# ITCC-P4 International Workshop
# IMPROVING PEDIATRIC ONCOLOGY DRUG DEVELOPMENT THROUGH PRECLINICAL RESEARCH 2018

## Breakout Session:
## Pediatric preclinical evaluation of IO compounds

**Moderators:**

**Sara Colombetti (Roche, Basel Switzerland)**

**Malcolm M Smith (NCI, Bethesda, USA)**

ITCC P4 PAEDIATRIC PRECLINICAL PROOF OF CONCEPT PLATFORM

This project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking under Grant Agreement No 116064 This Joint Undertaking receives support from the European Union's Horizon 2020 research and innovation programme and the European Federation of Pharmaceutical Industries and Associations.
http://www.imi.europa.eu/ - http://www.itccp4.eu

# Pediatric preclinical evaluation of IO compounds

- What are the specific needs/requirements for IO drugs?
- What are the current barriers for the preclinical evaluation of immuno-oncology drugs on pediatric tumors ?
- What is an optimal strategy
- Are there opportunities for a joint research project developed through a partnership between ITCC-P4 and PPTC

# Specific needs/requirements for IO drugs

- Therapeutic classes:
  - Checkpoint inhibitors (limited applicability as single agents)
  - T cell bispecific antibodies (TCBs)
  - CAR T cells

- Pediatric tumor specific antigens??
- Immune infiltrates in children and match to preclinical syngeneic models
- Pediatric cancer surfaceome
- MHC-presented peptides for pediatric cancers
- Pediatric research teams with experience using humanized mouse models or other model systems for evaluating BiTEs and TCBs

# Checkpoint inhibitors in pediatrics

ITCC P4 PAEDIATRIC PRECLINICAL PROOF OF CONCEPT PLATFORM

- Responding populations in adults
  - Tumors with high tumor mutational burden and corresponding high rates of tumor neoantigens
  - Hodgkin lymphoma, PMBCL
  - Others with low tumor mutational burden (e.g., polyoma-virus associated Merkel cell carcinoma)
- Pediatrics
  - Low tumor mutational burden with few patients with high tumor mutational burden (10 mutations/MB – primarily genetic conditions, e.g., BMMRD)
  - Hodgkin lymphoma
  - Clinical experience with checkpoint inhibitors: few responding patients
  - Need responder hypotheses that extend beyond tumor neoantigens and high tumor mutational burden
- Use of checkpoint inhibitors to enhance engineered T cell and antibody approaches may apply to both pediatric and adult cancers

imi innovative medicines initiative

# Barriers for the preclinical evaluation of immuno-oncology drugs on pediatric tumors

ITCC P4 PAEDIATRIC PRECLINICAL PROOF OF CONCEPT PLATFORM

Lack of antigens limited to pediatric cancers that could be targeted
Lack of experience with available preclinical IO testing systems for TCBs

imi innovative medicines initiative

# Optimal strategy for Pediatric Preclinical IO Agent Testing

- Agents with proven adult cancer activity
  - Agent expressed in children at comparable levels as adults
  - Absent toxicity concerns, proceed to clinical testing in children
  - Learn from the clinic and use preclinical models to understand clinical responses/resistance (co-clinical development)
- Agents with pediatric specific antigens and no proof-of-concept from adults
  - Develop preclinical package of data to support prioritization
- Minimal residual disease versus bulk disease??

# Opportunities for partnership between ITCC-P4 and PPTC for IO agent evaluations

Sharing of data regarding antigen expression and other relevant items