

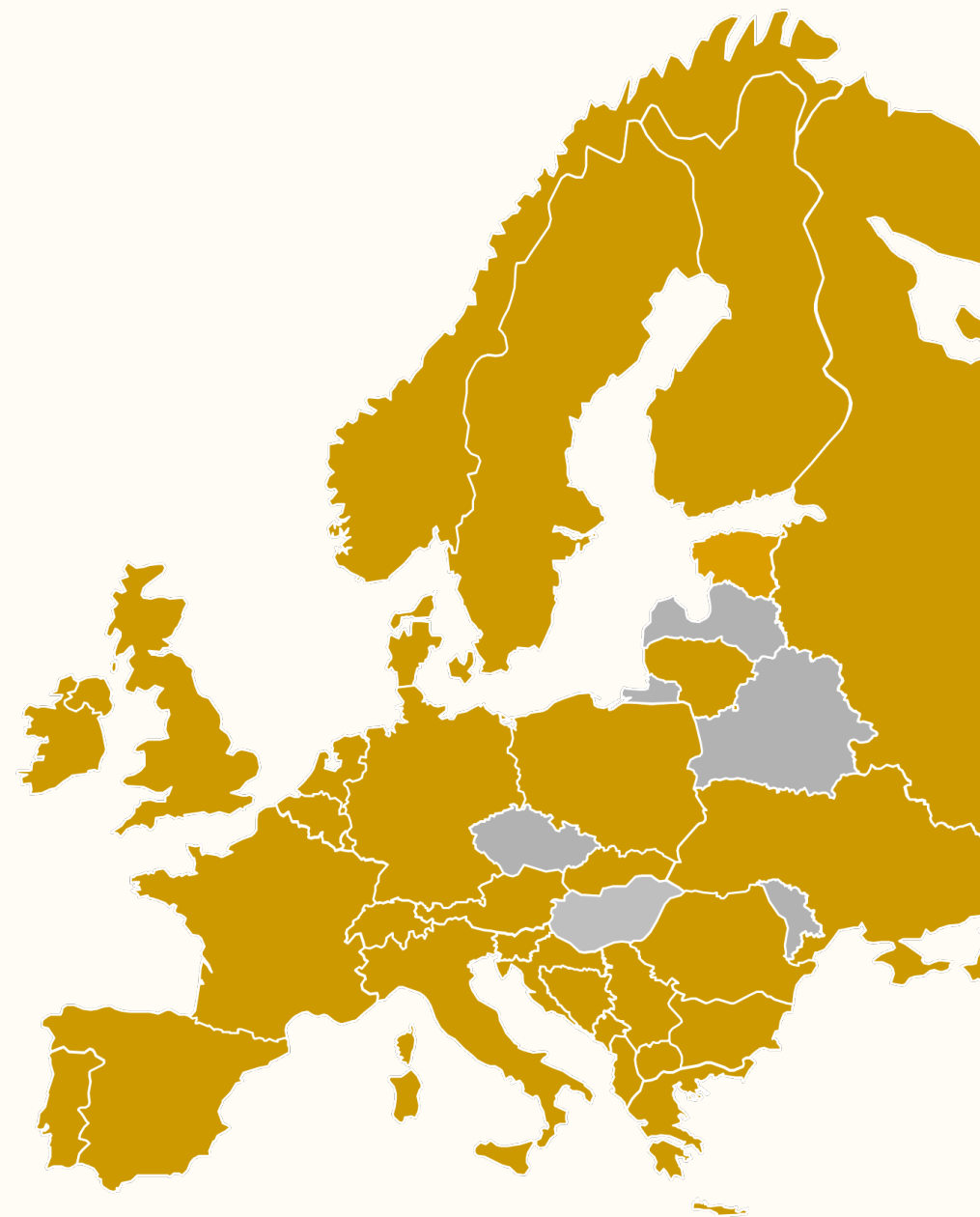


Understanding the EU Paediatric and Orphan Regulations

**This is what children with cancer need to get access
to better treatments!**



Co-funded by
the European Union



■ CCI-E - members
■ Non CCI-E members

Setting the scene: about the Paediatric and Orphan Regulations



Regulation on medicinal products for paediatric use

“Paediatric Regulation”

2007



From adults to children:

aims at improving the health of children by mandating the **development in paediatrics** of new medicines developed for adults

Regulation on orphan medicinal products

“Orphan Regulation”

2001



First-in-child:

aims at providing incentives for the research, development and marketing of medicines in **rare diseases**

2020

European Commission proposed a **joint revision** to **improve the therapeutic landscape** and **address unmet needs** in children

3 themes we want to tackle to ensure access to more efficient and kinder treatments

