EPTRI

European Paediatric Translational Research Infrastructure

Drug safety in translational paediatric research – How to anticipate and manage treatment related risks

Beate Aurich, Evelyne Jacqz-Aigrain

Department of Paediatric Pharmacology and Pharmacogenetics, Robert Debré Hospital,

APHP, Paris, France.

EPTRI Open Meeting, 02 - 03/04/2020

This project has received funding from the European Union's Horizon 2020 research and innovat programme under Grant Agreement No 777554

Hôpital universitaire Robert-Debré

Assistance Publique Hôpitaux de Paris

Declaration

The views and opinions expressed in the following PowerPoint slides are those of the individual presenter and should not be attributed to EPTRI or the European Commission.

This presentation has been funded by EPTRI (H2020-INFRADEV-2017-1, grant agreement number 777554). The authors consider not having any conflict of interest for this presentation. Beate Aurich has previously worked as a drug safety physician in pharmaceutical industry (GlaxoSmithKline and Novartis) and holds GSK shares.

EPTRI
European Paediatric Translational Research Infrastructure

Hôpital universitaire Robert-Debré
Assistance Publique Hôpitaux de Paris

How is knowledge of treatment risks included into a paediatric translational research program?

Aurich B, Jacqz-Aigrain E. *Drug safety in translational paediatric research – How to anticipate and manage treatment related risks.* EPTRI Meeting 3 April 2020.

Overview

- Anticipating treatment related risks: Safety profiling
- Paediatric protocol development and risk management
- Safety data review cycle
- Drug safety in paediatric translational research
- Summary

Anticipating treatment related risks: Safety profiling

Safety specification of study drug

General (all age groups) & paediatric data on

- Non-clinical data
- PK/PD (on & off-target)
- Pharmacogenetics
- Formulation (excipients, medication errors)
- Clinical data (clinical trial data & spontaneous reports)
- Pharmacoepidemiological data
- Class effects
- Literature

Paediatric study population

- Age corrected reference values (laboratory tests, vital signs, developmental assessment)
- Specificities of adverse drug reactions
- Comorbidities
- Comedications (safety profile, excipients, off-label/ unlicensed use, medication errors)
- Outcomes
- Limited availability of biosamples
- Limitations on invasive study procedures

