ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

European Society for Medical Oncology

Disparities of Cancer Medicine Access in Europe

Alexandru ENIU, MD, PhD

Chair, ESMO Emerging Countries Committee

Department of Breast Tumors

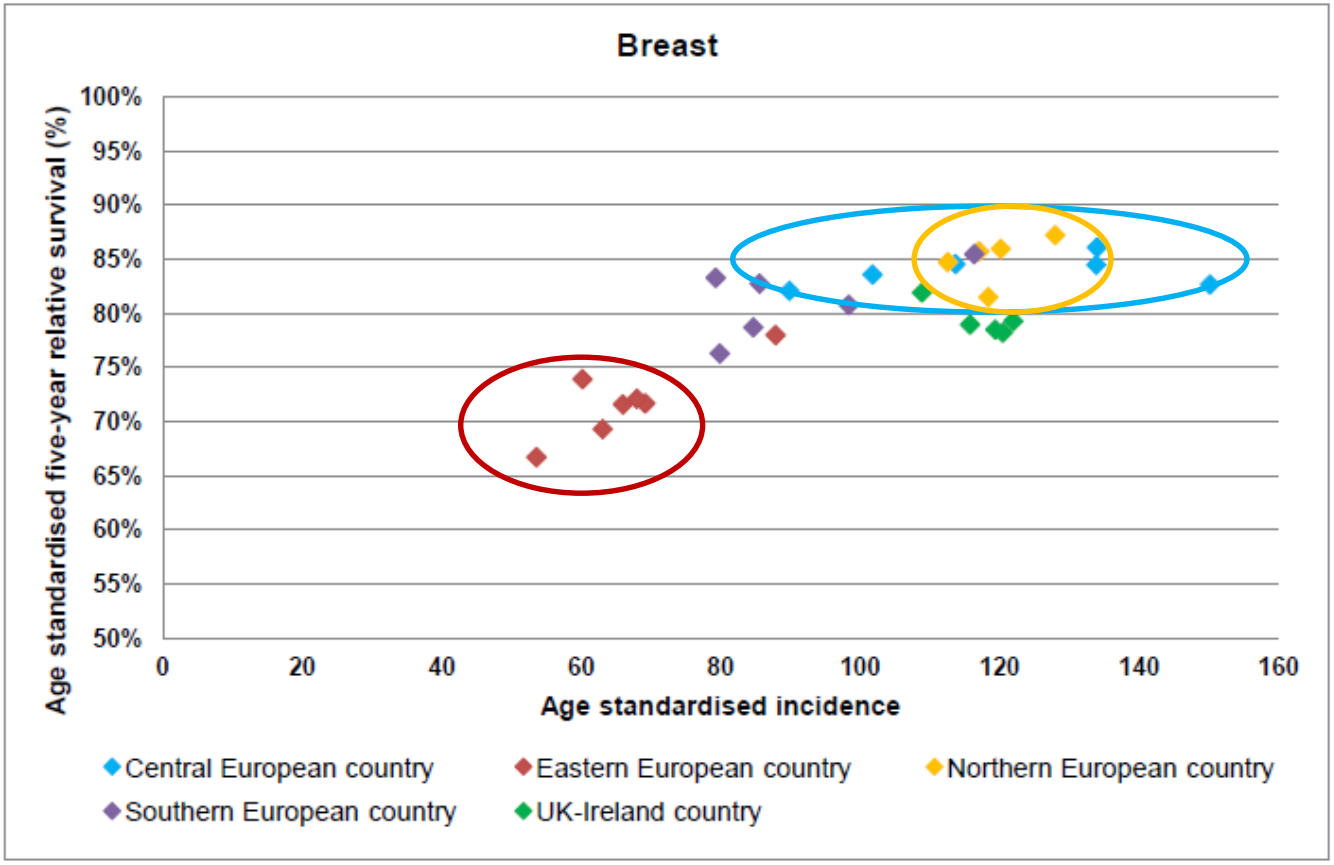
Head, Day Hospital Unit

Cancer Institute Ion Chiricuţă

Cluj-Napoca, Romania

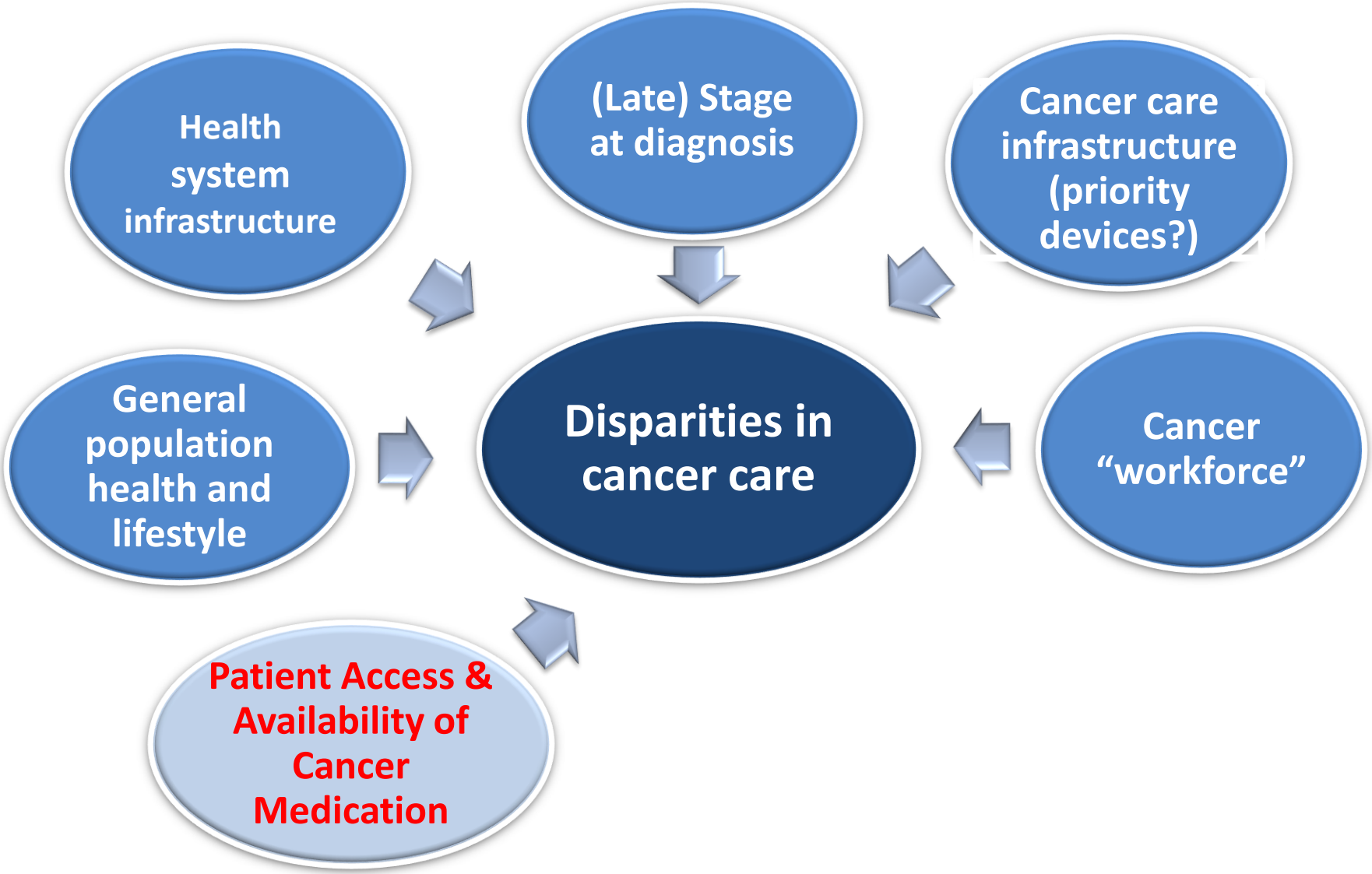
Disparities in cancer outcomes (survival) across Europe

Figures 2: Age-standardised incidence (rates per 100,000 person-year) vs. age-standardised five-year relative survival (%) for cancers of breast (women), prostate, skin melanoma by European region. Period of diagnosis 2000-2007. Countries represented by dots.