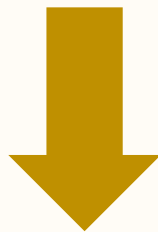
PR
OR
PR + OR

**Paediatric Regulation
(PR)**



Access to adult
medicines inexistant
or delayed

**Orphan Regulation
(OR)**



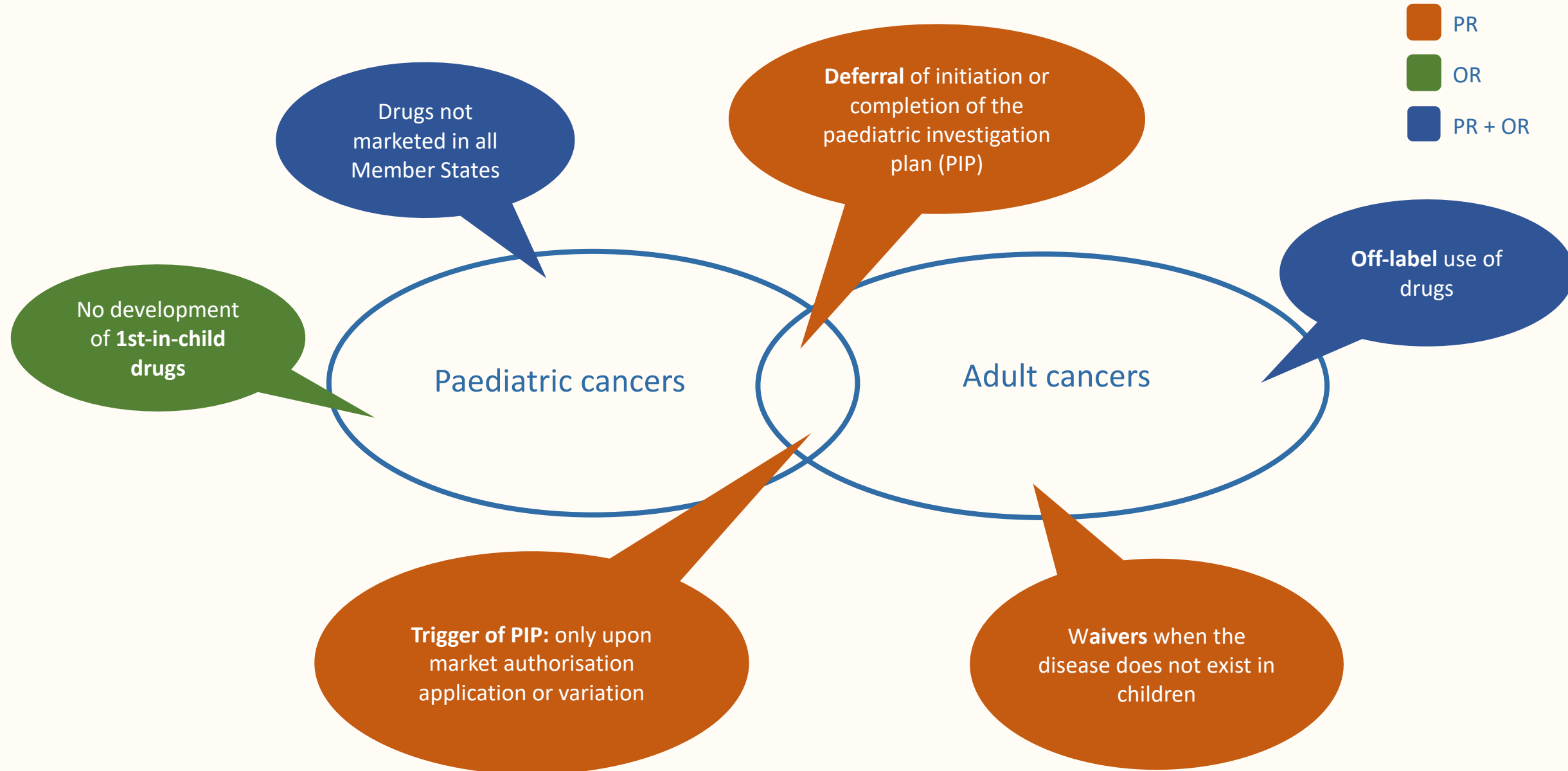
No medicines developed
specifically for
paediatric cancer

**Urgent needs in
a rare population**



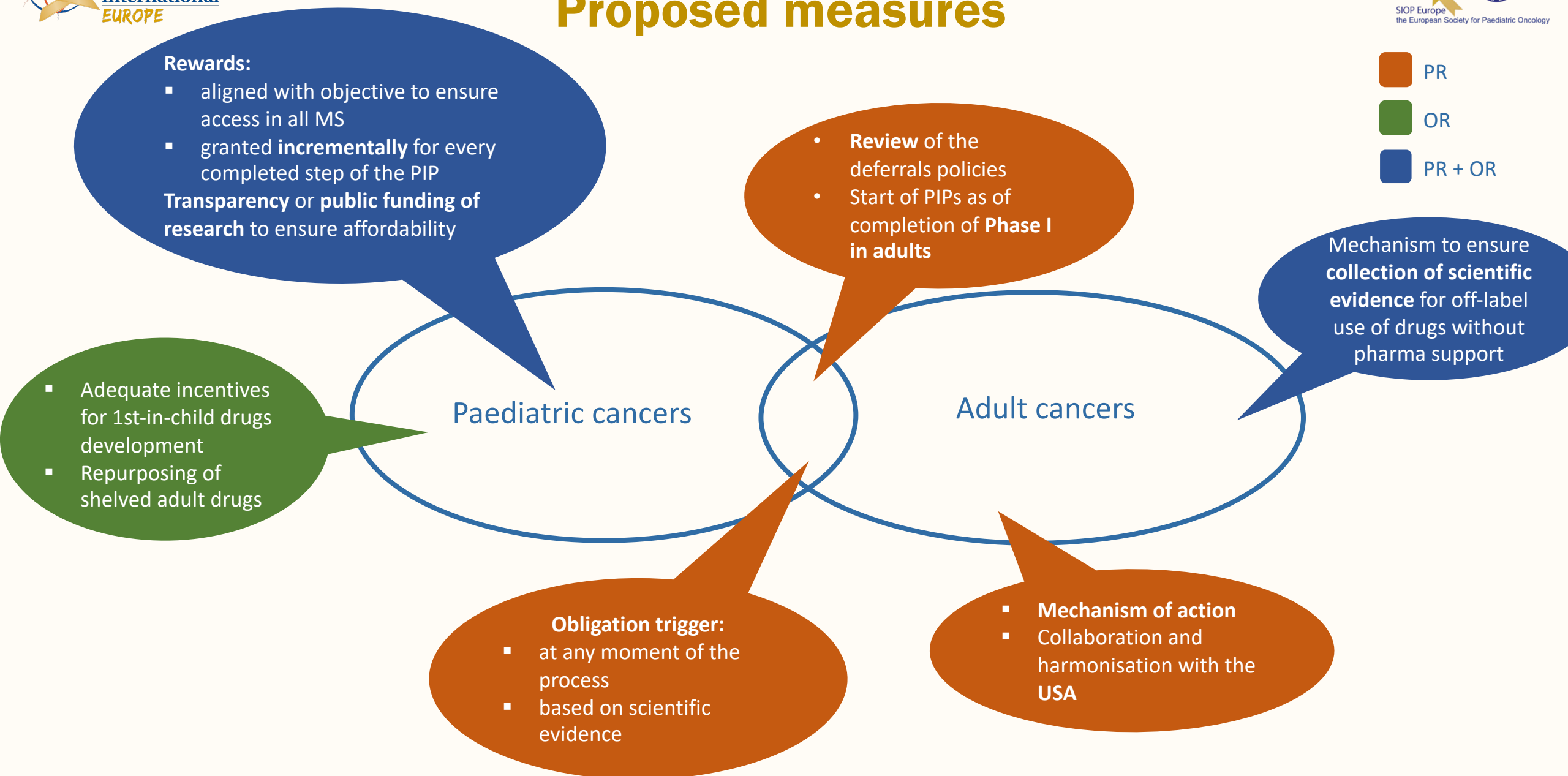
Developments not
systematically based on
science and properly prioritised

