European Federation of Pharmaceutical Industries and Associations

Compassionate Use Systems in the EU – How to improve for early access to patients

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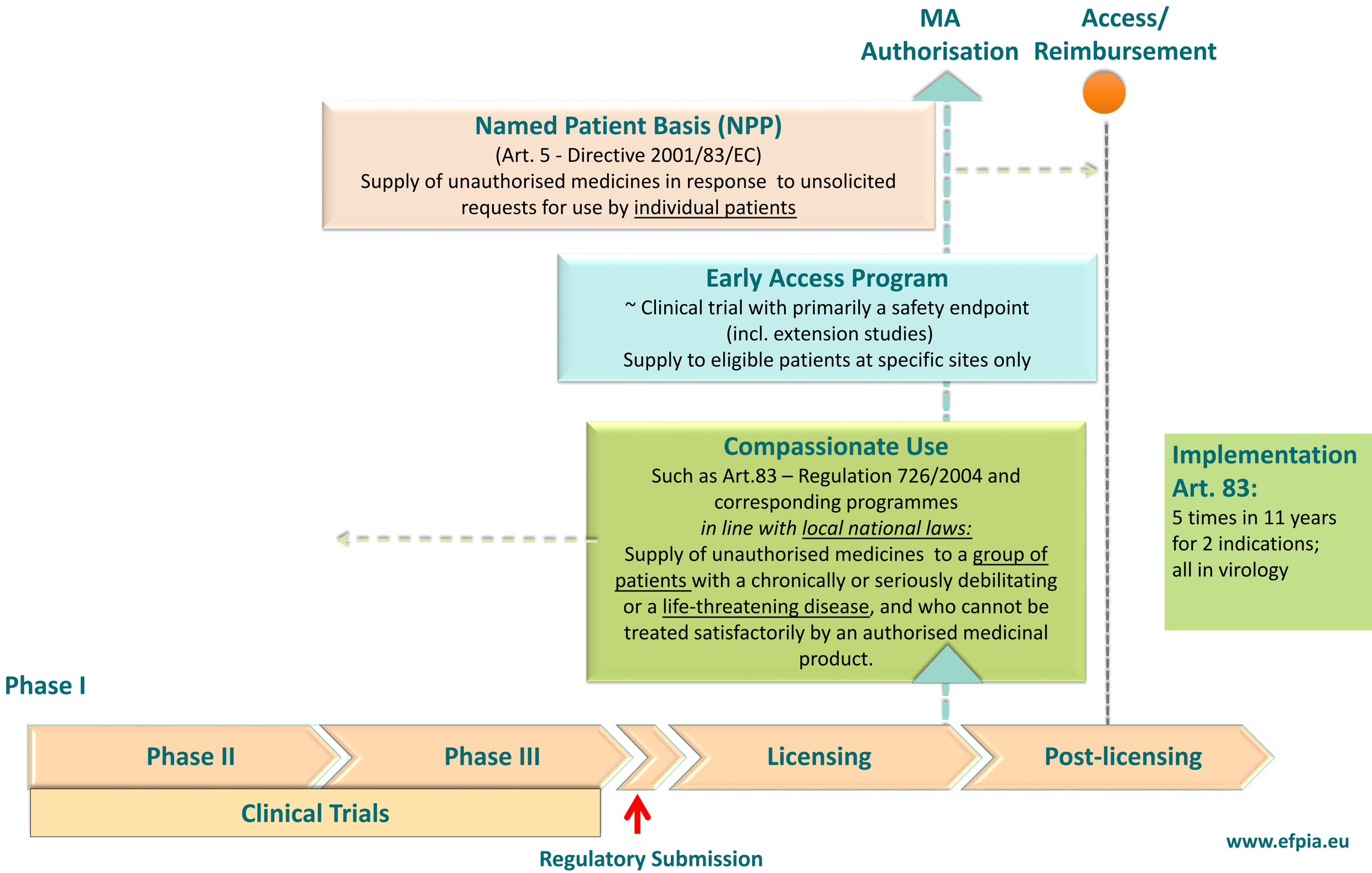
Agenda

