EARLY ACCESS TO MEDICINES IN EUROPE: HOW TO MAKE COMPASSIONATE USE BECOME A REALITY FOR ALL IN NEED

Joint Meeting of the Patients' And Consumers' Working Party and of the Healthcare Professionals Working Party

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http://www.eurordis.org/publication/early-access-medicines-europe-compassionate-use-become-reality

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A frequent situation in life-threatening or severely debilitating diseases

New drug being developed

New drug authorised

Marketing authorisation

Some patients have no more treatment options, their condition deteriorates. Not all are eligible for clinical trials. Some die. All know a product is being developed and may be there soon.

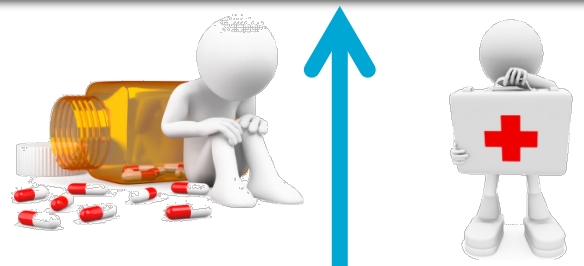
When the drug is authorised, patients can have access.

There is always one patient who will suffer the day before a drug is authorised and who knows the drug will be authorised next day

For all, this is a nightmare

Compassionate use is a response for patients with the most urgent need for a new option

