

Compassionate use What patients are expecting

CDDF Live Webinar - "Compassionate Use and EAP for Cancer Drugs – From Fragmentation to a Common Framework in Europe under the New Legislation"

26 October 2026

François Houyez

The origin

FDA Headquarters, Rockville, Maryland, October 11, 1988: AIDS activists advocated for a “parallel track”



News FDA Releases AIDS Drug on Parallel Track *Move Follows Intensive Pressure from Activists*

by Cliff O'Neill

WASHINGTON—DDI, an experimental anti-HIV drug, was released into a broad distribution program called a “parallel track,” by the U.S. Public Health Service on Sept. 28, after months of intense pressure from AIDS activists.

The drug, a less toxic relative of AZT, which is the only federally approved anti-HIV drug, will now enter broad Phase II clinical trials in which its effectiveness will be tested. In an unprecedented move, the Food and Drug Administration will also allow the drug's manufacturer to distribute the drug to a wide array of people with AIDS and advanced ARC who cannot tolerate AZT or do not qualify for the ddi clinical trials for a variety of other reasons.

DDI has raised hope of AIDS researchers after initial Phase I toxicity trials on 200 people showed that it appeared to be as effective, and less toxic than, AZT. However, clinicians have found that several patients taking high doses of ddi reported bouts of pain and numbness. New clinical trials have found that risk substantially minimized when the drug is taken at lower doses.

“The epidemic of AIDS is extraordinary and it must be met with extraordinary measures,” stated FDA

commissioner Frank Young on ddi's release. “Since ddi is still an experimental drug, it must be tested carefully and must demonstrate safety and efficacy before it can be approved. We believe, however, that it is important to offer the drug to people with

ddi if they don't have to. “I believe people who are stable on AZT right now would be wise to stay on AZT, unless they've been on it so very long that they and their physicians are virtually certain it's not helping,” stated Jim Ego of ACT UP.

The Public Health Service's announcement comes after months of intense pressure from AIDS activists, which initially came up with the concept of making experimental drugs available to AIDS patients on a parallel track after toxicity levels are established but before its effectiveness is proven.

To implement the new distribution system, the FDA, working with AIDS activists, has broadened its definitions of two existing programs, called “Treatment IND (Investigational New Drug)” and “compassionate use” protocols, to allow for the drug's release as soon as it enters Phase II effectiveness studies.

This plan offers some additional options for people with AIDS and particularly for the thousands of AIDS patients who cannot tolerate AZT,” said Secretary of Health and Human

Services Dr. Louis Sullivan, announcing the drug's release. “This plan for expanded testing and earlier availability of ddi, developed through the cooperation of several Public Health Service agencies and Bristol Myers, reaffirms our commitment to speeding both the development and the availability of

AIDS for whom the standard treatment of zidovudine (AZT) is not an option, even though there are some potentially serious side effects.”

AIDS activists were quick to caution that patients currently benefiting from AZT not drop the proven, although limited, drug in favor of the



AZT OK, TOO
Jim Ego

Photo: TL Litt

15 October 1989
BMS ddi trial: n= 2,600
Parallel track: n = 25,000

Compassionate use: a treatment for those who don't have the time to wait for the end of R&D

New drug being developed

New drug authorised



Compassionate
use

- For new active substances in R&D, or awaiting approval
- Up until effective reimbursement
- Early Access is part of CU

What is it about?

1

- End of trial: want to continue treatment? Trial extension (open-label), roll-over study (compassionate use in exceptional cases)

2

- Did not / could not join a clinical trial, product not yet evaluated? Compassionate use (to be continued with Early Access + Direct Access)

3

- Product authorised, no reimbursement decision yet? Early Access Programme, special fund, managed entry agreement, (& Direct Access)

4

- Negative reimbursement decision, or restrictive? Financial Assistance Programme

In Europe: most regulatory schemes for CU for a defined group of patients adopted after REG726/2004

Some named patient compassionate schemes existed

• **France**

- “Octroi humanitaire” by French Doctors NGOs in the 70s
- Law in 1994

• **Denmark**

- 1995
- Named patient basis, usually not enough patients for “programmes”