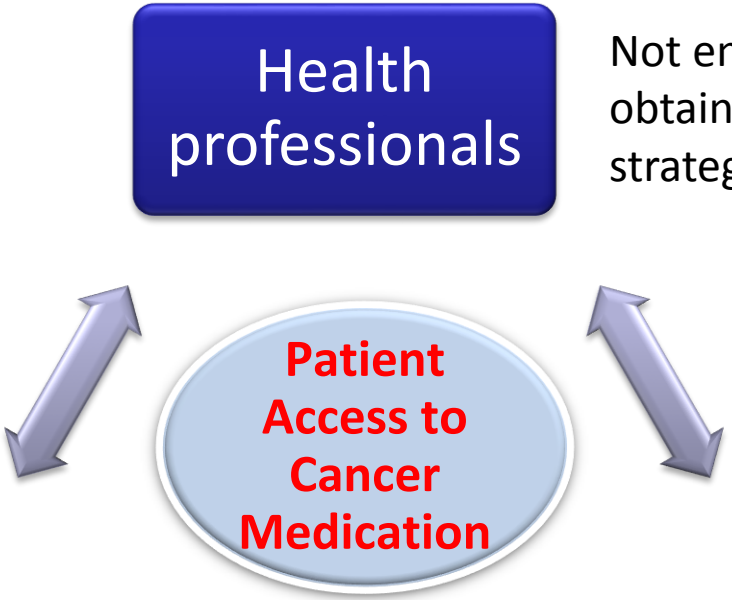
De Angelis, et al: Cancer survival in Europe 1999–2007 by country and age: EUROCARE-5 Lancet Oncol, 2013

Factors accounting for cancer outcomes disparities



ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE
European Society for Medical Oncology

Access to cancer medication: What are the obvious problems?



Not enough quality/benefit obtained with new strategies/drugs

Incoherent reimbursement strategy

Dramatically increased pricing

GOOD SCIENCE
BETTER MEDICINE
BEST PRACTICE

European Society for Medical Oncology

ESMO Anti-Neoplastic Medicines Survey

Perception survey to **map access to cancer medicines**, including WHO Essential Medicines, reporting on:

- **Approval status (yes/no) across Europe**
  - Informative for new drugs
- **Reimbursement (yes/no)**
  - Highlight differences in cancer policies
  - Residual (out of pocket) cost to patients
  - Delays in access due to special authorization
- **Actual availability**
  - Drug shortage for old drugs
  - Unavailability in the pharmacy (parallel export) for expensive drugs

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE
European Society for Medical Oncology

Coordinating & Collaborating Partners

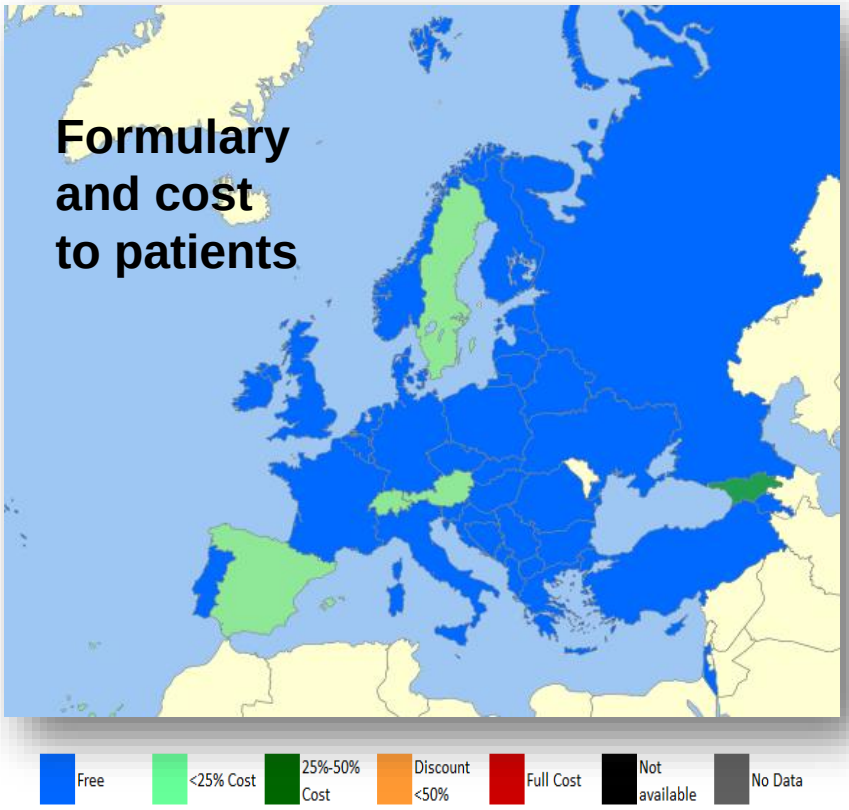
- **Coordinating Organization**
  - ESMO

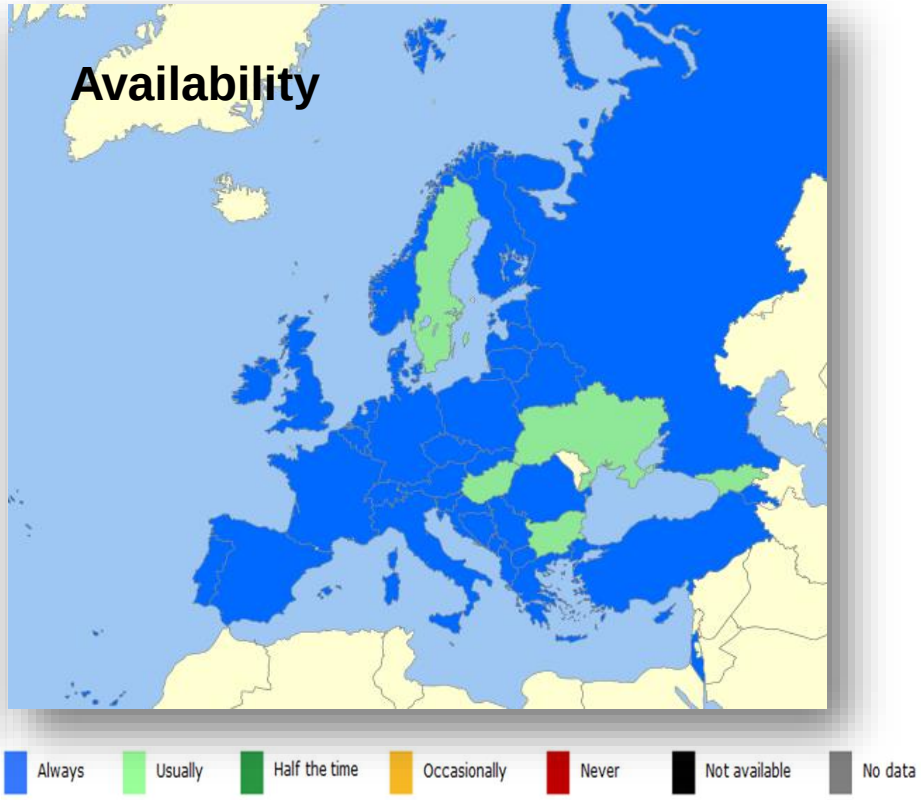
- **Collaborating Project Partners**

1. World Health Organization (WHO), Geneva, Switzerland
2. Union for International Cancer Control (UICC), Geneva, Switzerland
3. Institute of Cancer Policy, Kings College, London, UK
4. European Society of Oncology Pharmacists

- Breast Cancer
- Lung Cancer
- Colorectal Cancer
- Prostate Cancer
- Ovarian Cancer
- Sarcoma
- Pancreatic cancer
- Germ cell Tumors
- Renal cell Cancer
- GIST
- Urothelial Cancers
- Gastric and esophageal cancer
- Melanoma

Adjuvant breast cancer: : formulary inclusion and availability : TAMOXIFEN





- **Drug shortages affect several essential, old and inexpensive drugs** (tamoxifen, doxorubicin, cisplatin, 5-FU, bleomycin…)
- Not an issue of resources!