New drug being developed → New drug authorised

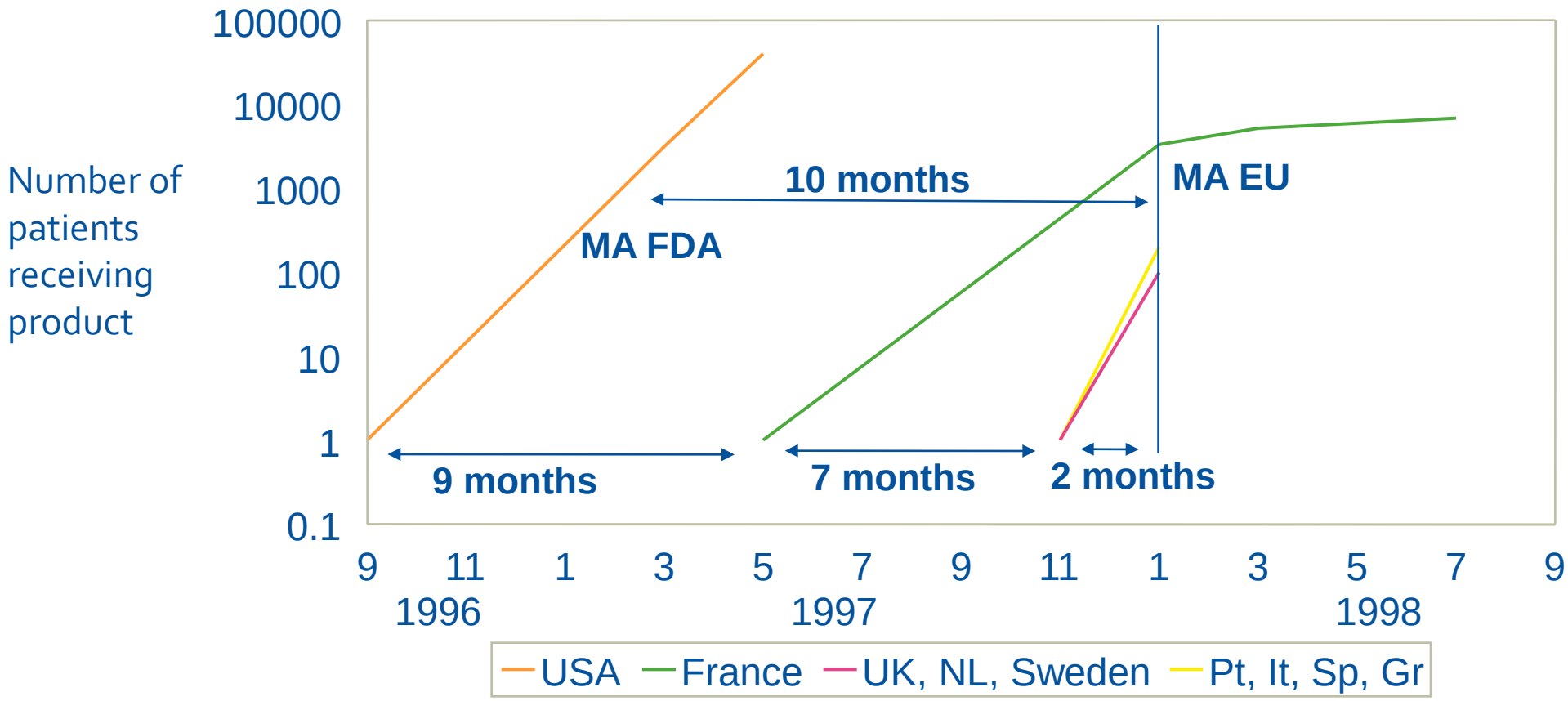


Compassionate use

Or adaptive licensing

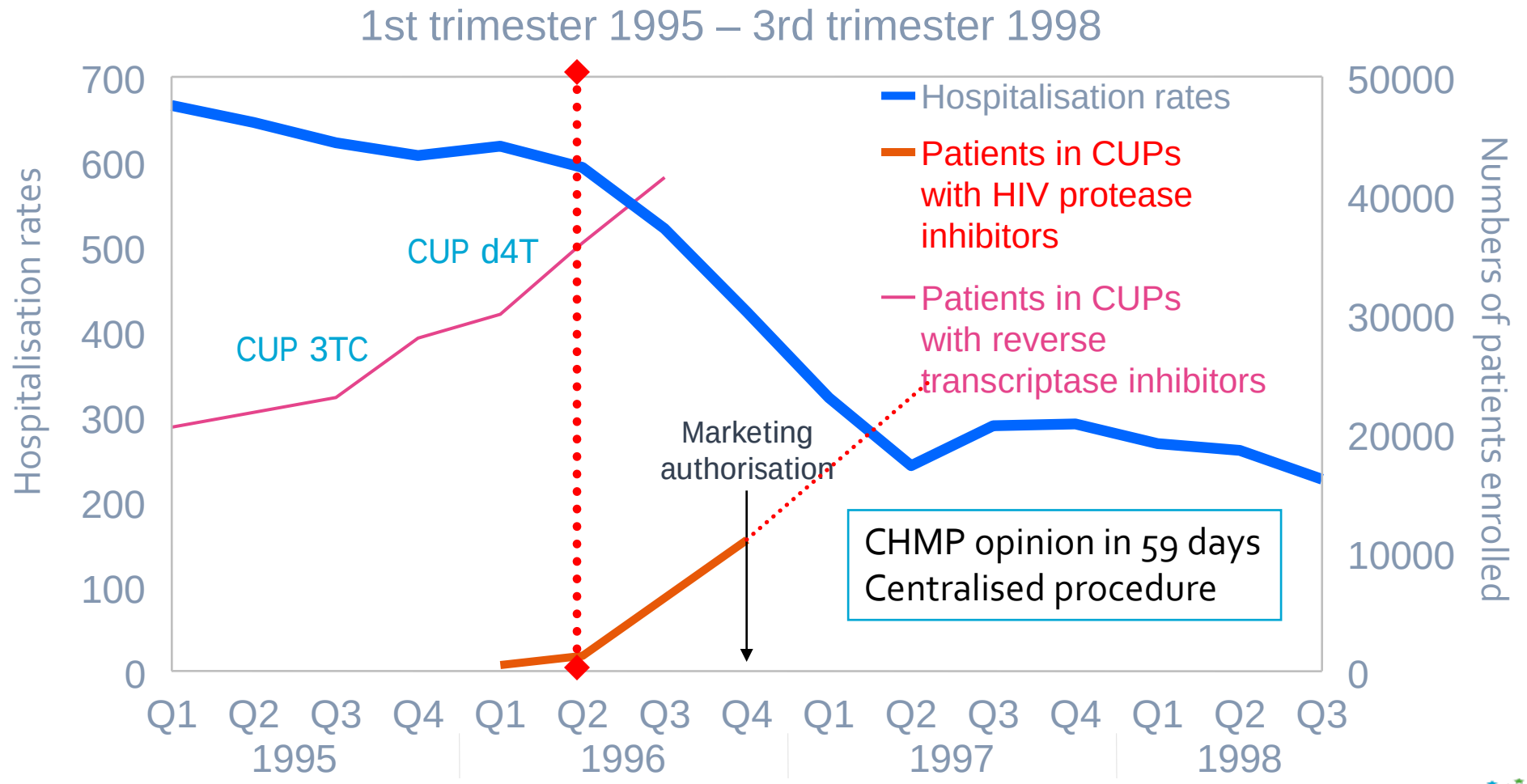
But whenever a compassionate use programme starts, there will always be patients for whom it will be too late.

