

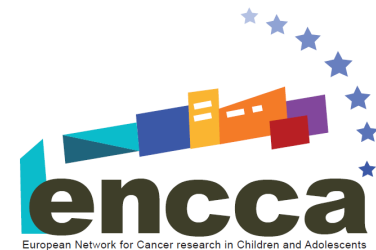
R CANCERS EUROPE E

Joining forces for action

Rare cancers in children and adolescents In Europe

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Bruxelles, February 10, 2012



Cancer in Children and Adolescents in Europe

- 15 000 new cases each year
- 80% can be cured with multidisciplinary treatments
- 3000 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

- More than 60 different diseases from newborns to teenagers (even more when biomarkers are considered)
- No private practice
 - ≈ 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



**SIOP
Brain
Tumour
Group**

**SIOP
Wilms
Tumor**



**I-BFM
group**

EIC-NHL

**EURAMOS I
TRIAL**

SIOPEN R NET

EuroEwing

**Hodgkin's
lymphoma
group**

**Myelodysplasia
Group**

**Rare
Cancers
Group**

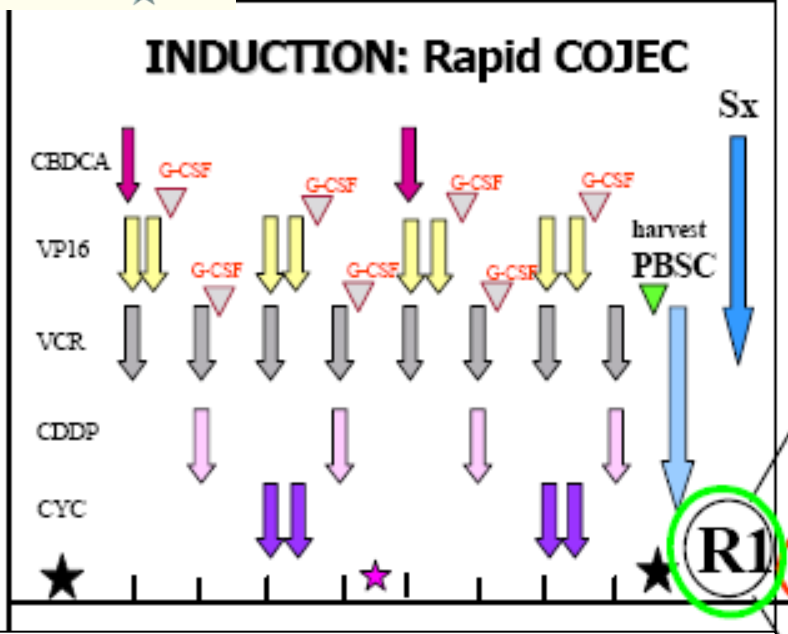
**EORTC
Childhood
Leukemia
group**

**Histiocyte
society**



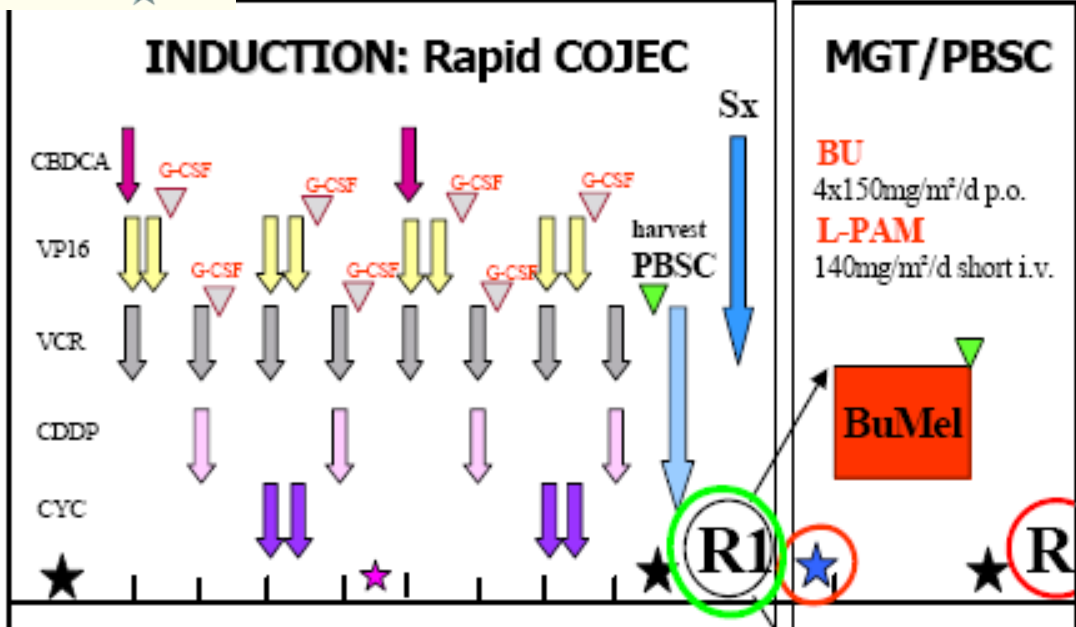
**Parents
Organisations**

- 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
total patients accrual
Feb 2002 – Sept 2010
1577 patients

