ACCESSING A MEDICINE BEFORE ITS AUTHORISATION? YES, WE CAN!

WE CAN MAKE A DIFFERENCE

EURORDIS OPEN ACADEMY 2025

- Responsibilities & expertise
  - Engagement with industry, EMA and HTA
  - Compassionate use
  - ACT EU
  - EuroCAB - Community Advisory Boards
  - Evaluation of the benefit/risks
  - Medicine Repurposing
  - Pharmacovigilance
  - Shortages
  - Information on medicines
  - Health Technology Assessment
  - Pricing
  - Market access

DIRECTOR OF TREATMENT INFORMATION AND ACCESS

PATIENT ADVOCATE SINCE 1989

REPRESENT EURORDIS AT EMA (PCWP)

AND AT THE HTA COOPERATION

CAMPAIGN FOR ACCESS To CARE FOR PEOPLE WITH RARE DISEASES

A response for patients with the most urgent need for new treatment options

New drug in R&D

Authorised

Available and reimbursed

Today

Future

Science fiction?

Compassionate use

Whenever a compassionate use starts, there are always patients for whom it is too late

CAMPAIGN FOR ACCESS To CARE FOR PEOPLE WITH RARE DISEASES

PIERRE
1988

20 YE
PN

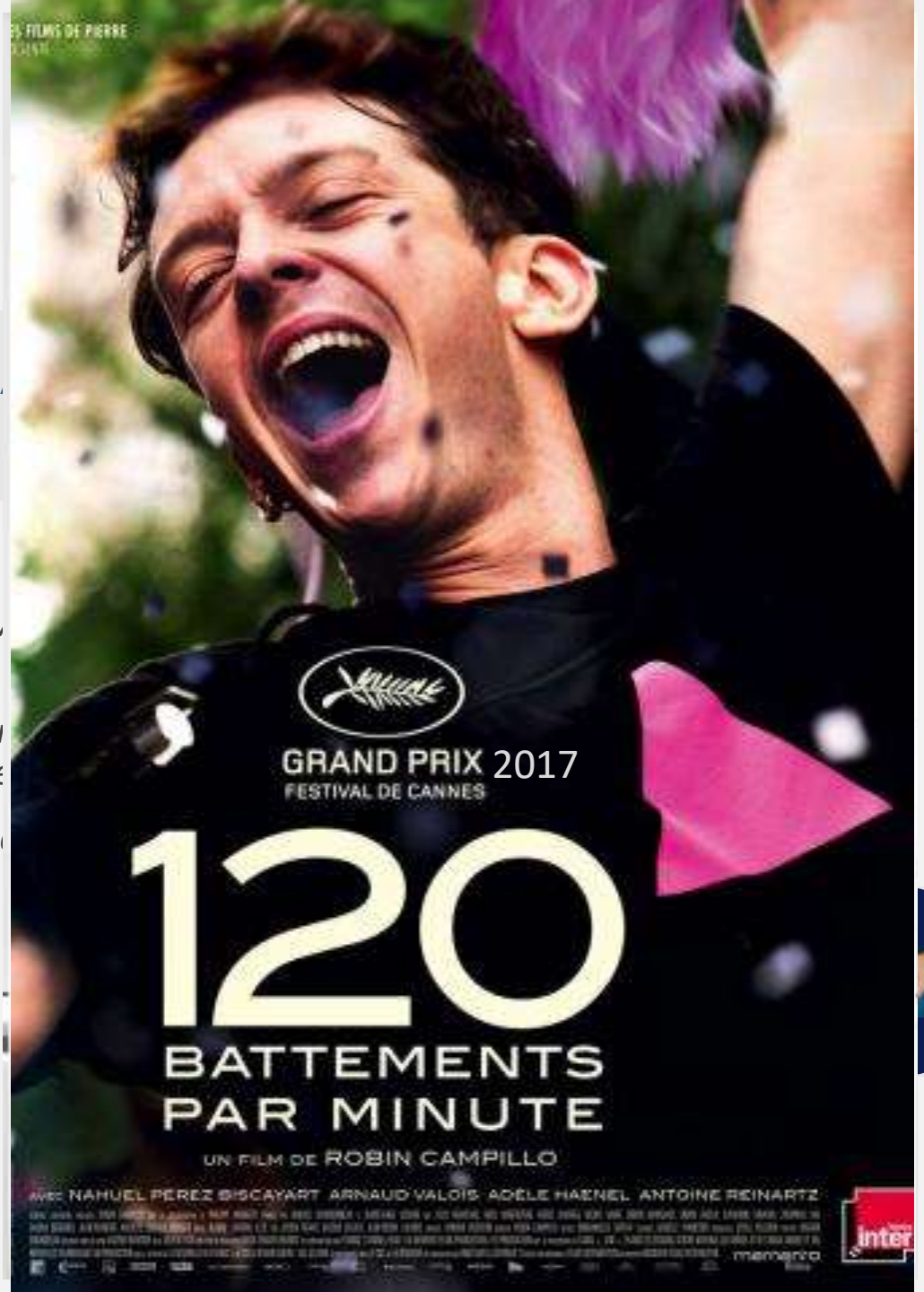
Media

Was on

In 1989, no i
be

Heard

Clinical trials in



Just had a lecture on the role of the military pharmacy in France: producing all medicines French troops might need, irrespective of IP rights

July 1989: wrote to Prof Dominique Dormont, head of the military pharmacy

Immediate response with phone numbers to contact him 24/24

"The role of the army is to protect the most vulnerable citizens, and this of course includes people living with AIDS"

Pierre: "that's all very nice, but you find a solution for all those in same case and I take it, or I don't".