Access to drugs is inexistant or delayed



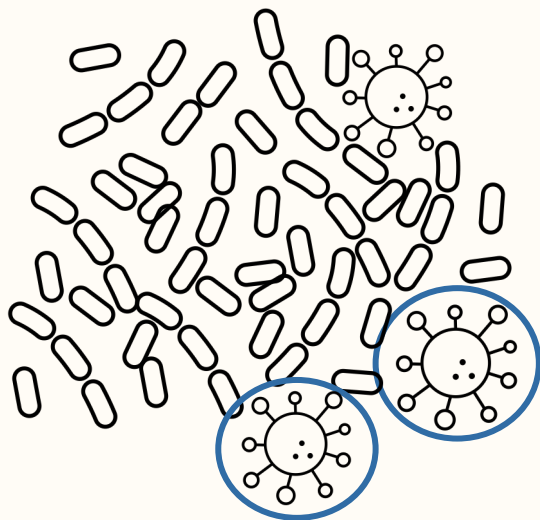
Proposed measures

- PR
- OR
- PR + OR

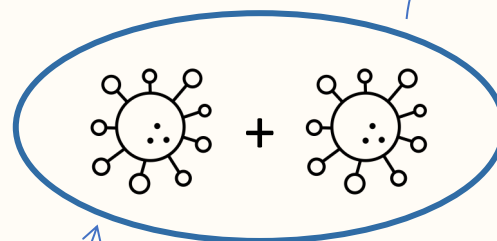
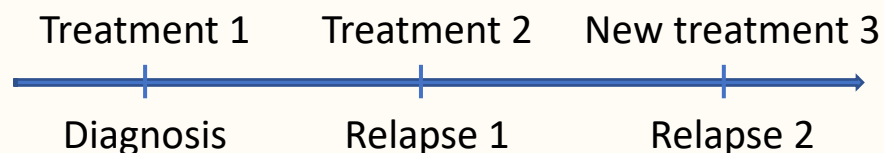


Children need treatments, not “a” drug

**Monotherapy does not
work in most cases**



**New treatments must benefit
patients faster in treatment
pathway**



**Academia proposes
combination trials
that are more
efficient**



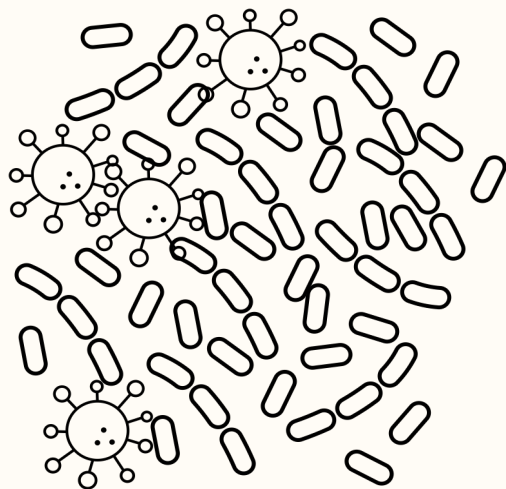
For efficient treatments



1. Academic combination trials, funded by public authorities (calls) or philanthropy (or both)
2. Mechanism to mandate the provision of the compound to be tested in academic trial
3. Innovation to move up treatments lines without delay to help all children faster
4. Review of the trial data by EMA

Paediatric cancers are rare diseases

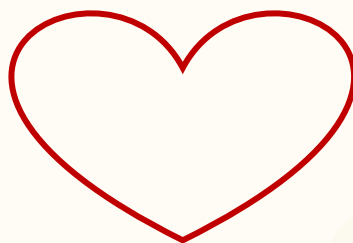
Many possible drugs



but a small patient population



only the **most relevant clinical trials**
must open to ensure a **swift**
recruitment of patients



**It is necessary to prioritise
the best drugs:**

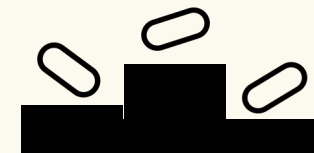
- For a given disease or
- Among drugs from the same class



ACCELERATE Paediatric Strategy Forums
to identify best possible treatment for
paediatric cancer, based on science

Ranking of the best drugs to be tested:

- for a given population or
- for a given indication



**Clinical trial landscape is not overcrowded &
all running trials
recruit meaningfully**

Summary of our proposed measures

1. Review of the PR

- Review of deferrals policies
- Mechanism of action
- Obligation trigger based on science
- Rewards granted incrementally

2. Review of the OR

- Adequate incentives for rare paediatric diseases
- Mechanisms to repurpose shelved drugs

3. Prioritisation

- Paediatric Strategic Forums at the heart of the process

4. Combination trials

- Public or philanthropic funding
- Access to compound
- Review of clinical data by EMA

- Rewards granted on basis of access in all MS
- Transparency on development costs and public funding for fundamental and clinical research
- Mechanism to collect scientific evidence about off-label use of drugs and review by EMA

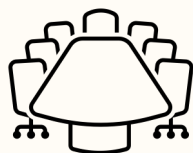
- Development of innovative drugs and combination treatments based on science and unmet needs
- Mechanisms to ensure swifter adaptation of treatments lines and warrant access to kinder drugs to all children without delay

How can you contribute?

