Erasmus School of
Health Policy
& Management

Inequalities in approval processes and access in EU

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Who am I?

Master Health Sciences (1985-1990)

PhD Health Economics : 1995

Director of institute for Medical Technology Assessment (from 2000 -)

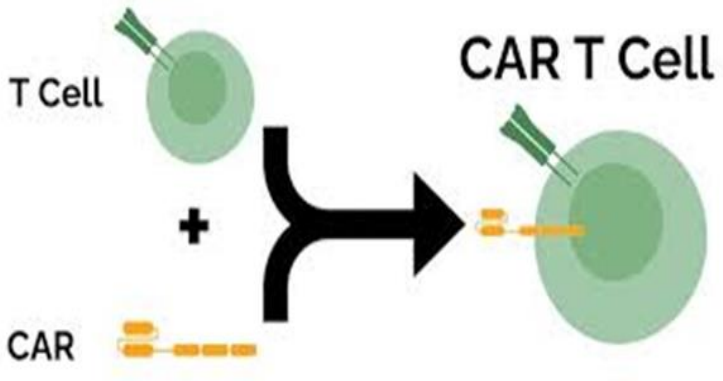
Professor of Health Technology Assessment (2005 -)

Principal Investigator of Horizon Europe project ASCERTAIN

Mission: To improve access to new promising (cancer) therapies for all patients in need

Many innovative cancer drugs and therapies

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



Process: From Early Development to EU Patient Access (I)

1. Early Development: Discovery & Preclinical Research:

1. Identification of potential drug compounds
2. Laboratory and animal studies to assess safety and efficacy

2. Clinical Development:

a. **Phase I:** First-in-human trials to evaluate safety and dosage
b. **Phase II:** Studies to assess efficacy and side effects
c. **Phase III:** Large-scale trials to confirm efficacy and monitor adverse reactions

3. Regulatory Submission:

Marketing Authorisation Application (MAA):

a. Submission of comprehensive data to EMA
b. Evaluation by the Committee for Medicinal Products for Human Use (CHMP)

4. EMA Assessment: Review Process:

a. Assessment of quality, safety, and efficacy data
b. Interaction with the applicant for clarifications

Process: From Early Development to EU Patient Access (II)

5. **Approval:**

   Centralised Marketing Authorisation:

   If approved, the medicine receives authorisation valid in all EU member states

6. **Health Technology Assessment (HTA):**

   National HTA Bodies:

   a. Evaluation of the drug's added value and cost-effectiveness

   b. Recommendations for reimbursement and pricing

7. **Market Access:**

   Negotiations & Reimbursement:

   a. Discussions with national health authorities

   b. Determination of pricing and inclusion in national formularies

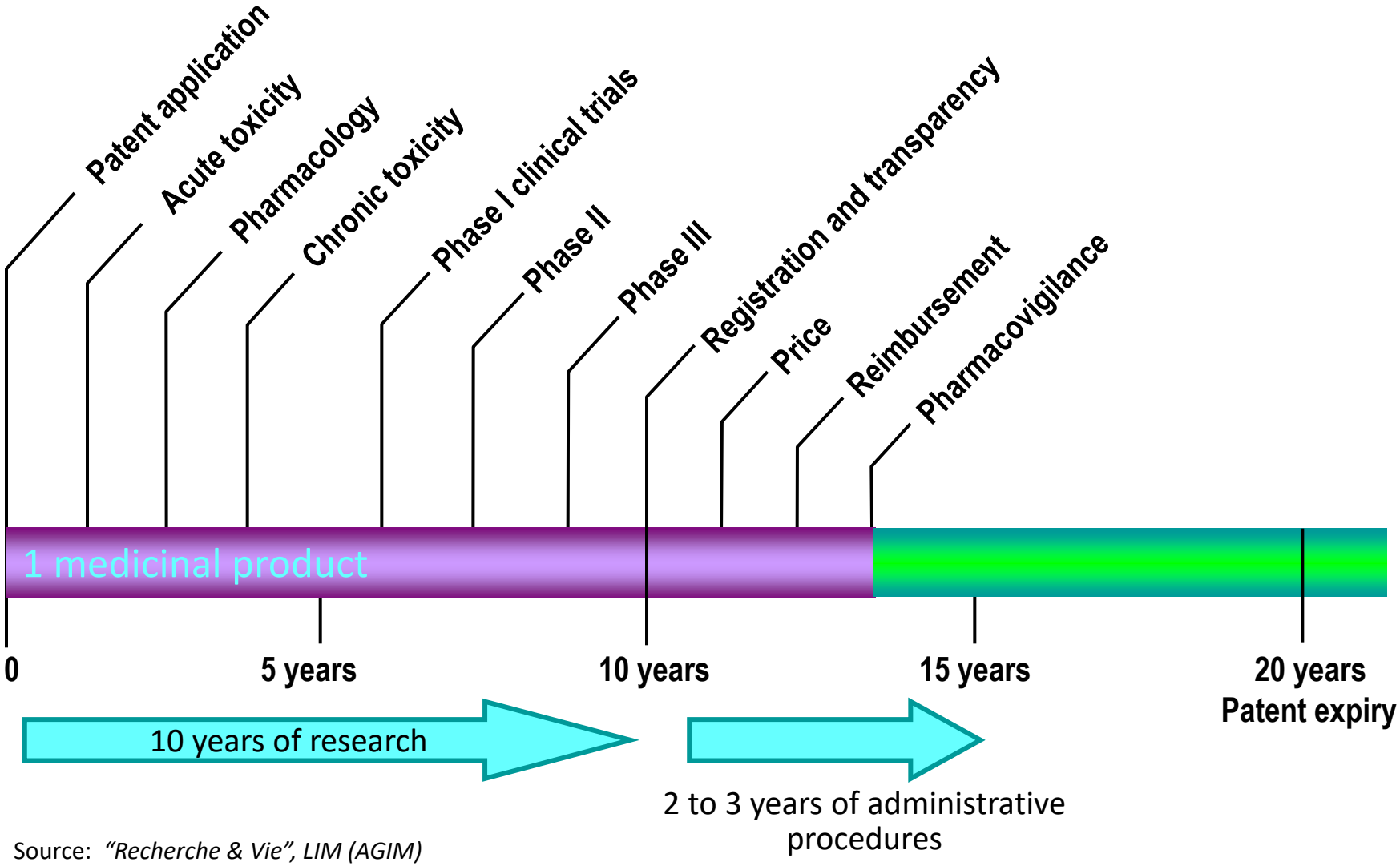
8. **Patient Access:**