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE
European Society for Medical Oncology

WHO ESSENTIAL MEDICINES LIST 2015
Solid Tumors

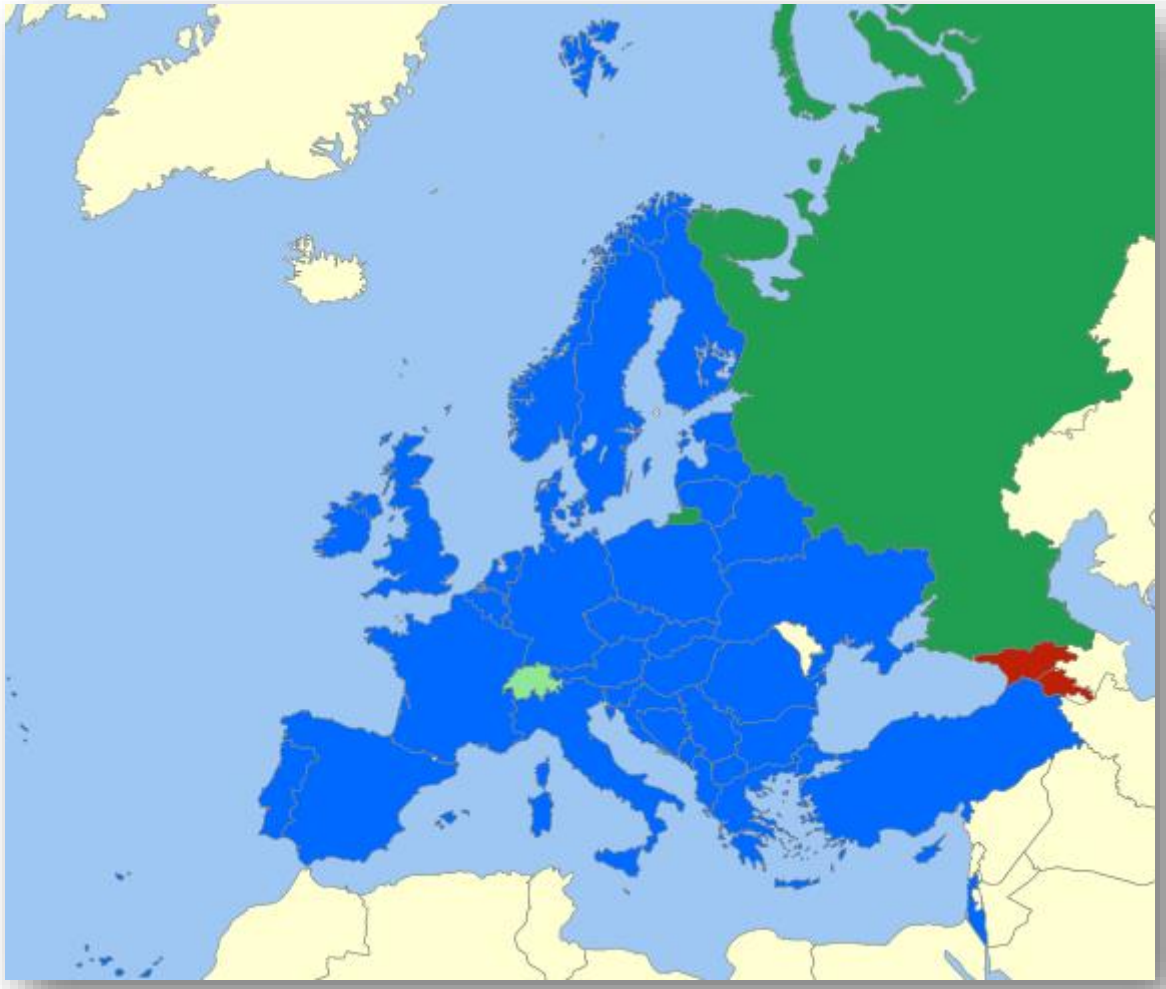
- **UICC Task Force on EML**: UICC, Dana Farber Cancer Institute, ESMO, ASCO, SIOP, US NCI, NCCN International & others
- New drugs, tumor-specific indications

Cytotoxics	Cytotoxics	Cytotoxics	Hormones
bleomycin	docetaxel	irinotecan	anastrozole
calcium folinate	doxorubicin	methotrexate	bicalutamide
capecitabine	etoposide	oxaliplatin	dexamethasone
carboplatin	fluorouracil	paclitaxel	leuprorelin
cisplatin	filgrastim	rituximab	tamoxifen
cyclophosphamide	gemcitabine	trastuzumab	
dacarbazine	Ifosfamide+mesna	vinblastine	
dactinomycin	imatinib	vincristine	
		vinorelbine	

http://www.who.int/medicines/publications/essentialmedicines/EML2015_8-May-15.pdf

ESMO
GOOD SCIENCE
BETTER MEDICINE
BEST PRACTICE
European Society for Medical Oncology

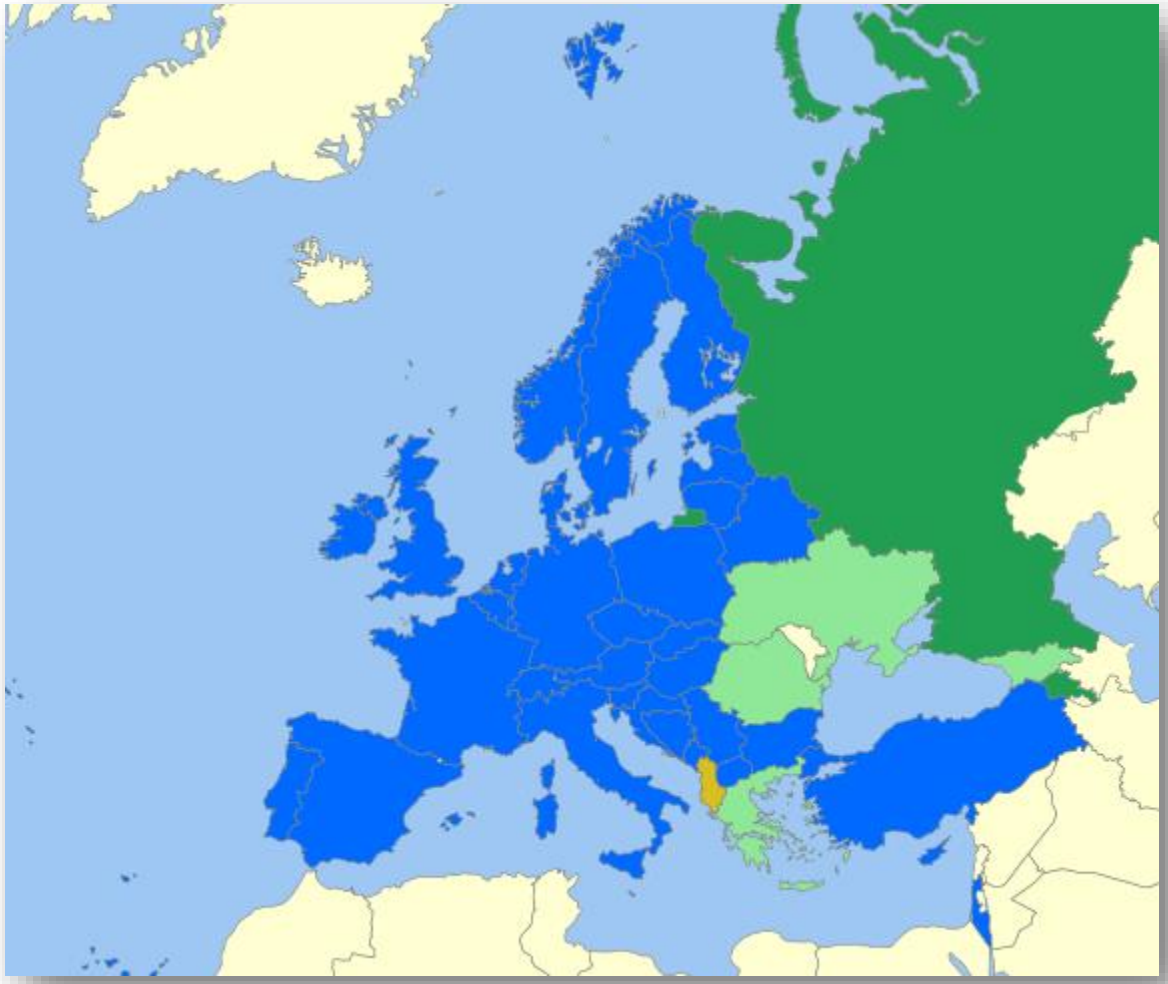
Adjuvant breast cancer: formulary inclusion and cost to patients - TRASTUZUMAB



Free
<25% Cost
25%-50% Cost
Discount <50%
Full Cost
Not available
No Data

ESMO
GOOD SCIENCE
BETTER MEDICINE
BEST PRACTICE
European Society for Medical Oncology