Access to compassionate use highly heterogeneous in the EU
(e.g. nelfinavir in 1997, as shown to CHMP): true in 1997, true in 2017



Compassionate use impact on public health – the case of HAART / AIDS

hospitalisation rates for 1000 AIDS patients, France 1995-1998



CUP: Compassionate Use Programme. Data from industry and BEH.

A.T.U* and orphan drugs

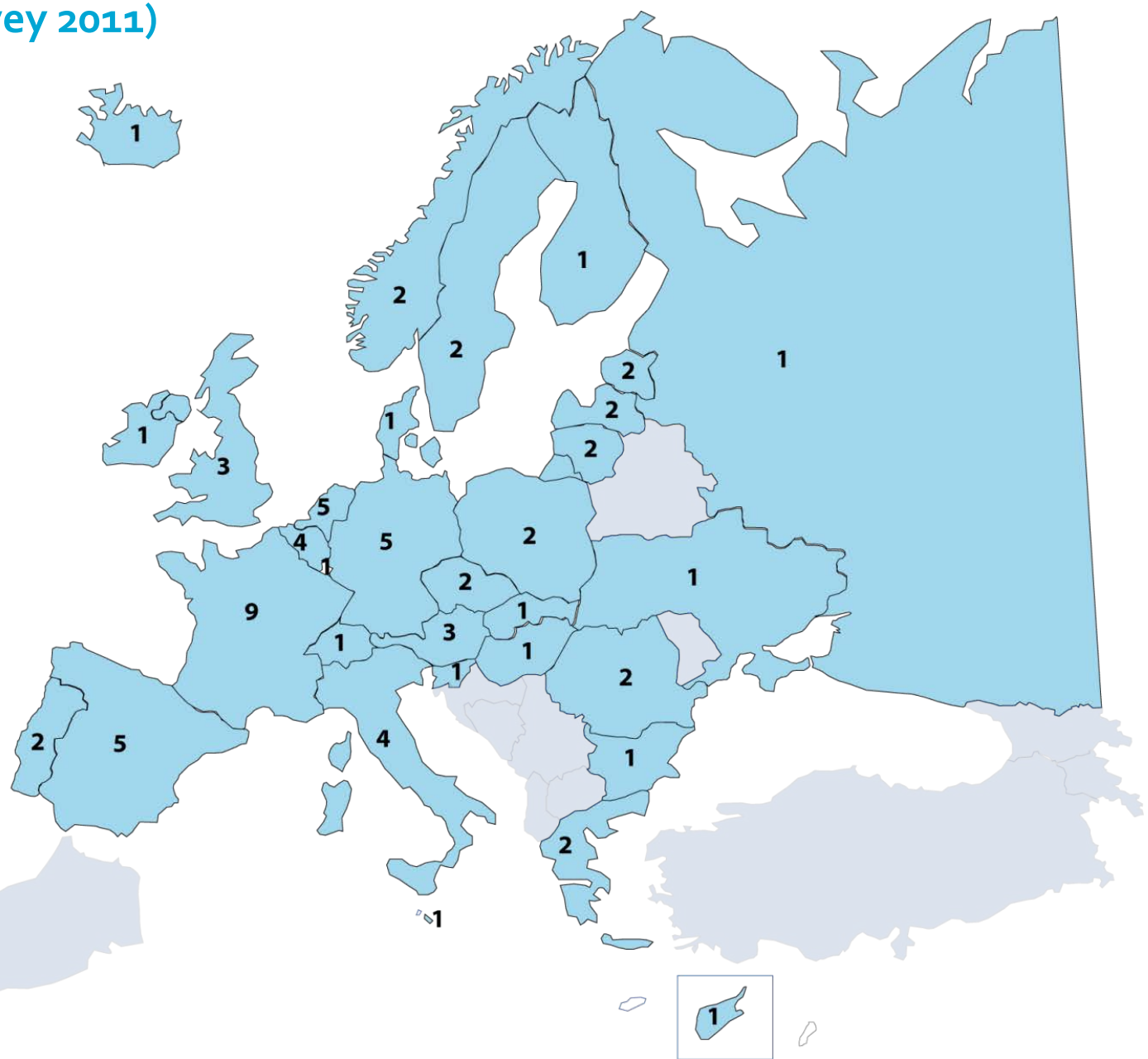
- Afssaps (now ANSM), annual report 2009

