Rare cancers in children and adolescents in Europe

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Cancer in Children and Adolescents in Europe

- 15,000 new cases each year
- 80% can be cured with multidisciplinary treatments
- 3,000 will die

The Goals for the next 15 years:

- Quality of cure and equal access to standard treatments across Europe
- Improving cure rate through Early access to innovative therapies and increased understanding of pediatric tumor biology

A significant Public Health Issue
Pediatric Oncology in Europe

• More than 60 different diseases from newborns to teenagers (even more when biomarkers are considered)
• No private practice
  \[\approx 250\] EU public specialized centers
• Networked since 1968 for clinical research
  – 40% of patients treated within trials (phase I to III)
  – 40% of patients treated according to standard within prospective studies
  – Less than 5% of pharma-sponsored trials
• Many high-level research teams dedicated to pediatric tumor biology
Pediatric Oncology in Europe

- 15 EU groups on solid tumors, hematological diseases, early drug development including joint programs with adult oncology
- A track record of high ranking publications
What is the best high dose Chemotherapy regimen?

6 Off-patent drugs
All approved in adults
(breast, lung, leukemias, ovary)
Not all fully authorized in children
HR-NBL-1 / ESIOP FLOWSHEET

INDUCTION: Rapid COJEC

MAT randomized patients:
563 patients
Randomization rate: 43%

HR-NBL 1
total patients accrual
Feb 2002 – Sept 2010
1577 patients

6 Off-patent drugs
All approved in adults
(breast, lung, leukemias, ovary)
Not all fully authorized in children

SIOPEN R NET
**EFS by Randomized Arm**

Intent to treat analysis from randomization

<table>
<thead>
<tr>
<th></th>
<th>Patients</th>
<th>Events</th>
<th>3-yr. pEFS</th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td>BUMEL</td>
<td>281</td>
<td>136</td>
<td>0.49±0.03</td>
<td>&lt;0.001</td>
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<tr>
<td>CEM</td>
<td>282</td>
<td>169</td>
<td>0.33±0.03</td>
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Europe is ready for new drug development

<table>
<thead>
<tr>
<th>Biology &amp; Preclinical Ev.</th>
<th>Phase I and early phase II</th>
<th>Late Phase II and Phase III</th>
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<tbody>
<tr>
<td>Euro Ewing</td>
<td></td>
<td>EpSSG (soft tissue sarcomas)</td>
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<tr>
<td>SIOPEN (neuroblastoma)</td>
<td></td>
<td>IBFM (leukemias)</td>
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<tr>
<td>SIOPE Brain Tumors</td>
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Current hurdles, pitfalls and limitations

• Fragmentation but a long history of networking
• Struggling to run investigator driven clinical trials within the 2004 clinical trial directive
• Lack of sustained and sufficient funding
• Extremely poor access to new drugs despite the 2007 Pediatric Medicine Regulation
• Insufficient integration between biology and clinical research but several examples of successful FP5 and FP6 projects (KidsCancerKinome, EET-pipeline,...)
• Inequal access to standard therapies across europe
• Pediatric Hemato-Oncology Sub-specialty not recognised in most countries
• Parents organisations need to better join forces
A Network of Excellence
Structuring clinical research in paediatric and adolescent oncology in Europe
HEALTH.2010.2.2.1-3

- Strategy
- Sustainability
- Tools and platforms
- Cooperation with all stakeholders
- Training
- Ethics

Launched in January 2011
Access to new anticancer drugs is a key issue for rare cancers in adults and children.

Do regulatory initiatives help in rare cancers?
2 Major EU Initiatives for Drug Development in Rare Cancers

Official Journal of the European Union

December 1999 : Orphan Medicinal Products

of 16 December 1999
on orphan medicinal products

December 2006 : Medicinal Products for paediatric use

of 12 December 2006
(Text with EEA relevance)

Pediatric Investigation Plans (PIPs); Waiver, Deferral
Orphan DRUGS – 10 years of EU regulation*

- 1235 applications
- 850 orphan designations
- 63 approved drugs
- 41% in oncology
  - Many hematological malignancies
  - Few solid tumors: kidney (3), GIST, Adrenal Glands, STS, osteosarcoma
  - Many rare cancers remain ORPHAN
  - No pediatric cancers

*As of December 2010

Nat Rev Drug Discov Vol10, May 2011, 341
PIPs in Oncology at year 5

41 approved PIPs in oncology*
17 (42%) drugs already have Marketing Authorisation

BUT

• Not all feasible
  - three PIPS in chronic myeloid leukemia
  - 4 drugs in non-hodgkin lymphomas (highly curable)

• Most of them have not been started
• Not all of them will be completed
• Important needs are ignored : eg – neuroblastoma
• No increase of drugs in early phase

Need to simplify and improve the implementation of the regulation

* As october 2011
Improving Drug Development in Rare cancers: the 4 Pilars

1. Networking of academic institutions for expertise, care and research (quality, accreditation)
2. Public funding of research to understand the diseases mechanisms (system biology) and support clinical research
3. Incentives/Obligations towards Pharma to develop oncology drugs for rare cancers and Innovative public/private partnerships
4. Partnership with patients and parents
• Run joint clinical research projects (adults and children) for early drug development
  – Eg Ewing, Osteosarcoma, NHL, GIST, ….

• Innovate together in new design and methodology

• Influence regulatory initiatives (CTD, Ped Med, Orphan, ….)

• Obtain recognition as a Health issue and priority by Eu and national authorities

• Obtain public research funding (because development of innovative therapies in rare cancers cannot rely only on Pharmas)

• Propose new models of partnership with Pharmas (precompetitive research, de-risking models, ….)