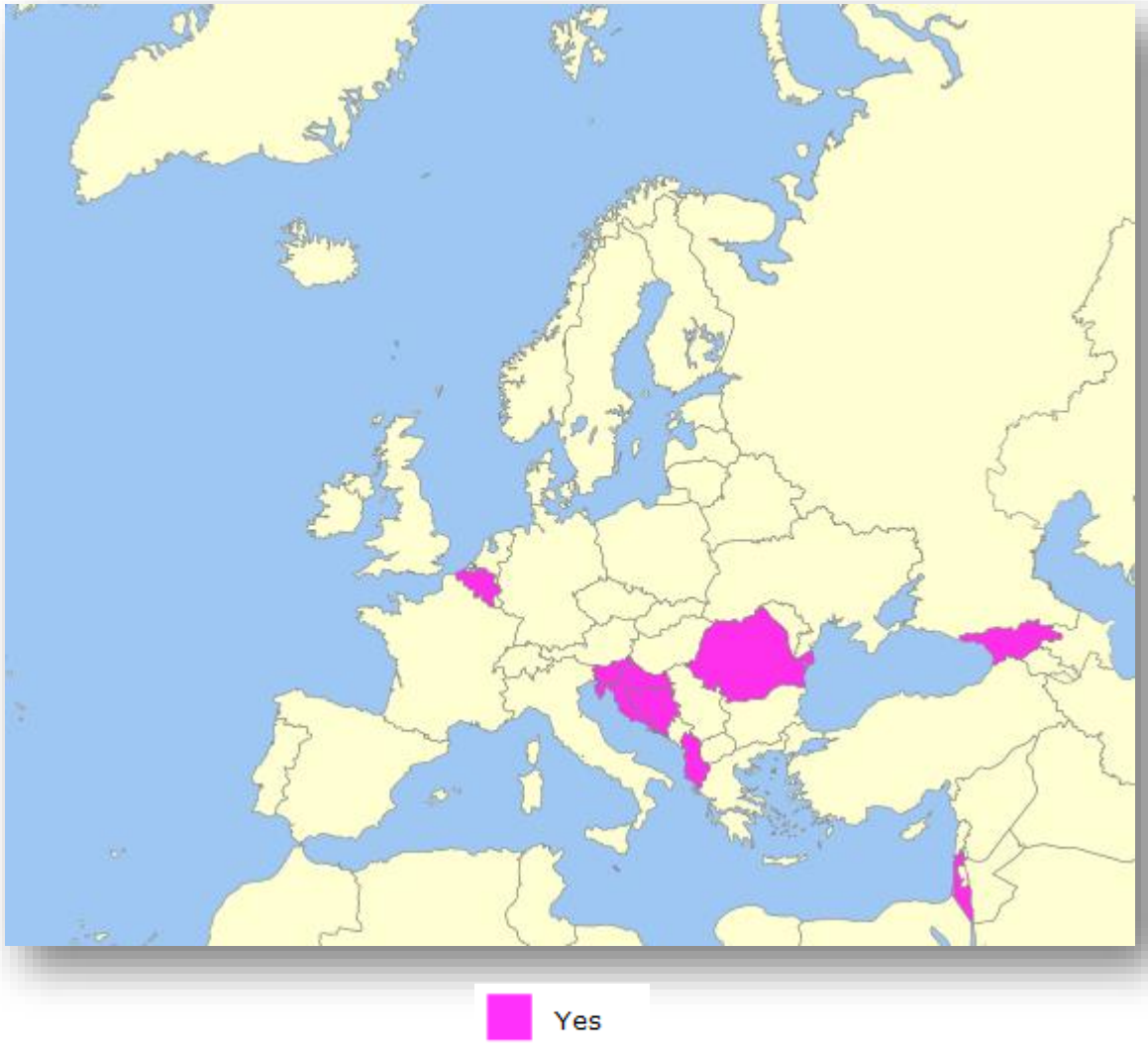
Adjuvant breast cancer: availability - TRASTUZUMAB



Always
Usually
Half the time
Occasionally
Never
Not available
No data

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE
European Society for Medical Oncology

