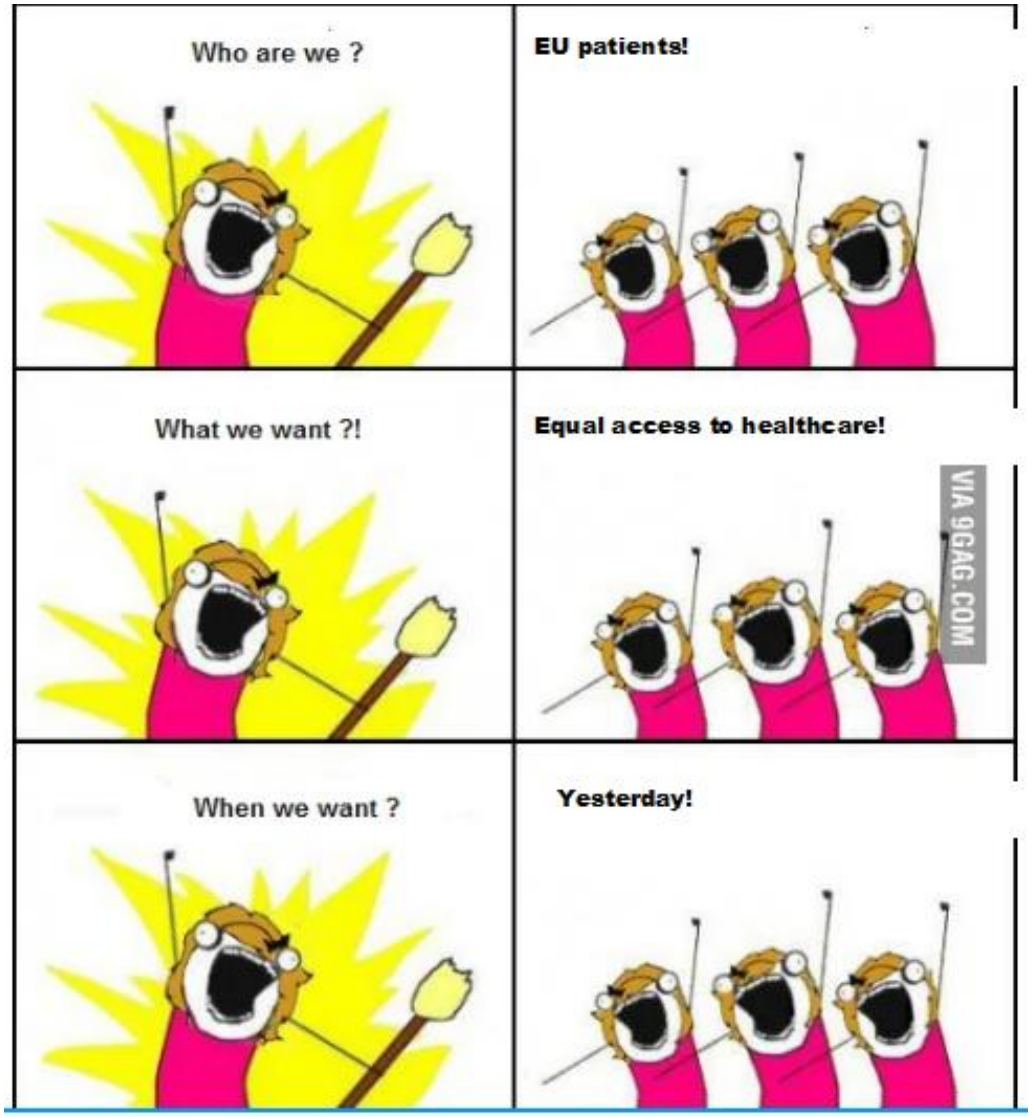
Let's talk about the elephant in the room

CECOG BREAST CANCER ACADEMY

EU patient


Who are we ?
EU patients!
What we want ?!
Equal access to healthcare!
VIA 9GAG.COM
When we want ?
Yesterday!

The clash of the titans FDA vs EMA

Table 1. FDA (Food and Drug Administration) and EMA (European Medicines Agency) new drug approvals for breast cancer (1995–2018).

eribulin	Halaven	**2010**	-	**FT**	-	**PR**	-	**2011**	-	-	-	-
pertuzumab	Perjeta	**2012**	-	-	-	**PR**	-	**2013**	-	-	-	-
everolimus	Afinitor	**2012**	-	-	-	-	-	**2012**	-	-	-	-
ado-trastuzumab emt.	Kadcyla	**2013**	-	**FT**	-	**PR**	-	**2013**	-	-	-	-
palbociclib	Ibrance	**2015**	**AA(+)**	-	**BT**	**PR**	-	**2016**	-	-	-	-
ribociclib	Kisqali	**2017**	-	-	**BT**	**PR**	-	**2017**	-	-	-	-
neratinib	Nerlynx	**2017**	-	-	-	-	-	**2018**	-	-	-	-
abemaciclib	Verzenio	**2017**	-	**FT**	**BT**	**PR**	-	**2018**	-	-	-	-
olaparib	Lynparza	**2018**	-	-	-	**PR**	-	**2019**	-	-	-	-
talazoparib	Talzenna	**2018**	-	-	-	**PR**	-	**2019**	-	-	-	-
TOTAL	**29**	**25**	**3**	**6**	**3**	**15**	**4**	**21**	**2**	**0**	**0**	**0**

Source: https://www.researchgate.net/publication/339386193_FDA_and_EMA_Approvals_of_New_Breast_Cancer_Drugs-A_Comparative_Regulatory_Analysis

BREAST CANCER ACADEMY

The clash of the titans FDA vs EMA

Table 1. FDA (Food and Drug Administration) and EMA (European Medicines Agency) new drug approvals for breast cancer (1995–2018).