Paediatric safety specification

- Identified treatment related risks
- Potential treatment related risks

Missing safety information

Safety profiles are population specific

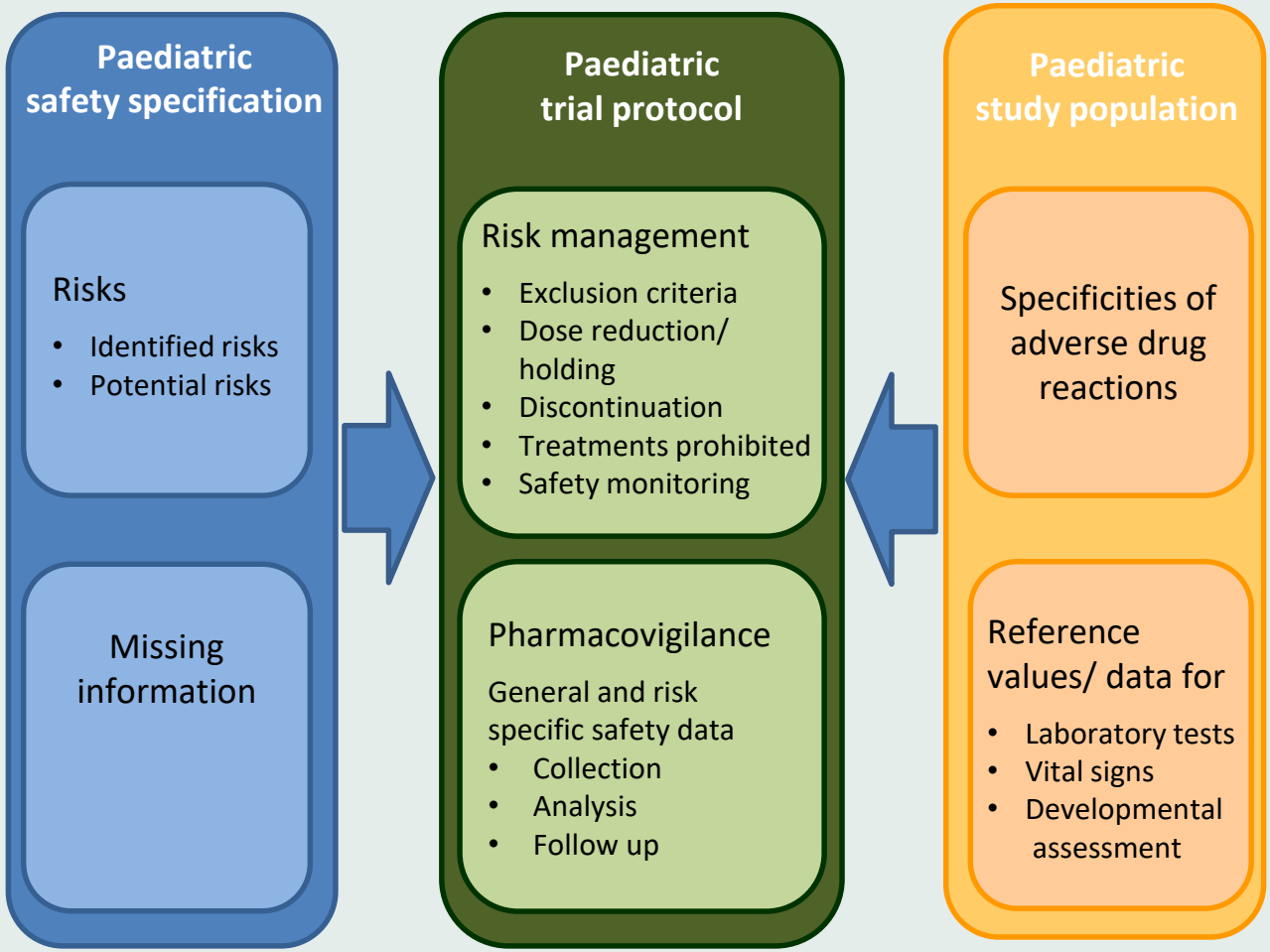
Safety profiling helps with

- Anticipating treatment related risks
- Identifying knowledge gaps
- Planning resources & priorities

ePTRI
European Paediatric Translational Research Infrastructure

Aurich B, Jacqz-Aigrain E. *Drug safety in translational paediatric research – How to anticipate and manage treatment related risks.* EPTRI Meeting 3 April 2020.