Your contact person is Marine Gouders:
m.gouders@ccieurope.eu



You can talk to your **local** politicians

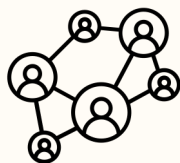


You can meet with your **national MEPs**:

- Contact us to check whether we have already met with them
- Make sure to prioritise those working in health sector - list of ENVI committee MEPS



You can **increase awareness** on the topic through your national medias



Coordinate with us in case you have a good relationship with your national Minister of Health



THANK YOU FOR YOUR ATTENTION!

FOLLOW US AND LEARN WHAT CCI EUROPE IS WORKING ON:



europe@cci.care



www.ccieurope.eu



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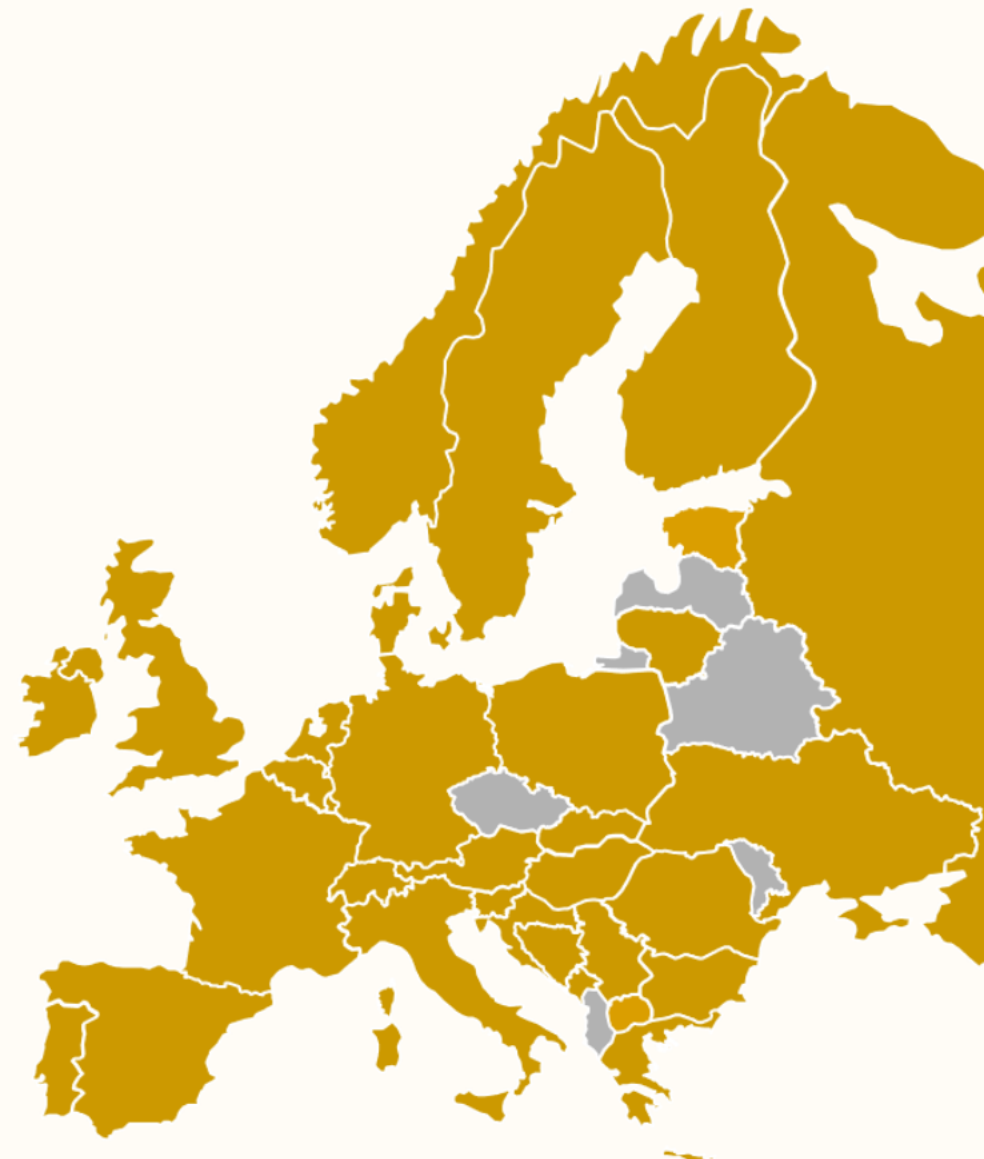
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[/cci_europe](https://twitter.com/cci_europe)



[/childhood-cancer-international-europe](https://www.linkedin.com/company/childhood-cancer-international-europe)