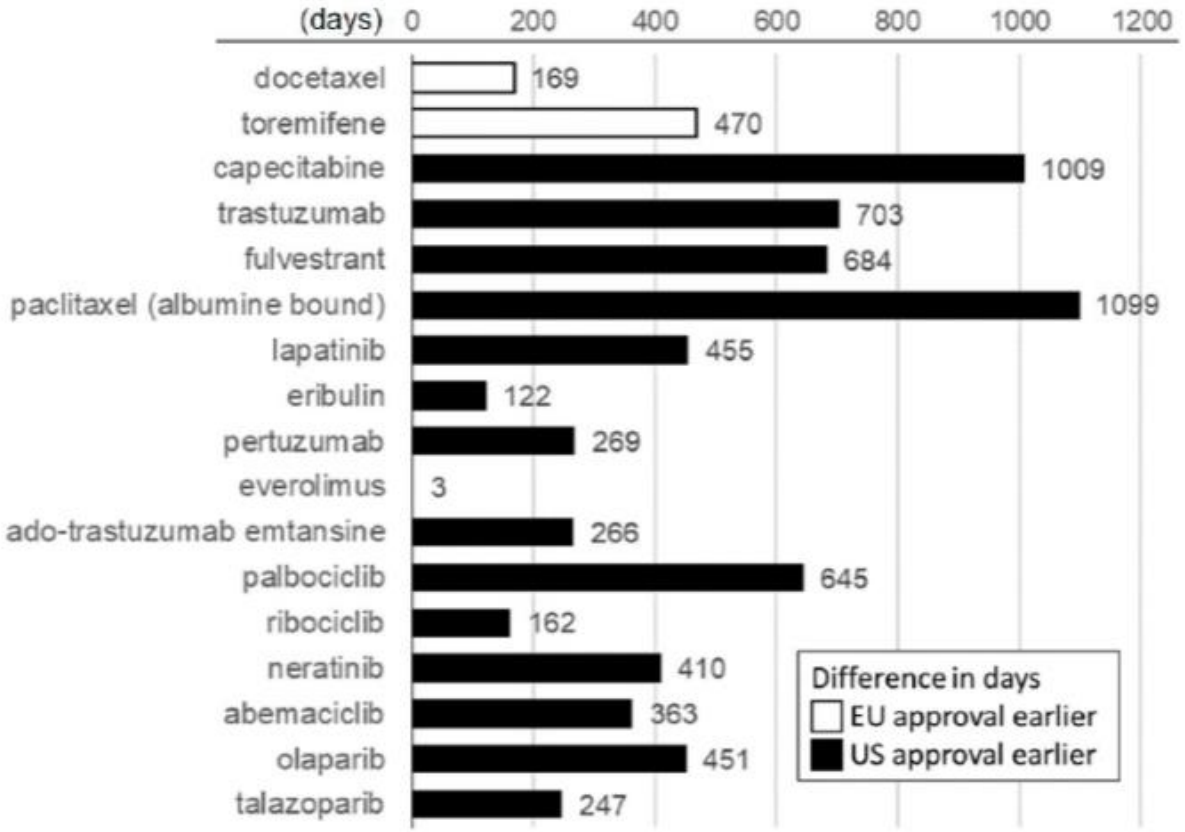
Generic Name	Brand Name	FDA Approval & Regulatory Designations						EMA Approval & Regulatory Designations				
		Year	Accelerated Approval (AA)	Fast Track (FT)	Breakthrough Therapy (BT)	Priority Review (PR)	Orphan Drug	Year	CMA/ExC	PRIME	Accelerated Assessment	Orphan Drug
anastrozole	Arimidex	1995	-	-	-	-	-	pre-EMA	n/a	n/a	n/a	n/a
goserelin	Zoladex	1995	-	-	-	-	-	pre-EMA	n/a	n/a	n/a	n/a
letrozole	Femara	1997	-	-	-	-	-	pre-EMA	n/a	n/a	n/a	n/a
epirubicin	Ellence	1999	-	-	-	PR	Orph	pre-EMA	n/a	n/a	n/a	n/a
exemestane	Aromasin	1999	-	-	-	-	Orph	pre-EMA	n/a	n/a	n/a	n/a
gemcitabine	Gemzar	2004	-	-	-	PR	-	pre-EMA	n/a	n/a	n/a	n/a
raloxifene	Evista	2007	-	-	-	-	Orph	not BC	n/a	n/a	n/a	n/a
ixabepilone	Ixempra	2007	-	-	-	PR	-	none	n/a	n/a	n/a	n/a
doxorubicin non-PEG	Myocet	none	n/a	n/a	n/a	n/a	n/a	2000	-	-	-	-
ibandronic acid	Bondronat	not BC	n/a	n/a	n/a	n/a	n/a	2003	-	-	-	-
doxorubicin PEG	Doxil	not BC	n/a	n/a	n/a	n/a	n/a	2003	-	-	-	-
docetaxel	Taxotere	1996	AA(+)	-	-	PR	-	1995	ExC(+)	-	-	-
toremifene	Fareston	1997	-	-	-	-	Orph	1996	-	-	-	-
capecitabine	Xeloda	1998	AA(+)	-	-	PR	-	2001	-	-	-	-
trastuzumab	Herceptin	1998	-	FT	-	PR	-	2000	-	-	-	-
fulvestrant	Faslodex	2002	-	-	-	-	-	2004	-	-	-	-
paclitaxel (alb. bound)	Abraxane	2005	-	FT	-	-	-	2008	-	-	-	-
lapatinib	Tykerb	2007	-	FT	-	PR	-	2008	CMA(+)	-	-	-
bevacizumab	Avastin	(2008)	AA(−)	-	-	(PR)	-	2007	-	-	-	-

