Roughly, 85% of preclinical drug candidates entering oncology clinical trials fail to demonstrate sufficient safety or efficacy to gain regulatory approval. Hence, there is a need for experimental systems which better mimic the inter-patient response heterogeneity observed in the clinic. Patient-derived tumor xenograft (PDX) mouse models have emerged as a relevant oncology research tool to study tumor evolution, drug response, biomarkers, resistance phenomenon and personalized treatments to each patient.

Oncodesign PDX Surrogate Clinical Trial

We will here expose the effectiveness of the Single Mouse Preclinical Trial (SMPT) paradigm for evaluating drug response, as mono or combo therapy using our well-characterized PDX collection. Based on the “1 PDX tumor/1 mouse/1 treatment” experimental design, a cohort of colorectal and breast PDX models was used to explore response to Standard Of Care (SOC) and combo therapy used in clinic.

**SMPT validation in breast PDX models**

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

The individual responses matched the majority response category in 78% for CR, 80% for PR and 63% for SD. No individual response were off by more than one mRECIST category. This analysis justify the 1x1x1 experimental approach. Furthermore, when we combined the response categories (mCR, mPR and mSD) into a single “responder” category, the response calls made on a single mouse were consistent with the majority response 100% of the time, which strongly support the rationale of using one animal to reflect the true response.

**SMPT study including 27 colon PDXs.** Tumor models were treated with SOC alone (5-FU or Oxaliplatin) and FOLFOX (5-FU, Oxaliplatin, folinic acid).

- FOLFOX increased the tumor response when compared with both mono therapies.

**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.