Precision Medicine in Pediatric Oncology drug development: The right time to accelerate innovation for children and adolescents with cancer

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Amsterdam, January 27, 2017
Cancer in Young People in Europe

• 6000 young people die each year of cancer
• Need for safe and effective innovative medicines rapidly introduced in frontline

Leading cause of death by disease beyond one year in the EU

http://www.siope.eu/SIOPE_StrategicPlan2015/
From 2011 to 2015, 70 new oncology treatments have been launched for over 20 uses in adults.
2008 – 2016: 4 new anticancer medicines* have been launched for 3 pediatric malignancies through a PIP

- **Unituxin®** (an anti-GD2 monoclonal antibody) for neuroblastoma
- **Votubia®** (mTOR inhibitor) for sub-ependymal giant cell astrocytoma,
- **Spectril®** (recombinant asparaginase) for ALL*
- **Xaluprine®** (mercaptopurine) for ALL*

* Asparaginase and mercaptopurine have been used for more than 40 years in the treatment of ALL

*1st marketing autorisation after 26 july 2008
THE SIOPE STRATEGIC PLAN
A European Cancer Plan for Children and Adolescents

http://www.siope.eu/SIOPE_StrategicPlan2015/
SIOP Strategic Plan;
The 7 objectives

1. Innovative therapies
2. Precision medicine
3. Knowledge on biology
4. Equal access
5. Teenager and young adults
6. Quality of survivorship
7. Causes of pediatric cancers

http://www.siope.eu/SIOPE_StrategicPlan2015/
How to accelerate?

- Science driven pediatric oncology drug development
- Early access to innovative medicines during their adult development
- Investment in developing specific pediatric oncology drugs
- Enlarge the number of drugs in trials through precision medicine
- Increase access to innovative medicines for children in relapse across Europe (goal > 1 in 2 children in 2025)
- Speed up introduction of innovative medicines in front line treatment of high-risk malignancies
Needs

- Science driven pediatric oncology drug development
- Early access to innovative medicines during their adult development
- Investment in developing specific pediatric oncology drugs
- **Enlarge the number of drugs in trials through precision medicine**
- Increase access to innovative medicines for children in relapse across Europe (goal > 1 in 2 children in 2025)
- Speed up introduction of innovative medicines in front line treatment of high-risk malignancies
The Innovative Therapies & PCM Programme²

1. A tumor molecular and Immunology portrait at relapse
   Molecular Matching Trials

2. Enriched Phase I and II Trials w single agents and combinations
   Targeted and immune therapies

All patients are proposed access to new drugs

3. New Knowledge

4. Specific Pediatric Drug Development

http://www.siope.eu/SIOPE_StrategicPlan2015/
MOlecular Screening for CAncer Treatment Optimization (MOSCATO-01) in pediatric patients:
A prospective molecular stratification trial
PI Birgit Geoerger

- Monocentric, non-randomized, prospective feasibility study (NCT01566019)
- 73 patients (biopsy at relapse) (median age, 11y)
- 42 (58%) with at least one actionable target
- Of whichn 14 (32%) received a matched therapy

Sponsor: Gustave Roussy, Villejuif, FRANCE
MAPPYACTS

PI: B Geoerger, CoPI: Gudrun Schleiermacher

Molecular Profiling for Pediatric and Young Adult Cancer Treatment Stratification

Children and Adolescents, in relapse, solid tumors and leukemias

Biopsy or resection at relapse → Tumor Molecular Profiling (WES/RNAseq/Immuno) → Molecular Report → Traitement

300 children in 3 years
FPI in January 2016
170 patients as of Dec 2016
INFORM

Pilot Phase

Feasibility-Registry Study (year 1+2)

Goals feasibility phase

Logistics
- molecular analysis, target identification, turnaround
- individualized risk management
- access mode compounds

Clinical data base
- molecular targets
- documentation of individualized treatments
- clinical courses, tox data

Molecular data
- genomic, epigenomic, transcriptomic profiles

Evaluation of data
- druggable target patterns within/across entities
- set of targeted compounds of interest “tool box”
- define number of eligible patients/year for clinical trial