Source: https://www.researchgate.net/publication/339386193_FDA_and_EMA_Approvals_of_New_Breast_Cancer_Drugs-A_Comparative_Regulatory_Analysis

BREAST CANCER ACADEMY

The clash of the titans FDA vs EMA

Figure 1. "Approval lag" between the U.S.A. and Europe, based on the relative timing of first approval for breast cancer.

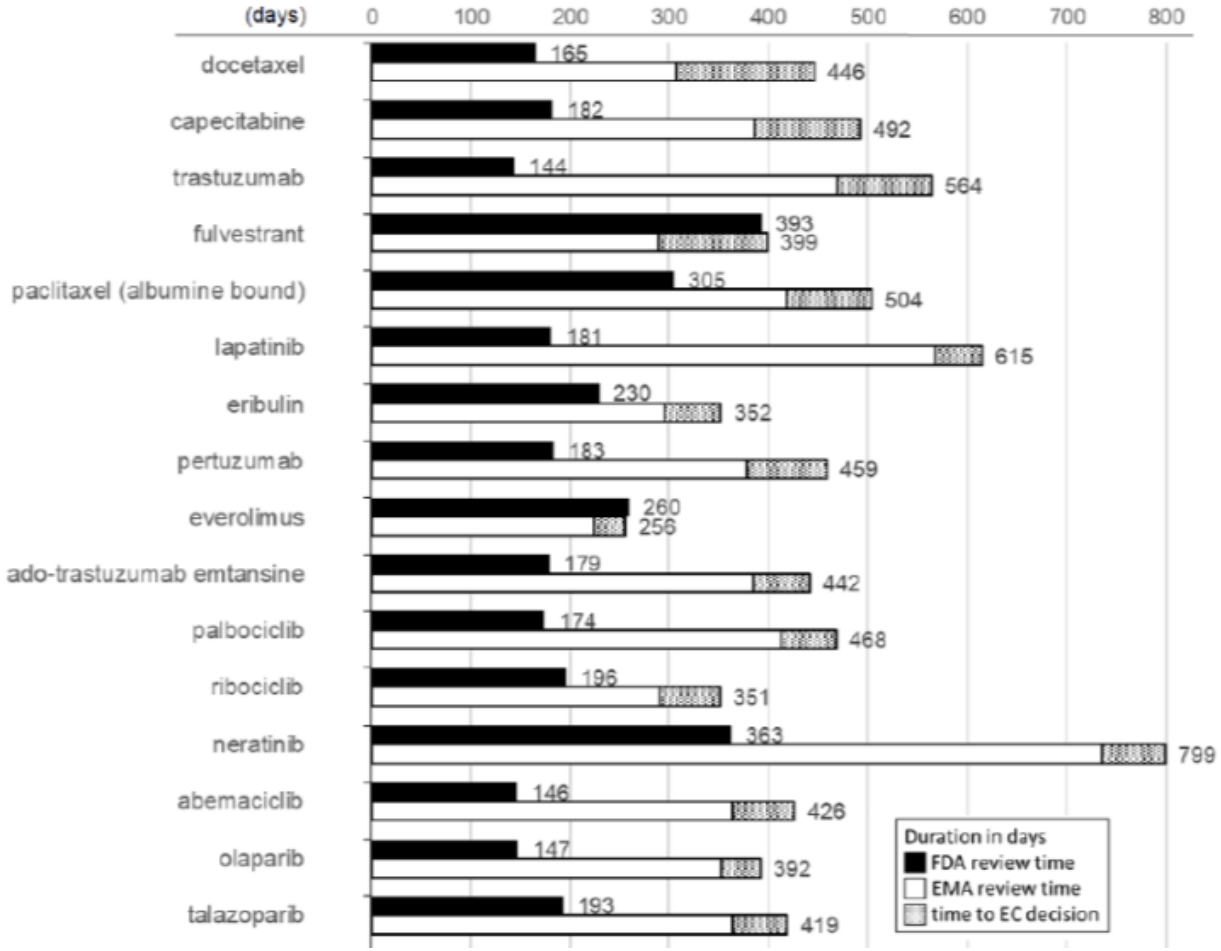


Source: https://www.researchgate.net/publication/339386193_FDA_and_EMA_Approvals_of_New_Breast_Cancer_Drugs-A_Comparative_Regulatory_Analysis