■ CCI-E - members
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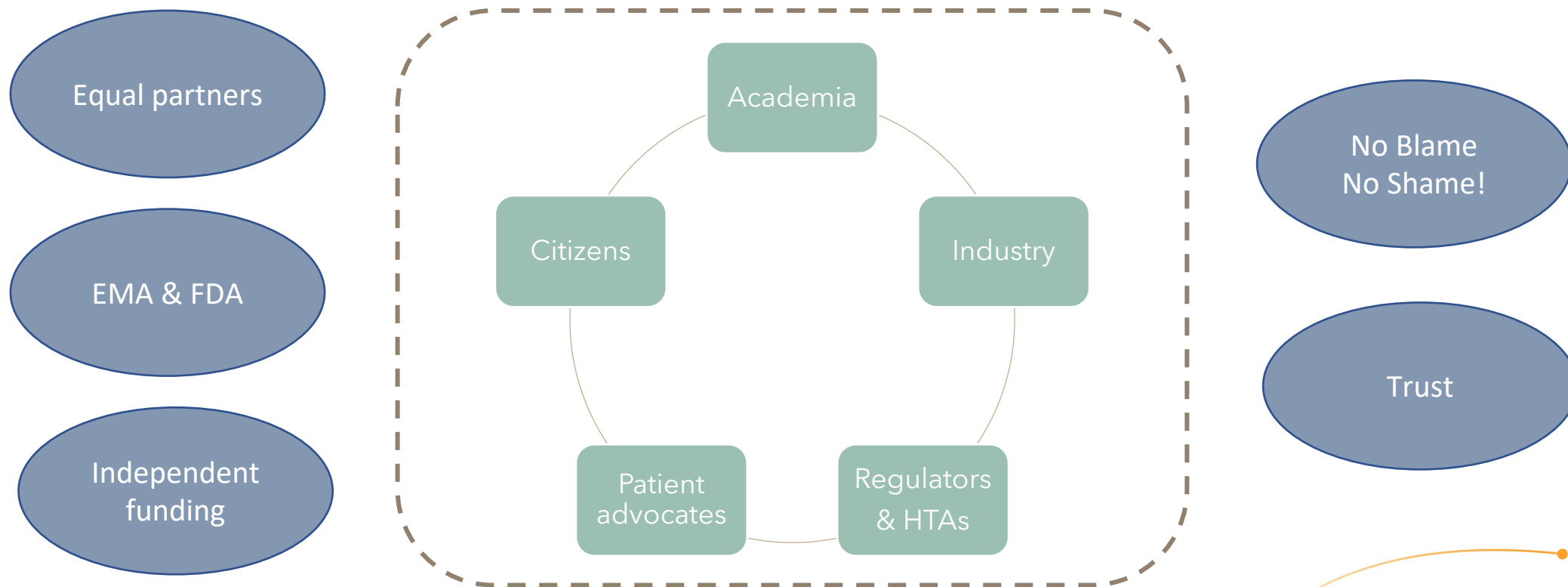


Paediatric Strategy Forums: What, Why & How

Dr. Teresa de Rojas, MD, PhD
Scientific Coordinator, ACCELERATE

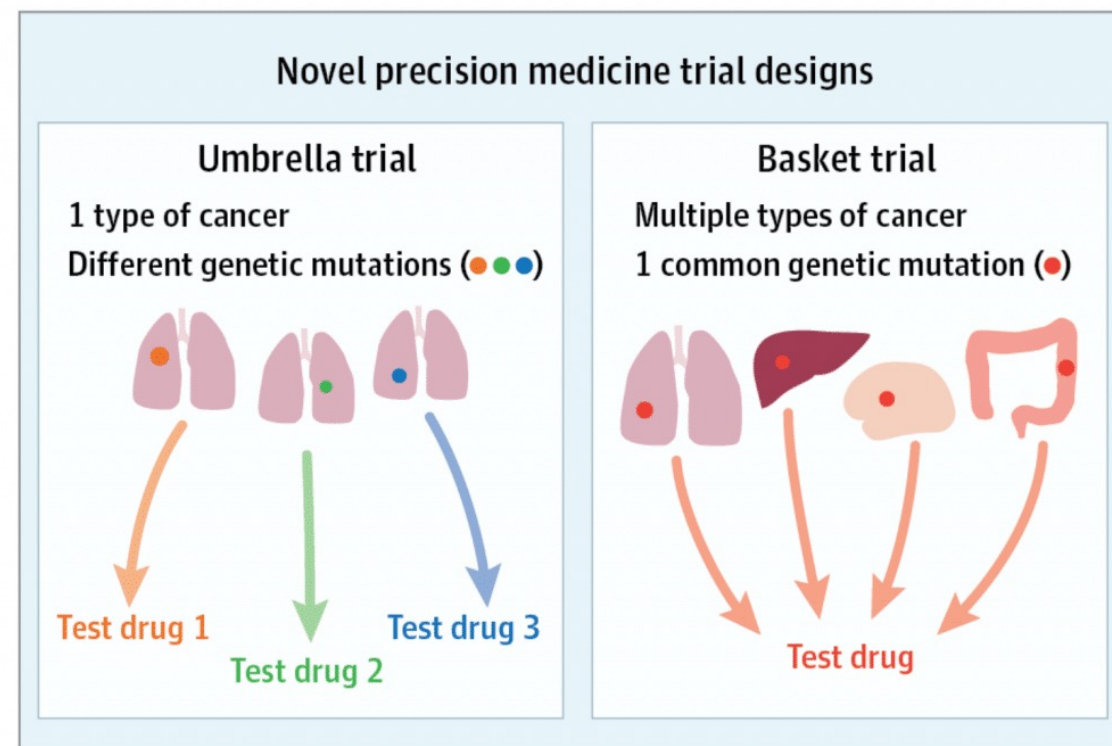
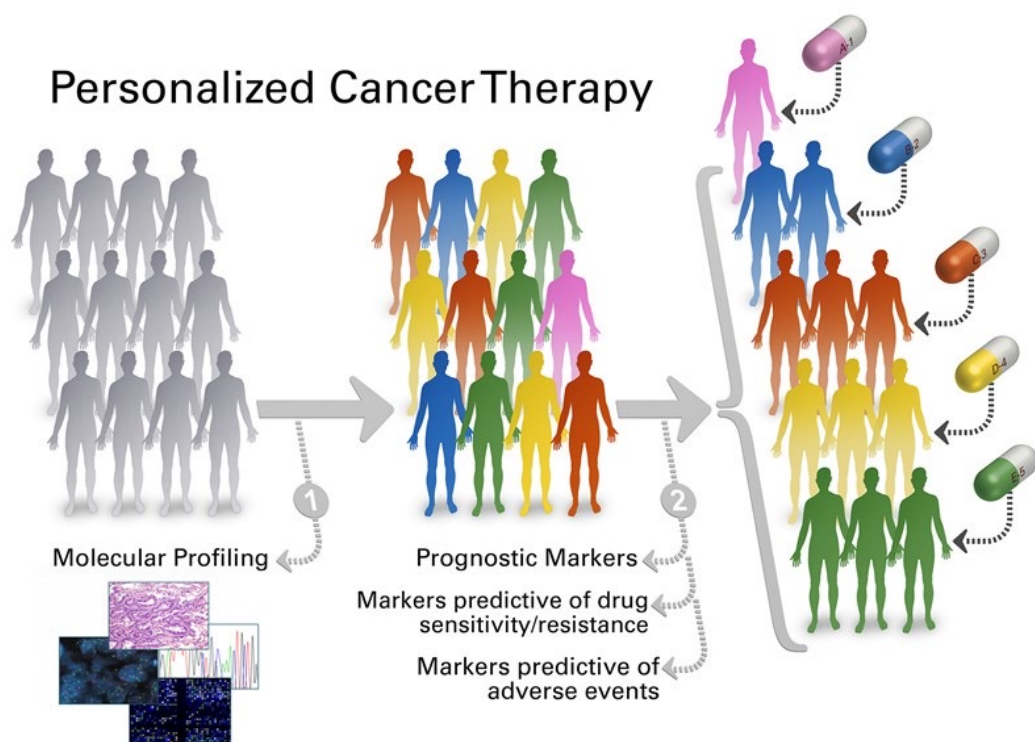
What are Paediatric Strategy Forums?

