Mechanism of action PIPs

Relevant and expected in Oncology

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Gustave Roussy, France
ENprEMA 2 october 2024

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ITCC
INNOVATIVE THERAPIES FOR CHILDREN AND ADOLESCENTS WITH CANCER

ACCELERATE
INNOVATION FOR CHILDREN AND ADOLESCENTS WITH CANCER

ITCC P4
PAEDIATRIC PRECLINICAL PROOF OF CONCEPT PLATFORM

Disclosure

Pr Gilles Vassal, MD, PhD

ITCC Industry strategy lead
ITCC-P4 COO
ACCELERATE Chair

Advice on pediatric oncology drug development to:
Astra-Zeneca, Bayer, BMS, Daichi, Merck, Novartis, Pfizer, Roche/Genentech, Sanofi

Do not accept personal remuneration.

REGULATION (EC) No 1901/2006 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 12 December 2006

on medicinal products for paediatric use and amending Regulation (EEC) No 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004

(Text with EEA relevance)

Adult condition driven pediatric developments

CHAPTER 2

Waivers

Article 11

1. Production of the information referred to in point (a) of Article 7(1) shall be waived for specific medicinal products or for classes of medicinal products, if there is evidence showing any of the following:

(a) that the specific medicinal product or class of medicinal products is likely to be ineffective or unsafe in part or all of the paediatric population;

(b) that the disease or condition for which the specific medicinal product or class is intended occurs only in adult populations;

(c) that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

2. The waiver provided for in paragraph 1 may be issued with reference either to one or more specified subsets of the paediatric population, or to one or more specified therapeutic indications, or to a combination of both.

Need to ACCELERATE Science driven pediatric anticancer drug development

10 YEARS

2011 ⋯⋯▸ **2012**

Marketing authorisation

U.S. FOOD & DRUG ADMINISTRATION — European Commission

Crizotinib in ALK+ Lung cancer

PREA stands for Pediatric Research Equity Act

Paediatric Regulation (EC) N°1901/2006

Waivered pediatric development

(lung cancer does not occur in children)

Academic pediatric development
More than 200 patients

2021 ⋯⋯▸ **2022**

Marketing authorisation

U.S. FOOD & DRUG ADMINISTRATION — European Commission

Crizotinib for children and adolescents with

ALCL and IMT

*anaplastic lymphoma kinase gene
** inflammatory myofibroblasic tumor

Need to ACCELERATE Science driven pediatric anticancer drug development

10 YEARS

2013

Marketing authorisation

Dabrafenib for BRAFmt melanoma

2023

Marketing authorisation

Dabrafenib for BRAFmt low and high grade gliomas >1 year (appropriate formulation)

In combinaton with

2013 **2014**

Trametinib for melanoma

2023 **2024**

Trametinib for low and high grade gliomas in children (appropriate formulation)

Multistakeholder working group on new development strategy to solve the ALK issue


Andy Pearson


Nicole Scobie

2016

European Journal of Cancer 62 (2016) 1–8

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

ELSEVIER

Current Perspective

Implementation of mechanism of action biology-driven early drug development for children with cancer

Andrew D.J. Pearson [a,*,1], Ralf Herold [b], Raphaël Rousseau [c], Chris Copland [d], Brigid Bradley-Garelik [e], Debbie Binner [f], Renaud Capdeville [g], Hubert Caron [h,i], Jacqueline Carleer [j], Louis Chesler [k], Birgit Geoerger [l], Pamela Kearns [m], Lynley Marshall [n], Stefan M. Pfister [o], Gudrun Schleiermacher [p], Jeffrey Skolnik [q], Cesare Spadoni [r], Jaroslav Sterba [s,t], Hendrick van den Berg [b], Martina Uttenreuther-Fischer [u], Olaf Witt [v], Koen Norga [w], Gilles Vassal [x] on behalf of Members of Working Group 1 of the Paediatric Platform of ACCELERATE[2]

Authors From Academia, Advocacy, Industry and Regulatory bodies

Request for Mechanism of action biology-driven early drug development

- Molecular profiling of paediatric tumours at diagnosis and relapse √
- Aggregated databases of paediatric biological tumour drug targets √
- Joint academic–pharmaceutical industry pre-clinical platform to analyse the activity of new drugs = ITCC-P4 and PIVOT √
- Paediatric Strategy Forums to define Unmet Needs and facilitate prioritisation √
- Change in Regulations (RACE and ongoing EU revision) √

FDA U.S. FOOD & DRUG ADMINISTRATION

PREA stands for Pediatric Research Equity Act

2017

RACE for Children Act

- **Requires pediatric evaluation of new molecularly targeted drugs and biologics "intended for the treatment of adult cancers** and **directed at a molecular target substantially relevant to the growth or progression of a pediatric cancer**."

