Single Mouse Preclinical Trial (SMTP): A tool for translational research

C. MIGNARD, M. HILLARRET DE BOISFERON, P. BICHAT, O. DUCHAMP, D. FRANCE

Oncodesign, Lyon (France)

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INTRODUCTION

Increase the power of translational research using predictive PDX (patient-derived xenografts) models. Each model represents 1 patient to:

- Support Go-Nogo decision for early clinical proof of concept
- Patient stratification: Identify responsive sub-populations
- Identification of drug resistance mechanisms
- Drug combination evaluation
- Drug positioning in repositioning
- Expansion of clinical indications by exploring other tumor types
- Biomarker identification and companion diagnostic development

With SMPT, increase the power of your translational research with limited cost:

One study with one pathology with several drug candidates
One study with several pathologies with one drug candidate

RESULTS

Evaluation of reproducibility of 225 single-animal response data among 24 treatments groups including 12 different breast PDX (patient-derived xenografts) subcutaneously xenografted in 7 to 10 mice per breast PDX treated model.

Readouts were based on RECIST criteria as adapted on readouts PDX SMPT and on RECIST - Mouse Response Evaluation Criteria in Solid Tumors. ΔV(t)=100%((V(t)-V(initial))/V(initial)) was calculated for each animal at each time. Best response is the minimum value of ΔV(t), for t=10 days. Avg of ΔV(t) was calculated for each t from t=1 to t=10 days. Best response Average is the minimum value of Average of ΔV(t).

PDX cohorts available to design SMPT

Colon PDX cancer collection (n=53)

Lung PDX cancer collection (n=16)

Breast PDX cancer collection (n=35)

Ovarian PDX cancer collection (n=30)

Pancreas PDX cancer collection (n=24)

Features PDX cancer collection (n=24)

More than 172 PDX well characterized tumor models are available
Highly conserved phenotype and genotype
Available annotation:
- Patient information (diagnostic and outcome)
- Histology
- Genomic profile (polymorphism exome seq, RNA seq)
- Pharmacological profile to 4 standard of care

All models were developed in partnership with the members of the consortium RECI3

SMPT validation in breast PDX models

- Sector: OXALIPAZIN
- Sector: FOLFOX

CONCLUSIONS AND PERSPECTIVES

- We demonstrate that individual response matched the treatment group data, supporting the concept to use SMPT.
- Our SMPT study demonstrates a synergy of combination compared with 2 standards of care alone in a cohort of 27 colon PDX.
- SMPT aims to predict the clinical outcome of new drug candidates.