Multi-stakeholder meetings with open dialog in a pre-competitive setting,
on a malignancy or class of compounds



What are Paediatric Strategy Forums?

Multi-stakeholder meetings with open dialog in a pre-competitive setting,
on a malignancy or class of compounds



What for?



- ❖ To *share* information between all stakeholders
- ❖ To *evaluate* science
- ❖ To *inform* pediatric drug development strategies and subsequent decisions



Improve the selection and **prioritisation** of innovative drugs
evaluated for children and adolescents cancer

Driven by **science** and to meet **patients' unmet needs**

Practicalities

- **Topics** decided by the multi-stakeholder pediatric oncology community
 - Proposal period
 - Voting at ACCELERATE Annual Conference
- Oversight Committee (all PSFs)
- Dedicated Program Committee (for each PSF)
- **2 days** → in presence – virtual – hybrid
- Preparation, preparation, preparation!!
- Funding → Charities, NGOs, ... NOT industry!!
 - In kind by EMA and other institutions
- Summary (online) & Publication in scientific journal within 6 months

Expectations



Bias, Motivation & Clash of interests



"Can't you see it?"



And yet, somehow...it works!!



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



PSF - 13
Topic To be decided

Overall, 134 assets discussed by 1019 participants

Original Research

ACCELERATE and European Medicine Agency Paediatric Strategy Forum for medicinal product development for mature B-cell malignancies in children

Andrew D.J. Pearson ^{a,*}, Nicole Scobie ^b, Koenraad Norga ^c, Franca Ligas ^d, Davy Chiodin ^e, Amos Burke ^f, Veronique Minard-Colin ^g, Peter Adamson ^h, Lynley V. Marshall ^{i,am}, Arun Balakumaran ^{j,2}, Bouchra Benettaib ^k, Pankaj Bhargava ^l, Catherine M. Bolland ^m, Ellen Bolotin ⁿ, Simon Bomken ^o, Jochen Buechner ^p, Birgit Burkhardt ^q, Hubert Caron ^r, Christopher Copland ^s, Pierre Demolis ^t, Anton Egorov ^u, Mahdi Farhan ^v, Gerhard Zugmaier ^w, Thomas Gross ^x, Danielle Horton-Taylor ^z, Wolfram Klapper ², Giovanni Lesa ^d, Robert Marcus ^{aa}, Rodney R. Miles ^{ab}, Kerri Nottage ^{ac}, Lida Pacaud ^{ad}, Rosanna Ricafort ^{ae}, Martin Schrappe ^{af}, Jaroslav Sterba ^{ag}, Remus Vezan ^{ah}, Susan Weiner ^{aj}, Su Young Kim ^{aj}, Gregory Reaman ^{ak}, Gilles Vassal ^{al}

Original Research

ACCELERATE and European Medicines Agency Paediatric Strategy Forum for medicinal product development of checkpoint inhibitors for use in combination therapy in paediatric patients

Andrew D.J. Pearson ^{a,*}, Claudia Rossig ^b, Giovanni Lesa ^c, Scott J. Diede ^d, Susan Weiner ^e, John Anderson ^f, Juliet Gray ^g, Birgit Geoerger ^h, Veronique Minard-Colin ^h, Lynley V. Marshall ⁱ, Malcolm Smith ^j, Paul Sondel ^k, Marcis Bajars ^l, Claudia Baldazzi ^m, Elly Barry ⁿ, Sam Blackman ^o, Patricia Blanc ^c, Renaud Capdeville ^p, Hubert Caron ^q, Peter D. Cole ^r, Jorge Camarero Jiménez ^s, Pierre Demolis ^t, Martha Donoghue ^u, Mabrouck Elgadi ^v, Thomas Gajewski ^w, Sara Galluzzo ^x, Robert Ilaria Jr ^y, Alessandro Jenkner ^z, Dominik Karres ^c, Mark Kieran ^{aa}, Franca Ligas ^c, Israel Lowy ^{ab}, Michael Meyers ^{ac}, Corina Oprea ^{ad}, Vijay G.R. Peddareddigari ^{ae}, Jaroslav Sterba ^{af}, Paul K. Stockman ^{ag}, Peter Suenaert ^{ah}, Uri Tabori ^{ai}, Cornelis van Tilburg ^{aj}, Todd Yancey ^{ak}, Brenda Weigel ^{aj}, Koenraad Norga ^{am}, Gregory Reaman ^u, Gilles Vassal ^h