August 1989, joined Act-Up Paris, just created, and together we advocated for compassionate use

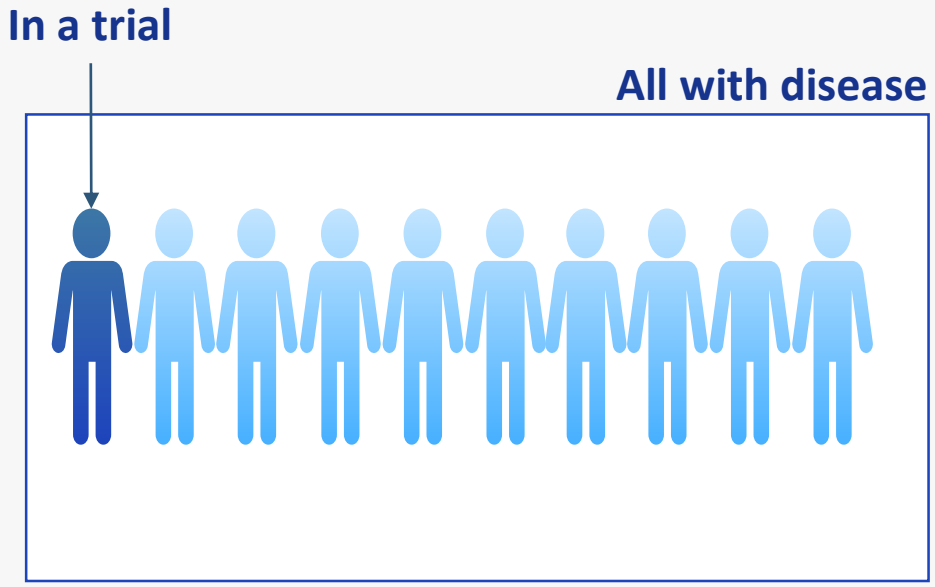
Pierre died in 1991, few months before a CU could start

When your health is deteriorating fast, and you know a product is out there, soon to arrive, what can you do?

CAMPAIGN FOR ACCESS To CARE FOR PEOPLE WITH RARE DISEASES

Food and Drug Administration Headquarters, Rockville, Maryland, October 11, 1988
Advocates Seizing Control of the FDA, requesting "Parallel track"
https://www.theatlantic.com/health/archive/2011/12/before-occupy-how-aids-activists-seized-control-of-the-fda-in-1988/249302/

CAMPAIGN FOR ACCESS To CARE FOR PEOPLE WITH RARE DISEASES

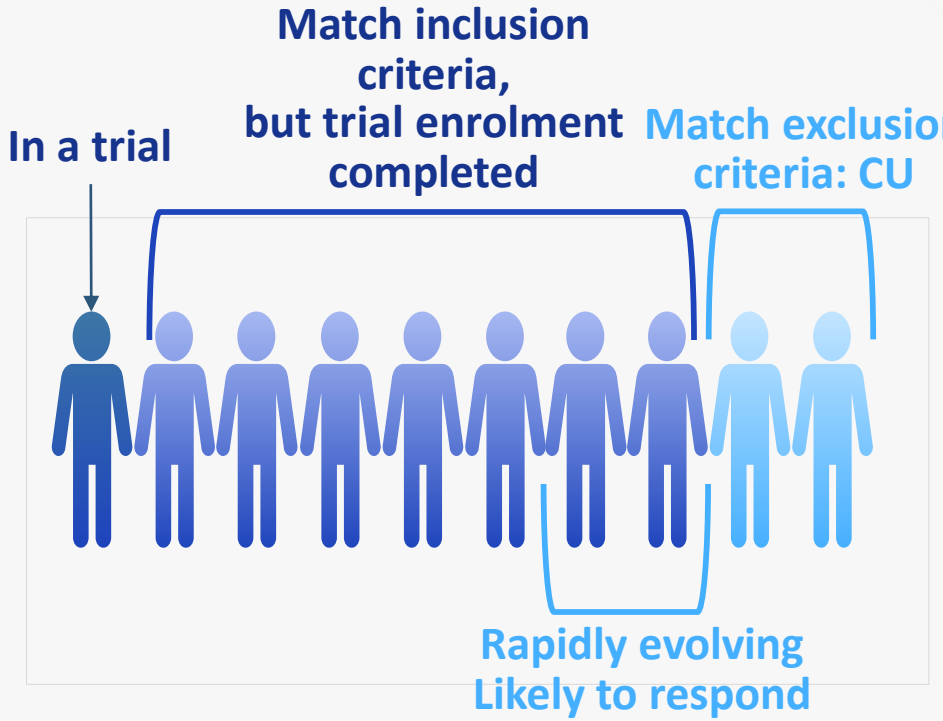


- Suppose a prognosis of 3-year life expectancy at diagnosis (eg Amyotrophic Lateral Sclerosis ALS ORPHA803)
- For 1 person in a randomised clinical trial (2-year duration), 9 are not enrolled in the trial
- 500 in the trial, 4,500 not in the trial
  - of whom 3,000 will be dead in 2 years
- Parallel track: 4,500 receive the investigational product, data are collected
- In total, 4,500 + 250 access the investigational product, 250 other after a placebo period (how long?)