1. Early Access Schemes in the Member States – Heterogeneity
2. Experience with National & “Centralised” Compassionate Use Programmes – Case Study
3. Future Opportunities – Priorities for Improvement

1. Early Access Schemes in the Member States (MSs) - Heterogeneity

Early Access Programmes in EU

Implementation is based on applicable national laws



Specific Differences in MS Schemes

Approval or notification, dossier content, EC approval, timing, applicant, length of validity, protocol, safety reporting

Allowed, required, safety, efficacy

Necessary or not

General system

NPP, Cohort, Both, direct import, different terminology

Approval

Liability

Physicians, Company, hospital or applicant

Data collection

Medicine

IMP or commercial supply. Labeling requirements, how long need/allowed to supply

Import process

Payment

Companies, hospitals, insurance or patients

EC – Ethics Committee

2. Experience with National and “Centralised” Compassionate Use Programmes (CUPs)

Case Study

BMS- Overall CUP Experience with Daclatasvir

Treatment of Hepatitis C in combination with Sofosbuvir +/- Ribavirin

Combined & tailored approach:

- Name Patient Programme (NPP)
- Compassionate Use Treatment Protocol – Cohort, in some EU countries

Regulatory & Medical Implementation

- Article 83 dossier: collaboration with EMA excellent in all steps
- Regulatory environment highly varied across MSs
- Not a 'clinical trial' but interest to maximise data collection via treatment protocol (incl. efficacy)
- "Real life" safety & efficacy data collected
- Interim data published & presented in international congresses (dissemination of knowledge)
- Opportunity for thousands of patients with no other treatment options and highest medical need

Timeline Overview – Daclatasvir

Art. 83 CHMP Opinion: November 2013

2013												2014					
Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun

Implementation of CUP in EU, all cohorts running by the end June

Ph 2 Study AI444040:
DCV+SOF +-RBV
Unmet medical need
EASL: compelling data presented

CHMP request art. 83

CHMP Opinion art 83

DCV MAA validated

MAA Accelerated Assessment

CHMP Opinion

27 June 2014, EMA site:

***"EMA recommends approval of Daklinza in chronic hepatitis C. First-in-class medicine to offer new treatment option for patients*". Authorised by European Commission on 22 Aug. 2014**

CUP – Compassionate Use Programme
MAA – Marketing Authorisation Application
DCV- Daclatasvir
SOF- Sofosbuvir
RBV - Ribarivin

BMS Experience for Daclatasvir with MSs

- **Majority of MSs have national laws on CU:**
  - Named patient programme (NPP)
  - Cohort compassionate use
  - both or other mechanisms
- **Primary purpose: provide early access to patients in urgent need**
- **BMS Experience:**
  - Tailoring implementation:
    - Cohort treatment in line with Art. 83: established in 7 MSs
      Opinion recommendation followed & adapted by MSs (with in some cases broader use)
    - NPP: several countries
  - Challenges resulting from mutual lack of experience (company and MSs), since this provision of the EU law is rarely used, e.g:
    - Varied requirements, review of treatment protocol, varied approval timelines, lack of guidance templates (e.g as in ATU French system)
  - Excellent interactions with MSs health authorities

CUP Daclatasvir and Real World Data

Some key efficacy data collected from the cohort program

- Situation mimicked the “real world setting” for the sickest patient population, for which clinical studies were not available in EU.
- Collection & reporting of safety data followed national & EU laws: varied.
- Patient population included patients with common co-morbidities - highest medical need. Welcomed by treating physicians.