- 72% of authorised orphan drugs received ATU* status
- In average 34 months before their authorisation via the centralised procedure

* Temporary Use Authorisation

9 products, 42 countries, 74 programmes

(Eurordis survey 2011)



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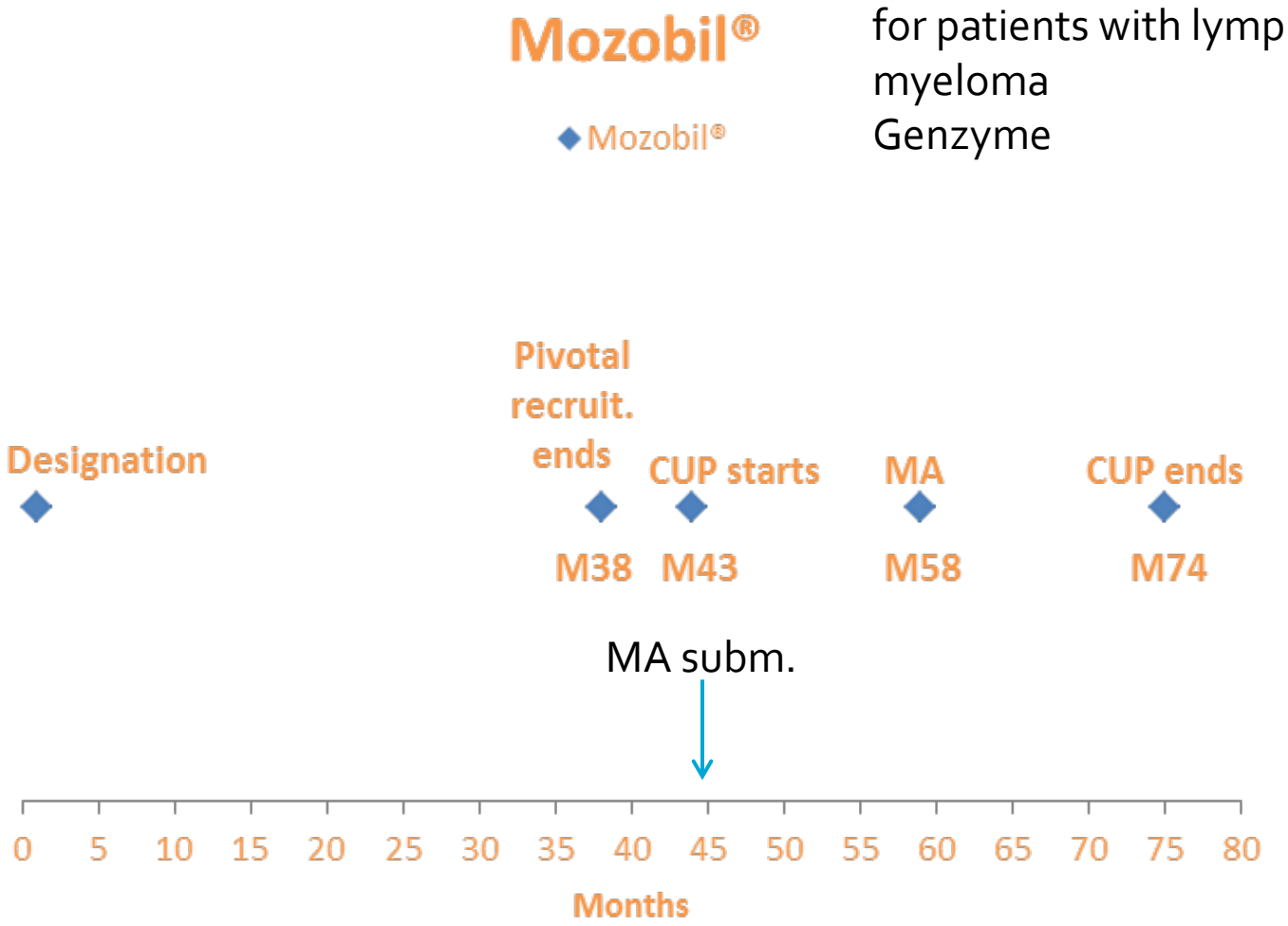
Completed programmes (1)

