikbaar te maken in Nederland?
9. Hoe gaat u ervoor zorgen dat de sluisprocedure voor met name dure geneesmiddelen wordt verkort?

[1] Parool, 15 september 2020, 'Kankermedicijnen hier maanden later op de markt dan in de VS: lange wachttijd dodelijk' (https://www.parool.nl/nederland/kankermedicijnen-hier-maanden-later-op-de-markt-dan-in-de-vs-lange-wachttijd-dodelijk~b44d2523/).

Het Parool

'Lang kank lever

Kanke maand markt wacht

Nieuwe kanke maanden later Deze vertragir en onnodig st

Irene van den Berg

Beeld ANP

ANP 15 septem

Nieuwe kan later beschil blijkt uit on Erasmus Un dat kankerp

Uyl-de Groo medicijnen, goedkeurin huidkanker

De Telegraaf

NIEUWS SPORT ENTERTAINMENT FINANCIEEL VROUW LIFESTYLE WAT U ZEGT

NPO Radio 1 @NPORadio1 · 3 u
Goedemorgen! @Kirstenkdomp bekijkt weer de kranten deze ochtend:

Vereniging Innovatieve Geneesmiddelen @wewordenbeter
'Bureaucratie bij **kankermedicijnen** kost levensjaren. Daarom is gr herijking van de toelating voor nieuwe medicijnen hard nodig', zeg directeur Gerard Schouw. Hij reageert op nieuw onderzoek van Ca

Irene van den Berg @ivandenberg
Vandaag komt de opening van het **kankermedicijnen** hier veel later op

EuropeesParlementNL
Wat moeten de prioritei
Volg LIVE op 16 sept om
#SOTEU #StrongerToget

ton huise
iets ander
Europese
VS,hier zo
mogelijk

'Lange wachttijden nieuwe kank
Nieuwe kankermedicijnen zijn in
beschikbaar voor patiënten dan
telegraaf.nl

Hoo

Ka toe

Nieuwe kank komen in Eu acht maand markt dan in ten. Deze ve dat mensen nodig sterve raar Carin U

Irene van de Rotterdam

Uit een stud aan de Erasm terdam blijkt kermedicijn deld 403 dage In de Verenig sneller: al na Volgens Uy in dat Europ beduidend la dagen – op le cijnen moete kerpatiënten Eén van de Europees Ger

Da_Brownie 6 d

Opvallend is d jongetjes van dit aan een er

Respect 11 Re

Arjan_Koole 6 d

Een reden hie medicijnen da het geld toch belangen te g

Respect 18 Re

Hich Hichi
Hou op man k
Leuk · Beantwo
2 antwoor

Diana Alberts
lekker dan!!!!!
Leuk · Beantwo

The good news (1).....

Cancer survival in Europe 1999–2007 by country and age: results of EUROCARE-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 EUROCARE-5 Working Group**

Summary

Background Cancer survival is a key measure of the effectiveness of health-care systems. EUROCARE—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. EUROCARE-5 assesses their effect on 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 2007 and followed up to 2008. Uniform quality control procedures were applied to all datasets. For patients diagnosed in 2000–07, we calculated 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.

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

Lancet Oncol 2014; 15: 23–34
Published **Online**
December 5, 2013
http://dx.doi.org/10.1016/S1470-2045(13)70546-1

See **Comment** page 2
See **Articles** page 35
See **Online** for an author interview with Roberta de Angelis