   Availability:

   a. Drug becomes available to patients in EU countries.

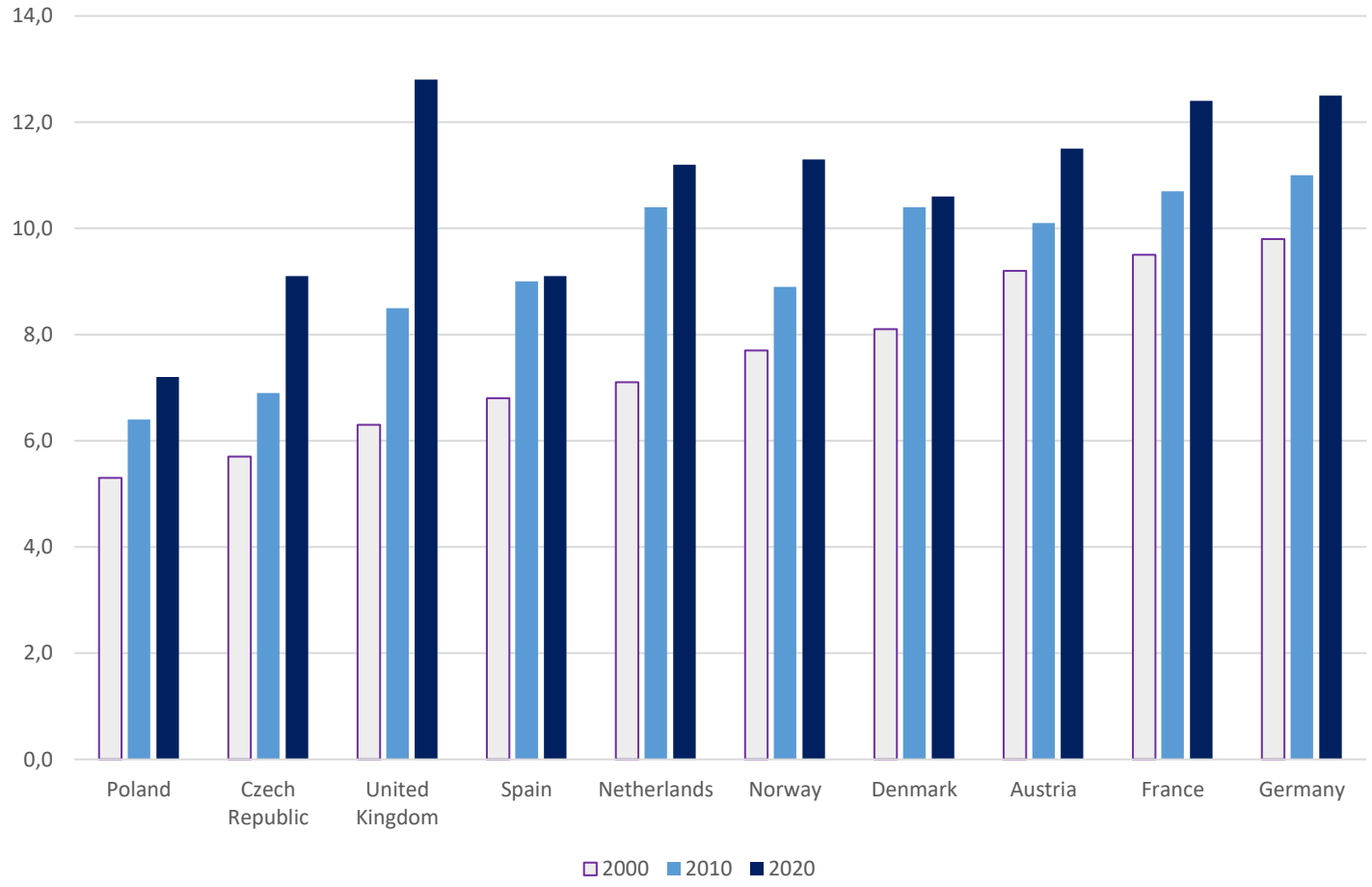
   b. Ongoing pharmacovigilance to monitor safety in the real-world setting.

