Innovative Therapies for Children with Cancer (ITCC)  
**Pediatric Preclinical Proof-of-Concept Platform (ITCC-P4)**

*A preclinical filtering platform to prioritize new therapies for children with cancer*

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Children are not small adults

~1%
(yet ~50% of gained years of life!)

~99%
The clinical need

Cure rates have mostly plateaued over the last >20 years

→ the „last 20%“ will probably not be cured by „more of the same“!
The regulatory environment is changing

Mandate for pediatric development has changed from „tumor type“ to „relevance of the mechanism-of-action“

Almost all new oncology drugs HAVE to be explored for potential pediatric indications
The challenge

Pharma „pipelines“: ~1000 new oncology drugs

A (smaller) fraction to be prioritized for clinical trials with a good rationale in pediatric oncology

→ **Needs:**

- Prioritize preclinically effective treatments
- De-prioritize non-effective treatments
- Identify rational combinations
- Identify/validate predictive biomarkers
The potential solution: ITCC-P4

15 academic institutions, 10 EFPIA companies and 3 CROs
The approach

- 400 PDX models/5 years, 2 GEMMs per entity, extension to leukemia & lymphoma in 2020
- Full molecular characterization
- 3 standard-of-care drugs and 6 selected compounds
- Proof-of concept for immunotherapies in humanized models
- Proof-of-concept for organoids
ITCC-P4 Models

Most common solid tumors

- Brain tumors are orthotopic; all others flank
- Ependymoma supratentorial [EPD_ST]
- Ependymoma infratentorial [EPD_IT]
- Medulloblastoma WNT [WNT]
- Medulloblastoma SHH [SHH]
- Medulloblastoma Group3 [GR3]
- Medulloblastoma Group4 [GR4]
- Atypical teratoid/rhabdoid tumor [ATRT]
- High grade glioma other [HGGothers]
- High grade glioma K27Mmut [KGG_K27M]

Rarer entities

- ETMR
  - Desmoplastic small round cell tumor
  - HGNET-BCOR
  - CNS neuroblastoma (FOXK2)
  - Inflammatory myofibroblastic tumor
  - Renal cell carcinoma
  - Hepatocellular carcinoma

2020: Liquid Tumors

1. BCP-ALL
   - ETN-RUNX1
   - Hyperdiploid
   - Hypodiploid
   - TCF3-ILF2
   - TEK/PKS-I
   - Bcr/abl
   - BCR-ABL/BCR-ABL-like
   - LAMFII

2. T-ALL
   - Early cortical (11q23-mut)
   - Late cortical (1A4, LM02-mut)

3. AML
   - RUNX1-RUNX1T2/CFB-MYH11
   - RUNX1-mut, TP53-mut, APL1-mut
   - DUX4-P214
   - MLL2 (8q21.1q22.1q23.32)
   - complex karyotype
   - monosomai karyotype
   - NPM1-mut
   - NUP98
   - other

4. Infant ALL/ALL
   - MLL2 (8;14)(q21.1;q11.2), (11q23)
   - others

~250 models with full molecular characterization to date

Derivation of organoids from all these + selection of controls
ITCC-P4 Testing: An example

Testing in one (neuroblastoma) model:

MV17458_ITCC:P4_NB0026

- vehicle
- Etoposide
- Topotecan
- Cisplatin + Cyclophosphamide
- Idasanutlin
- JQ-1
- Prexasertib
- Cobimetinib
- Lorlatinib
- Copanlisib

control

Standard of care

x40 for each tumor type for 9 selected treatment conditions

Tumor progression

Tumor shrinkage

www.itccp4.eu
ITCC-P4 Recommendations

International Consensus on Minimum Preclinical Testing Requirements for the Development of Innovative Therapies For Children and Adolescents with Cancer

Gilles Yassat, Peter J. Houghton, Stefan M. Pfister, Malcolm A. Smith, Huib N. Caron, Xiao-Nan Li, David J. Shields, Olaf Witt, Jan J. Molenaar, Sara Colombetti, Julia Schüler, and Lou F. Stancato

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…to be submitted to regulatory authorities (EMA +/- FDA) for endorsement
**ITCC-P4 Sustainability**

**Goal:** Build a sustainable post-IMI2 infrastructure that will provide the biological and preclinical data to identify and prioritize new oncology drugs for children and adolescents with cancer.

**Progress to date:**
- Preferred model defined
- Service, not models will be sold
- Will serve the needs of both academic and industrial customers
- Plan to ensure the platform and the science carries on
The ITCC-P4 Managing Board

...a great team effort!

www.itccp4.eu
re-launched today!

www.itccp4.eu
Questions?