BREAST CANCER ACADEMY

The clash of the titans FDA vs EMA

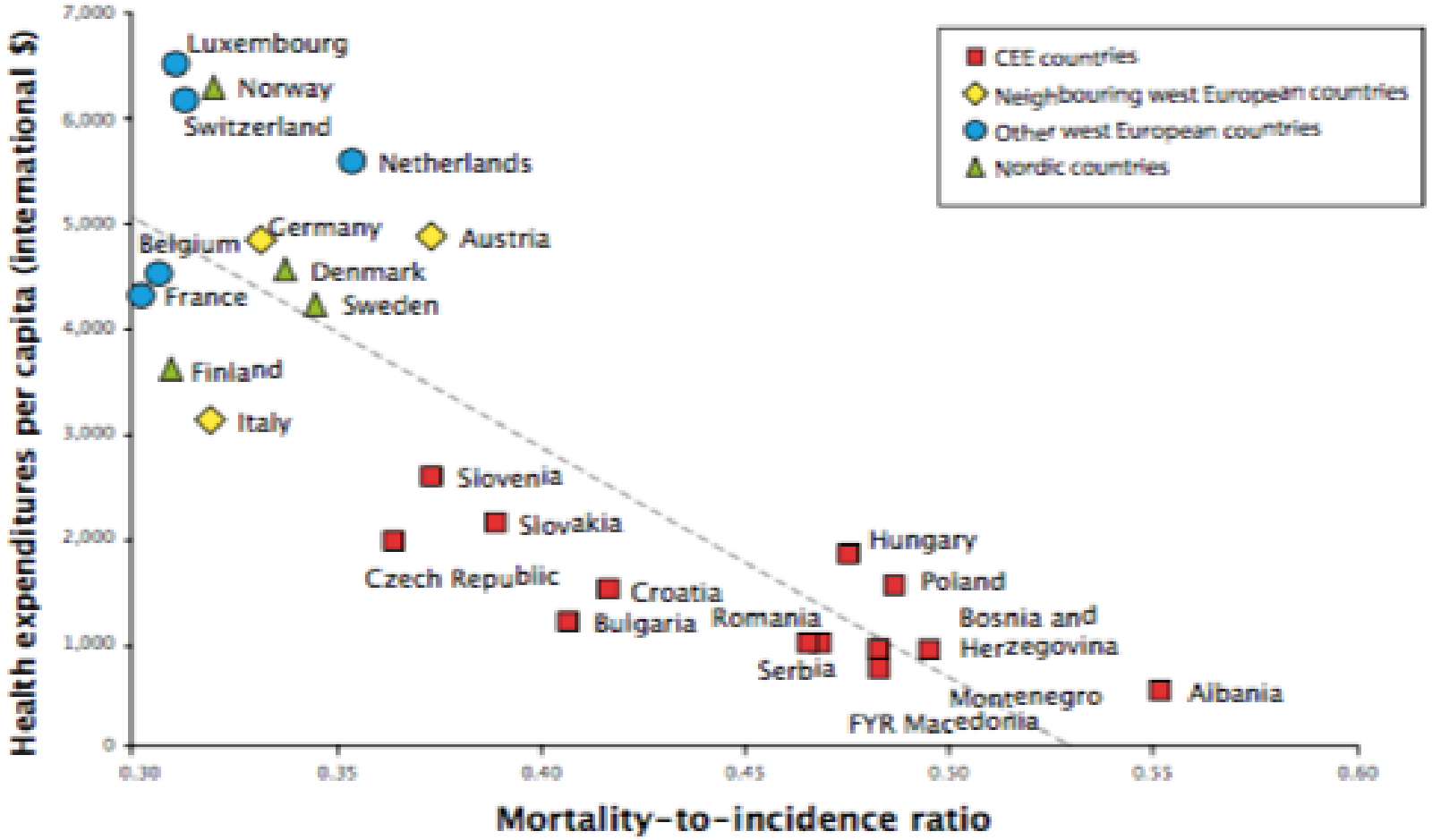
Figure 2. Duration of approval process in the U.S.A. vs. Europe, based on time from NDA (New Drug Application) or MAA (Marketing Authorization Application) submission to approval.



Source: https://www.researchgate.net/publication/339386193_FDA_and_EMA_Approvals_of_New_Breast_Cancer_Drugs-A_Comparative_Regulatory_Analysis

BREAST CANCER ACADEMY

Lets talk about the elephant in the room



Sources: https://cancerworld.net/systems-services/bad-for-budgets-but-also-for-patients-challenging-the-in-patient-culture-of-central-and-eastern-europe/

BREAST CANCER ACADEMY

Is it white?

- Shortage of essential oncology drugs

WHO: Shortages of essential drugs are becoming increasingly frequent globally, burdening health systems with additional costs and posing risks to the health of patients who fail to receive the medicines they need.

Our role? Advocating for equal access to quality treatment and for cancer prevention

Country	Extent of the shortages
Germany	27 (2017)
France	35 (2017)
Ireland	Over 200 (2017)
Spain	244 (2017)
Romania	Over 500 (2017)
Slovenia	60% of hospital pharmacists said they experience shortages on a weekly basis (2014)

Source: National Medicines Agencies' websites # (last checked 15 May 2017)

Is it white?