Lab => bedside

21.10.2013

19.1.2015

SAB1: 11/2015

SAB2: 11/2015

Q2-3 2017:
The ITCC Precision Cancer Medicine program

1. Generate molecular profiling for each patient

Molecular Matching Trials at relapse

- INFORM (Germany)
- MAPPYACTS (France, Spain, Denmark, Italy)
- iTHER (Netherland)
- SM-PAED (UK)

Platform, pipelines and data harmonization

- WES, RNA seq, methylome
- immunophenotype

- Evaluate drugs and combinations

- European clinico-biological database

- New knowledge

- WES, RNA seq, methylome, immunophenotype

- Platform, pipelines and data harmonization

- INFORM2
- 1000 exomes in relapse

- Platform, pipelines and data harmonization

- eSMART trial
- IST multi-agent from multi-company

- Phase 1 & 2 ITCC Trials (sponsored by industry and ISTs)
The ITCC Precision Cancer Medicine program

1. Generate molecular profiling for each patient

**Molecular Matching Trials at relapse**

- **INFORM** (Germany)
- **MAPPYACTS** (France, Spain, Denmark, Italy)
- **iTHER** (Netherlands)
- **SM-PAED** (UK)

2. MATCH

3. Evaluate drugs and combinations

**Phase 1 & 2 ITCC Trials** (sponsored by industry and ISTs)

- **MATRIX trial** (Genentech/Roche)

- **eSMART trial**
  - IST multi-agent from multi-company
    - AcSé
    - Gustave Roussy
    - Imagine
    - Mari 90

4. Create

**European clinico–biological database**

1000 exomes in relapse

5. New knowledge

*new druggable pathways for specific pediatric drug development*
Patient with tumor molecular profile at relapse (WES, RNAseq, Immuno)

MATCH

Portfolio of ITCC phase I and phase II trials

IST - phase I/II single agent and combo
Goal >10 drugs from >3 Companies

Wave 1: 7 treatment arms with 5 drugs from AZD, Novartis, BMS

launched august 2016
Multistakeholder Paediatric Oncology Platform

To improve new oncology drug development for children

Creating a unique, multi-stakeholder Paediatric Oncology Platform to improve drug development for children and adolescents with cancer


Gilles Vassal\textsuperscript{a,*}, Raphaël Rousseau \textsuperscript{b}, Patricia Blanc \textsuperscript{c}, Lucas Moreno \textsuperscript{d}, Gerlind Bode \textsuperscript{e}, Stefan Schwoch\textsuperscript{f}, Martin Schrappe\textsuperscript{g}, Jeffrey Skolnik\textsuperscript{h}, Lothar Bergman\textsuperscript{i}, Mary Brigid Bradley-Garelik\textsuperscript{j}, Vaskar Saha\textsuperscript{k}, Andy Pearson\textsuperscript{l}, Heinz Zwierzina\textsuperscript{m}

Academia, Industry, Parents, Regulatory Bodies

ACCELERATE

INNOVATION FOR CHILDREN AND ADOLESCENTS WITH CANCER

www.accelerate-platform.eu
Proposals

1. Pediatric development should be based on drug mechanism of action instead of adult indication

2. Prioritisation should be set up to choose compounds to be evaluated or not in children
   – Based on MOA, needs, feasibility
   – Using stronger biological and preclinical data

3. Reduce delay in starting pediatric development

4. Break the 18 years dogma

5. New incentives and rewards
Cause of children with cancer

Champions in the Parliament

Elena Gentile, Françoise Grossetête, Alojz Peterle, Glenis Willmott

Resolution of the EU Parliament voted in 15 December 2016 (2016/2902(RSP))
Conclusion

• Precision Medicine in Pediatric Oncology drug development: The right time to accelerate innovation for children and adolescents with cancer

• Work together and re-invent partnerships
5th Annual Paediatric Oncology Conference

SAVE THE DATE

2 - 3 March 2017 | Brussels, Belgium

March 2nd & 3rd, 2017