Development phase
From discovery to patient

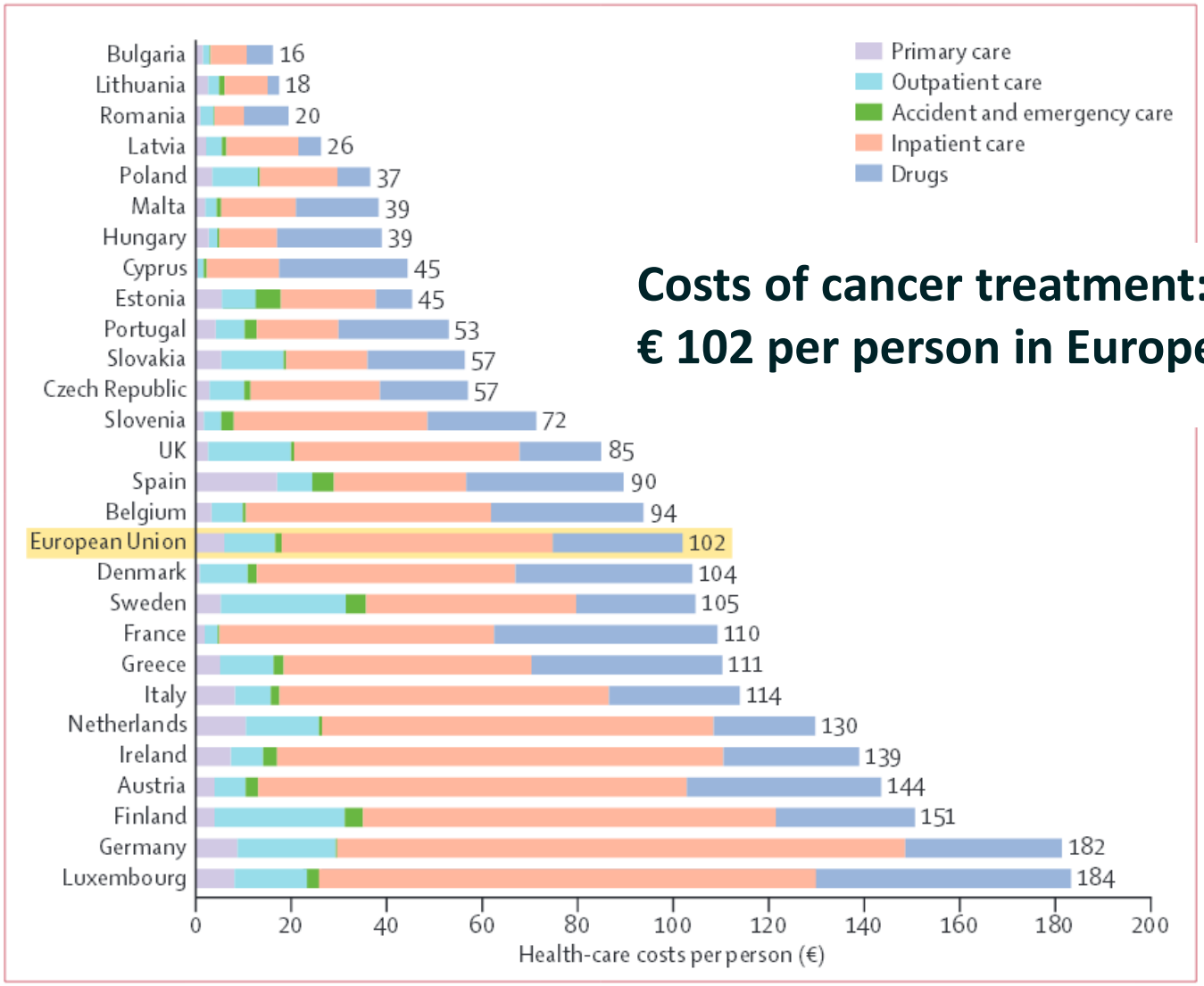


Source: *"Recherche & Vie", LIM (AGIM)*

Rise in health expenditures 2000-2020 as share Gross Domestic Product (GDP) in several European countries



Huge differences within EU, unequal access

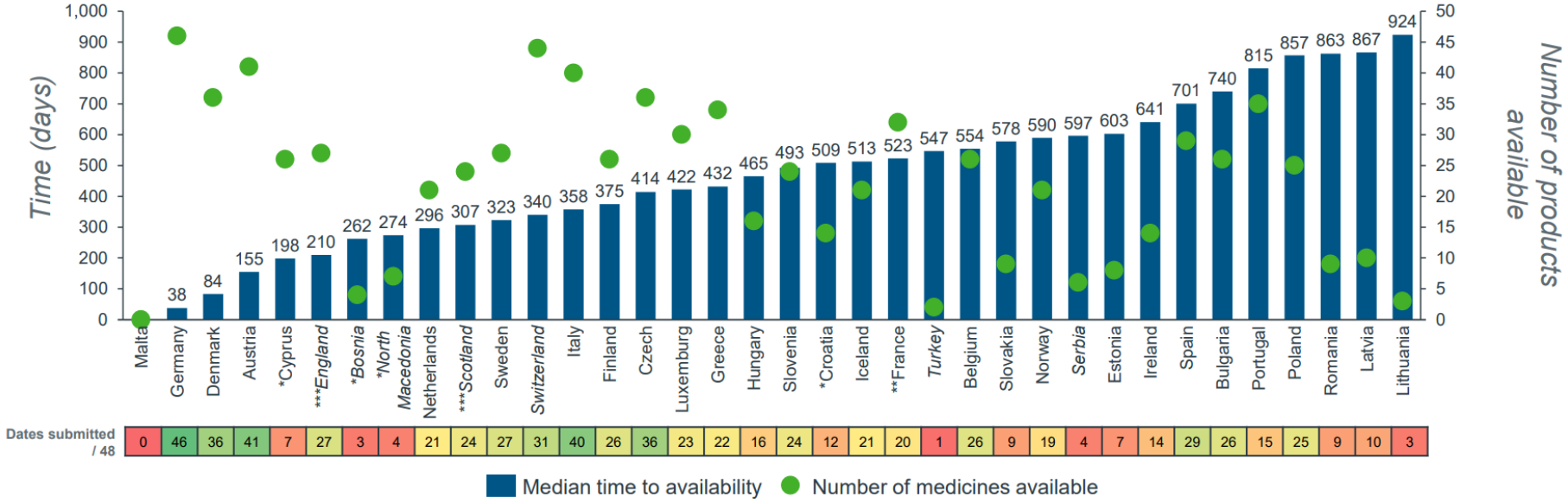


Costs of cancer treatment:
€ 102 per person in Europe

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

Oncological medicines median time to availability (2019-2022): from market authorisation to access/reimbursement



EFPIA patient wait indicator June 2024,

Annual price of a newly-launched cancer drug in the United States averaged $283,000 in 202

U.S. cancer d

Despite the Inflation Re s cancers are poised to rise in the coming years.