Shortage of essential oncology drugs

Figure 3. Countries in Europe where there was a list of medicines shortages as of 2017

Source: EIU research; Pauwels et al. 2014[20]

Sursa: http://www.eiu.com/graphics/marketing/pdf/ESMO-Cancer-medicines-shortages.pdf

BREAST CANCER ACADEMY

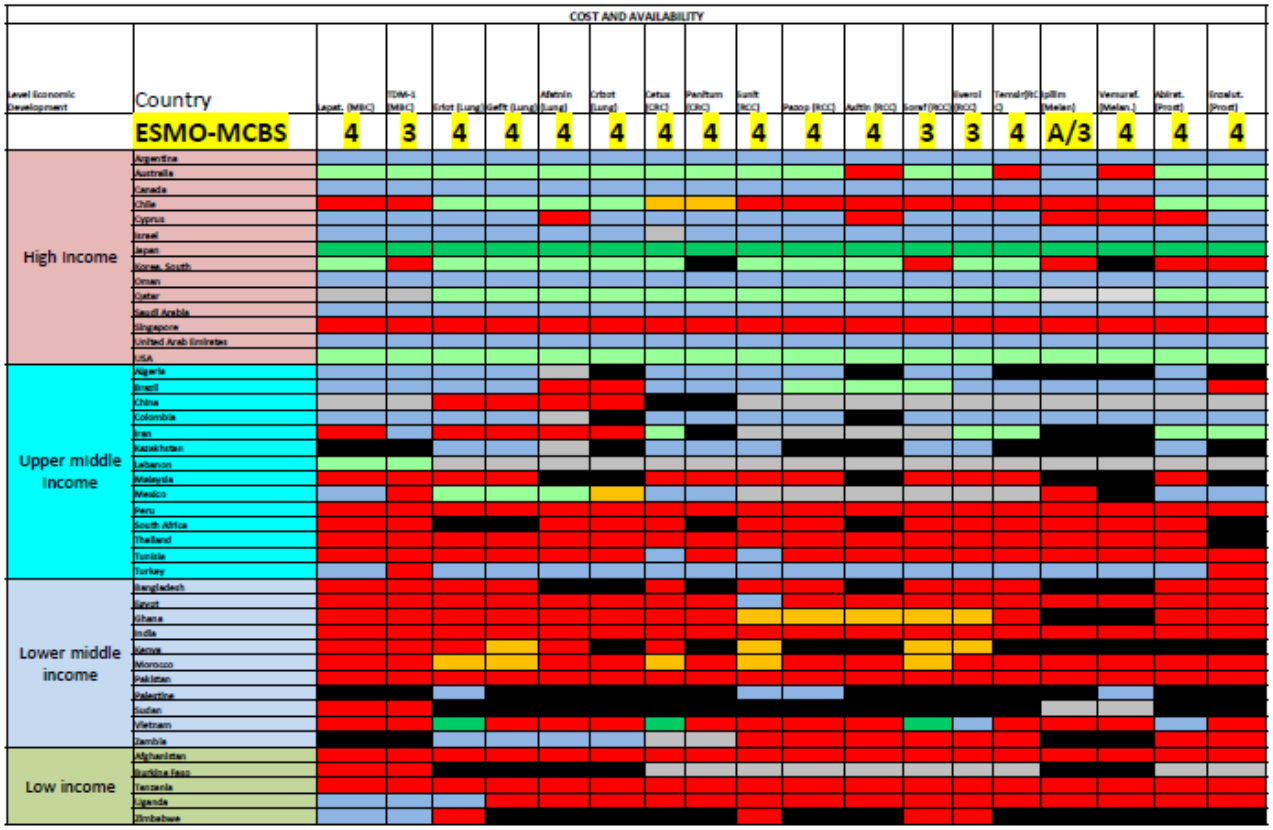
Is it white?

Shortage of essential oncology drugs

NEW CANCER MEDICATIONS WITH AN ESMO-MAGNITUDE OF CLINICAL BENEFIT SCALE SCORE >3: COUNTRIES OUTSIDE EUROPE

AVAILABILITY

	Always
	Usually
	Half the time
	Occasionally
	Never
	Not available
	Missing data



Sursa: https://www.researchgate.net/figure/A-Anticancer-medications-on-World-Health-Organization-Essential-Medicines-List-2015_fig1_305647141

BREAST CANCER ACADEMY

Is it white?

EUROPEAN PARLIAMENT LAUNCH OF THE ECONOMIST INTELLIGENCE UNIT–ESMO REPORT ON HOW TO PREVENT AND MANAGE CANCER MEDICINES SHORTAGES IN EUROPE

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Is it white?

RECOMMENDATIONS

1. **Introduce legislation** for early notification requirements for medicines shortages.
2. **Establish European strategic plans** for medicines shortages.
3. **Introduce incentives for production infrastructure improvements** including financial incentives to address the economic causes of manufacturing issues. Incentives for suppliers to remain in these markets should also be considered.
4. **Develop catalogues of shortages** based on a common minimum set of data requirements, including a common EU definition of medicines shortages.
5. **Develop national essential medicines lists** based on the World Health Organization's Model List of Essential Medicines.
6. **Establish procurement models** designed to prevent medicines shortages, including tender-cycle harmonisation.