*Members of the EUROCARE-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**

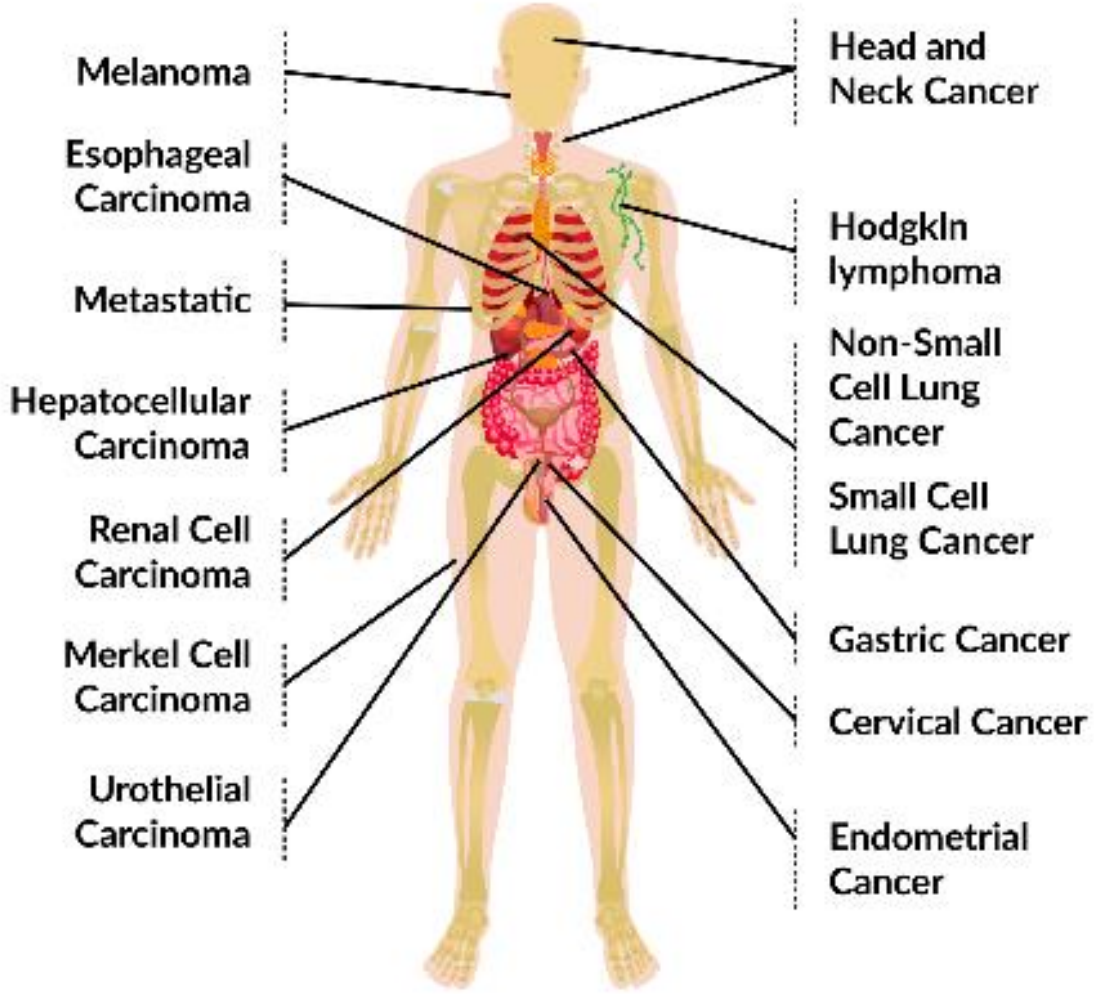
De Angelis et al. Lancet Oncology 2014;15:23-34

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

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

Pembrolizumab

As of 1st January 2020 is FDA approved for treating:



The bad news (1):