MAT
randomized
patients:
563 patients
Randomization rate: 43%

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

150

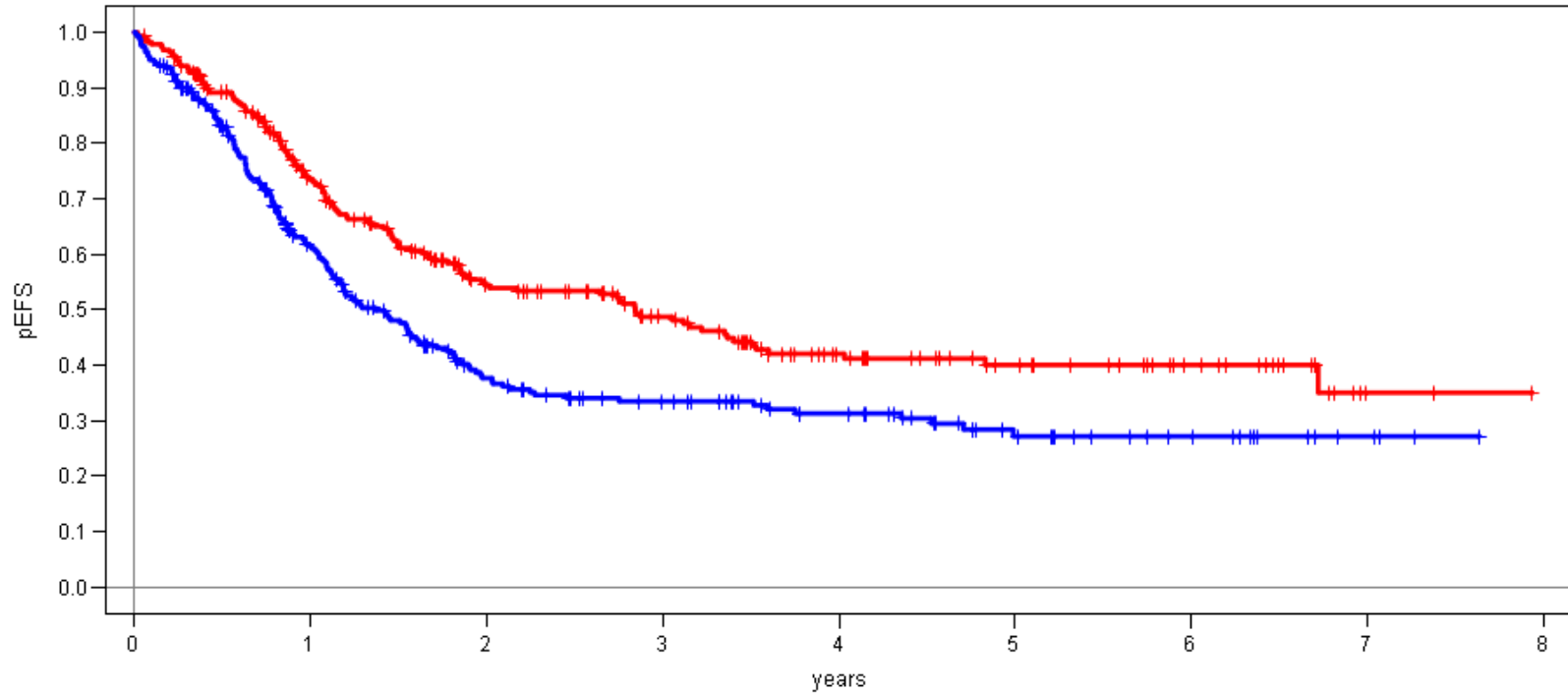
CBDCA
4x ctn iv 425mg/m²

VP16
4x ctn iv 338mg/m²

L-PAM
3x short iv 70mg/m²

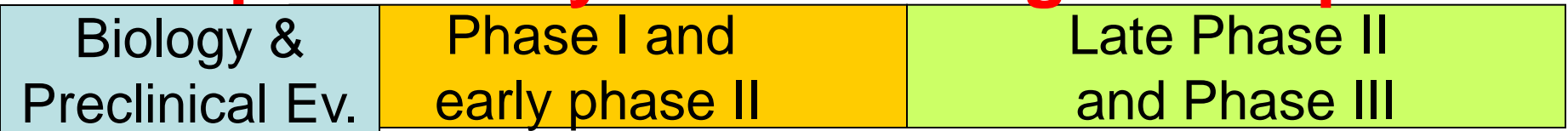
EFS by Randomized Arm

Intent to treat analysis from randomization



	Patients	Events	3-yrs. pEFS	p-value
BUMEL	281	136	0.49±0.03	<0.001
CEM	282	169	0.33±0.03	.