Adjuvant breast cancer: preapproval required: TRASTUZUMAB

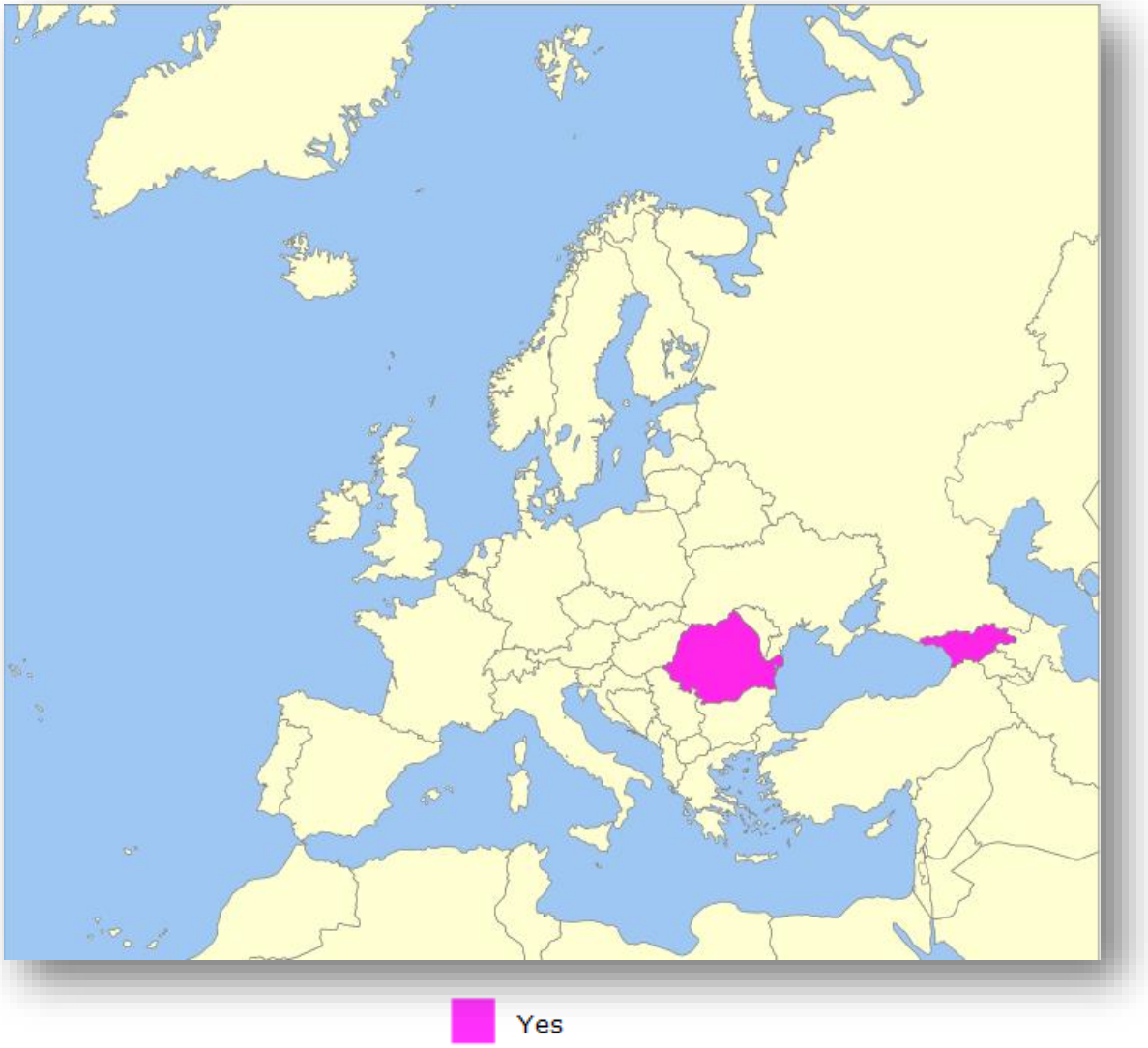


GOOD SCIENCE
BETTER MEDICINE
BEST PRACTICE

European Society for Medical Oncology

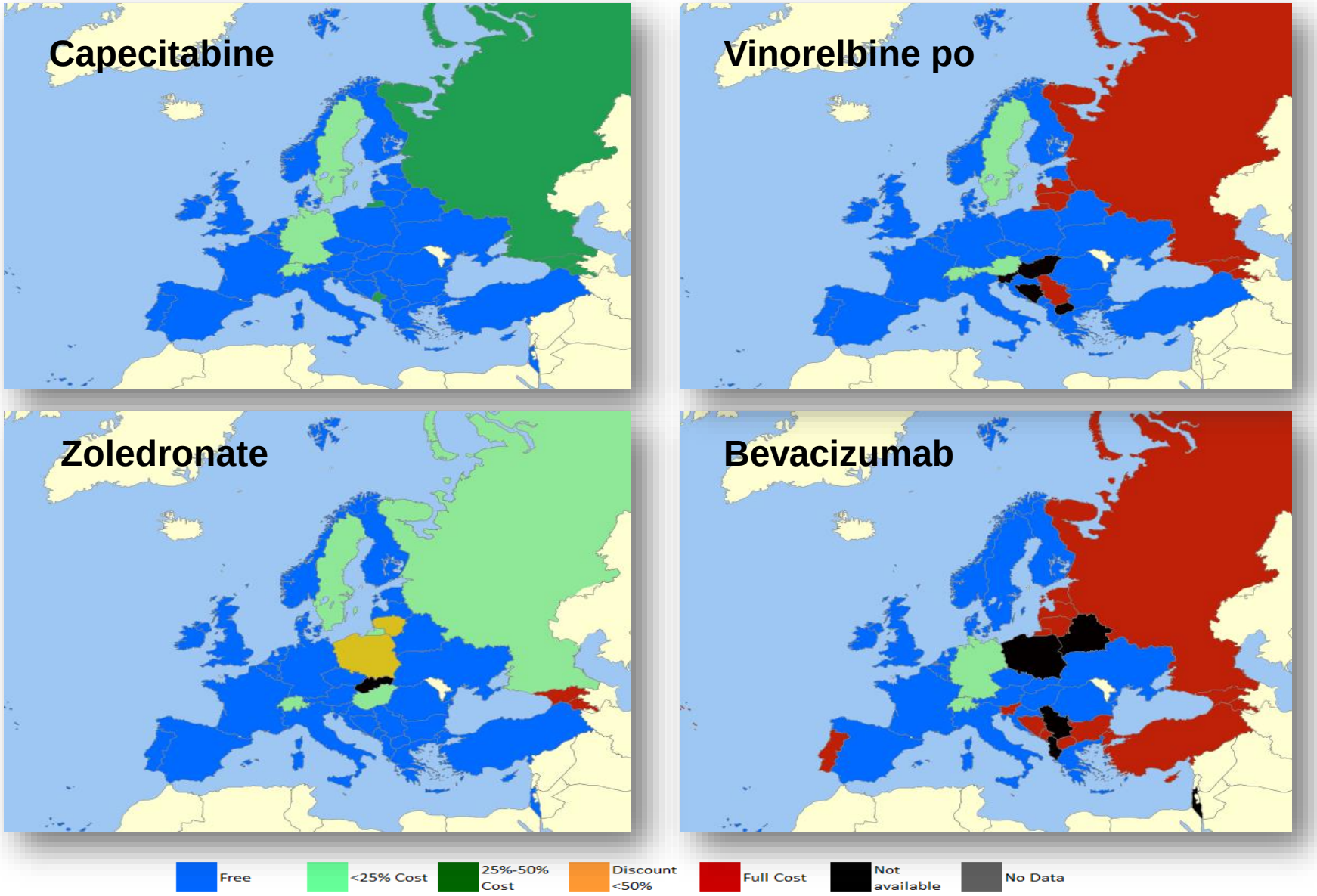
Adjuvant breast cancer

(Pre-approval causing >4 weeks delay): TRASTUZUMAB



ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE
European Society for Medical Oncology

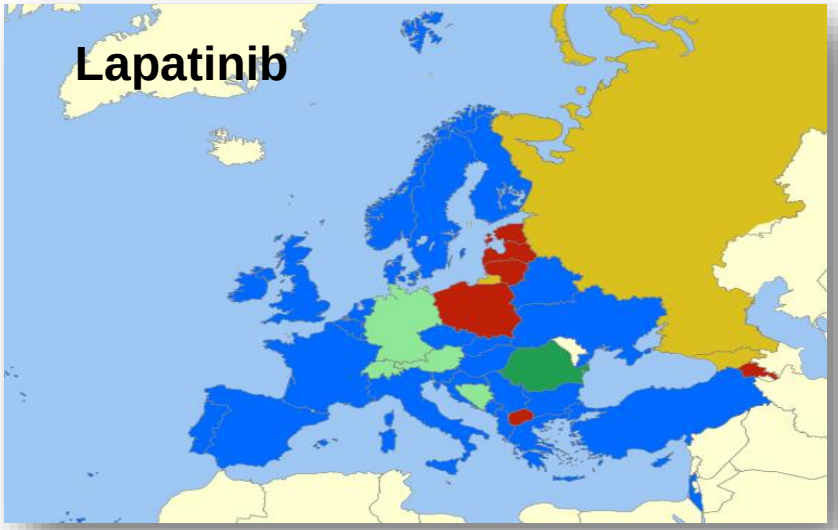
Metastatic breast cancer
(formulary inclusion & cost to patients)

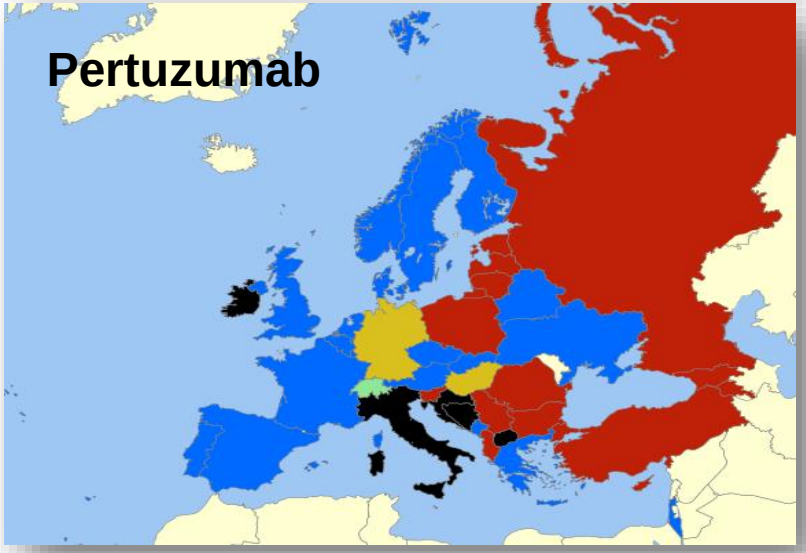


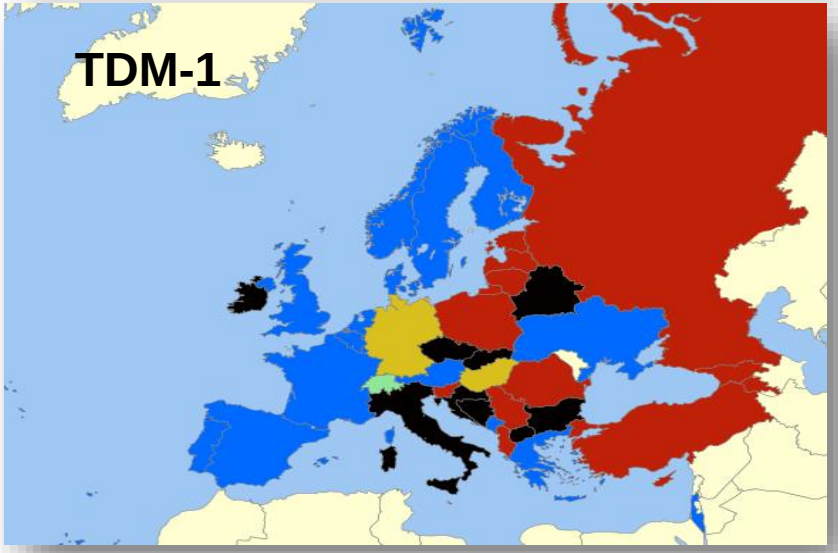
ESMO
GOOD SCIENCE
BETTER MEDICINE
BEST PRACTICE
European Society for Medical Oncology