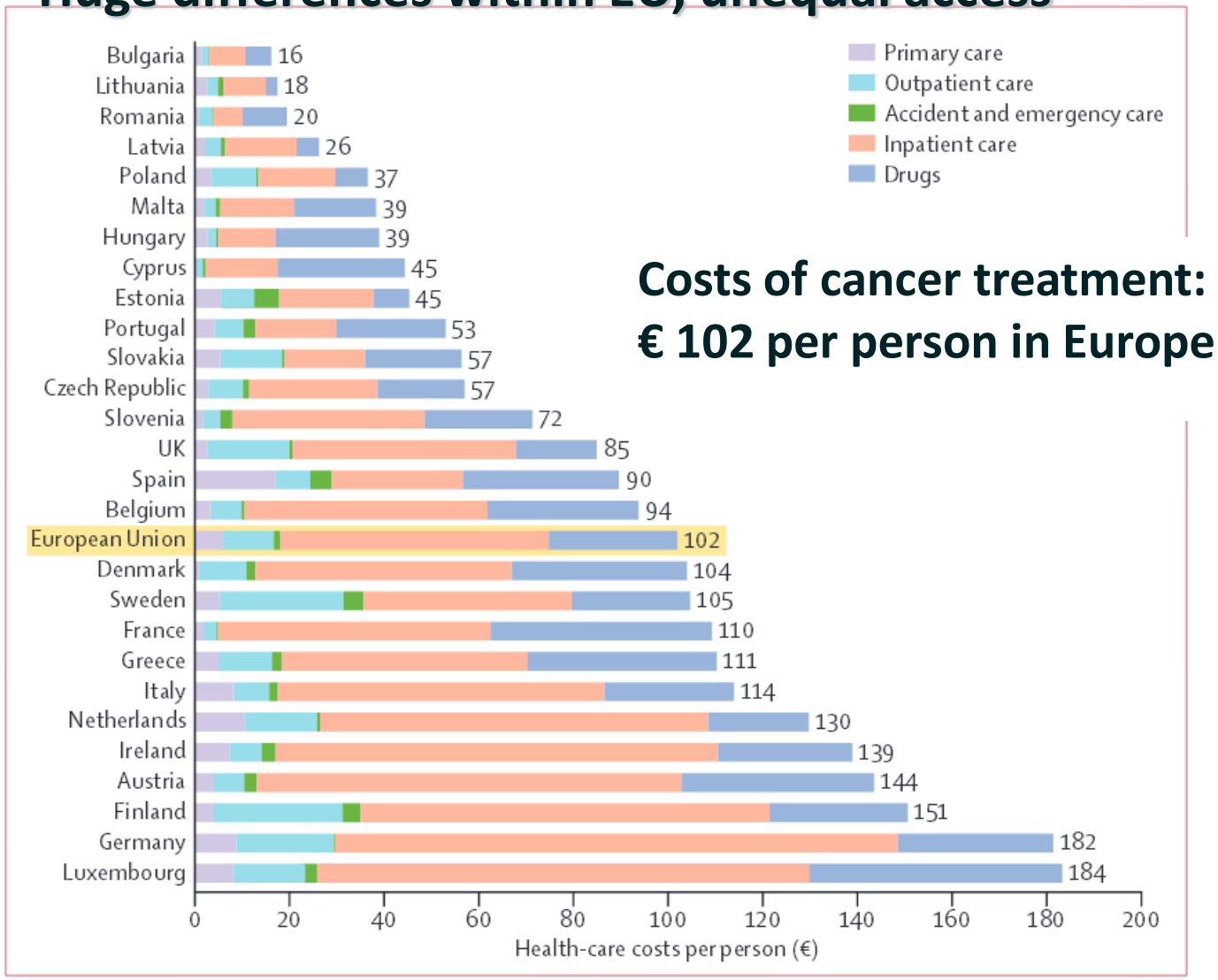
Rise in health expenditures 2000-2015

as share Gross Domestic Product (GDP)

Country	2000	2005	2010	2015
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
Average EU	**7.3**	**8.2**	**8.9**	**9.0**

The bad news (2):

Huge differences within EU, unequal access



Costs of cancer treatment:
€ 102 per person in Europe

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.

Luengo-Fernandez et al. Lancet Oncology 2013;14:1165-1174

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
Nivolum			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

Opportunity cost

Issues around sustainability and accessibility:

Sustainability: How to reduce spending?

- Shift from expensive to cheap technologies
- Make patients or the insurance pay a larger part
- Reduce the total use of drugs
- Reduce the prices of drugs

Accessibility: How accessible are our cancer treatments/drugs?