• **EU Reg.**

- 2004
- CHMP opinion if requested by 2 MS
- All authorised CU notified to EMA

• **Germany**

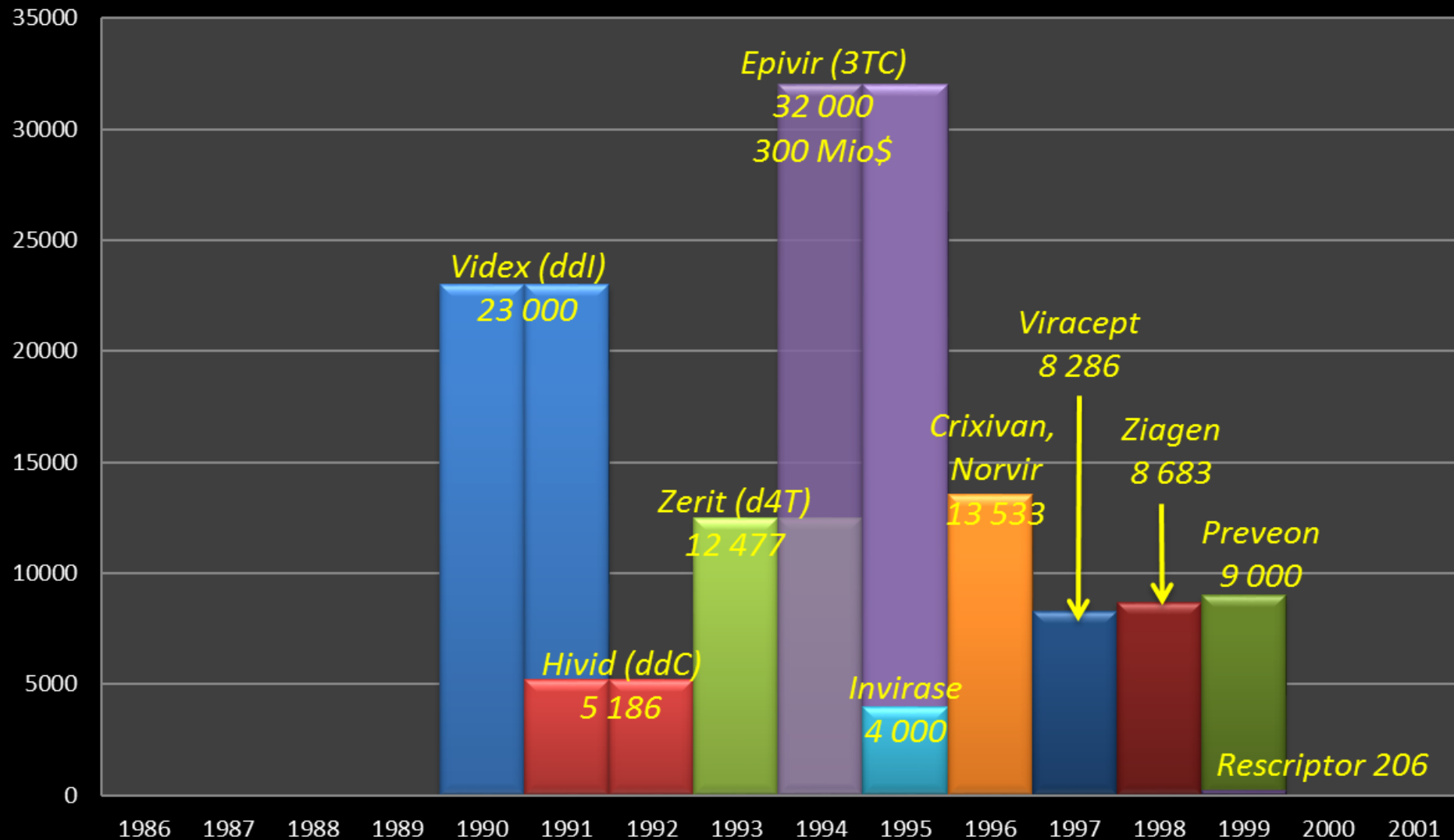
- Before 2005: import via international pharmacies (US GIs)
- After 2005: AMHV