Paediatric protocol development & risk management



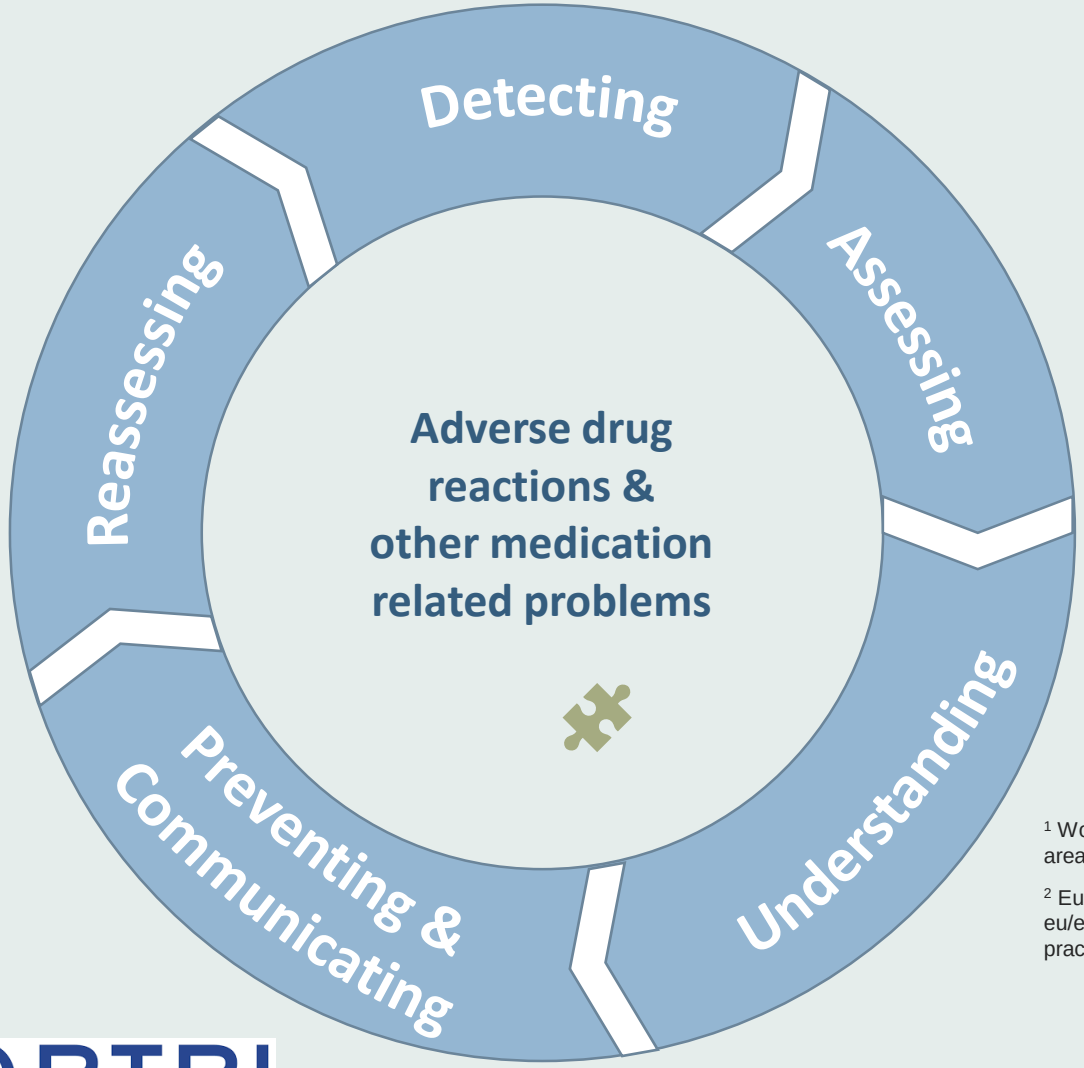
Paediatric protocol development includes

- Paediatric risk management
- Paediatric pharmacovigilance

ePTRI
European Paediatric Translational Research Infrastructure

Aurich B, Jacqz-Aigrain E. *Drug safety in translational paediatric research – How to anticipate and manage treatment related risks.* EPTRI Meeting 3 April 2020.

Safety data review cycle



Pharmacovigilance is defined as

the science and activities relating to the

- detection
- assessment
- understanding
- prevention

of adverse drug reactions or any other medication-related problems.[1]