Reduce price of drug: A novel pricing model

- 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

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

Profit margin should depend on clinical value: e.g. ESMO Magnitude of Clinical Benefit Score

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ESMO > Guidelines > ESMO-MCBS

ESMO-MCBS SCORECARDS

ESMO-MCBS

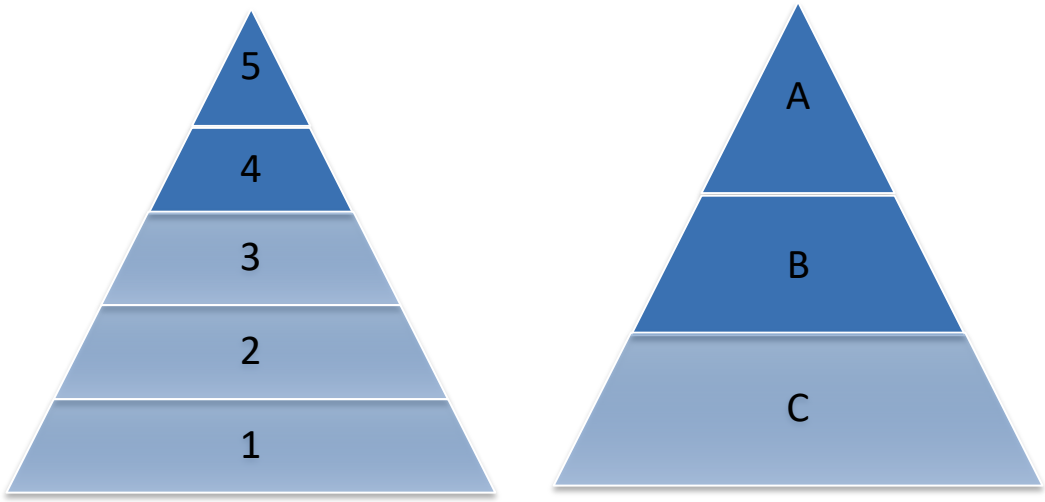
ESMO-Magnitude of Clinical Benefit Scale

SCORECARDS

The searchable portal provides a centralised location of cancer medicines that have been scored and published by ESMO.

How to assess the new drugs: ESMO Magnitude of Clinical Benefit Scale

- A standardized, generic and validated tool, aimed at quantifying the clinical benefit for anti-cancer drugs for solid tumours.
- Considers outcomes of survival, quality of life (QoL) or surrogates thereof (DFS, EFS, TTR, PFS and TTP) and treatment toxicity.



[2] Cherny NI; Ann Oncol2015 Aug;26(8):1547-7

Cancer drugs with **score 4 or 5 and A or B** should be accessible for **ALL** European cancer patients

cancers

MDPI

Article

Unequal Access to Newly Registered Cancer Drugs Leads to Potential Loss of Life-Years in Europe

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Topics

Aim

Methods

Results

Conclusions

Questions

Aim

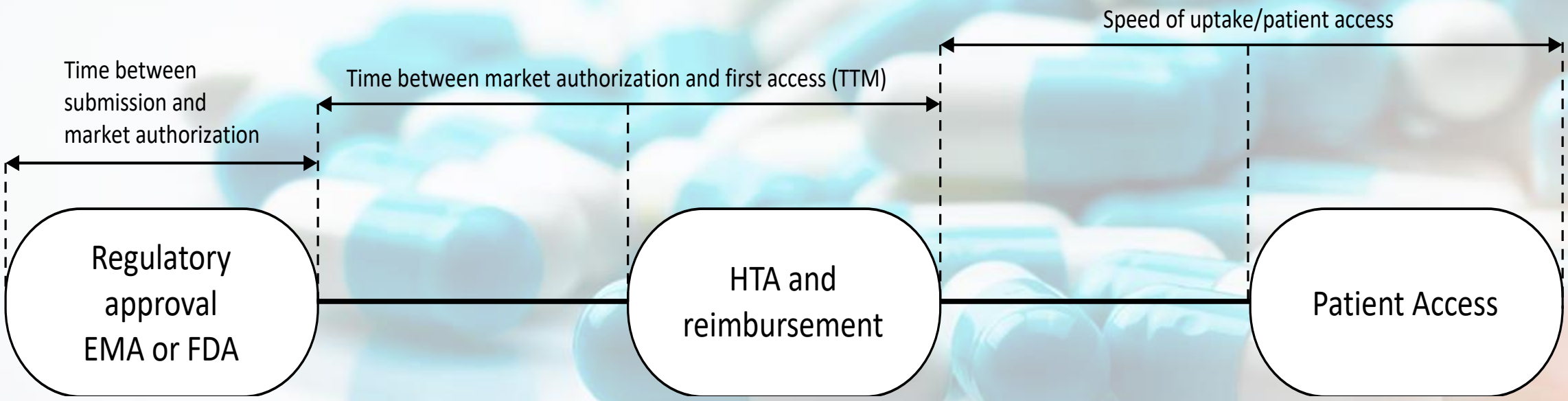
“To assess variations in national patient access to several newly registered cancer drugs across Europe.”