• **Other**

- Italy: 2006
- Spain: 2009
- Romania: 2012
- UK: 2014

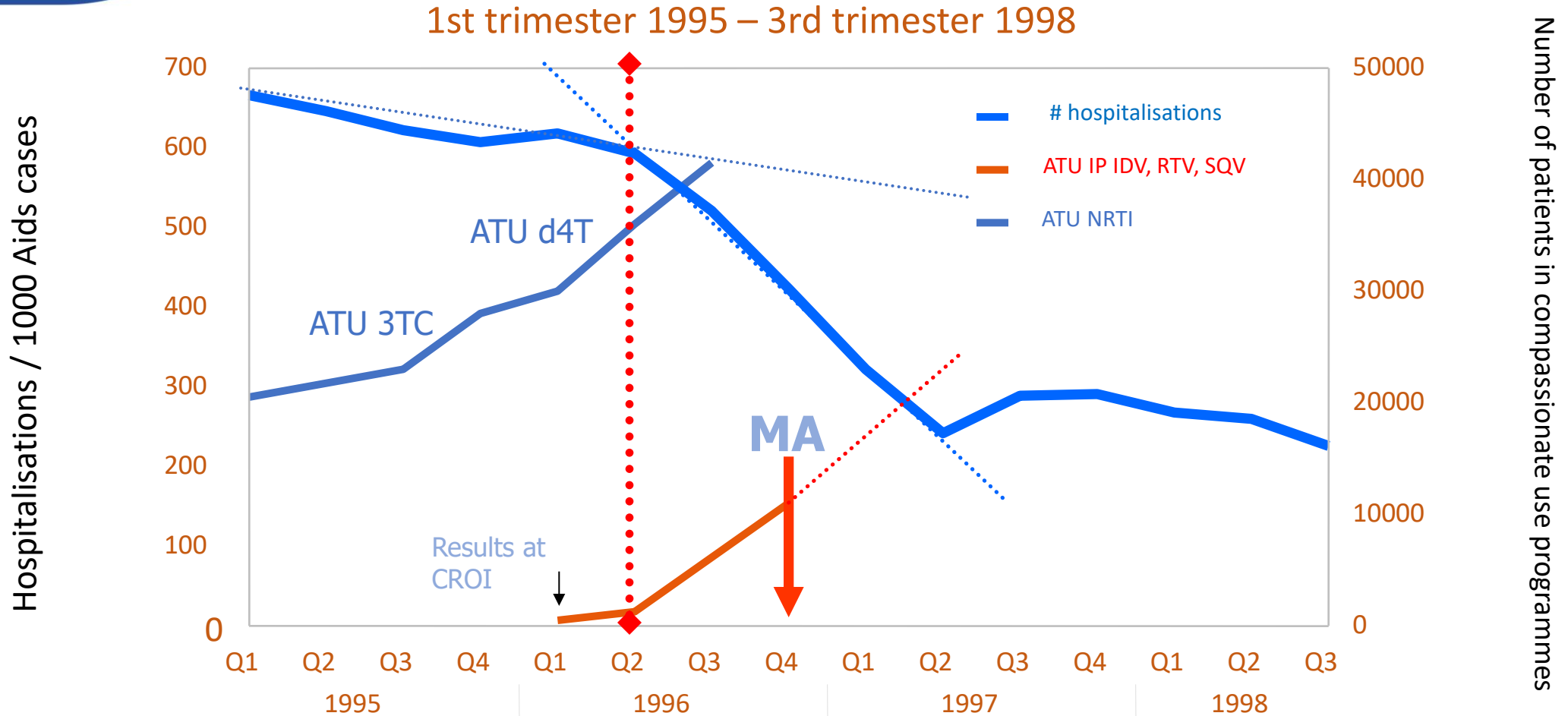
The importance of compassionate use

Number of PLWAIDS in compassionate use programmes worldwide (1986-1999)



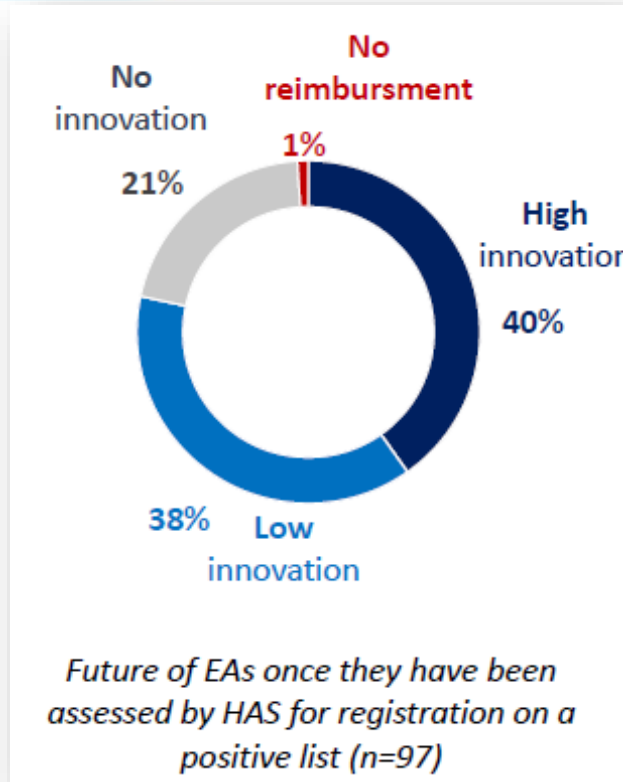
Clinical effectiveness of compassionate use

