EUROPEAN MEDICINES AGENCY
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European perspective on collaborations to accelerate global paediatric oncology drug developments

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Presented by Dominik Karres on 8 February 2022
Paediatric Medicines Office

An agency of the European Union

Disclaimer

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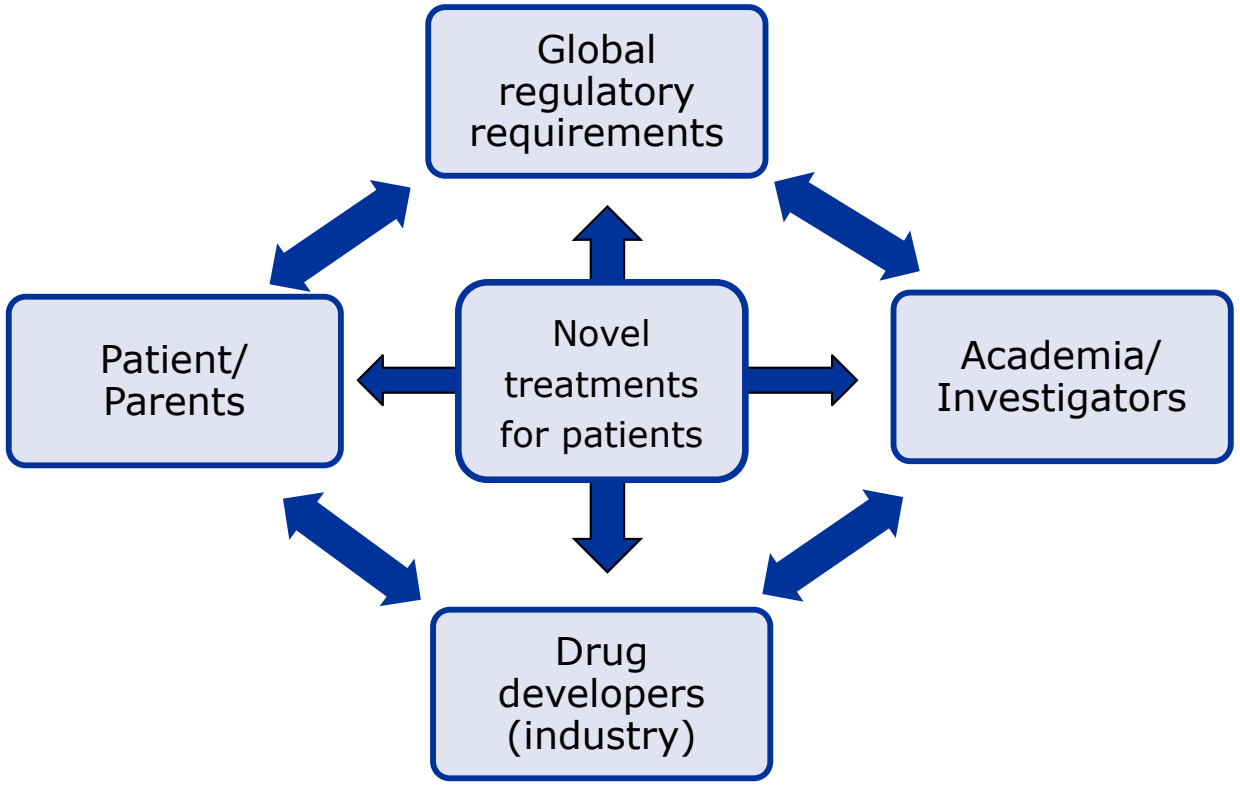
Challenges with paediatric drug development

- Conceptually
  - Unmet medical need
  - Target population
  - Timing
- Content
  - Standard of care
  - Study design
- Operational
  - Different regulations



How to address these challenges in a global setting

Need for international cooperation and collaboration across/ between all stakeholders

1. Multi-stakeholder interaction
   - To foster early, focused academia/ multi companies' collaboration and prioritisation and coordination discussions

2. International regulatory coordination
   - Paediatric Cluster calls as platform for regulatory exchange to foster coordinated approach towards global development plans

1. Multi-stakeholder interaction – Paediatric oncology strategy forums

Meetings organized by ACCELERATE together with EMA and FDA participation created to:

- evaluate the current state of the science
- facilitate dialogue and provide an opportunity for constructive discussions between relevant stakeholders (patient advocates, clinicians, academics, biotechnology/pharmaceutical companies and regulators) on specific topics in an open forum
- assure development of medicines in the best interests of children and adolescents with cancer

Paediatric Oncology Strategy Forums

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ACCELERATE
INNOVATION FOR CHILDREN AND ADOLESCENTS WITH CANCER

FDA U.S. FOOD & DRUG ADMINISTRATION

Paediatric Strategy Forums

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 — RAF and MEK inhibitors
- PSF - 10 — To be decided
- PSF - 11 — To be decided

Continually evolving

Slide provided by Prof Andy Pearson – ACCCELATE & Chair of Oversight Committee of Paediatric Oncology Strategy Forums