Entered into force August 2020

Proposal for a

REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing rules governing the European Medicines Agency, amending Regulation (EC) No 1394/2007 and Regulation (EU) No 536/2014 and repealing Regulation (EC) No 726/2004, Regulation (EC) No 141/2000 and Regulation (EC) No 1901/2006

Released on April 26, 2023

A science driven and patient centric regulation

Article 75

Waivers

1. In accordance with the procedure set out in Article 78, the Agency may decide that the production of the information referred to in, Article 6(5), point (a), of [revised Directive 2001/83], shall be waived for products or for classes of medicinal products, if there is evidence showing any of the following:

(a) that the specific medicinal product or class of medicinal products is likely to be ineffective or unsafe in part or all of the paediatric population;

(b) that the disease or condition for which the specific medicinal product or class is intended occurs only in adult populations, unless when the product is directed at a molecular target that on the basis of existing scientific data, is responsible for a different disease or condition in the same therapeutic area in children than the one for which the specific medicinal product or class of medicinal products is intended for in the adult population;

(c) that the specific medicinal product is likely to not represent a significant therapeutic benefit over existing treatments for paediatric patients.

2. The waiver provided for in paragraph 1 may be issued with reference either to one or more specified subsets of the paediatric population, or to one or more specified therapeutic indications, or to a combination of both.

3. On the basis of the experience acquired as a result of the operation of this Article or of scientific knowledge the Commission is empowered to adopt delegated acts in accordance with Article 175 to amend the grounds for granting a waiver detailed in paragraph 1.

Not limited to cancer
But in the same therapeutic area

Development of an anticancer asset in adults: 3 questions

- Is mechanism of action relevant for pediatric malignancies?
- Is the asset potentially active (preclinical data) on childhood cancers?
- Would the asset address an Unmet Medical Need?

Relevant questions outside oncology

Think Early, no later than when an asset is enterin g first in human trial

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ANDREW McDONOUGH B+ FOUNDATION

To design MOA PIPs or scientifically relevant waiver

Request for Mechanism of action biology-driven early drug development

√ • Molecular profiling of paediatric tumours at diagnosis and relapse

√ • Aggregated databases of paediatric biological tumour drug targets

• Joint academic–pharmaceutical industry pre-clinical platform to analyse the activity of new drugs = ITCC-P4 and PIVOT

• Paediatric Strategy Forums to define Unmet needs and facilitate prioritisation

• Change in Regulations (RACE and ongoing EU revision)

ITCC pedcan portal:
Federated agreggation of more than 6500 complete sequencing of pediatric malignancies at relapse

www.pedcanportal.eu

To design MOA PIPs or scientifically relevant waiver

Request for Mechanism of action biology-driven early drug development

- Molecular profiling of paediatric tumours at diagnosis and relapse
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√