Note: 2021 is actual year-end

Source: Office of U.S. Represe

Examples of HTA bodies for pharmaceutical assessment in Europe

- France – Haute Autorité de Santé (HAS) – http://www.has-sante.fr
- Germany – Gemeinsamer Bundesausschuss (GBA) – https://www.g-ba.de/
- Scotland – Scottish Medicines Consortium (SMC) – scottishmedicines.org.uk/Home
- Sweden – Tåndvards Och Läkemedelsförmänsverket (TLV) – tlv.se/In-English/in-english/
- Netherlands – Zorg Instituut Nederland (ZIN) https://www.zorginstituutnederland.nl/

Health Technology Assessment (HTA)

"A multidisciplinary process that uses explicit methods to determine the value of a health technology at different points in it's lifecycle.

The purpose is to inform decision-making in order to promote an equitable, efficient, and high-quality health system."

Question: Reimbursement, based on what criteria?

WHAT OTHER CRITERIA CAN WE USE

BESIDE COST-EFFECTIVENESS

Reimbursement, based on what criteria?

- Efficacy/effectiveness?
- Total budget impact?
- Number of patients?
- Cost-effectiveness?
- Health gain per patient?
- Disease severity?
- Rarity of disease?
- Own responsibility?
- Strength of lobbies stakeholders?
- Etc?

cancers

MDPI

Article

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

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Aim

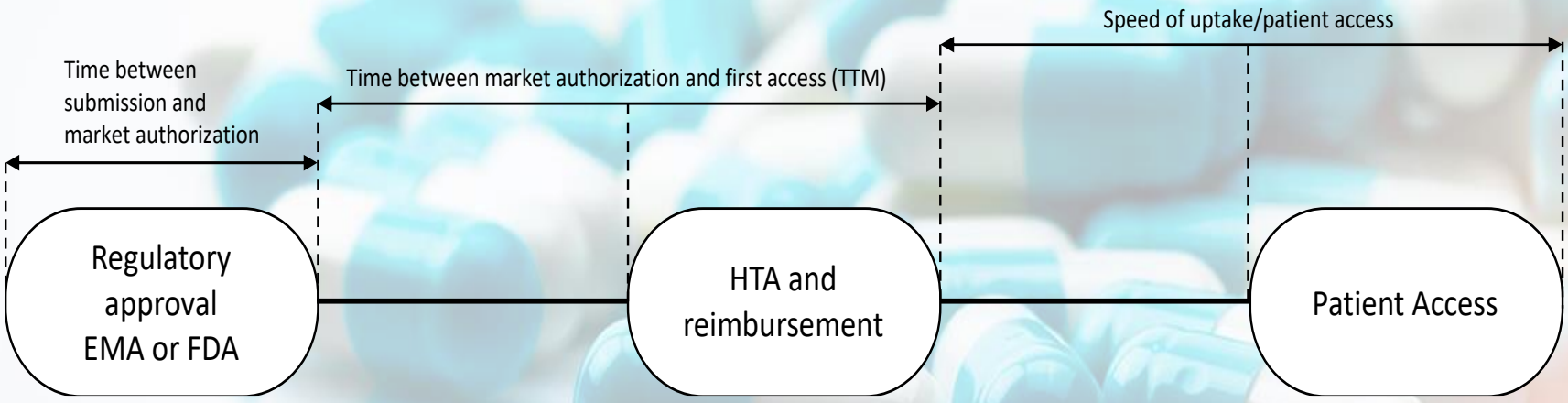
"To assess variations in national patient access to several newly registered cancer drugs across Europe."

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
- Specific cancer mortality data (Eurostat)