FDA Expanded access: in parallel to the trial(s), **all** can access

Issues:

- competition between recruitment/retention in the trial and in the expanded access
- If another product is in R&D, no “treatment naïve” patients available for other trials



- Suppose a prognosis of 3-year life expectancy at diagnosis (eg ALS)
- For 1 person in a randomised clinical trial (2-year duration), 9 are not enrolled in the trial
- 500 in the trial, 4,500 not in the trial
  - 3,500 match trial inclusion criteria, but came too late
  - 1,000 match exclusion criteria, can't take part in trial
- These 1,000 can enter a compassionate use
- In total, 1,000+250 receive the investigational product

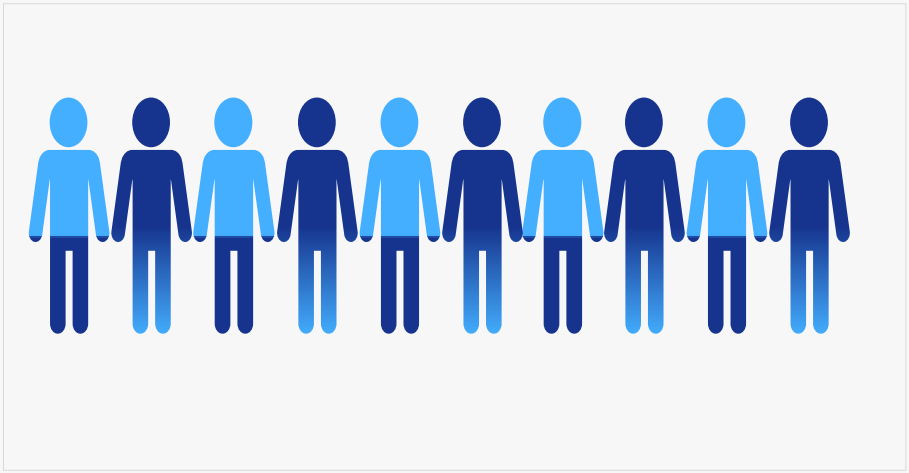
EU Compassionate use: after trial(s) have completed recruitment, for those matching exclusion criteria (eg comorbidities, co-medications, age, end-stage of the disease…)

Issues:

- Among those matching inclusion criteria, some evolve rapidly and want CU
- Difficulties to define clear criteria for accessing compassionate use
  - End-stage of disease: but maybe the less likely to respond?
    - Ethical dilemma
- What if finally not authorised?

CAMPAIGN FOR ACCESS To CARE FOR PEOPLE WITH RARE DISEASES

All in a trial, treatment or placebo



- All trial participants are randomised to investigational treatment or to a control
- Double-blinded or open label, but randomisation for a certain duration
- End of trial: sponsors should make provisions for participants wishing to continue or start treatment

Open Label Extension phase (roll-over study, or extension): provisions should exist for those wishing to continue treatment or wishing to start it, if there are benefits (Declaration of Helsinki Art 22 and 34, CIOMS guideline 6)

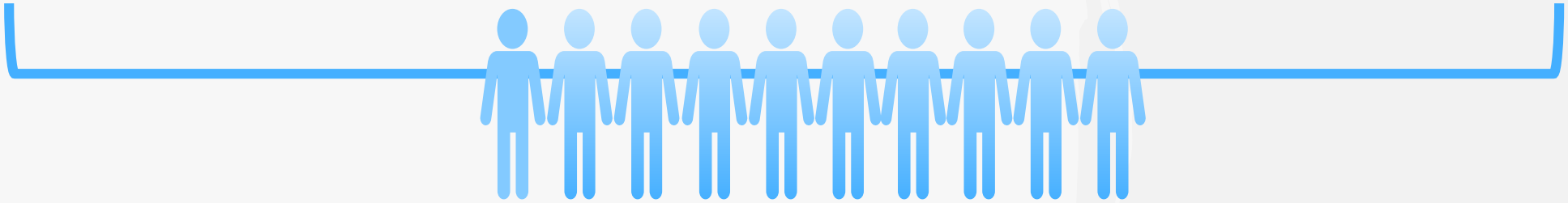
Issues:

- Not to be confused with compassionate use
- Regulated via Clinical Trial regulations
- More a kind of early access / key role of Community Advisory Boards

CHMP evaluation (=marketing authorisation application submitted, 210 days +)

Authorised

HTA, pricing, reimbursement, distribution chain - in healthcare system



Placed on market, commercial route

Early access: can start before the marketing authorisation, but after an application has been submitted. Or after the authorisation has been granted, and during the price negotiation, the reimbursement decision, the organisation healthcare delivery etc.

Issues:

- The whole indication? A selected sub-group?
- What if product finally not reimbursed?
- Can data be collected, including on efficacy / impact for patients?

CAMPAIGN FOR ACCESS To CARE FOR PEOPLE WITH RARE DISEASES

Compassionate use?