Original Research

Paediatric Strategy Forum for medicinal product development for acute myeloid leukaemia in children and adolescents[☆]
ACCELERATE in collaboration with the European Medicines Agency with participation of the Food and Drug Administration

Andrew D.J. Pearson ^{a,*}, C.Michel Zwaan ^{b,c,1}, E.Anders Kolb ^{d,1}, Dominik Karres ^c, Julie Guillot ^f, Su Young Kim ^g, Lynley Marshall ^h, Sarah K. Tasian ⁱ, Malcolm Smith ^j, Todd Cooper ^k, Peter C. Adamson ^l, Elly Barry ^m, Bouchra Benettaib ⁿ, Florence Binlich ^o, Anne Borgman ^p, Erica Brivio ^{b,c}, Renaud Capdeville ^q, David Delgado ^r, Douglas V. Faller ^s, Linda Fogelstrand ^t, Paula Goodman Fraenkel ^u, Henrik Hasle ^v, Delphine Heenen ^w, Gertjan Kaspers ^{b,c}, Mark Kieran ^x, Jan-Henning Klusmann ^y, Giovanni Lesa ^c, Franca Ligas ^c, Silvia Mappa ^z, Hesham Mohamed ^{aa}, Andrew Moore ^{ab}, Joan Morris ^{ac}, Kerri Nottage ^{ad}, Dirk Reinhardt ^{ae}, Nicole Scobie ^{af,ag}, Stephen Simko ^{ah}, Thomas Winkler ^{ai}, Koen Norga ^{aj}, Gregory Reaman ^{ak}, Gilles Vassal ^{a,al}

Review

Paediatric Strategy Forum for medicinal product development of epigenetic modifiers for children
ACCELERATE in collaboration with the European Medicines Agency with participation of the Food and Drug Administration

Andrew D.J. Pearson ^{a,*}, Kimberly Stegmaier ^{b,1}, Franck Bourdeaut ^{c,1}, Gregory Reaman ^d, Delphine Heenen ^e, Michael L. Meyers ^f, Scott A. Armstrong ^g, Patrick Brown ^g, Daniel De Carvalho ^h, Nada Jabado ⁱ, Lynley Marshall ^j, Miguel Rivera ^k, Malcolm Smith ^l, Peter C. Adamson ^m, Amy Barone ^d, Christian Baumann ⁿ, Samuel Blackman ^o, Vickie Buenger ^p, Martha Donoghue ^q, Aundrietta D. Duncan ^q, Elizabeth Fox ^r, Brian Gadbow ^s, Maureen Hattersley ^t, Peter Ho ^u, Ira Jacobs ^v, Michael J. Kelly ^w, Mark Kieran ^x, Giovanni Lesa ^y, Franca Ligas ^y, Donna Ludwinski ^z, Joe McDonough ^{aa}, Zariana Nikolova ^{ab}, Koen Norga ^{ac}, Adrian Senderowicz ^{ad}, Tilmann Taube ^{ae}, Susan Weiner ^{af}, Dominik Karres ^y, Gilles Vassal ^{ag}

Review

Second Paediatric Strategy Forum for anaplastic lymphoma kinase (ALK) inhibition in paediatric malignancies
ACCELERATE in collaboration with the European Medicines Agency with the participation of the Food and Drug Administration

Andrew D.J. Pearson ^{a,*}, Elly Barry ^b, Yael P. Mossé ^c, Franca Ligas ^d, Nick Bird ^e, Teresa de Rojas ^f, Zachary F. Zimmerman ^f, Keith Wilner ^g, Willi Woessmann ⁿ, Susan Weiner ^l, Brenda Weigel ^l, Rajkumar Venkatramani ^k, Dominique Valteau ^l, Toby Trahair ^m, Malcolm Smith ⁿ, Sonia Singh ^o, Giovanni Selvaggi ^p, Nicole Scobie ^q, Gudrun Schleiermacher ^r, Nicholas Richardson ^o, Julie Park ^k, Karsten Nysom ^l, Koen Norga ^u, Margret Merino ^o, Joe McDonough ^y, Yousif Matloub ^o, Lynley V. Marshall ^x, Eric Lowe ^y, Giovanni Lesa ^d, Meredith Irwin ^z, Dominik Karres ^d, Amar Gajjar ^{aa}, François Doz ^r, Elizabeth Fox ^{aa}, Steven G. DuBois ^{ab}, Martha Donoghue ^o, Michela Casanova ^{ac}, Hubert Caron ^{ad}, Vickie Buenger ^{ae}, Diana Bradford ^{af}, Patricia Blanc ^{af}, Amy Barone ^o, Gregory Reaman ^o, Gilles Vassal ^{aj}

Review

Paediatric Strategy Forum for medicinal product development of chimeric antigen receptor T-cells in children and adolescents with cancer
ACCELERATE in collaboration with the European Medicines Agency with participation of the Food and Drug Administration²