Hospitalisation rates for 1000 AIDS patients, France 1995-98



Sources: François Houÿez
Hospitalisation rates DMI2 - Direction des Hôpitaux - BEH n°44/96
Abbott Laboratories, Merck Sharp & Dohme, Glaxo Wellcome, Bristol Myers Squibb, Roche

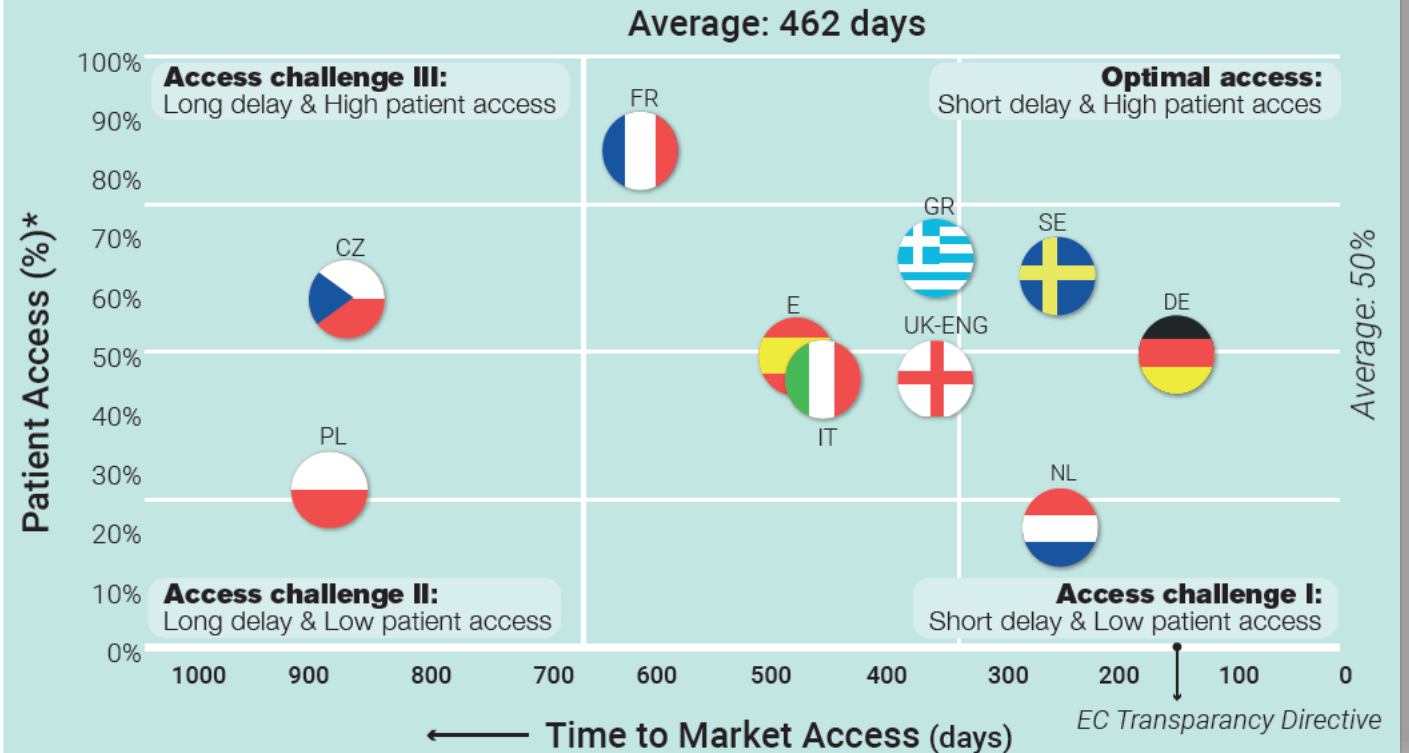
IMPACT: CU/EA make a difference



HAS 2-year evaluation EAP

Fig. 3

Within Europe, huge inequalities exist in time to Market Access and Patient Access to new oncology therapies