We compared the dates of submissions to FDA and EMA, the time to first uptake, and speed of uptake of these drugs and explored the impact of observed variations in access in terms of health outcomes.

Methods

- Retrospective database study
- 12 Innovative “end of life” cancer drugs (2011 – 2017)
- Various indications: breast cancer, gastric cancer, prostate cancer, and melanoma
- Drugs with various ESMO-MCBS scores
- Pharmaceutical sales data was obtained from IQVIA’s MIDAS® database, Netherlands missing, data from manufacturers (n=8)
- Specific cancer mortality data (Eurostat)

Newly registered drug access pathway

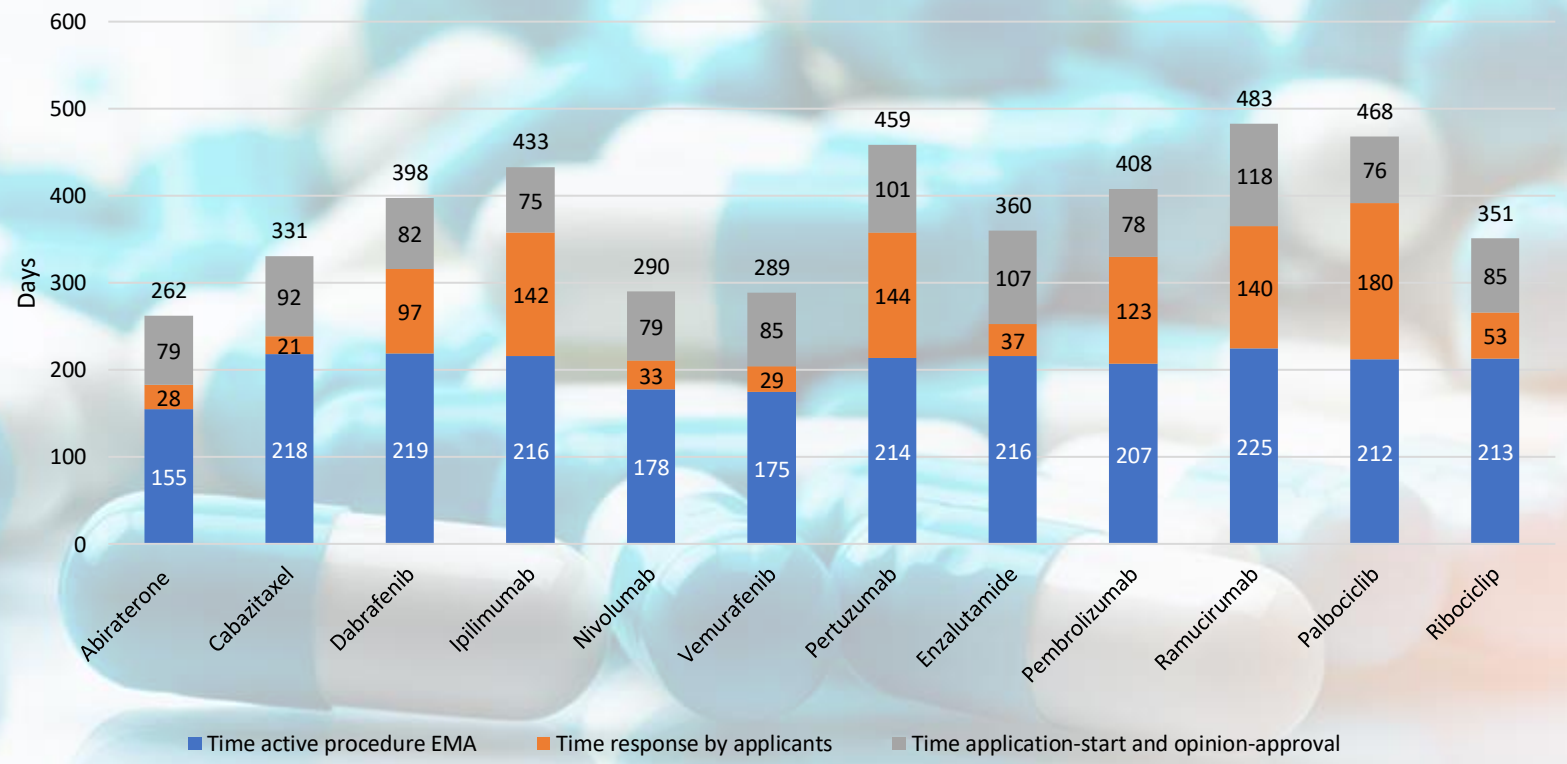


Newly registered first indications, clinical values, FDA and EMA procedures

	First indication	Gain PFS, OS, TTP (median, months)	ESMO-MCBS*	Total time EMA (in days)	Total time FDA (in days)	Time between EMA and FDA approval (in days)
Abiraterone	Prostate cancer	3·9 months OS	4	262	129	130
Cabazitaxel	Prostate cancer	2·4 months TTP	2	331	78	273
Dabrafenib	Melanoma	2·4 months PFS	4	398	303	89
Ipilimumab	Melanoma	3·7 months OS	4	433	278	119
Nivolumab	Melanoma	4·0 months PFS	4	290	145	179
Vemurafenib	Melanoma	3·7 months PFS	4	289	111	184
Pertuzumab	Breast cancer	6·1 months PFS	4	459	185	269
Enzalutamide	Prostate cancer	4·8 months OS	4	360	101	294
Pembrolizumab	Melanoma	1·3 months PFS	3	408	188	317
Ramucirumab	Gastric cancer	2·2 months OS	2	483	241	242
Palbociclib	Breast cancer	10·3 months PFS	3	468	218	645
Ribociclib	Breast cancer	PFS not reached	3	351	196	162
Average time (in days)				378	181	242
Average time accelerated assessment/priority review (in days)				280	139	n.a.
Average time in case no accelerated assessment/no priority review (in days)				410	223	n.a.

Regulatory approval EMA vs FDA

- **FDA** procedure time on average = 181 days (range 78 – 303) **vs**
  EMA = 378 days (range 262 – 483).
- On average **EMA** is 242 days slower than **FDA**