KEY STEPS

1. Develop an EU-wide study on the issue of medicines shortages and their overarching impact on the European Union through independent EU advisory bodies on social and economic affairs.
2. Work towards creating a common definition of medicines shortages in the European Union.
3. Position inexpensive essential medicines shortages as a key political priority for the European Union's 2019-2024 legislature.

BREAST CANCER ACADEMY

Is it red?

Table 10: Sales of cancer medicines by cancer type in Europe, 2018

Cancer type	Chemical name	Sales (million €)	Year of EMA approval
Breast cancer	trastuzumab	1803.2	2000
	palbociclib	854.3	2016
	pertuzumab	847.9	2013
	trastuzumab emtansine	334.9	2013
	fulvestrant	278.0	2004
	docetaxel	246.0	1995
	eribulin	91.6	2011
	ribociclib	60.6	2017
	lapatinib	47.0	2008
	abemaciclib	0.5	2018
	toremifene	0.1	1996

Source: IHE Report 2019

BREAST CANCER ACADEMY

Is it red?

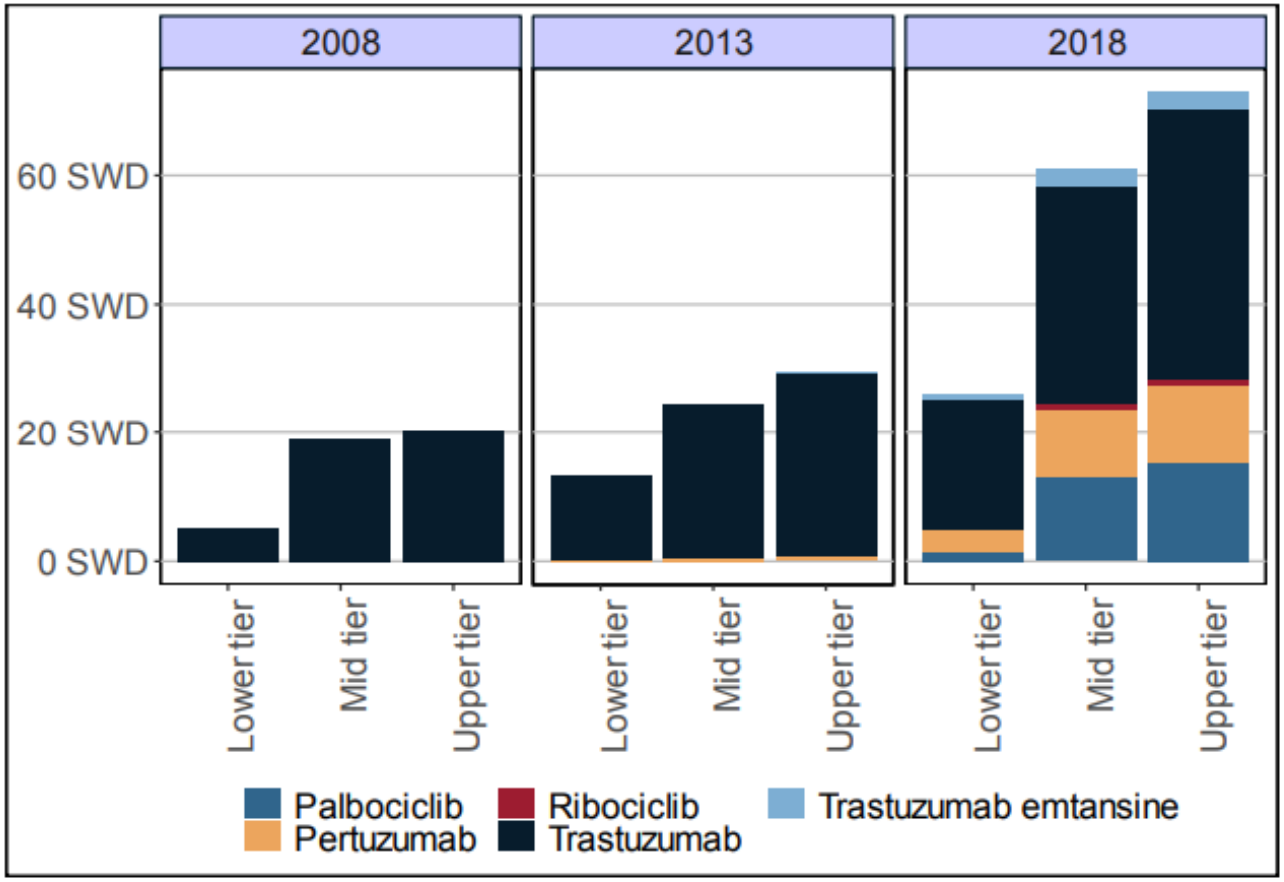

Figure 56: Uptake of medicines in breast cancer expressed as sales in SWD per case – groups of countries

Source: IHE Report 2019

BREAST CANCER ACADEMY

Is it red?