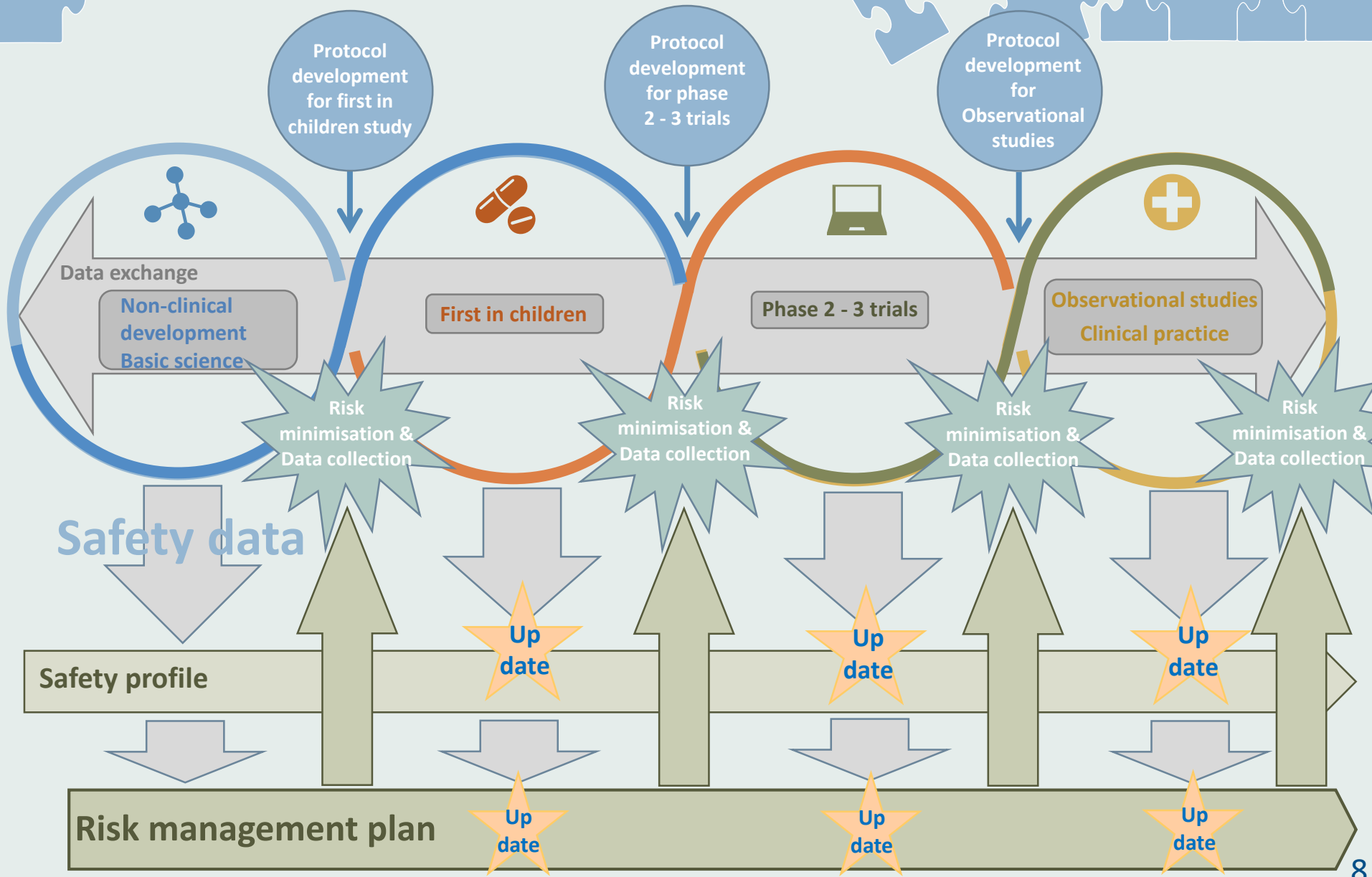
Risk management in drug safety is defined as the overall aim of

ensuring that the benefits of a medicinal product exceed the risks by the greatest achievable margin.[2]

[1] World Health Organisation, 2018. Available at: https://www.who.int/medicines/areas/quality_safety/safety_efficacy/pharmvigi/en/

[2] European Medicines Agency, 2017. Available at: https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-good-pharmacovigilance-practices-module-v-risk-management-systems-rev-2_en.pdf

Drug safety in paediatric translational research



Drug safety in paediatric translational research - EPTRI

Paediatric safety profile

- Identified risks
- Potential risks
- Missing information

Human Development and Paediatric Medicines Discovery (WP 5)

- Animal studies
- Assessment of toxicity and ADME properties

Paediatric Biomarkers and Biosamples (WP 6)

- Validation of paediatric biomarkers

Developmental Pharmacology (WP 7)

- Marker tests and techniques for efficacy testing and adverse drug reactions
- Pharmacogenetics and developmental interplay

Paediatric Formulation Science (WP 8)

- Prevention of medication errors
- Safety of excipients

- **Paediatric studies**
- **Paediatric clinical practice**

Paediatric safety profiling in translational research informs

- Non-clinical studies
- Clinical studies
- Clinical practice

EPTRI
European Paediatric Translational Research Infrastructure

Aurich B, Jacqz-Aigrain E. *Drug safety in translational paediatric research – How to anticipate and manage treatment related risks.* EPTRI Meeting 3 April 2020.