83.8 *Where a compassionate use programme has been set up, the applicant shall ensure that patients taking part also have access to the new medicinal product during the period between authorisation and placing on the market*

REGULATION (EC) 726/2004 art. 83.2

- Running a Compassionate Use Programme (CUP) consists in making a not yet authorised medicinal product available, for compassionate reasons, to a group of patients
- EMA can provide an opinion on the target patient population for a CUP
- MS have an obligation to notify their programmes to EMA

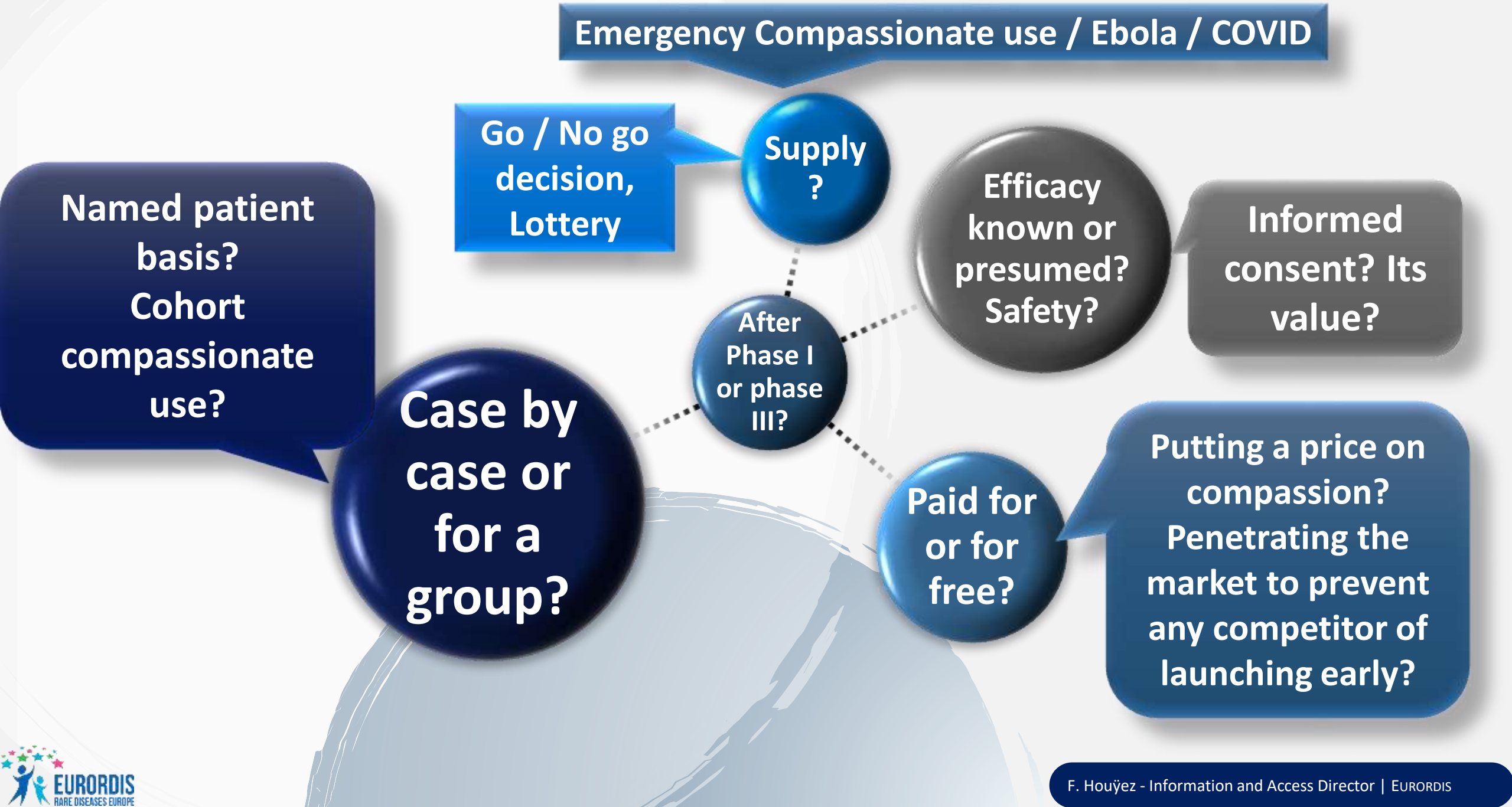
Conditions (for a defined group of patients)

- The medicinal product concerned must either be
  - the subject of an application for a marketing authorisation
  - or must be undergoing clinical trials

Usually no conditions for a named-patient basis

- Case-by-case, regulatory authorisation needed for each patient
- Even earlier than the compassionate use programme for a group of patients

CAMPAIGN FOR ACCESS To CARE FOR PEOPLE WITH RARE DISEASES


Emergency Compassionate use / Ebola / COVID
Go / No go decision, Lottery
Supply ?
Named patient basis? Cohort compassionate use?
Efficacy known or presumed? Safety?
Informed consent? Its value?
After Phase I or phase III?
Case by case or for a group?
Paid for or for free?
Putting a price on compassion? Penetrating the market to prevent any competitor of launching early?