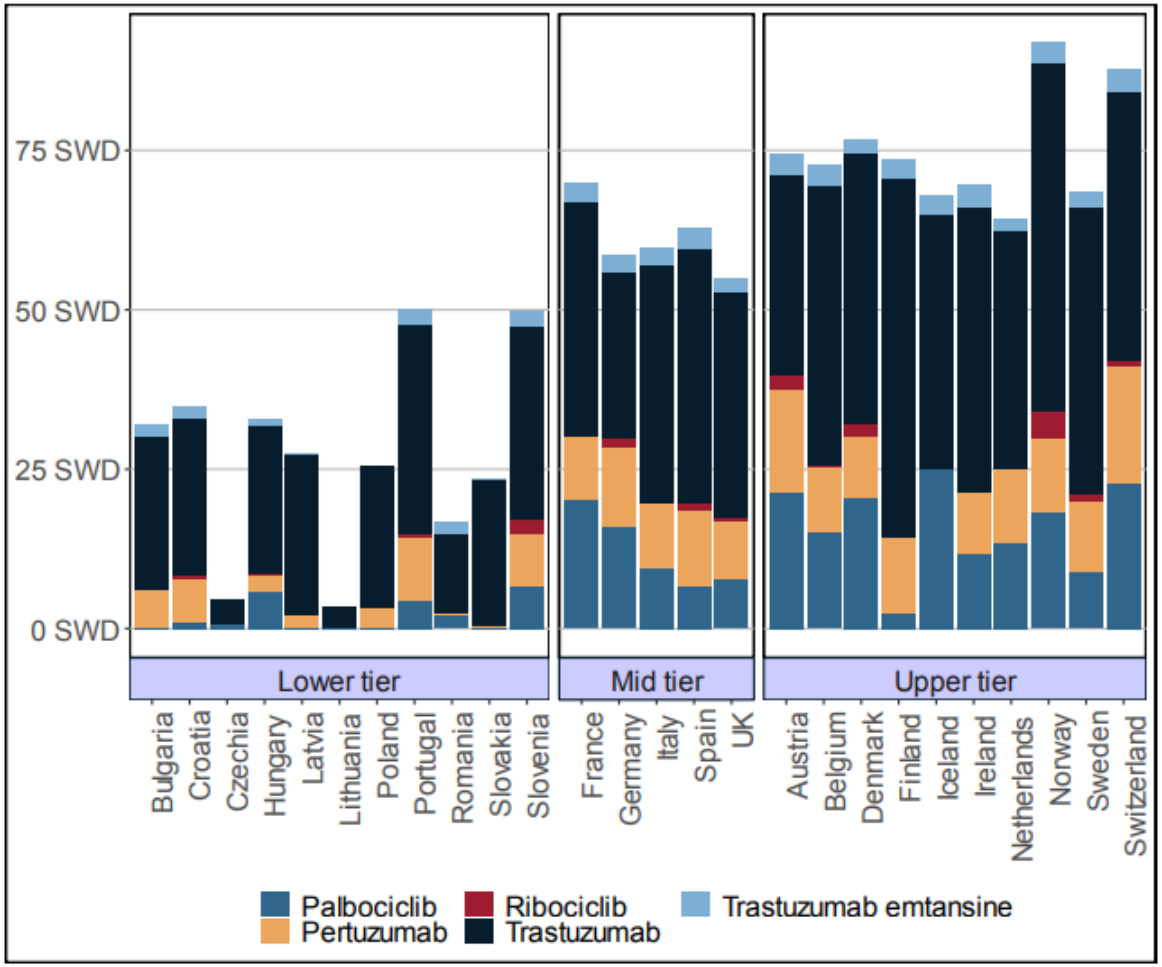

Figure 57: Uptake of medicines in breast cancer expressed as sales in SWD per case, 2018

Source: IHE Report 2019

BREAST CANCER ACADEMY

Red! Red! Red! Romania case

- **Tyverb (DCI LAPATINIBUM)**

Authorization (centralized procedure) Decision of the European Medicines Agency - June 2008

National HTA evaluation

a) Submission of the medical technology evaluation file for all 3 lines - August 2014
    a) Publication of ETM report with positive decision - "in combination with an aromatase inhibitor for women with metastatic disease with hormonal receptors present, postmenopausal, for whom chemotherapy is not currently indicated" - April 2015
    b) Publication of the report of ETM with negative decision - "in combination with capecitabine, in patients with advanced or metastatic breast cancer, progressive following previous therapies, which must have included anthracyclines and taxanes and trastuzumab therapy, in metastatic context" - April 2015
    c) Publication of the report of ETM with negative decision - "in combination with trastuzumab, in patients with metastatic disease with hormone receptors absent, progressive following previous therapies with trastuzumab in combination with chemotherapy" - April 2015

    * Publication of the protocol - December 2016

BREAST CANCER ACADEMY

Red! Red! Red! Romania case

Submission of the medical technology evaluation file for line 1 - June 2017

a. Publication of ETM report with positive decision - "in combination with capecitabine, in patients with advanced or metastatic breast neoplasm, progressively following previous therapies, which should have included anthracyclines and taxanes and trastuzumab therapy, in metastatic context" - July 2017

* Update of the protocol - February 2018

Conclusion: Tyverb is currently compensated in Romania for 1st and 3rd therapeutic lines.