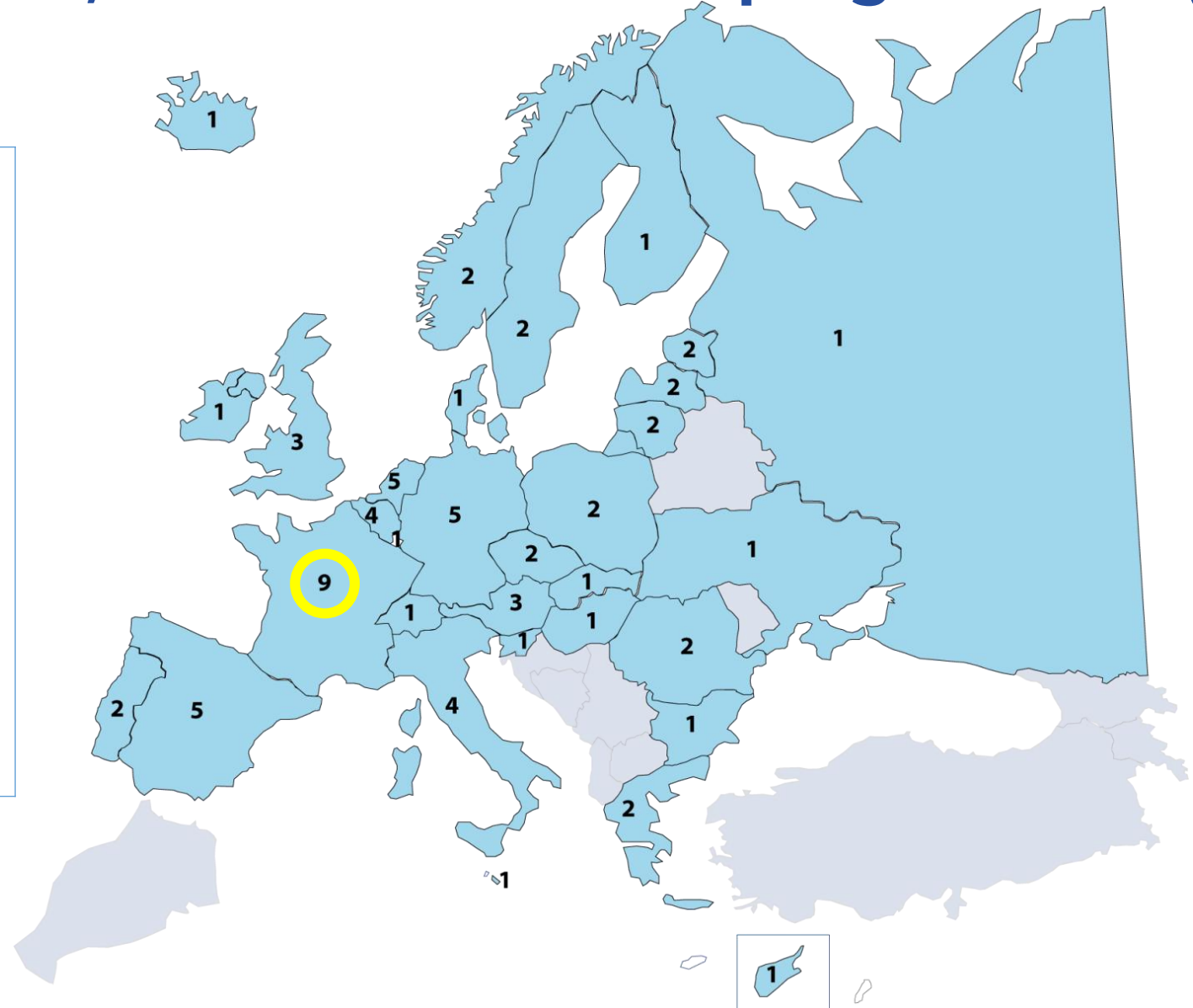
Vintura July 2020 Every Day Counts

Eurordis research 2011, OMPs

9 products, 42 countries = 74 programmes (378)

Products

Mozobil® (Genzyme)
vandetanib (AstraZeneca)
inolimomab (Eusa Pharma)
Kuvan® (Merck Serono)
Carbaglu® (Orphan Europe)
Yondelis® (Pharma Mar)
decitabine (Johnson & Johnson)
Vpriv® (Shire Pharmaceuticals)
Xyrem® (UCB)