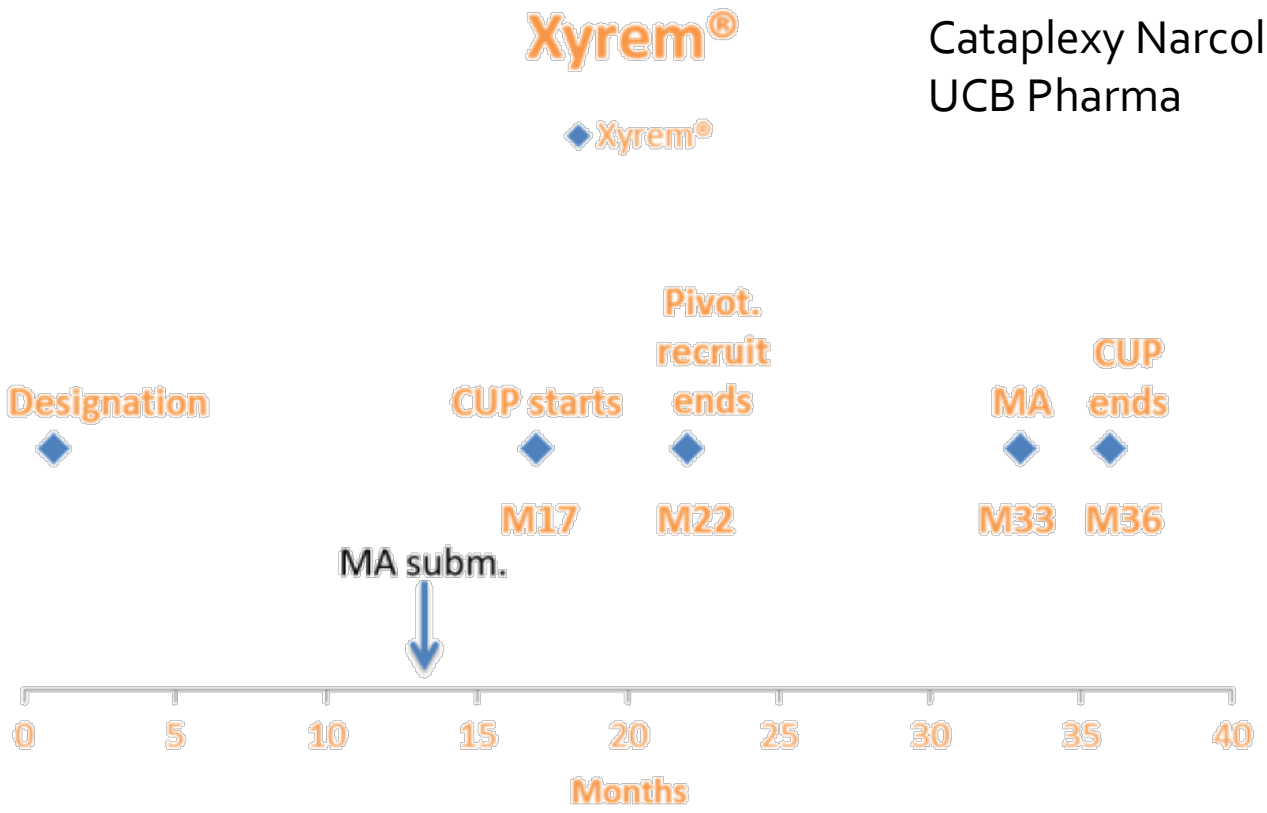
(EURORDIS survey 2011)

prior to autologous stem cell transplantation, for patients with lymphoma or multiple myeloma
Genzyme



Completed programmes (2)

(EURORDIS survey 2011)



Cataplexy Narcolepsy
UCB Pharma

Figure 1: CUP for Xyrem® to treat narcolepsy

Typically

Patients treated via a CUP reflect different patient populations than for clinical studies

- Comorbidities (liver or kidney-impaired, end-of-life…)
- Other co-medications than in CTs (drug-drug interactions)

Safety can be explored, but which control group?

- Exposure analysis (on-treatment)
- Ok for activities such as real-life evaluation of risk minimisation measures

Difficulty to measure efficacy – most, or many, will die or worsen anyway

- Look at prescription renewals?