BREAST CANCER ACADEMY

Red! Red! Red! Romania case

- **Kisqali (DCI RIBOCICLIBUM)**

Authorization (centralized procedure)

Decision of the European Medicines Agency - August 2017

National HTA evaluation

a) Submission of the medical technology evaluation file - July 2018

a. Publication of ETM report with positive decision - "in combination with an aromatase inhibitor is indicated for the treatment of postmenopausal women, with breast cancer, in advanced stage or locally metastasized, with hormone receptors (RH) positive and without factor 2 receptor epidermal growth factor (HER2), as initial hormone therapy ”with addressability for patients receiving ribociclibum in combination with letrozole, in the absence of symptomatic visceral impairment with major implications on short-term life prognosis - July 2019

b. Publication of the report ETM with negative decision - "in combination with an aromatase inhibitor is indicated for the treatment of postmenopausal women, with breast cancer, in advanced stage or locally metastasized, with hormone receptors (HR) positive and without human factor receptor 2 epidermal growth factor (HER2), as initial hormone therapy, with addressability for patients receiving ribociclibum treatment in combination with other aromatase inhibitors, except letrozole - July 2019

**** Publication of the protocol - not yet published***

Conclusion: Kisqali has not yet been introduced in GD 720/2008, but patients have access to treatment through an access program provided by the company, for the indication for which a positive decision was received from ANMDMR.

BREAST CANCER ACADEMY

Is it blue?

Row	Saved	Status	Study Title	Conditions	Interventions	Locations
1	☐	Recruiting	Study of Nivolumab Versus Placebo in Participants With High-Risk **Breast Cancer**	• **Breast Cancer**	• Biological: nivolumab • Drug: paclitaxel (PTX) • Other: nivolumab placebo • (and 4 more...)	• Local Institution Mobile, Alabama, United States • Marin Cancer Care, Inc Greenbrae, California, United States • Local Institution Los Angeles, California, United States • (and 165 more...)
2	☐	Recruiting	A Study Of Ipatasertib in Combination With Atezolizumab and Paclitaxel as a Treatment for Participants With Locally Advanced or Metastatic Triple-Negative **Breast Cancer**.	• Triple-Negative **Breast Cancer**	• Drug: Atezolizumab • Drug: Ipatasertib • Drug: Paclitaxel • (and 2 more...)	• USA Mitchell Cancer Institute Mobile, Alabama, United States • Highlands Oncology Group Fayetteville, Arkansas, United States • CBCC Global Research Inc., at Comprehensive Blood and Cancer Center Bakersfield, California, United States • (and 303 more...)
3	☐	Recruiting	A Study Comparing Atezolizumab (Anti PD-L1 Antibody) In Combination With Adjuvant Anthracycline/Taxane-Based Chemotherapy Versus Chemotherapy Alone In Patients With Operable Triple-Negative **Breast Cancer**	• Triple Negative **Breast Cancer**	• Drug: Atezolizumab • Drug: Paclitaxel • Drug: Dose-dense Doxorubicin or dose-dense Epirubicin • Drug: Cyclophosphamide	• John Muir Health Clinical Research Center Concord, California, United States • Cedars-Sinai Medical Center Los Angeles, California, United States • Martin-O'Neil Cancer Center Saint Helena, California, United States (and 425 more...)

Romania status: not recruiting yet

Is it blue?

Row	Saved	Status	Study Title	Conditions	Interventions	Locations
1	☐	Recruiting	Study of Nivolumab Versus Placebo in Participants With High-Risk **Breast Cancer**	• **Breast Cancer**	• Biological: nivolumab • Drug: paclitaxel (PTX) • Other: nivolumab placebo • (and 4 more...)	• Local Institution Mobile, Alabama, United States • Marin Cancer Care, Inc Greenbrae, California, United States • Local Institution Los Angeles, California, United States • (and 165 more...)
2	☐	Recruiting	A Study Of Ipatasertib in Combination With Atezolizumab and Paclitaxel as a Treatment for Participants With Locally Advanced or Metastatic Triple-Negative **Breast Cancer**.	• Triple-Negative **Breast Cancer**	• Drug: Atezolizumab • Drug: Ipatasertib • Drug: Paclitaxel • (and 2 more...)	• USA Mitchell Cancer Institute Mobile, Alabama, United States • Highlands Oncology Group Fayetteville, Arkansas, United States • CBCC Global Research Inc., at Comprehensive Blood and Cancer Center Bakersfield, California, United States • (and 303 more...)
3	☐	Recruiting	A Study Comparing Atezolizumab (Anti PD-L1 Antibody) In Combination With Adjuvant Anthracycline/Taxane-Based Chemotherapy Versus Chemotherapy Alone In Patients With Operable Triple-Negative **Breast Cancer**	• Triple Negative **Breast Cancer**	• Drug: Atezolizumab • Drug: Paclitaxel • Drug: Dose-dense Doxorubicin or dose-dense Epirubicin • Drug: Cyclophosphamide	• John Muir Health Clinical Research Center Concord, California, United States • Cedars-Sinai Medical Center Los Angeles, California, United States • Martin-O'Neil Cancer Center Saint Helena, California, United States (and 425 more...)

Romania status: not recruiting yet

Is it blue?

Barriers - We have identified five major challenges to accessing innovative cancer treatments to be addressed :

1. Delayed regulatory approval and marketing authorization
2. Limited availability of health insurance and insurance coverage
3. Lagging disease awareness and screening
4. Restricted reimbursement and access
5. Low affordability for patients and their families

BREAST CANCER ACADEMY

Thank you!

Alina Comanescu

Fouder

Community Health Association

Romania

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BREAST CANCER ACADEMY