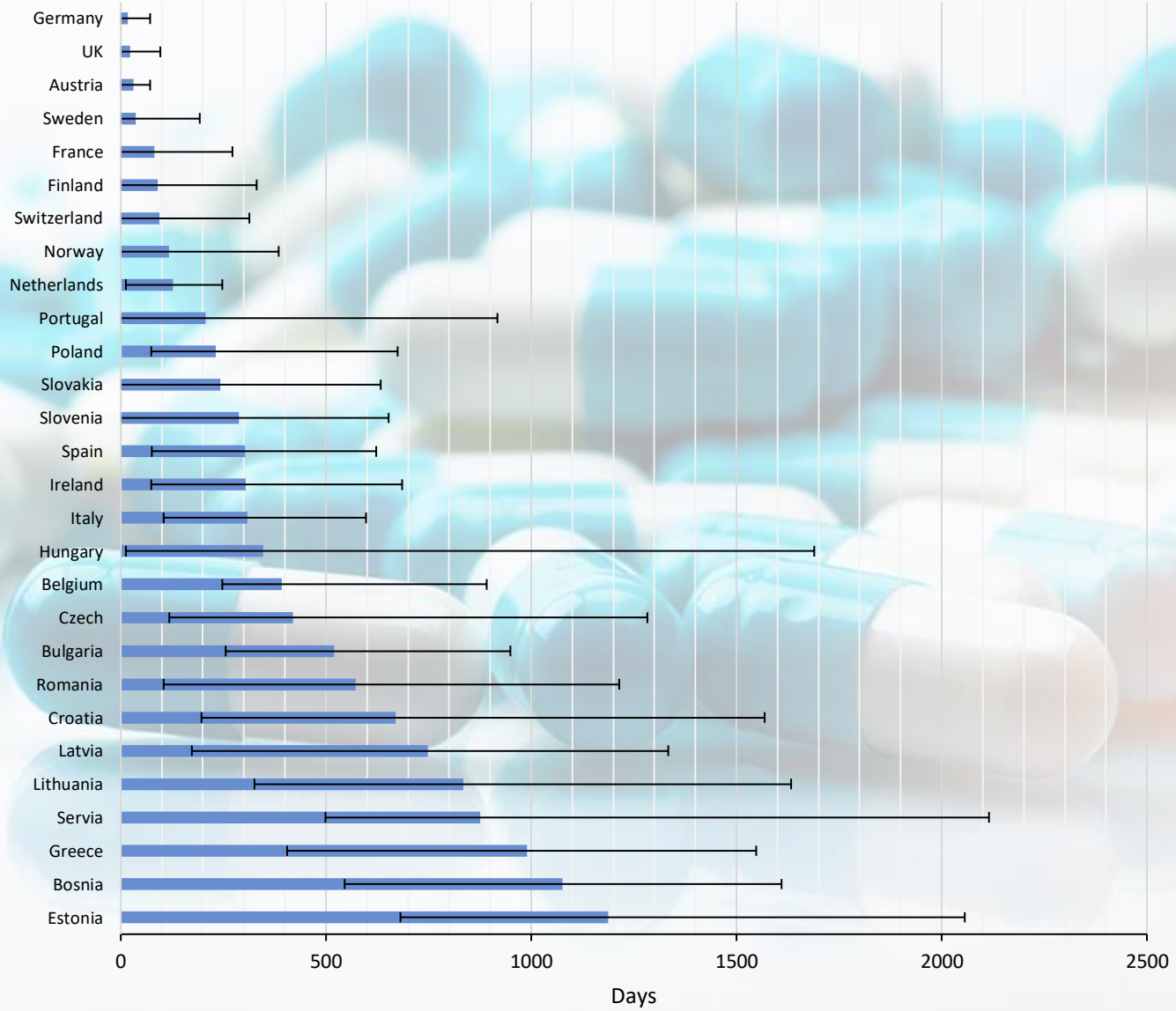


Time between authorization and first access

Germany: early patient access 17 days on average

Netherlands: doing reasonably well 128 days

Estonia: 1187 days on average (only 4 out of 12)