Before you meet with developer

(ideally as part of a Community Advisory Board discussion, or a Scientific Advice meeting / Protocol Assistance at the EMA)

As this is in parallel to clinical trials

•1

- Know how compassionate use programmes are run in your country here

•2

- Have an eye on the pipeline in your disease and engage with developer around phase 1: **when could a CU be envisaged in the future?**

•3

- Discuss if you can think of a patient population that would not be eligible for clinical trials but for CU

•4

- Think of data that would be worth collecting from a CU, and how to see an impact (if product works)

•5

- Before early results at conference: remind company, they are fully responsible for the hype they create

CAMPAIGN FOR ACCESS To CARE FOR PEOPLE WITH RARE DISEASES

WHICH COMPASSIONATE USE SCHEME IS THE MOST EFFECTIVE IN THE EU?

FROM THE PERSPECTIVE OF PATIENTS

CAMPAIGN FOR ACCESS To CARE FOR PEOPLE WITH RARE DISEASES

COMPASSIONATE USE PROGRAMMES IN PROGRESS

LAST CHECK: 27 MAY 2025

France: 79% of innovative medicines authorised in the EU are available on a compassionate basis in average 24 (AAC) to 9 months (EA) before the marketing authorisation

- 34 (AMHV here and here)

Germany 

- 5 (EAMS here)

United Kingdom (average/year) 

- 2* (see here)

Netherlands 

- 282** (here)

France 

*: 1 or 2 granted per year

**: 38 early access (98 from 2021 to 2023, 100,000 patients), and 244 products on a named patient basis

https://www.has-sante.fr/upload/docs/application/pdf/2023-10/synthese_aap_2ans.pdf

CAMPAIGN FOR ACCESS To CARE FOR PEOPLE WITH RARE DISEASES

A SUCCESS STORY

CHMP EARLY DIALOGUE

12/2021

Xenpozyme® for Niemann Pick A/B or B

Mild to massive hepatosplenomegaly, hypersplenism leading to thrombocytopenia, interstitial lung disease, dyslipidaemia and CNS manifestations

FRANCE: AAC FOR XENPOZYME

01/2022

Interviews with 5 patients

2 from UK
1 from Norway
1 from France
1 from Spain

UK, mother and son: 17 yo, spleen enlarged by 12x, liver 8x
Exhausted, can't stand it anymore.
What about a CU ? Unaware
EURORDIS explained the procedure

CU STARTED, NICE

17/04/22

Dose escalation

7 doses before maximum dose

Hospital every 2 weeks until July, then home

3 to 4h infusion

EU MA

24/06

UK MHRA

08/2022

Mother consulted by NICE (appraisal)

Son just had his first full dose at the end of his escalation.

"He feels good and benefits are already showing in his blood. Can walk with much less fatigue"