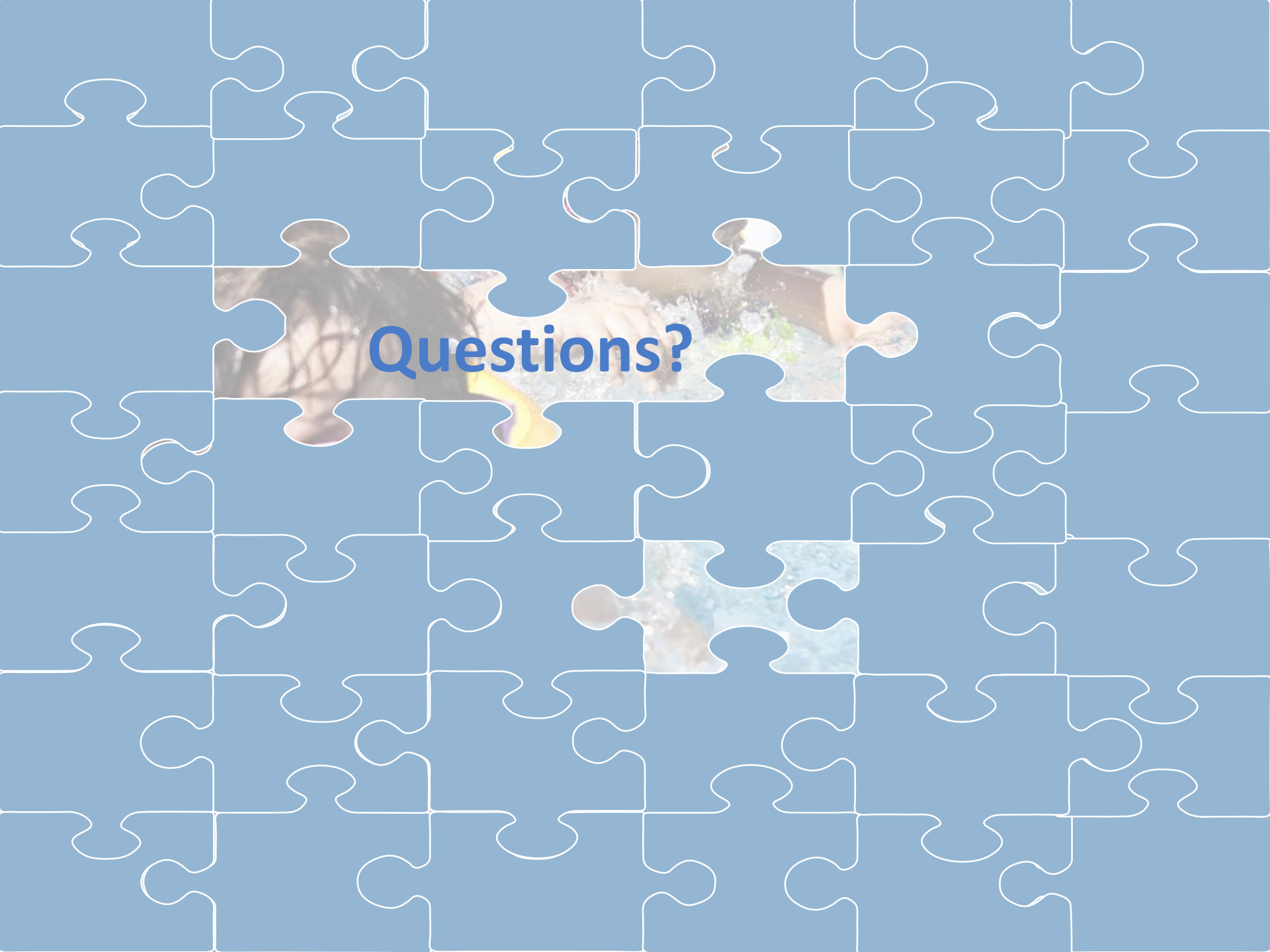
Summary

- Paediatric drug safety forms an integral part of translational research in children
- Paediatric safety profiling helps with the identification of
  - Treatment related risks
  - Knowledge gaps
  - Planning resources and priorities
- Paediatric safety profiling in translational research informs
  - Non-clinical studies
  - Clinical studies
  - Clinical practice
- Paediatric drug safety
  - Is a continuous process throughout the life cycle of a medicinal product/ device
  - Includes pharmacovigilance and risk management in clinical studies & practice
  - Informs the benefit-risk balance of treatments

ePTRI
European Paediatric Translational Research Infrastructure

Aurich B, Jacqz-Aigrain E. *Drug safety in translational paediatric research – How to anticipate and manage treatment related risks.* EPTRI Meeting 3 April 2020.

Hôpital universitaire Robert-Debré
Assistance Publique Hôpitaux de Paris


Questions?


Thank you.

Backup slides

Useful references

European Medicines Agency (EMA)
https://www.ema.europa.eu/en/human-regulatory/overview/paediatric-medicines-overview

Food and Drug Administration (FDA)
https://www.fda.gov/science-research/science-and-research-special-topics/pediatrics

World Health Organisation (WHO)
https://www.who.int/ictrp/child/ethics/en/

Council for International Organisations of Medical Sciences (CIOMS)
https://cioms.ch/shop/product/management-of-safety-information-from-clinical-trials-report-of-cioms-working-group-vi/

Abstract (1/4)

Introduction

Translational paediatric drug development includes the multidirectional exchange between basic, clinical and population based research to improve the health of children. Integral part of such development is the assessment of treatment related risks and their management.

Objectives

To search and summarise the literature for practical guidance on how to anticipate and manage treatment related risks in translational paediatric research.

Abstract (2/4)

Methods

Pubmed, Embase, Web of Science, health authority (EMA and FDA) and learned society websites (WHO and CIOMS) were searched for publications up to 31/12/2019 providing practical guidance on how to anticipate and manage treatment related risks in translational paediatric research. Search terms are available on request and will be published in the upcoming article.