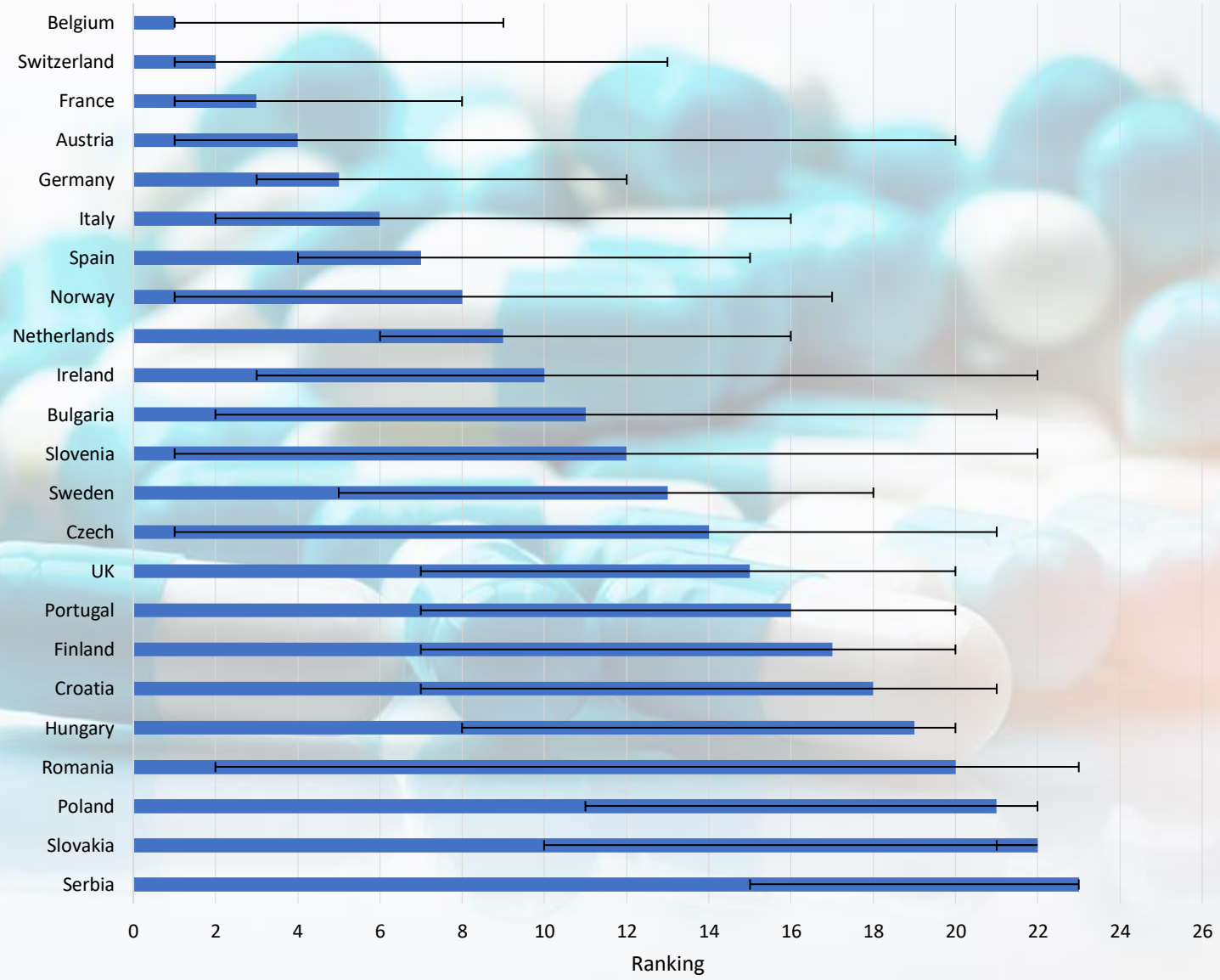


Ranking based on speed of drug uptake

Belgium: fast uptake of innovative cancer drugs

Netherlands: 9th in the ranking, slower than Italy and Spain

UK: 15th in the ranking, not great



Potential life years lost due to delayed access

Two examples:

- Abiraterone
- Ipilimumab

Assumptions:

- 80% need
- based on trial OS gain

Result: **30,000 potential life year lost**

	Abiraterone			Ipilimumab		
	Difference in track FDA -EMA	Delay in access after EMA registration	Total life years lost	Difference in track FDA -EMA	Delay in access after EMA registration	Total life years lost
Austria	115	204	318	50	31	81
Belgium	140	376	516	69	26	95
Bulgaria	89	249	338	40	13	53
Croatia	72	203	275	46	15	62
Czech Republic	157	440	597	114	38	152
Estonia	25	70	95	14	4	18
Finland	85	234	319	50	18	68
France	854	1803	2657	185	150	336
Germany	1126	2466	3592	394	219	613
Hungary	119	334	453	100	33	133
Ireland	84	234	318	44	17	61
Italy	602	1691	2293	433	143	576
Latvia	37	104	141	19	6	25
Lithuania	55	155	211	26	8	34
Netherlands	292	733	1025	194	72	266
Norway	117	273	390	94	31	125
Poland	507	1416	1923	385	127	512
Portugal	164	456	621	63	21	84
Romania	225	632	857	45	36	81
Serbia	102	287	389	68	22	90
Slovakia	92	256	349	58	19	77
Slovenia	41	113	155	32	11	42
Spain	580	1545	2126	240	79	318
Sweden	235	583	818	132	46	178
Switzerland	136	305	440	57	32	89
United Kingdom	1170	2988	4159	495	200	695
Total life years lost	**7221**	**18152**	**25373**	**3448**	**1418**	**4867**

Conclusion

- Patients in the US have faster access to innovative cancer treatments than European patients.
- Great inter-country variation in access to new cancer treatments exists among European countries.
- The delay in access may result in a potential loss of many life years


Effective
Cost-effective
Personalized
Timely
The health outcomes of European patients can substantially be improved
by enabling faster and more general use of available new medicines.