All children on Board!

Why the Paediatric Regulation must be amended to benefit all children
Unite2Cure works closely with professionals
Presentation objectives

- State of play for children with cancer: **specific urgent needs**;
- Mitigated success of the Paediatric Medicines Regulation: **call for amendments**;
- No impact of Orphan Drugs Regulation;
- 10-years review process: **mixed feelings and our plan going forward**.
State of play for children with cancer
SPECIFIC URGENT NEEDS
Paediatric cancers are a public health concern

1. Every kid cancer is a rare disease

60 different paediatric malignancies, each of them requiring a specific scientific attention.

35 000 new diagnoses* /year

2. 1st cause of death by disease**

Some cancers are so rare that they receive little attention, despite a very poor cure rate (below 50%).

6 000 deaths* /year

* Children, adolescents and young adults up to 24 years
** Among children aged 1 year or more
QoL of survivors and cure rate must improve

3. Cure rate stalled over last 15 years

Curing cancer is making progress, except with children.

4. 2/3 survivors suffer long term side effects

Survivors will represent about half a million people in Europe by 2020. LTEs must be prevented and reduced.

Blindness, hearing loss
Amputation (foot, leg, hand...)
Organ removal (kidneys)
Coronary or artery disease
Cardiac failure
Secondary cancers
Post-traumatic stress disorders
Innovation does not reach children who most need it

5. High-risk=poor outcome

The cure rate of certain high risk cancers remains shockingly low. For those, cancers, we need new drugs.

[Bar chart showing cure rates for High Risk NB, High risk MB, and DIPG with 40%, 30%, and 1% respectively.]

6. Adults 70 – Kids 2

From 2011 to 2015, 70 new anti-cancer drugs were approved for adult cancers. For kids, only 2.

[Bar chart showing 70 adults and 2 children.]
**Paediatric cancer is not seen as a profitable market**

1. **Less than 1% of all cancers are paediatric**

And yet that 1% needs to be split again into 16 different cancers and 60 different sub-types...

2. **Cancer is still an acute disease (>> chronic)**

With the aim of curing cancer, treatments are to be administered for one to two years at most.

3. **Children with cancer still have specific needs**

- Age-adapted formulas
- Age-group specific toxicities
- Patients recruitment complexity

---

Mitigated success of the Paediatric Regulation (PMR)
CALL FOR AMENDMENTS
The review report notes the PMR’s weaknesses

• Regulation works best where the needs of adult and paediatric patients overlap
• The SPC reward is most attractive in areas where the drug is a blockbuster in adults
• The PMR only has limited possibilities to steer developments towards certain specific areas
• The article 11 waiver poses problems where the compound can be beneficial for children, albeit in a different condition
Cancer is a problematic area when it come to waivers

- The requirement for a PIP may be waived if the disease or condition for which the product is intended occurs only in adults.
- While many paediatric cancers share biological similarities with adult cancers, they occur in different organs and are therefore usually considered as different conditions.

**PIP will only occur on a voluntary basis** when the mechanism of action of the compound is expected to be effective in paediatric cancers.
In Europe, children should not have to wait for voluntary initiatives to access life-saving drugs developed in adults.

Call for a moral stance
Most waivers are granted in oncology

- All class waivers: 214
- Class waivers in oncology: 154
- Approved class waivers in oncology: 147

PDCO minutes from June 2012 to June 2015 + Literature search then blinded panel of 16 ITCC experts
Most drugs waived could benefit children with cancer

PDCO minutes from June 2012 to June 2015 + Literature search then blinded panel of 16 ITCC experts
We are calling for two amendments

1. Waivers for paediatric developments should be based on the evaluation of its potentially significant therapeutic benefit (including the relevance of its mechanism of action) over existing treatments in the paediatric population.

2. The selection between comparable compounds (i.e., with the same MoA) to be developed in children must be based on well-informed decisions taken during forums where all stakeholders participate.
3. **Delays in paediatric developments must be reduced** and PIPs have to be submitted early during product development in adults in order to address the needs of the paediatric population in good time, as stated in Recital 10 and Article 16.
No impact of Orphan Drugs Regulation (ODR)
NEW COMMERCIAL PARADIGM REQUIRED
ODR aim is to foster an interest in rare conditions

• A rare condition is defined as a disease with a prevalence of less than 5 of 10,000, meaning approximately less than 250,000 patients based on a European population of 506 million

• Each paediatric cancer is an ultra-rare condition according to the ODR
~40% of MAs under ODR are in oncology

Though they generated little interest under ODR

![Graph showing interest levels in different conditions.

- Children only condition: 2
- Adults & children condition: 31
- Adults only condition: 32]
Though they generated little interest under ODR

Children only condition: 2
Adults & children condition: 31
Adults only condition: 32
Only 10 compounds have an authorised paediatric indication

Focus on drugs for conditions occurring both in adults and children

- 1st MA: 8
- MA variation: 2
- No Paediatric Indication: 21
ODR and PMR serve completely different purposes

Paediatric Medicines Regulation → Innovation for adults brought to children

Orphan Drugs Regulation → Policy tool to foster innovation in any rare disease

Joint review is questionable
10-years review process: mixed feelings
OUR PLAN GOING FORWARD
Mixed feelings about the 10-year report

<table>
<thead>
<tr>
<th>Satisfied</th>
<th>Doubtful</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Specific needs of children with cancer are recognised;</td>
<td>• Any amendments are deferred until 2019.</td>
</tr>
<tr>
<td>• Policy on deferrals will be reviewed to speed up access to innovation;</td>
<td>• Implementation of waivers on basis of mechanism of action is seen as possibly impacting the predictability of the scope of a PIP and a risk to the overall product development;</td>
</tr>
<tr>
<td>• EU Commission will propose implementation improvements of the PMR.</td>
<td></td>
</tr>
</tbody>
</table>
A person that submit, (...) an original application for a new active ingredient (...) shall submit with the application reports on [paediatric investigation plan] if the drug or biological product that is the subject of the application is

(i) intended for the treatment of an adult cancer; and

(ii) directed at a molecular target that the Secretary determines to be substantially relevant to the growth or progression of a pediatric cancer.”;
Conclusion and our plan going forward

- The Commission’s Report supports our call for revision
  - PMR has failed to meet the needs of children with cancer
  - ODR has not been used in the context of children with cancer
    - We have already shown this inadequacy: why wait?
- The Commission’s Report calls for more review but this delays definitive action!
- We will monitor the implementation in the US of the Race for Children Act
- As parents of children with cancer we
  - do not want to see more delay and will keep pressing for changes in the PMR
  - propose:
    - to participate in discussions about improving the PMR implementation
    - to swiftly start preparing a plan for a 2019 revision
Presentation objectives: Recap

• State of play for children with cancer: **specific urgent needs**;

• Mitigated success of the Paediatric Medicines Regulation: **call for amendments**;

• No impact of Orphan Drugs Regulation;

• 10-years review process: **mixed feelings and our plan going forward**.