An example of search terms for Pubmed is:

((“clinical trials as topic”[MeSH Terms] OR (“clinical”[All Fields] AND “trials”[All Fields] AND “topic”[All Fields]) OR “clinical trials as topic”[All Fields]) AND (“pharmacovigilance”[MeSH Terms] OR “pharmacovigilance”[All Fields])) NOT (“vaccines”[MeSH Terms] OR “vaccines”[All Fields] OR “vaccine”[All Fields]) AND (“humans”[MeSH Terms] AND English[lang] AND (“infant”[MeSH Terms] OR “child”[MeSH Terms] OR “adolescent”[MeSH Terms]))

Titles and abstracts were screened and full text articles were reviewed where information was not clear. Both health authorities and the WHO have a dedicated paediatric section. Documents on regulatory authority and learned society websites were reviewed by title and full text where applicable.

Abstract (3/4)

Results

A total of 1829 publications were identified. After the removal of 46 duplicates 1783 were reviewed. No article was identified providing practical guidance. However, general guidance documents of health authorities and learned societies were combined with the specificities of paediatric research providing practical guidance on how to anticipate and manage treatment related risks in translational paediatric research and are summarised here.

Paediatric risk assessment in translational research is based on the integrated analysis of non-clinical, clinical and population based data from all age groups. It includes considering how identified and potential risks may present in children and which information is missing. This informs the paediatric drug development program by, for example, highlighting the need for a pharmacokinetic study prior to a paediatric trial. It also informs safety related protocol sections such as exclusion criteria, safety monitoring and risk management.

Abstract (4/4)

Conclusions

The paediatric safety profile informs translational paediatric research including safety related protocol sections and data analysis and reporting. Safety data from carefully planned paediatric research provides valuable information for children, parents and healthcare providers about the benefit-risk of available treatment options.