Metastatic breast cancer

(formulary inclusion and cost to patients): Anti-Her2 therapy







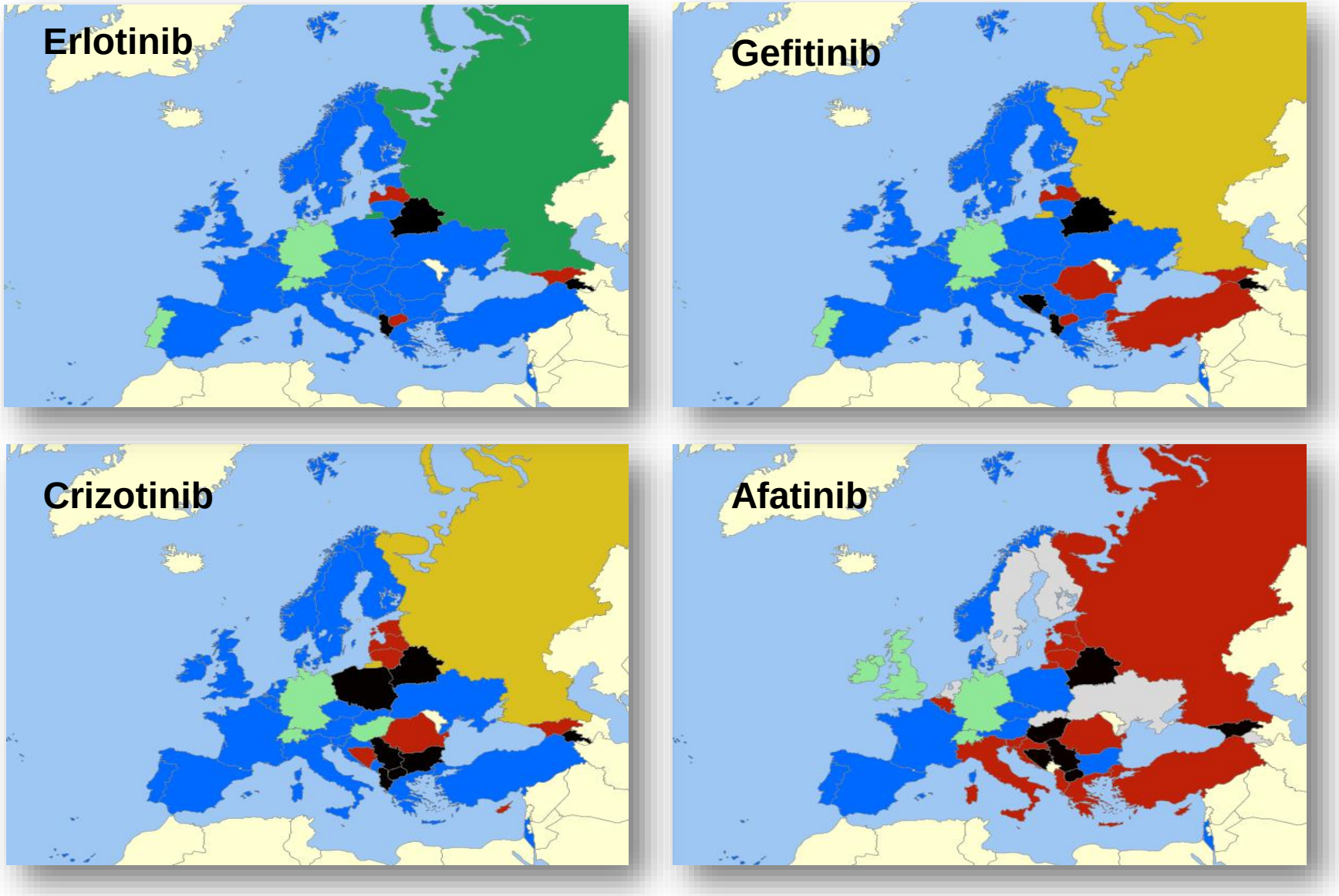
Free
<25% Cost
25%-50% Cost
Discount <50%
Full Cost
Not available
No Data

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

European Society for Medical Oncology

Lung cancer :formulary inclusion and cost to patients:

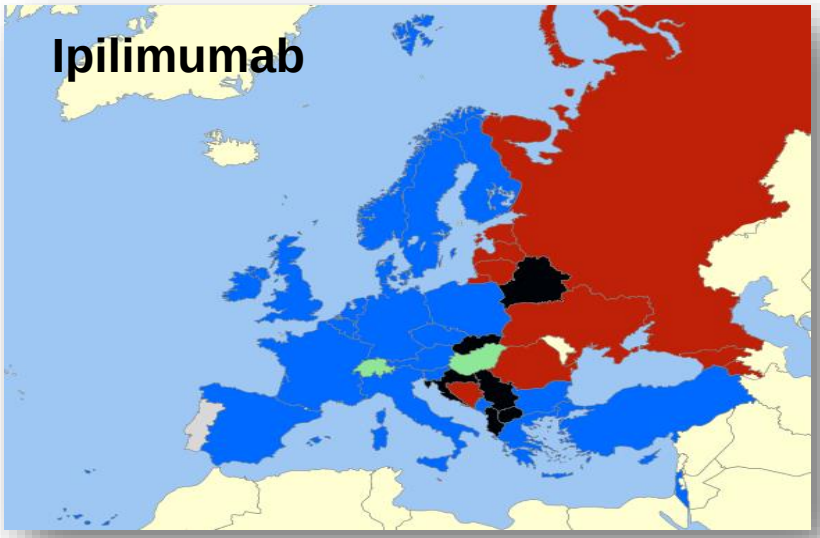
Targeted therapy

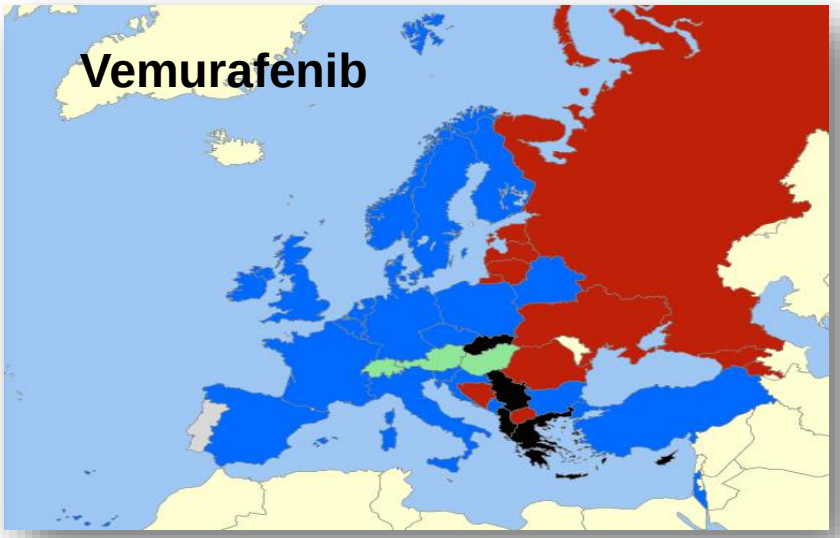


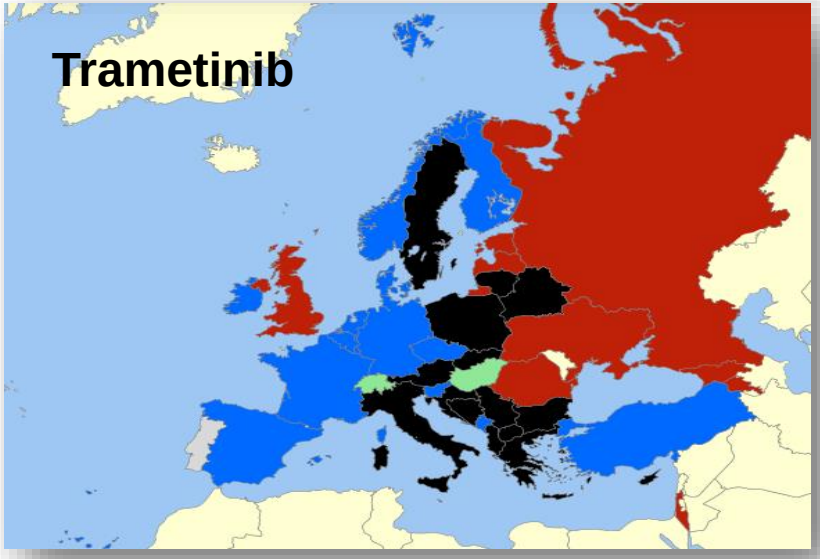
ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