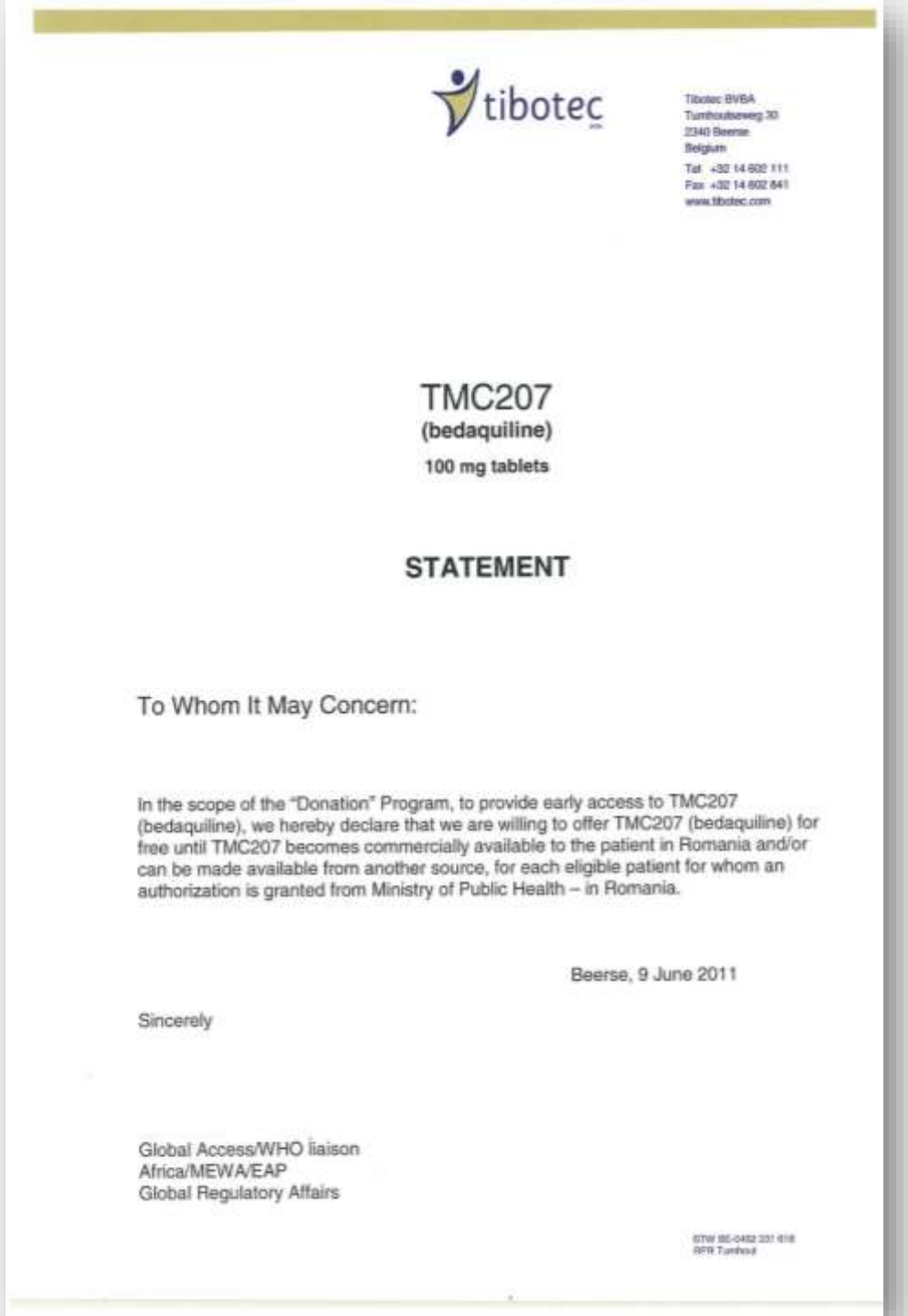
NICE CONCLUSIONS

03/2024

For this adolescent, CU started 120 days before MA and 704 days before NICE conclusion.

Not reimbursed, product is effective, but price too high. *People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this decision*

For a 70kg person, annual price ≅ 744 000€



tibotec

Tibotec BVBA
Turnhoutseweg 30
2340 Beerse
Belgium
Tel +32 14 602 111
Fax +32 14 602 841
www.tibotec.com

TMC207
(bedaquiline)
100 mg tablets

STATEMENT

To Whom It May Concern:

In the scope of the "Donation" Program, to provide early access to TMC207 (bedaquiline), we hereby declare that we are willing to offer TMC207 (bedaquiline) for free until TMC207 becomes commercially available to the patient in Romania and/or can be made available from another source, for each eligible patient for whom an authorization is granted from Ministry of Public Health – in Romania.

Beerse, 9 June 2011

Sincerely

Global Access/WHO liaison
Africa/MEWA/EAP
Global Regulatory Affairs

- **Compassionate use and urgency?**

2011 Multidrug resistant tuberculosis

Request from a patient in Romania, cousin of a member of the National Rare Disease Alliance

CU in France for TMC207 (orphan), but no patient

EURORDIS contacted the developer: Immediate positive response from developer, but 6 months to organise the programme

Anticipate! CAB+++

- Consider 2 to 6 months in average for the first patient to be treated (more rapid for patient named basis CU)

CAMPAIGN FOR ACCESS To CARE FOR PEOPLE WITH RARE DISEASES

RESOURCES

HELPING YOU ADVOCATING FOR CU / EA

CAMPAIGN FOR ACCESS To CARE FOR PEOPLE WITH RARE DISEASES

To advocate for fewer inequalities in accessing promising treatments on a compassionate basis

In the context of the pharmaceutical legislation revision, a concrete proposal to facilitate access to medicines

https://download2.eurordis.org/positionpapers/early-access-to-medicines-in-europe-compassionate-use-to-become-a-reality.pdf

Heads of Medicines Agencies

https://www.hma.eu/fileadmin/dateien/Human_Medicines/01-About_HMA/Working_Groups/Timely_Access/2020_04_Compassionate_use_program.pdf

Compassionate use program

The EU regulatory framework makes it possible for non-authorized medicines to be made available under certain circumstances. This is achieved through a compassionate use program.

Relevant regulation

According to article 83 of Regulation (EC) No 726/2004, medicinal products without a Marketing Authorisation *may be made available for compassionate reasons to a group of patients with a chronically or seriously debilitating disease or whose disease is considered to be life-threatening, and who can not be treated satisfactorily by an authorized medicinal product*.

National jurisdiction

Compassionate use programs falls under national jurisdiction and, in most Member States under the remit of National Competent Authorities (NCA). Article 83 of Regulation (EC) No 726/2004, states that the Committee for Medicinal Products for Human Use (CHMP) has an advisory role at the request of a Member State. The individual NCA decide whether or not to approve the use of medicinal products without a market authorization.

The NCA in the Member State decides if such a program fulfils an unmet medical need according to their clinical practices and available alternatives. Some Member States have a long tradition on early access programs, including compassionate use, and others have different provisions in their national legislation.

Refused to create an online catalogue. Instead:

- Czech Republic – State Institute for Drug Control (SUKL)
  http://www.olecich.cz/encyklopedie/dostupnost-leciv-v-cr
  Information about actual use of non-authorised medicinal products is published regularly at http://www.sukl.cz/hodnoceni-neregistrovanych-lp
- Denmark -Danish Medicines Agency
  https://laegemiddelstyrelsen.dk/en/licensing/compassionate-use-permits/
- Estonia – Ravimiamet agency
  https://www.ravimiamet.ee/en/medicines-used-cup-and-npp-programs
- France - French National Agency for Medicines and Health Products Safety (ANSM)
  https://www.ansm.sante.fr/Activites/Autorisations-temporaires-d-utilisation-ATU/Faire-une-demande-d-autorisation-temporaire-d-utilisation/(offset)/3
- Germany – Federal Institute for Drugs and Medical Devices (BfArM)
  https://www.bfarm.de/EN/Drugs/licensing/clinicalTrials/compUse/_node.html
- Germany – Paul-Ehrlich-Institut (PEI)
  http://www.pei.de/EN/information/license-applicants/clinical-trial-authorisation/compassionate-use/compassionate-use-node.html