Obstacles, and what patients are proposing

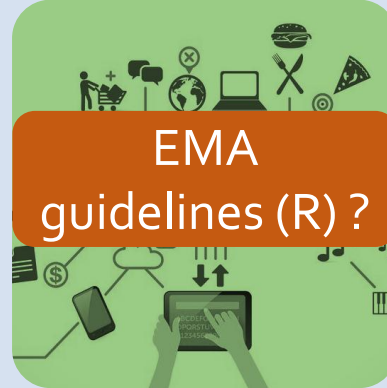
FREQUENT OBJECTIONS – MS, INDUSTRY, OR CLINICIANS



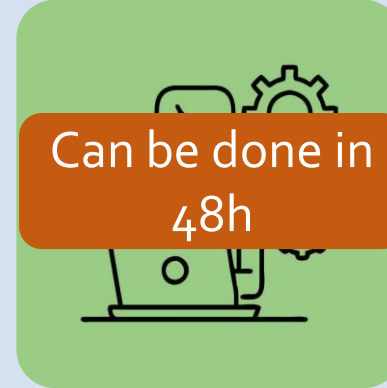
Dialogue with
patients



Price-volume
agreements



EMA
guidelines (R) ?



Can be done in
48h



Dialogue with
patients

Exit rules

MS afraid
they can't
stop if
product not
authorised /
not
reimbursed

Costs

If unpaid,
company has
no resources

Difference
with end
price

Data

Not a
substitute for
clinical trials

Forbidden to
collect data
in some MS

Standardisation

Complexity

Particularly
for named
patient basis:
paperwork
for each
patient

Too early

No efficacy
data

Too risky

Not enough
product

What patients recommend to industry (and more, see Position)

Discuss timing and criteria early in R&D

Be transparent on manufacturing and supply

Accept information on CU cannot be confidential

Collect information, toxicity data and special populations

Don't interrupt the programme abruptly if negative CHMP opinion

Don't present the programme as a gift for clinical trials

A revision of EMA guidelines on CUP, as proposed in Commission Communication on Rare Diseases in 2008?

- EMA guidelines: very restrictive interpretation of the Regulation
 - *CHMP adopt opinions on the conditions for use, the conditions for distribution and the patients targeted*
- EMA interprets conditions for distribution only as
 - Medicinal product is subject to medical prescription, or whether it is subject to special or restricted medical prescription.
- Where in fact EMA guidelines could propose to
 - Discuss the possibility of a future CU at SA
 - Estimate how many patients could benefit from the CU and when it could start
 - Standardisation of data collection, including PED
 - Propose measures when the demand exceeds available supplies, ensuring a fair distribution of available stock among MS
 - Accept patients' organisations and/or healthcare professionals ask CHMP for an opinion

Can we learn from data collected during compassionate use?

PRAC and CHMP precedents

1995
(Vistide®)

- CMV retinitis
Renal toxicity: probenecid + hydration
- Validation of risk minimisation measures in ATU
- MAA: 28/12/95
- ATU: 12/03/96
- MAH: 18/12/96

1996
HIV prot. inhib.

- HIV infection
- Unexpected spontaneous haemorrhage in 52 haemophiliacs in ATU
- → SmPC before marketing authorisation

2003-2007
Thalidomide®

- Multiple Myeloma
- Teratogenicity
- Validation of Pregnancy Prevention Prog with 1,289 women of child-bearing potential in ATU over 9 years

2009
(Xagrid®)

- Essential thrombocytopenia
- Single arm CTs ATU with 451 patients, subset evaluable for efficacy (*"trend in favour"*)

2025 Kaftrio®

- Cystic Fibrosis
- Extension of the indication
- New data submitted from various studies (RCT, RWD data, compassionate use)

Summary

We need to
identify and
share best
practices

Compassionate use programmes: a win-win for all.
For the patients, for public health, for authorities and
for the developer

In many domains (viral diseases, HIV, Hep, Covid,
Ebola): 100% of medicines with compassionate use.
Patients' advocates on the front line

Plans for future CUs: Anticipate!
Ensuring equity is in our hands (no one privileged)

Contact EURORDIS or relevant patient organisations to
discuss compassionate use



THANK YOU!