Challenges with the current situation

EU legislation

- Objectives of the legislation
  - Harmonisation
  - Common approach between MSs
  - Equal treatment for patients across the EU

Not met

- Role of the EMA (*may* provision)
  - Evaluation
  - Opinion (*may* adopt an opinion)
- Role of the MSs final decision (take into account)

Main concerns: MAA needs an army of staff
(EURORDIS survey 2011)

- Differences between MSs policies difficult to understand (authorisation, documentation, prescription, assessment time, validity, follow up)
- Interference with the marketing authorisation procedure and whether or not the data collected in a programme can be part of the dossier submitted to regulatory authorities
- Liability risks
- Lack of transparency
- Supply and logistics, information/language
- Pressure on supply under compassionate use including off-label
- Free of charge/prices

Hell is in the details, but priority should be clinical trials (or collect quality data from CUP = real life evidence)

Germany

- CUP to be initiated by the company, not by clinicians
- CUP must be for free
- CUP must use commercial batches of highest quality
- Unclear who pays for other expenses (surgery…)

France

- CUP can be on doctor's request
- CUP can be free of charge or paid for
- CUP can use pilot batches for clinical trials
- Healthcare system pays for all related expenses

Another hot topic: when supply is limited

- Equity:
  - Members of patients' organisations should not be advantaged compared to non-members (no advantage for the best informed)
  - Medical criteria: doesn't work, doctors write what they want
  - If extremely limited supply: random draw to enrol patients
  - Don't let the company set its own "independent ethics committee"

- French Ethics Council Opinions 1996

  Since patients will be selected randomly by computer, there will be no conscious or unconscious emotional preference or pressure. Drawing lots will relieve doctors of the responsibility of choice and preserve patients' trust in their attending physicians. Lots will be drawn each time supplementary drug doses are made available, with the aim of including all eligible patients.

- If such a system is in place, need for a European coordination and a European waiting list: not a MS by MS procedure

What EURORDIS is proposing

Policy options (not mutually exclusive)

- Promote the French ATU system (similar scheme in the Netherlands)
- Adopt an EU Regulation / amend article 83
- Apply the Directive on Patients' Rights in Cross-Border Healthcare
- Generalise the Medicines Adaptive Pathways to Patients
- Amend the EMA guidelines for compassionate use

Revise EMA guidelines on CUP, as proposed in ComCom on RD 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.
- What should be addressed by EMA
  - Anticipation of the programme during early SA
  - Estimates on how many patients could benefit from the CUP in the EU and when in the development it could be started
  - Criteria to increase the number of patients when more product is available
  - Measures when the demand exceeds available supply
  - Measures to ensure a fair distribution of available stock among Member States

In addition to policy proposals, 28 recommendations to:

- Patients' organisations (3)
- Industry (18)
- Member States (4)
- European Authorities (EC, EMA, HMA) (3)

Next steps

- Position public release and press: April 2017
- Presented to the Commission Expert Group on Safe and Timely Access to Medicines for Patients (STAMP) on 27 June 2017
- Planned
  - EMA/FDA Rare Diseases Cluster Meeting, 21 September 2017
  - Heads of Medicines Agencies (date to be defined)

Discussion

As for clinical trials, a facilitation group with MSs for compassionate use programmes?

Transparency: how to make MS respect Regulation (EC) N° 726/2004 and notify the EMA?

MS and MS only can request a CU opinion to the EMA. EU organisations as well (PCO, HCP)?

If data collected from CUP were better quality (standardisation) would regulators look at them?

Shouldn't discussions on CUP be systematic in all SA discussions?

Is it time for the revision of EMA guidelines?

Thank you for your attention.

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REGULATION (EC) Nº 726/2004 art. 83

- *Defines what compassionate use programmes are*
- *Explains the conditions (the medicinal product concerned must either be the subject of an application for a marketing authorisation or must be undergoing clinical trials)*
- *Organises the CHMP opinion on MS request*
- *Requests MS to notify to EMA CUP they authorise*
- *Requests CUPs to be continued during the period between authorisation and placing on the market*

What patients recommend to industry

(18 recommendations total, see the position)

- Discuss relevance and timing of CUP with patients' advocates and doctors early in the development of a medicine
- Define inclusion criteria for the compassionate use with patients and doctors
- Accept information on CUPs cannot be confidential
- Collect information from the CUP, in particular toxicity data and special populations
- Involve and coordinate different departments within the company: medical affairs, clinical development, regulatory, pharmacovigilance, finance and supply chain