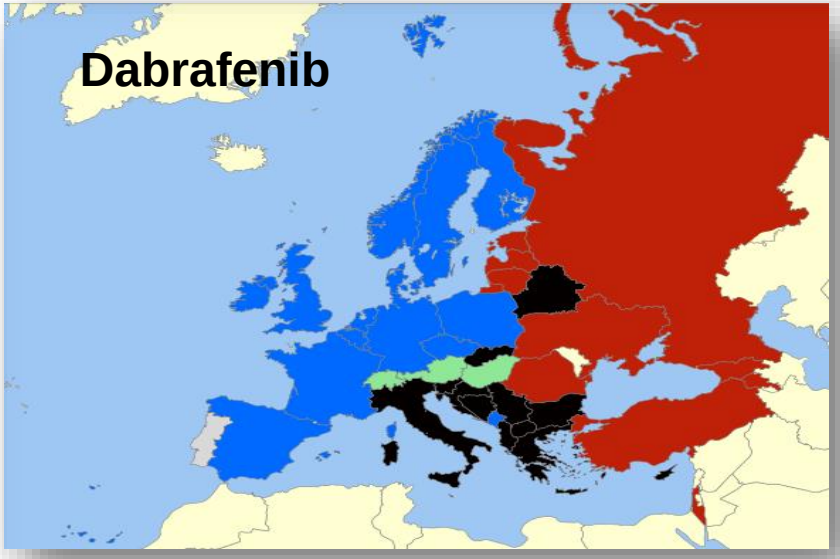
European Society for Medical Oncology

Melanoma : formulary inclusion and cost to patients







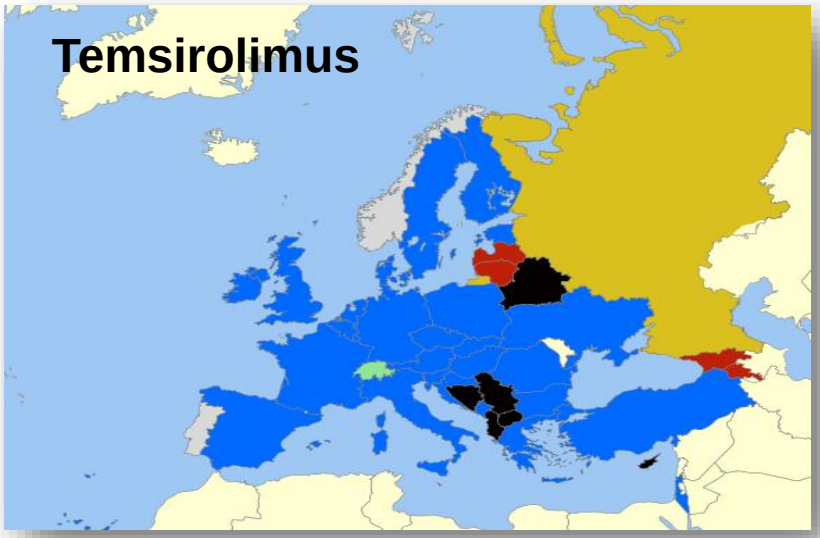


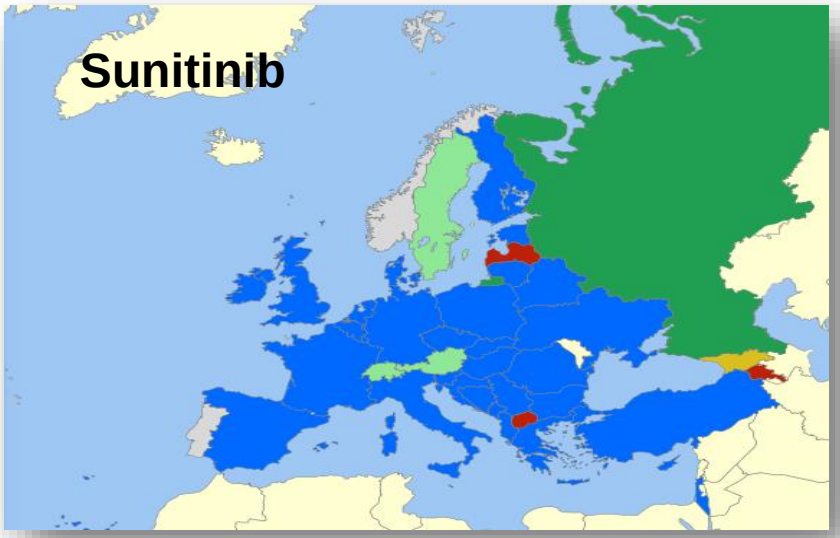
Free | <25% Cost | 25%-50% Cost | Discount <50% | Full Cost | Not available | No Data

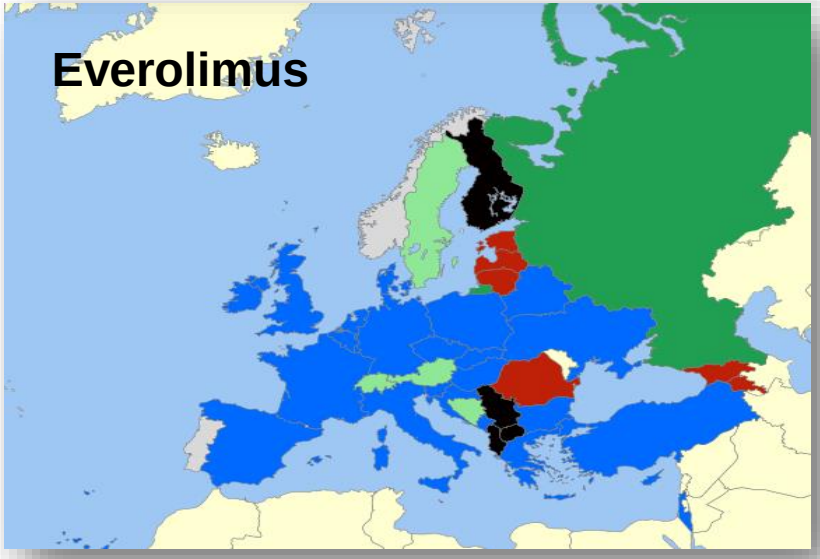
ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

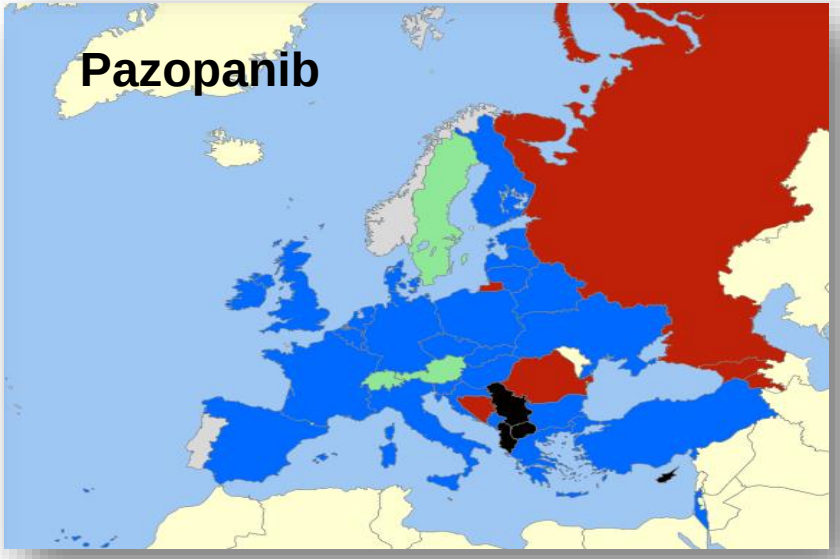
European Society for Medical Oncology

Renal Cancer : formulary inclusion and cost to patients









Free | <25% Cost | 25%-50% Cost | Discount <50% | Full Cost | Not available | No Data

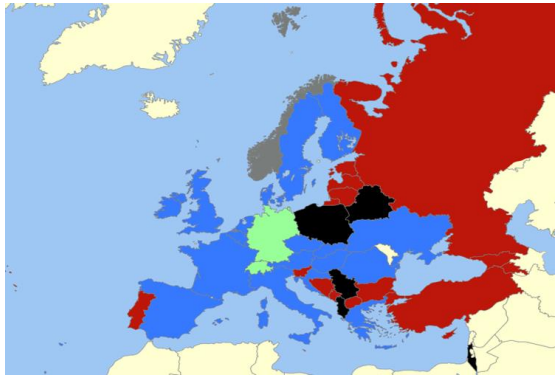
ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE
European Society for Medical Oncology

The present scenario

The pharmaceutical company requests marketing authorization
Evaluation by EMA (high degree of transparency!)
Approval by the European Commission

Time 0: the new drug is effective and safe – valid for whole EU

Europe explodes into 28 different countries…



ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE
European Society for Medical Oncology

The nightmare of the cancer medicines journey

- Many national commissions and expert committees-replicating at a lower level the same assessment done at the EMA stage
- A few HTA bodies
  - Working on few and weak data
  - With limited consultive value
- Fruitless sessions of negotiation, looking for creative/desperate strategies

The problem: *JUSTUM PRETIUM* is utopia

- The price proposed by pharmaceutical companies is
  - dramatically increasing
  - frequently **unrelated to the size of the benefit produced by the new medicine**
- Little transparency (if any) in the way the price is decided

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.

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE
European Society for Medical Oncology

Example of using MCBS data: Lung cancer, Romania

Medication	Setting	Primary outcome	ESMO-MCBS
Erlotinib vs carboplatin gemcitabine	1st line stage 3b/4 non-squamous + EGFR mutation	PFS	4
Erlotinib vs Pt-based chemo doublet	1st line stage 3b/4 non-squamous + EGFR mutation	PFS, crossover allowed	4
Gefitinib vs carboplatin + paclitaxel	1st line stage 3b/4 non-squamous + EGFR mutation	PFS, crossover allowed	4
Afatinib vs cisplatin + pemetrexed	1st line stage 3b/4 non-squamous + EGFR mutation	PFS, crossover allowed	4
Crizotinib vs chemo	1st line stage 3b/4 non-squamous + ALK mutation	PFS, crossover allowed	4
Crizotinib vs cisplatin + pemetrexed	1st line stage 3b/4 non-squamous + ALK mutation	PFS	4
Cisplatin pemetrexed vs **c**isplatin gemcitabine	1st line 3b/4 (non-squamous)	PFS	**4**
Erlotinib vs placebo	Stage 3b/4 disease	PFS	1

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE
European Society for Medical Oncology