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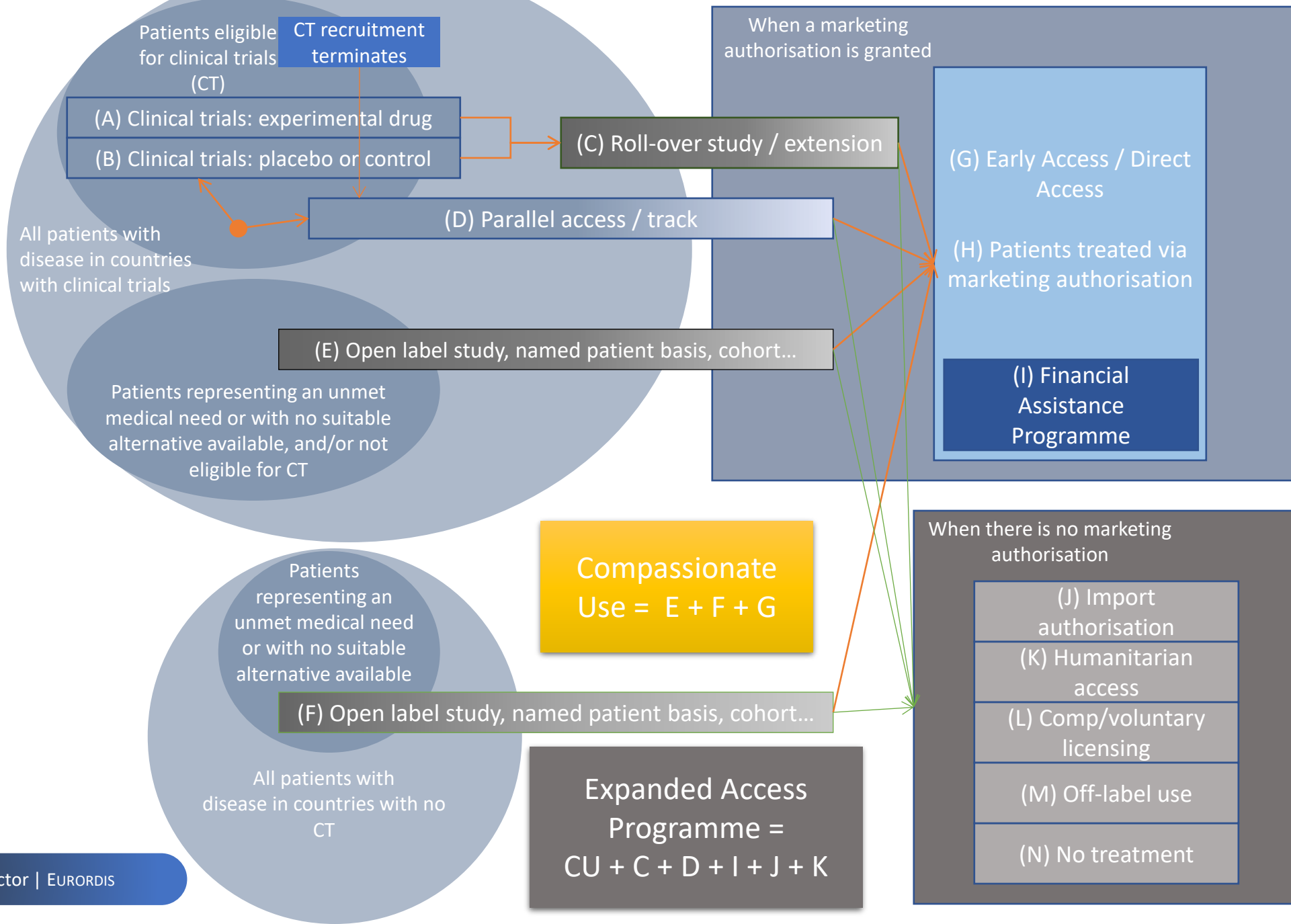
Compassionate use programmes for rare diseases: proposals for actions

François Houyez, Chantal Bélorgey, Arielle North, Etelka Czondi, and Michele Lipucci di Paola

Orphanet J Rare Dis. 2012; 7(Suppl 2): A28

Eurordis position

<https://www.eurordis.org/improve-compassionate-use-programmes-to-ensure-patients-early-access-to-medicines>



Regulatory

- EMA mandate too restricted
- National schemes heterogenous
- Paid CU only in some countries (USA, France)

Industry

- Resources not always adequate: how many to treat? How much supply?
- Diverging policies and practices (“ethics committee”)
- No anticipation of consequences of early communication on results
- Objective difficulty when defining inclusion criteria