Paediatric Oncology Strategy Forums' deliverables

- Publications of the outcome of the forums in peer reviewed journals (https://www.accelerate-platform.org/publications-reference-documents/)

- Follow-up activities
  - e.g. LLS PedAL/EUpAL initiative - platform for real-time matching of children with relapsed acute myeloid leukaemia to early-phase clinical trials (1)
  - GloBHNL platform- international clinical platform trial designed to study novel in children with relapsed or refractory B-cell Non-Hodgkin Lymphoma (2)
  - Follow-up meetings between academia and several industry partners to prioritise (3)

1. Eur J Cancer. 2020 Sep;136:116-129
2. https://www.accelerate-platform.org/2020/09/10/glo-bnhlan-opportunity-pharma/
3. Eur J Cancer. 2021; 146:115-124.

Multi Stakeholder interaction – oncology experience

- Call for early academia/ industry collaboration with objective to prioritise based on unmet needs (through follow up meetings)
- Development of 'living' prioritisation structure as proof of concept
- Calling for focused and sequential developments across compounds and companies

- Conclusions of Strategy Forums have supported regulatory decision making
  - Mature B cell malignancies – more focused PIPs (1)
  - Checkpoint inhibitors – more focused PIPs, more combination developments

1. https://www.accelerate-platform.org/wp-content/uploads/sites

Conclusions Part 1

Acknowledgment that regulatory decision making on mandated (global) paediatric developments cannot take place in isolation.

There is a shared responsibility to ensure development efforts address unmet medical needs and prioritise developments accordingly.

Multi-stakeholder engagement can support regulatory decision making (1)

1. Karres et al; Clin Pharmacol Ther. 2020, Sep;108(3):553-556.

2. Need for international regulatory coordination

- Paediatric cancer drug development is a global enterprise
- Sponsors need to satisfy different regulatory requirements globally (e.g. PIP/iPSP)
- Changing regulatory landscape (through RACE Act) underlined the need for further strengthening of international/global collaboration also in the regulatory field

Background on Paediatric Cluster calls

- Monthly meetings between regulatory agencies under confidentiality agreements
- Participants
  - EMA, FDA, TGA, PMDA, HC
- Platform for regulatory bodies to exchange and discuss
  - Regulatory submissions (PIPs/iPSP/ PPSR etc)
    - Design aspects of paediatric drug development
    - Ensuring mutual understanding of methodological concepts etc.

Paediatric Cluster calls

- Call for transparency on sponsors on plans to fulfil all regulatory requirements (PIPs and iPSP)

- Call for simultaneous PIP/iPSP submissions (co-authored by FDA/ EMA, Reaman G et al; JCO, Sept 2020)


comments and controversies

Accelerating the Global Development of Pediatr Cancer Drugs: A Call to Coordinate the Submissions of Pediatric Investigation Plans and Pediatric Study Plans to the European Medicines Agency and US Food and Drug Administration

The Continuing Unmet Clinical Need

Regulations Guiding Drug Approval in the United States and the European Union

Paediatric Cluster calls

- Publication of a generic common commentary by EMA/ FDA (March 2021) (1)
- Facilitates early focused discussions amongst regulators on key (design) issues at Paediatric cluster calls
- Allowing early regulatory coordination of global development plans (eg through common commentary)
- Differences in regulations can be overcome (2)


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Common Commentary - EMA/FDA
Common issues requested for discussion by the respective agency (EMA/PDCO and FDA) concerning paediatric oncology development plans (Paediatric Investigation Plans [PIPs] and initial Pediatric Study Plans [iPSPs])

Background

DIA

Common Commentary on Paediatric Oncology Drug Development Published: Another Step in Optimising Global Regulatory Coordination of Paediatric Development Plans

1. https://www.ema.europa.eu/en/documents/other/common-commentary-ema/fda-common-issues-requested-discussion-respective-agency-ema/pdco-fda-concerning-paediatric-oncology-development-plans-paediatric-investigation-plans-pips_en.pdf
2. Ther Innov Regul Sci. 2021 Nov;55(6):1109-1110

Additional international regulatory collaboration

- EMA participation to FDA Type F meetings as observers (subject to request and agreement of the sponsor)

- FDA participation as observers to PIP clarification TCs in case of simultaneous PIP/iPSP submissions and prior discussion of the product in a Paediatric cluster call

Conclusion Part II

Despite different regulatory processes and timelines, early coordinated discussions between regulatory agencies at Paediatric cluster calls on mandated paediatric development plans can assure timely initiation of early-phase studies and a coordinated approach to later phase developments.

Summary and lessons learnt

- Early academia-(multi)-company engagement followed by early involvement of regulators is key.
- Multi-stakeholder discussions can support identification of unmet medical needs and priorities.

- Transparency by industry to regulators on paediatric plans beyond EU is important.
- Simultaneous PIP/iPSP/PPSR submissions allow early and coordinated discussions between agencies at the monthly paediatric cluster calls.

Thank you very much

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Any questions?

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