Example of using MCBS data: Renal cancer, Romania

Medication	Setting	Primary outcome	ESM0-MCBS
Pazopanib vs sunitinib	1st line metastatic with clear cell component	PFS non inferiority	4
Temsirolimus vs interferon vs combined	1st line poor-prognosis metastatic	OS	4
Sunitinib vs interferon	1st line metastatic	PFS, crossover allowed	4
Axitinib vs sorafenib	Previously treated metastatic	PFS	3
Everolimus vs placebo	2nd or 3rd line after TKI metastatic	PFS, crossover allowed	3
Pazopanib vs placebo	2nd line locally advanced or metastatic	PFS, crossover allowed	3
Interferon +/- **bevacizumab**	1st line metastatic with clear cell	PFS	3
Interferon +/- **bevacizumab**	1st line metastatic with clear cell	PFS	1

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE
European Society for Medical Oncology

Example of using MCBS data: Melanoma , Romania

Medication	Setting	Primary outcome	ESM0-MCBS
Ipilimumab +/- glycoprotein 100 vaccine vs vaccine alone	Previously treated metastatic	OS	**4**
Vemurafenib vs dacarbazine	1st line or 2nd line after IL-2 metastatic + BRAF V600E mutation	PFS and OS	**4**
Trametinib vs dacarbazine or paclitaxel	Unresectable or metastatic + BRAF V600E mutation	PFS (crossover allowed)	**4***
Dabrafenib +/- **trametinib**	1st line unresectable or metastatic + BRAF V600E mutation	Toxicity, PFS	**4**
Dabrafenib vs dacarbazine	1st line unresectable or metastatic + BRAF V600E mutation	PFS (crossover allowed)	**4**

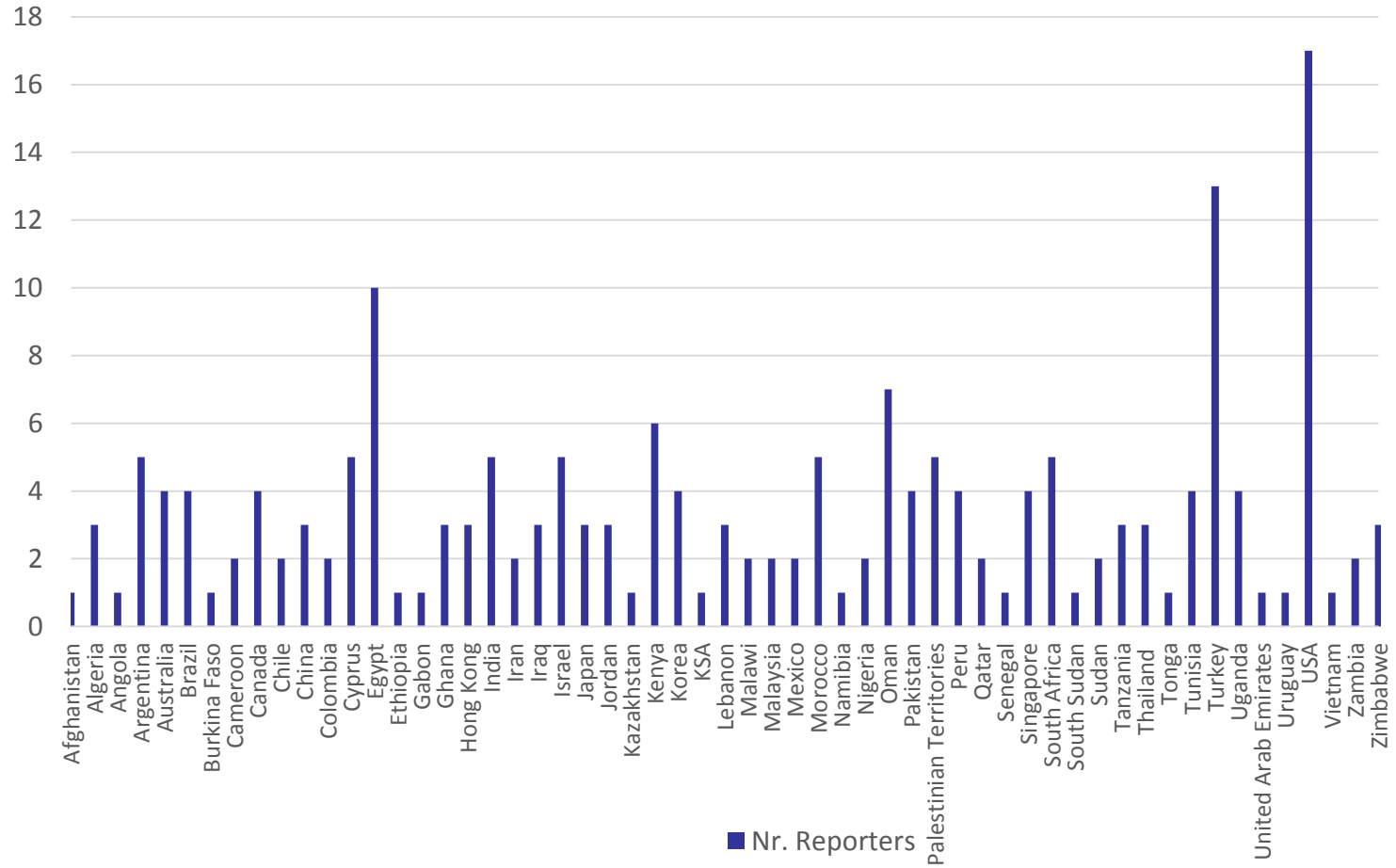
ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE
European Society for Medical Oncology

Example of using MCBS data: Breast cancer, Romania

Medication	Setting	Primary outcome	ESMO-MCBS
Chemotherapy +/- trastuzumab	(Neo)adjuvant HER-2 positive tumours	DFS	**A**
T-DM1 vs lapatinib + capecitabine	2nd line metastatic after trastuzumab failure	PFS and OS	**5**
Trastuzumab + chemotherapy +/- pertuzumab	1st line metastatic	PFS	**4**
Lapatinib +/- trastuzumab	3rd line metastatic	PFS	**4**
Capecitabine +/- lapatinib	2nd line metastatic after trastuzumab failure	PFS	**3**
Eribulin vs other chemotherapy	3rd line metastatic after anthracycline and taxane	OS	**2**
Paclitaxel +/- bevacizumab	1st line metastatic	PFS	**2**
Exemestane +/- everolimus	Metastatic after failure of aromatase inhibitor (with PFS > 6 mth)	PFS	**2**

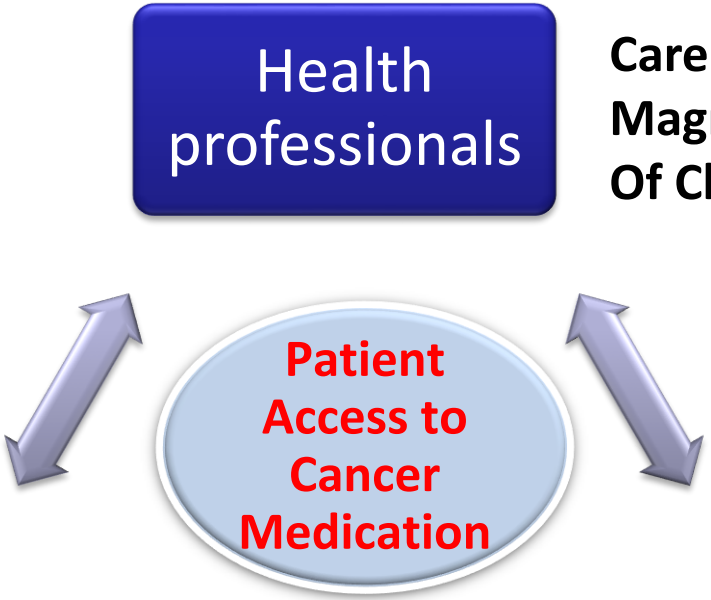
International Survey - Ongoing

ESMO Int'l Consortium Study on the Availability of Anti-Neoplastic Medicines



Collaborating Partners (international study): USA, South America, Japan, China, Korea, India, Malaysia, Thailand, Australia, New Zealand, etc.

What are the solutions to improve cancer medicine access?



Care about benefit:
Magnitude
Of Clinical Benefit Scale

Reimburse the reasonable medicines (public policy)

Justum Pretium

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE
European Society for Medical Oncology

Conclusions

- Disparities exist across Europe in access to cancer medicines
- Drug shortages affect several “essential”, old and inexpensive drugs
  - THIS SHOULD BE UNACCEPTABLE !
- Inequalities exist in availability and patient costs, especially for newer, more expensive drugs, across Europe
- The **ESMO Magnitude of Benefit Scale**, applied on the availability data (**ESMO Antineoplastic Medicines Survey)** can inform the process of prioritization access to medicines, when resources are limited