Exit rules, how to end CU

- Reg 726/2004 Article 83.8, gap with commercial sales
- What if not approved or not reimbursed? Cf scheme in Japan

Patients

- Unreasonable expectations (developer’s constraints poorly understood)
- Unaware how these programmes work, how they can contribute

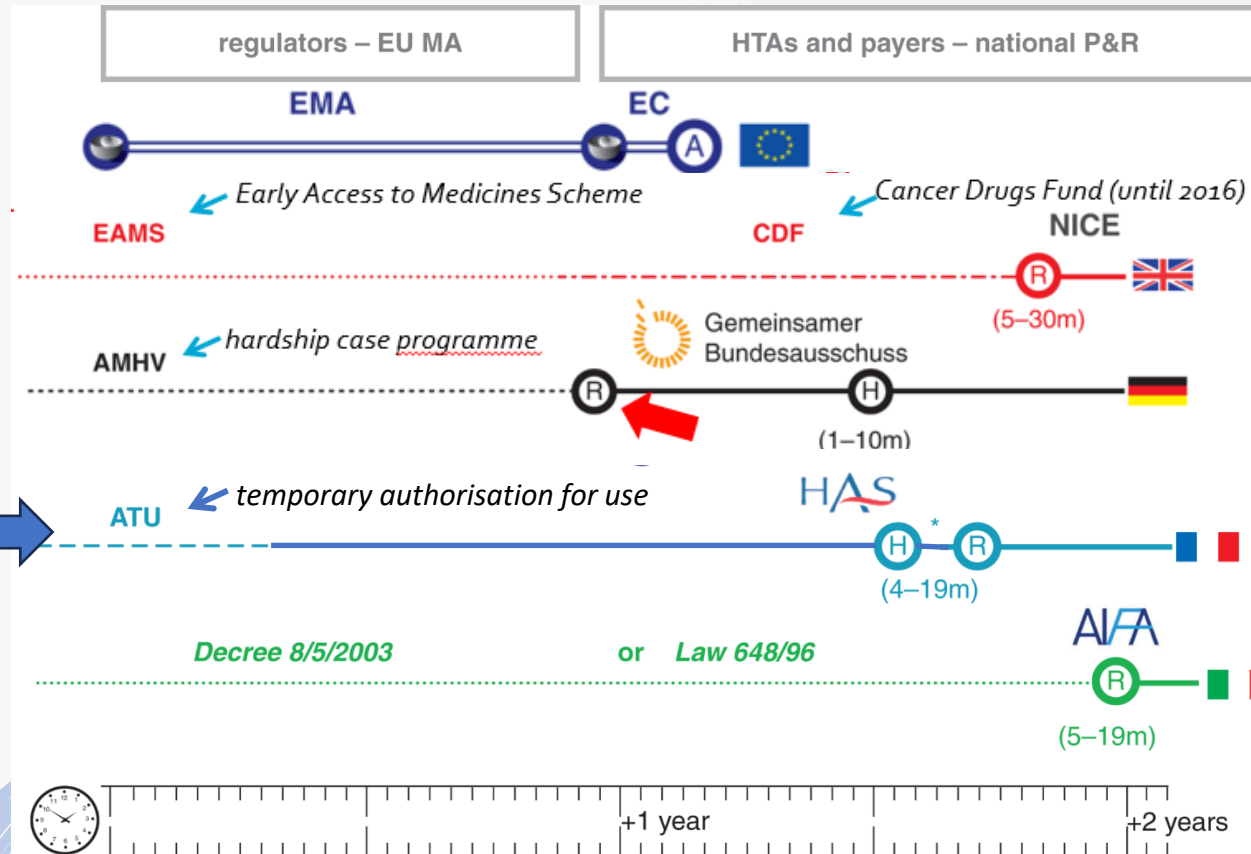
Timelines

New Drugs: Analysis of timelines of approval and HTA/P&R decisions for oncological products in EU

J. Martinalbo et al. "Early market access of cancer drugs in the EU" *Ann Oncol.* 2015;27(1):96-105. doi:10.1093/annonc/mdv506

Until 2021: 80% of new active substances authorised available as compassionate use in average 24 to 36 months before marketing authorisation

Dashed lines: national compassionate use / early access



Sample size N=15 (oncological drugs with regular approval in EU between 2011-2013) based on median times from EU marketing authorisation (MA) in months