Andrew D.J. Pearson ^{a,*}, Claudia Rossig ^{b,1}, Crystal Mackall ^{c,1}, Nirali N. Shah ^{d,1}, Andre Baruchel ^{c,1}, Gregory Reaman ^l, Rosanna Ricafort ^g, Delphine Heenen ^h, Abraham Bassan ⁱ, Michael Berntgen ^j, Nick Bird ^k, Eric Bleickardt ^l, Najat Bouchkouj ^f, Peter Bross ^l, Carrie Brownstein ^m, Sarah Beaussant Cohen ⁿ, Teresa de Rojas ^d, Lori Ehrlich ^f, Elizabeth Fox ^o, Stephen Gottschalk ^o, Linda Hanssens ^p, Douglas S. Hawkins ^q, Ivan D. Horak ^r, Danielle H. Taylor ^s, Courtney Johnson ^t, Dominik Karres ^l, Franca Ligas ^l, Donna Ludwinski ^u, Maksim Mamontkin ^v, Lynley Marshall ^w, Behzad K. Masouleh ^x, Yousif Matloub ^y, Shannon Maude ^z, Joe McDonough ^{aa}, Veronique Minard-Colin ^{ab}, Koen Norga ^{ac}, Karsten Nysom ^{ad}, Alberto Pappo ^o, Laura Pearce ^{ac}, Rob Pieters ^{ae}, Martin Pule ^{af}, Alfonso Quintás-Cardama ^{ah}, Nick Richardson ^l, Martina Schüßler-Lenz ^{ai,am}, Nicole Scobie ^{aj}, Martina A. Sersch ^{ak}, Malcolm A. Smith ^{al}, Jaroslav Sterba ^{am}, Sarah K. Tasian ^z, Brenda Weigel ^{an}, Susan L. Weiner ^{ao}, Christian Michel Zwaan ^{af,ap,ar}, Giovanni Lesa ^l, Gilles Vassal ^{a,aq}

Review

Bromodomain and extra-terminal inhibitors—A consensus prioritisation after the Paediatric Strategy Forum for medicinal product development of epigenetic modifiers in children—ACCELERATE

Andrew D.J. Pearson ^{a,*}, Steven G. DuBois ^b, Vickie Buenger ^c, Mark Kieran ^d, Kimberly Stegmaier ^b, Pratiti Bandopadhyay ^b, Kelly Bennett ^e, Franck Bourdeaut ^f, Patrick A. Brown ^g, Louis Chesler ^h, Jessica Clymer ^h, Elizabeth Fox ⁱ, Christopher A. French ^j, Eva Germovsek ^k, Francis J. Giles ^l, Julia G. Bender ^m, Maureen M. Hattersley ⁿ, Donna Ludwinski ^{o,p}, Katarina Luptakova ^q, John Maris ^r, Joe McDonough ^s, Zariana Nikolova ^t, Malcolm Smith ^u, Athanasios C. Tsiatis ^v, Rajeev Vibhakar ^w, Susan Weiner ^x, Joanna S. Yi ^z, Fred Zheng ^l, Gilles Vassal ^{a,aa}

Endorsement by FDA & EMA



**FDARA Implementation
Guidance for Pediatric
Studies of Molecularly
Targeted Oncology Drugs:
Amendments to Sec. 505B of
the FD&C Act
Guidance for Industry**

December 2019



**Can a Multistakeholder Prioritization Structure
Support Regulatory Decision Making? A
Review of Pediatric Oncology Strategy Forums
Reflecting on Challenges and Opportunities of
this Concept**

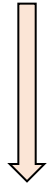
Dominik Karres^{1,*}, Giovanni Lesa¹, Franca Ligas¹, Pia Annunen^{2,3}, Maaïke van Dartel^{3,4}, Pierre Demolis^{5,6}, Sara Galluzzo^{3,7}, Ralf Herold⁸, Olga Kholmanskikh van Crickingen⁹, Violeta Stoyanova-Beninska^{8,10} and Koen Norga^{1,11,12,13}

CPT, 108, 3, 553, 2020

An example: Mature B-Cell malignancies (Nov. 2017)

Unmet needs

- i) Develop innovative treatments for incurable patients
- ii) Reduce high acute toxicity of current therapy

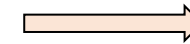


Conclusions

- Successful de-escalation at low risk in front line therapy can only be undertaken with an effective salvage regimen
- **Priority** = developing treatment for **relapse**
 - Very small number of patients = global strategy
 - Combination approach rather than monotherapy

Consensus of clinicians on priorities

- Antibody drug conjugates
- CAR-T cells
- T-cell Engagers



GloBNHL

- International academic platform trial
- For relapsed/refractory B-NHL
- COG (US), C17 (Canada), ITCC (EU), ANZCHOG (Australia)
- Drugs prioritized by the PSF!



An example: Mature B-Cell malignancies (Nov. 2017)



THE LANCET
Oncology

COMMENT | VOLUME 23, ISSUE 11, P1354-1357, NOVEMBER 01, 2022

ACCELERATE Paediatric Strategy Forums: an advance for oncological drug development?

Andrew D J Pearson • Teresa de Rojas • Dominik Karres • Gregory Reaman • Nicole Scobie • Elizabeth Fox • et al.

[Show all authors](#)

Published: November, 2022 • DOI: [https://doi.org/10.1016/S1470-2045\(22\)00619-2](https://doi.org/10.1016/S1470-2045(22)00619-2) • [Check for updates](#)



- Prioritisation → Reduced PIPs
- Medically and scientifically justified waivers

Time Period	Number of Products	PIP	Full-Waivers
B-cell products			
July 2007 – November 2017	27	15/27 (56%)	12/27 (44%)
December 2017 – June 2021	36	9/36 (25%)	27/36 (75%)

No "blah-blah", ACTION!



ACCELERATE Paediatric Strategy Forums in a nutshell



- ✓ Multi-stakeholder meetings on a malignancy or class of compounds
- ✓ No blame, no shame → Trust
- ✓ Prioritisation of innovative drugs for children with cancer
- ✓ Driven by Science and to fulfil patients' unmet needs
- ✓ They work! 10 conducted so far, with concrete actions and outputs