CAMPAIGN FOR ACCESS To CARE FOR PEOPLE WITH RARE DISEASES

A Helping Hand for People with no Treatment Options

IHI consortium co-lead by Eurordis
4-year
Submitted April 2025
Response: before 30/09/2025

Public partners
KU Leuven
EURORDIS
Uni Gröningen
Hospices Civils de Lyon
UMIT Tirol
Erasmus MC
Eupati-Spain
Tehistark
Syreon Institute
TeamIT
ANSM
HAS
MEB
AEMPS
Bfarm
Genethon
Hospital Clinic BCN

Pharma partners
Servier
Jazz Pharma
Sanofi (Mytonic Dystrophies DM1)
Roche
Novartis
BMS
Italfarmaco
NovoNordisk
Ferrer
SOBI

Summary

Definitively a role for you

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

In some domains (viral diseases): 100% of medicines have a compassionate use – as patient advocates are on the front line

You can initiate the preparation of a CUP
CAB+++ CAB+++ CAB+++

Contact EURORDIS if you need help, information, support for your campaign to access compassionate use. See EURORDIS's position here

CAMPAIGN FOR ACCESS To CARE FOR PEOPLE WITH RARE DISEASES

CAMPAIGN FOR
ACCESS
To
CARE FOR
PEOPLE WITH
RARE DISEASES

TIME FOR QUESTIONS

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Over 10 or 20 years of drug development: when is best timing to request compassionate use? Is your own organisation ready?

CAB +++

When more safety data are available?

When interim analysis results are known?

During CHMP evaluation ?

After MA, before reimbursement decision? Early access, special funds…

Lab research → Animal testing → FIM studies (first in men) Tested in 10-20 → Proof-of-concept studies Tested in 30-50 → Confirmatory studies Tested in hundreds → Regulatory evaluation MAA → HTA, reimbursement and pricing: commercial access

Here? Here? Here? Here? Here? Here?

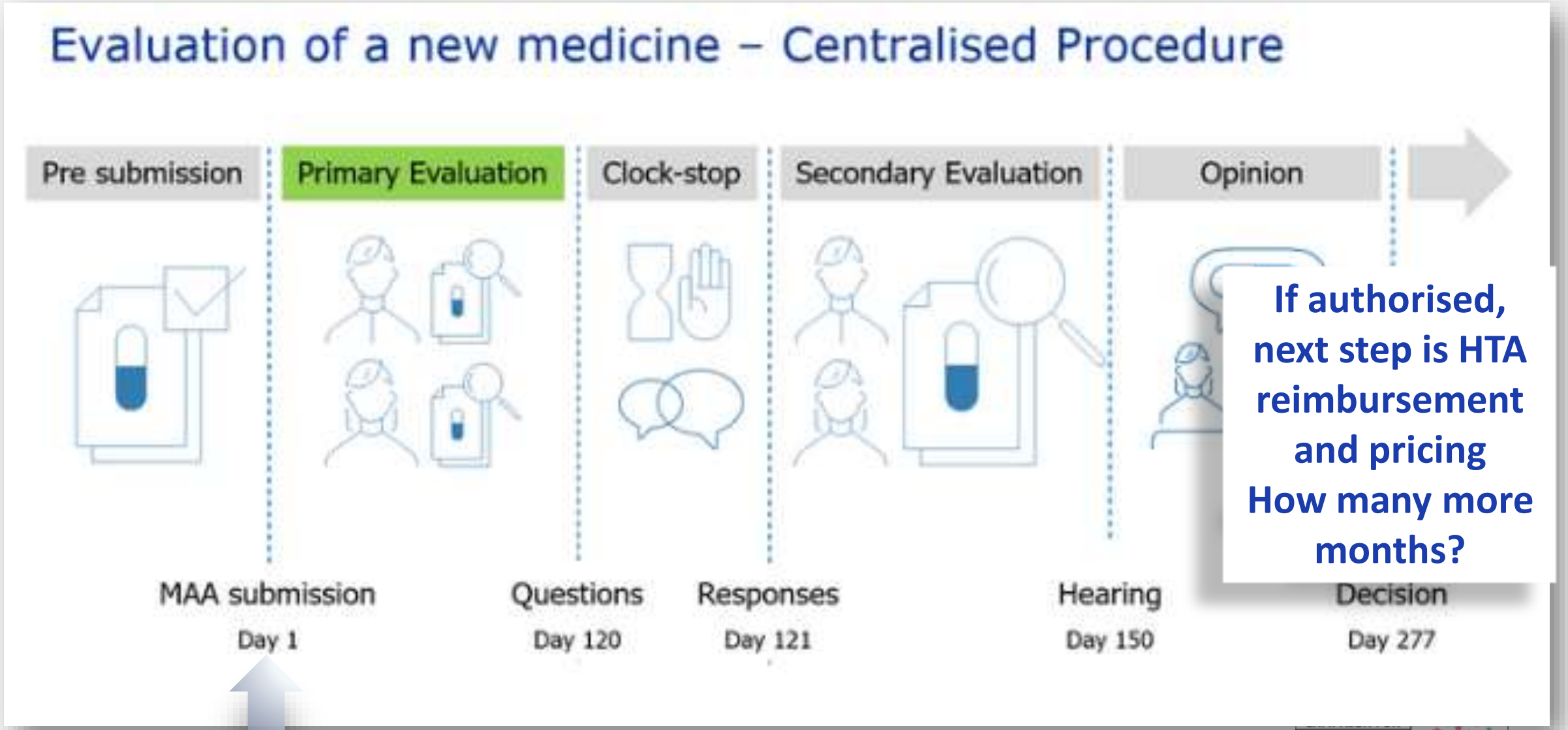
When early safety data are available?