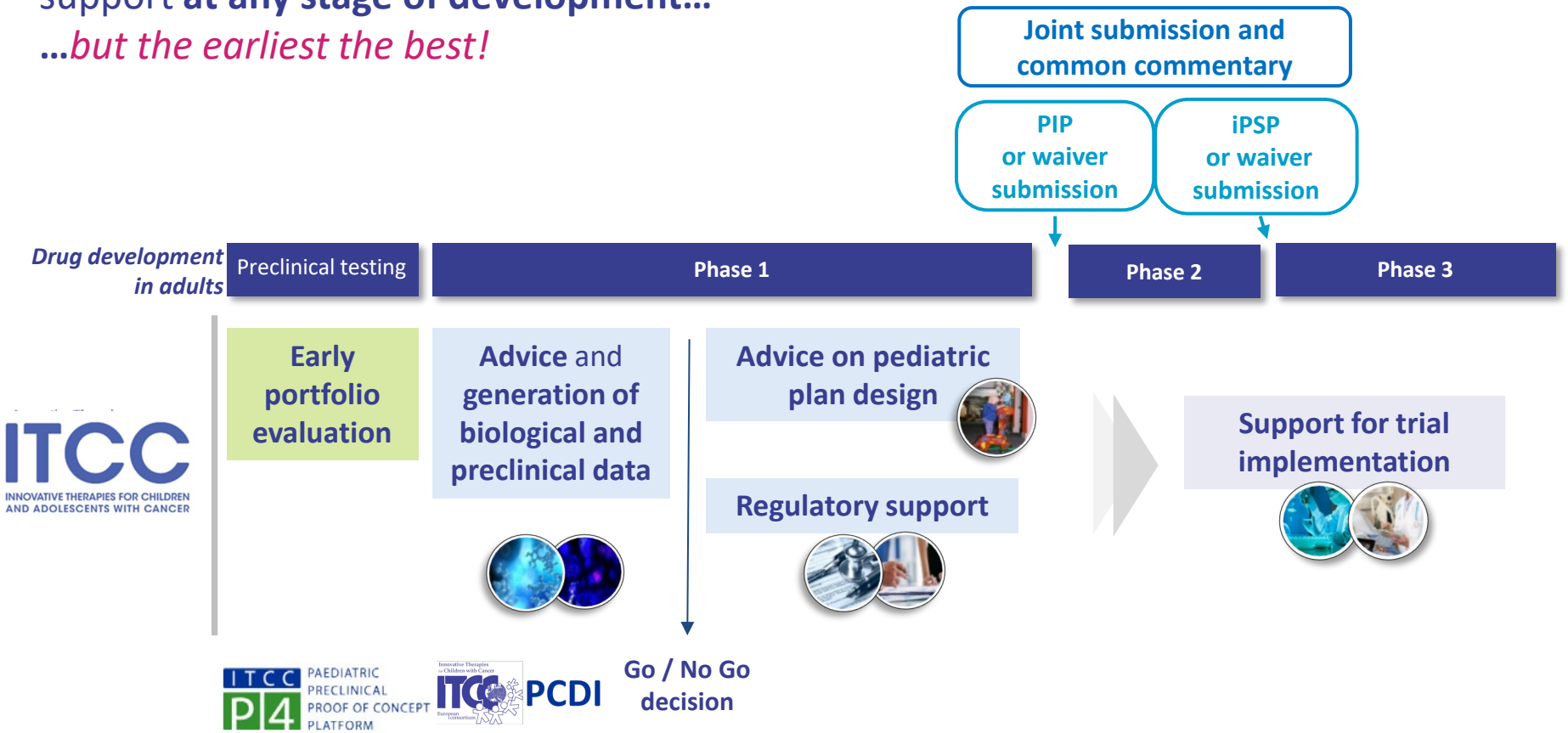
ITCC P4

gGMBH

www.itccp4.com

Advice to industry

support **at any stage of development…**
…*but the earliest the best!*



FDA participation

Paediatric Strategy Forums

Overall more than 300 assets discussed by 2000 participants.

2017

- PSF - 1 **ALK inhibition**
- PSF - 2 **Mature B-cell lymphoma**

2018

- PSF - 3 **CheckPoint Inhibitors**

2019

- PSF - 4 **Acute Myeloid Leukemia**
- PSF Prioritisation **Acute Myeloid Leukemia**

2020

- PSF - 5 **Epigenetic modifiers**
- PSF Prioritisation **BET inhibitors**

2021

- PSF - 6 **Second ALK inhibition**
- PSF - 7 **CAR T cells**
- PSF - 8 **TKI in Sarcomas**

2022

- PSF - 9 **MAPK inhibitors**
- PSF -10 **DNA Damaging agents**

2023

- PSF - 11 **PI3K/AKT/mTOR Pathway**
- PSF - 12 **CDK 4, 6 & 9 inhibitors**

2024

- PSF - 13 **Diffuse Midline Gliomas**
- PSF - 14 **GD2 therapies**

Conclusions

Clarify the scope of article 75

3 questions:

- Is mechanism of action relevant for a pediatric disease different from the adult indication?
- Is the asset potentially active (preclinical data)?
- Would the asset address an Unmet Medical Need?

Need for Close collaboration between Industry, pediatric specialists, advocates and regulators

We are ready in pediatric oncology

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