Different mechanisms for collection of efficacy data needed to be implemented

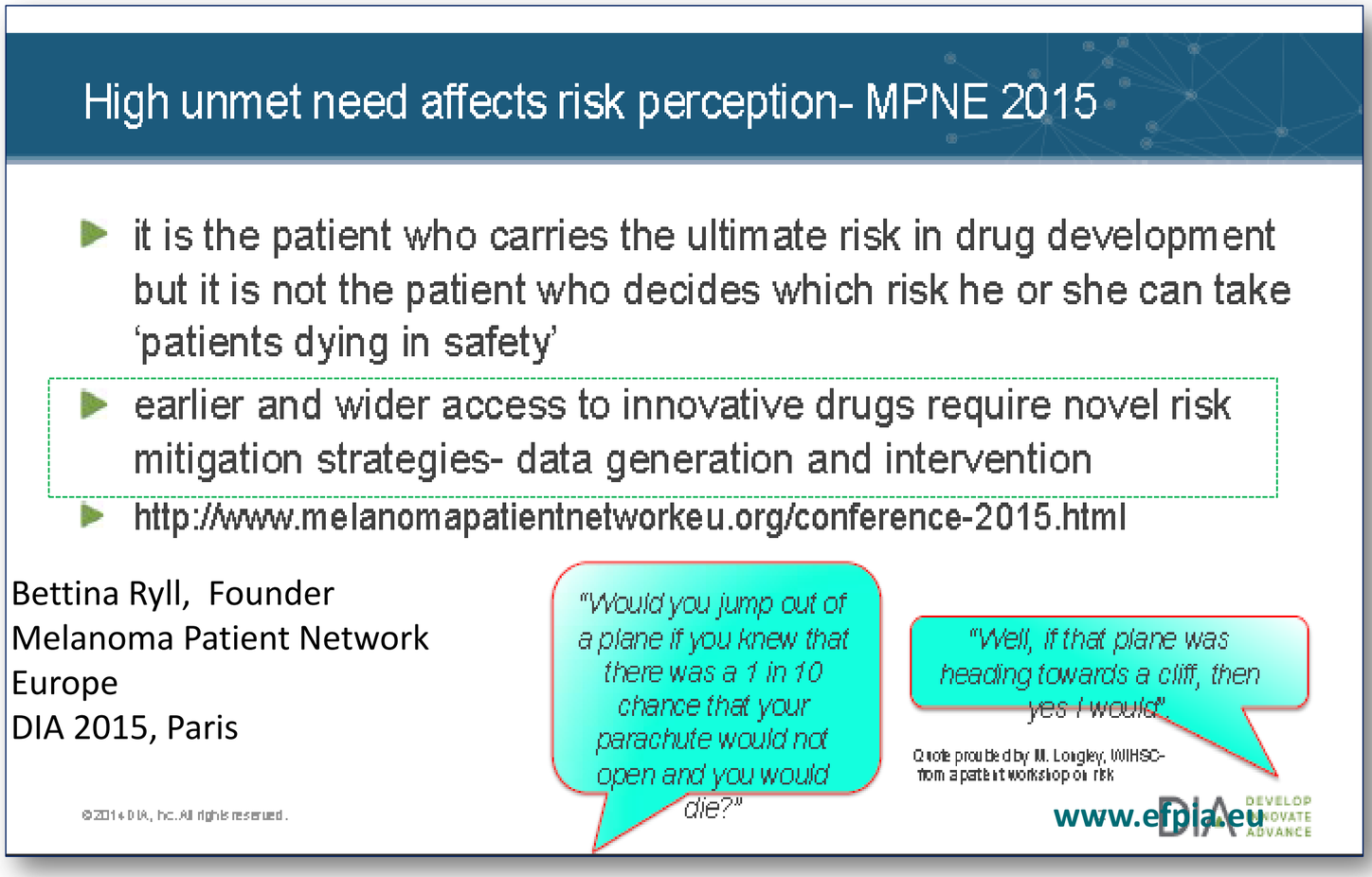
- Further alignment across MSs on principles of implementation of CUP and collection of data (efficacy and safety) would be very beneficial given high interest by multiple stakeholders, including patients.