Newly registered drug access pathway

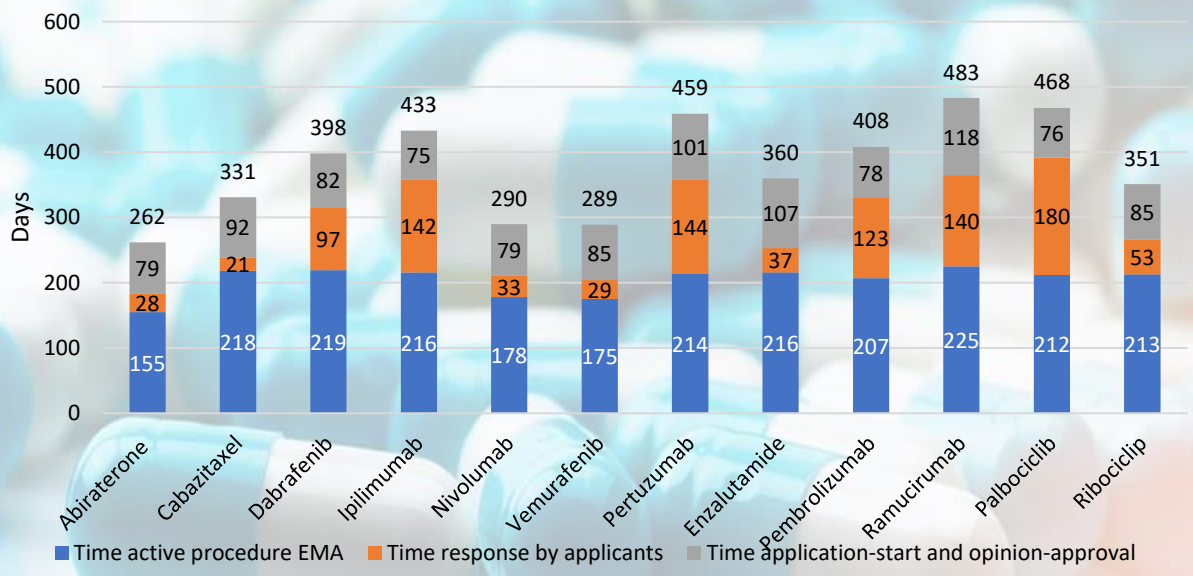


Newly registered first indications, clinical values, FDA and EMA procedures

	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**

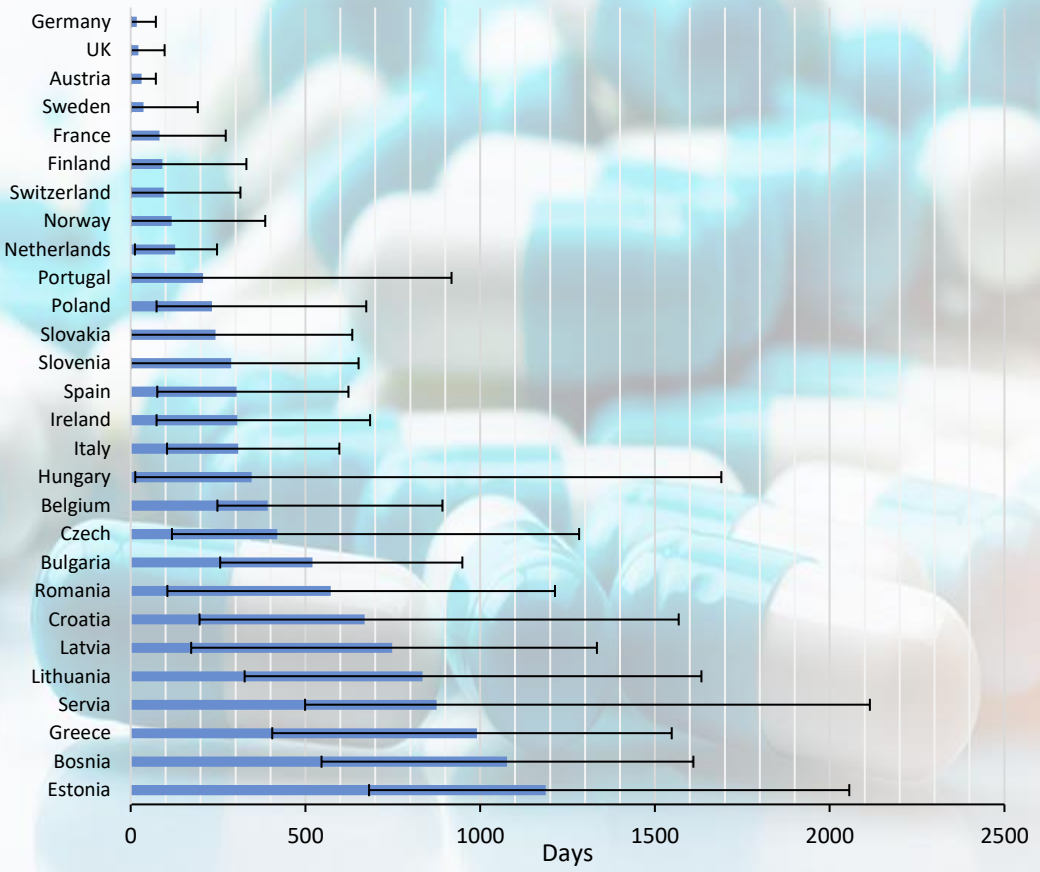


Time between authorization and first access

Germany: early patient access 17 days on average

Netherlands: doing reasonably well 128 days

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

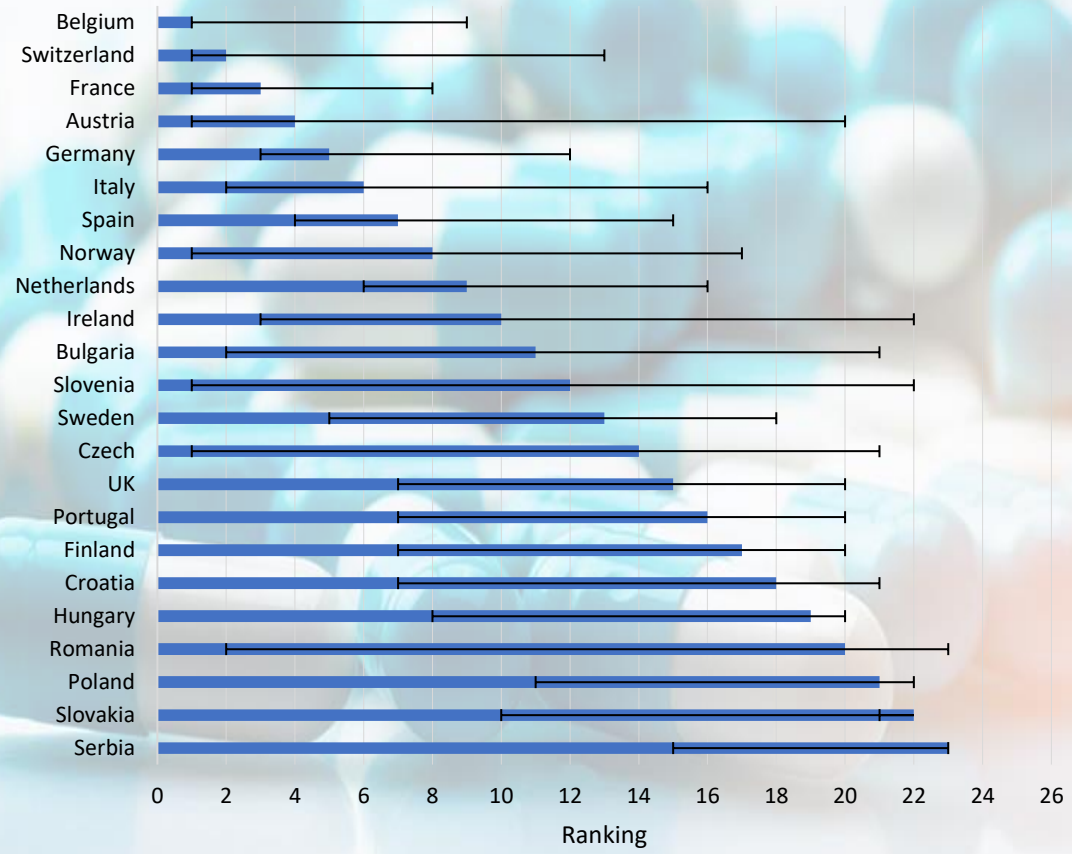


Ranking based on speed of drug uptake

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

Policy goals in health care

Goal: Ensure *affordable* and *equitable* access for (all) patients to *effective* therapies in a *sustainable* manner.

Sustainability

Financial: rational use of medicines
Research: promote innovation

Equity

No systemic disparities

Quality

Person centered, safety, evidence based, etc.

ASCERTAIN

Affordability and **S**ustainability improvements through new pricing, **C**ost-**E**ffectiveness and **R**eimbursemen**T** models to **A**ppraise **IN**novative health technologies

ASCERTAIN

Start: December 2022

Duration: 4 years.

Budget: 5 million

Funded by the European Union

Funded by the European Union. Views and opinions expressed are however those of the author(s) only and do not necessarily reflect those of the European Union or HaDEA. Neither the European Union nor the granting authority can be held responsible for them. Grant 101094938

ASCERTAIN (www.access2meds.eu)

Focus

INNOVATIVE HEALTH TECHNOLOGIES

THREE USE CASES:

Aim

- Improve **affordability**
- Improve **access**
- Improve **sustainability**

ASCERTAIN: methodology

Model

Pricing of technologies

Cost-effectiveness; value assessment; budget impact

Reimbursement / payment

Usability

Application of models in supporting policy-making tools

User evaluation

Quick overview of ASCERTAIN

Video

- https://www.youtube.com/watch?v=fvjJ4-2nOxk

Song

https://www.youtube.com/watch?v=KMLzUddVFRI

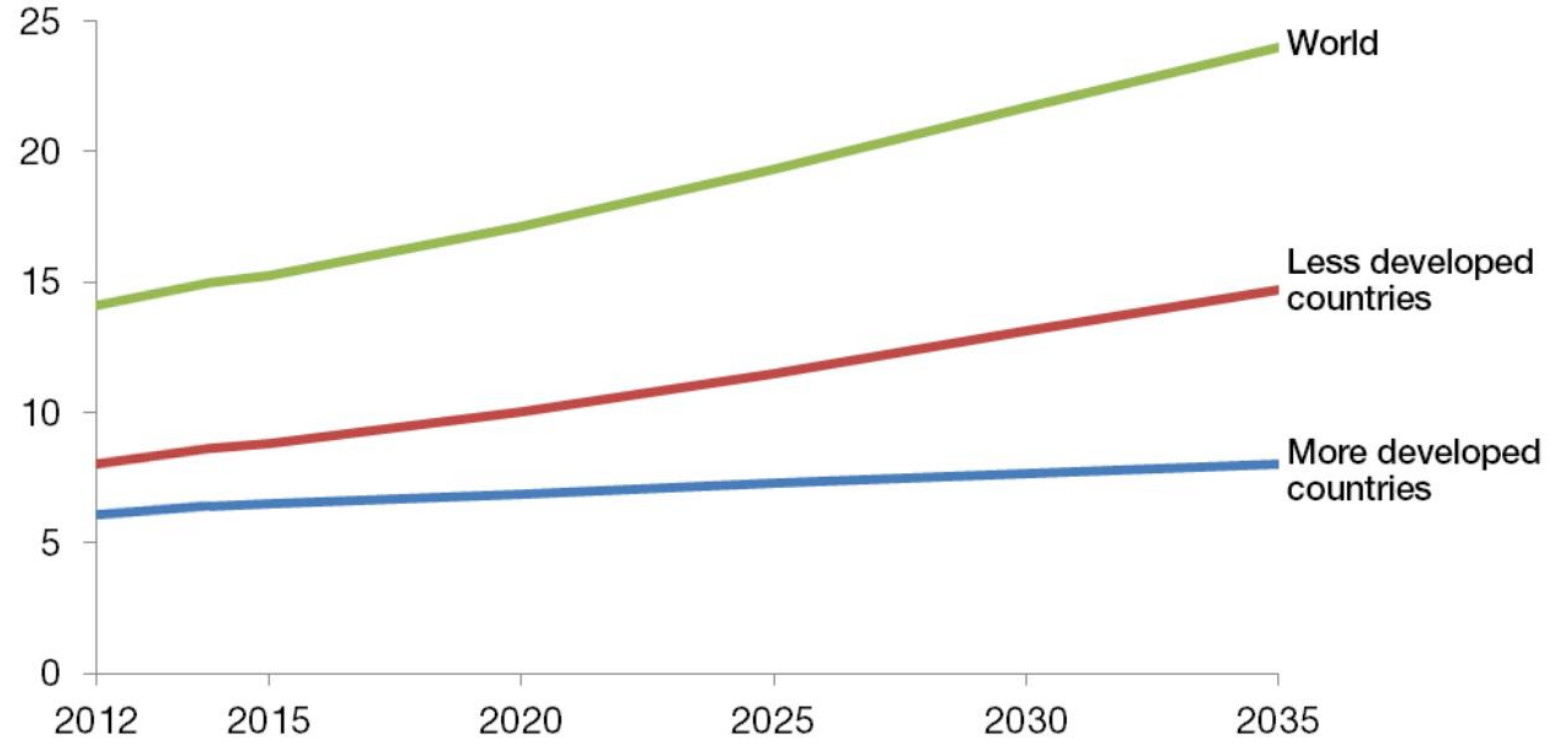
The journey is the destination

- Engagement process with all stakeholders
- Define, agree and prioritize the expectations/ values among the following:
  - Encourage innovation
  - Cover R&D costs with RoI
  - Limit budget impact
  - Improve cost effectiveness
  - Ensure appropriate drug use
  - Ensure access
  - Ensure sustainability
- Design a journey (process) that can be considered fair and transparent

Predicted global cancer cases, 2012-2035

Cases (millions)

WORLD ECONOMIC FORUM
COMMITTED TO IMPROVING THE STATE OF THE WORLD



Source: WHO GloboCan, BBC

Thank you!