Europe is ready for new drug development



Innovative Therapies
for Children with Cancer



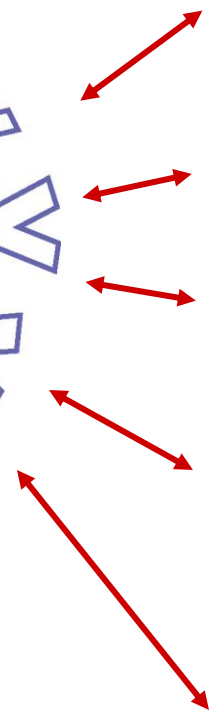
Euro Ewing

EpSSG
(soft tissue sarcomas)

SIOPEN
(neuroblastoma)

IBFM
(leukemias)

SIOPE Brain TUmors



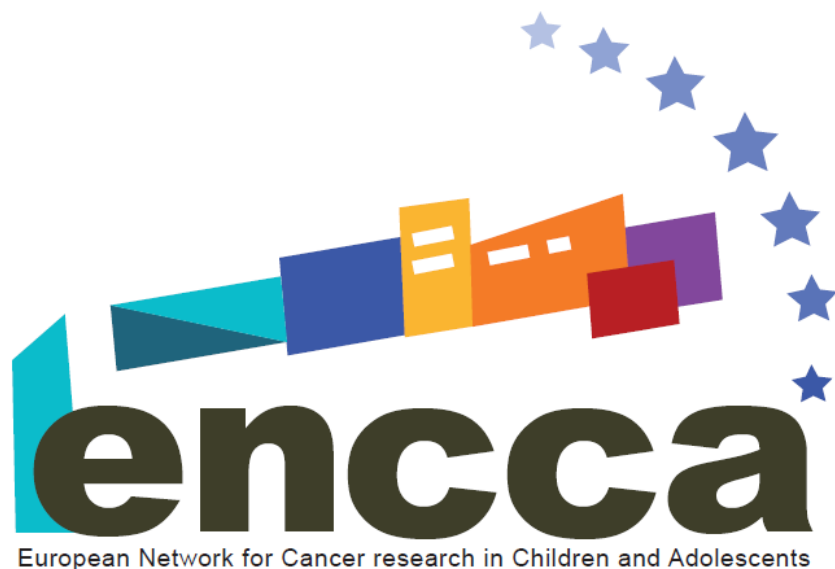
Current hurdles, pitfalls and limitations

- 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



Launched in January 2011

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

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

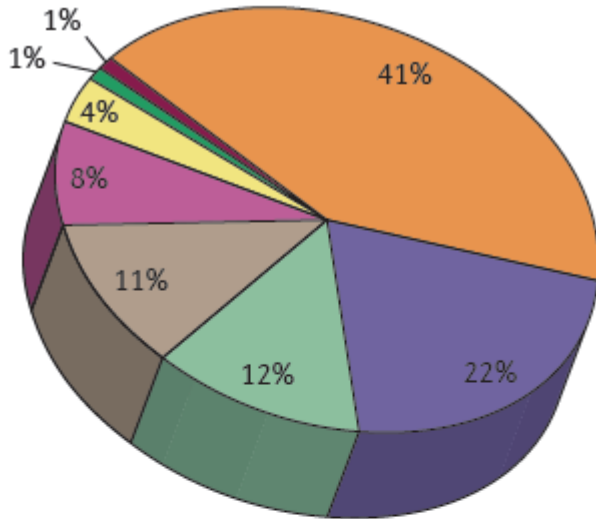
REGULATION (EC) No 141/2000 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL
of 16 December 1999
on orphan medicinal products

December 2006 : Medicinal Products for paediatric use

REGULATION (EC) No 1901/2006 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL
of 12 December 2006
on medicinal products for paediatric use and amending Regulation (EEC) No 1768/92, Directive
2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004
(Text with EEA relevance)

Pediatric Investigation Plans (PIPs); Waiver, Deferral

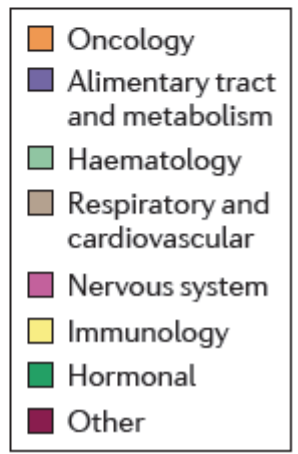
Orphan DRUGS – 10 years of EU regulation*



- 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

Improving Drug Development in Rare cancers : the 4 Pillars

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

R CANCERS in adults, adolescents & children EUROPE E

Joining forces for action → **WHY?**

- 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,.....)