Patients' Perspective

According to feedback heard:

- Expect to receive proper education/ information via patient groups
- Expect to obtain equal chance across MSs for early access
- Need to decrease administrative burden and procedure time for early access
- Expect different approach of health authorities to risk-taking
- Very positive feedback on DCV Art. 83 implementation

„There is nothing worse for a patient, from a psychological and human standpoint, than being severely ill or even dying from a disease, when experimental treatments are out there, pending final evaluation."
/EURORDIS/



3. Future Opportunities Priorities for Improvement

Priorities for Improvements (1)
Use/ Request of Art. 83

Problem Statement:

- It seems that very few MSs have requested Art. 83 opinions (according to available info):
  - Ireland (1)
  - Sweden (3)
  - Finland (1)
- Lack of transparency on whether MSs notify EMA of “compassionate use” (Art. 83 (3)

Proposals:

- Research (survey/ study) needed on
  - Overview on
    - ongoing CU Programs in MSs
    - functioning of reporting mechanisms to EMA (Art. 83(3))
  - Root cause analysis why MSs are not requesting an Article 83 opinion
  - Root cause why only few MSs established the framework to support cohort CUPs

Priorities for Improvements (2)
Article 83 Process

Problem Statements:

- *Request*: Currently only MS can request Art. 83 opinion
- *Guidelines:* Lacking considerations of real world/ efficacy data collection and clarification on timelines

Proposals:

- *Request:*
  - Consider how patient groups and industry can trigger requests (via MSs)
  - PRIME designation/ use of Adaptive Pathways could trigger (Co-) rapporteur MS to request Article 83 opinion after consultation with applicant (optional) → in case of unmet medical need and availability of adequate data
- *Guidelines:*
  - CUP to allow for critical real world data gathering
  - Guidelines for collection and more structured assessment of this first real world data could be developed for public benefit
  - Further clarification on timelines to be detailed and published by EMA/CHMP

Priorities for Improvements (3)
Alignment by Member States

Problem Statement:

- Current different approaches by Member States on compassionate use lead to
  - disparities in access to new innovative medicines by patients
  - high administrative efforts by all stakeholders

Proposals:

- Establishment of a framework for cohort CUPs across Member States is critical to allow full operation of Article 83
- Better alignment required between different national compassionate use systems in particular with respect to
  - scientific criteria
  - procedures (timelines)
  - standardised documents (e.g. CUP protocol templates)

Priorities for Improvements (4)
Integration of Patient Perspectives

Problem Statements:

- Disparities in patient access to innovative medicines across MSs
- Limited/ lack of patient involvement into set up of programmes/ current system

Proposals:

- Education/ info of patients on early access programs via patient groups
- Integration of patient perspectives into set-up of compassionate use programmes
- IMI projects may explore/identify opportunities and methodology for better patient involvement

Summary - Improve Current System

Within the existing framework

- **Application:** MSs to make more use of Art 83 and leverage the CHMP expertise.
- **Request:** Possibilities for patient groups and industry to request Art. 83 via MSs. (Co-) Rapporteur identified early in PRIME to allow for early request of Art. 83 opinions after consultation with applicant (optional).
- **Real world data:** Utilise CUPs to allow for critical real world data gathering and establish guidelines for collection and more structured assessment of this first real world data.
- **Alignment:** MSs to drive for stronger alignment between different national compassionate use systems in particular with respect to scientific criteria, procedures, standardised documents (e.g CUP protocol templates).
- **IMI projects** may explore/identify opportunities and methodology to enhance patient perspectives into setup of CUPs and improve current systems.

Future additional/ legislative changes

- **National framework for cohort CUPs:** Systematic national implementation of a framework for cohort CUPs in all MSs to allow operation of Article 83 across all MSs.

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