At the Go/No go decision?

When final results are known, before MA submission?

CAMPAIGN FOR ACCESS To CARE FOR PEOPLE WITH RARE DISEASES

CHMP Early Contact – is it the right timing to request a compassionate use?



The Zolgensma® controversy: authorised 18 May 2020

- Further reading

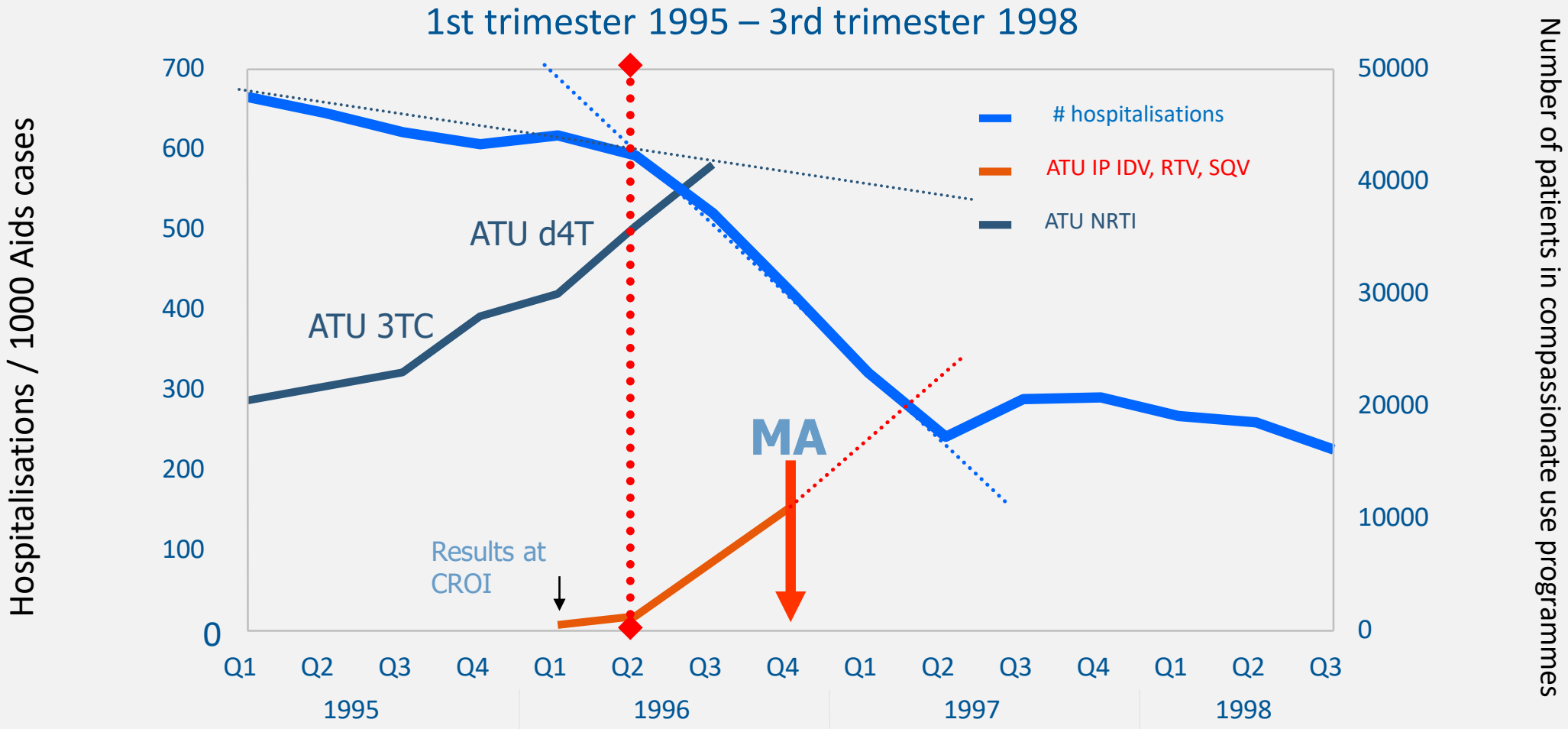
Firth, I., Schirrmacher, H., Hampson, G. and Towse, A. (2021)

Key Considerations for Early Access Schemes for Single-Administration (One-Time) Therapies.

OHE Consulting Report. Available from https://www.ohe.org/publications/key-considerations-early-access-schemes-single-administration-one-time-therapies

Clinical effectiveness of a compassionate use programme

Hospitalisation rates for 1000 AIDS patients, France 1995-98



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

9 orphan products, 42 countries, 75 programmes

(EURORDIS SURVEY 2011

RETROSPECTIVE ANALYSIS - DATA PROVIDED BY MAH)

ONLY FRANCE PROPOSED ALL 9 PRODUCTS ON A COMPASSIONATE BASIS

CAMPAIGN FOR ACCESS To CARE FOR PEOPLE WITH RARE DISEASES