

Case Study



Combination Feasibility Prediction for Checkpoint Inhibitors for a Biologic

The Purpose

The partner had a large molecule in the development pipeline for cancer indications. They were interested in combining their proprietary molecule with already approved immune check-point inhibitors to improve therapeutic efficacy.

About the Client



INDUSTRY Biotech

2	LOCATION
	Europe



THERAPEUTIC AREA Oncology

Client Requirement

To prioritize cancer indications based on their sensitivity towards the combination of the biologic with a check point inhibitor (anti-PD-1/PDL-1). Publicly available data on successful and failed drug combinations was used for building predictive models.

The Excelra Approach

Machine learning models were built using to assess the sensitivity of cancer indications as well as patients to the drug combination. Based on the analysis, some cancer indications were prioritized for further assessment. A biological hypothesis was built to establish the synergistic role of the combination partners for cancer treatment.

Algorithms





Network Based Analysis



Scoring System

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	Overall cancer level				Each patient level insight			
	Anti-PD1 Sensitivity (RPART)	Anti-PD1 PLS score	Drug X PLS score	Both (Anti PD1+ DrugX) Sensitive	Total Sample	Sensitive sample (both Drug X+Anti PD1)	Resistant Sample	Response Rate (Anti-PD1 blocker)
ALL	0	2.08	0.55	Yes	750	131	619	17.47
LIHC	-1	0.01	0.31	Yes	373	185	188	49.60
PAAD	-1	0.74	0.29	Yes	179	57	122	31.84
OV	0	0.34	0.93	Yes	558	497	61	89.07
AML	0	2.26	0.72	Yes	542	77	465	14.21
BLCA	-1	2.44	-0.40	No	408	199	209	48.77
CHOL	-1	-0.83	-0.30	No	36	13	23	36.77
STAD	-1	0.41	0.61	No	415	164	251	39.52
TNBC BL1	-1	0.88	0.32	Yes 💌	20	16	4	80.00
BRCA	-]	-0.20	-1.05	No				

Color scheme is based on Drug X response

RPART 0→Resistant, 1→Sensitive -1→Partial Sensitive

PLS score Positive → Sensitive Negative → Resistant

Yes → Must be Drug X positive and either of Anti PD1 predictor (RPART or PLS) as sensitive

Excelra's Contribution

Prioritize the indication where indication therapy with PD-1 willwork the best. Custom pathways were generated to understand crosstalk between the drug-induced signaling and checkpoint inhibitor signaling pathways.

Feasibility/synergy prediction of the two-drug combination.

Widen the list of indication where the query drug may be developed. Indications resistant or were partially sensitive to the monotherapy were predicted to be sensitive towards combination with the checkpoint inhibitor.

Excelra's Service Portfolio

		Insights	Data
	Discovery	 Data Science Driven Drug Discovery Target Identification Target Dossier Services 	 Chemistry Curation Services GOSTAR Structure Activity Relationship database
	Translational	 Biomarker Discovery Drug Repositioning Life Cycle Management Systems Biology Informatics 	 Biology Curation Services GOBIOM Biomarker intelligence database
បំប៉ិប៉ិ	Clinical	 Precision Oncology Informatics Clinical Pharmacology	 Clinical Trial Outcomes Database
	Value Evidence	 Outcomes Research Epidemiology Modelling Economic Modelling Value Evidence Communication 	 RWE & Big Data Realization SLR & Meta-analysis
	Technology Solutions	 Enterprise Data Strategy Enterprise Cloud Ops Enterprise Digital Transformation 	

For more information, visit https://www.excelra.com/clinical/#precision_oncology



About Excelra

Excelra's data and analytics solutions empower innovation in life sciences across the value chain from discovery to market. The Excelra Edge comes from a seamless amalgamation of proprietary curated data assets, deep domain expertise and data science. The company's multifaceted teams harmonize and analyse large volumes of disparate unstructured data using cutting-edge technologies. We galvanize data-driven decisions to unlock operational efficiencies to accelerate drug discovery and development. Over the past 18 years, Excelra has been the preferred data and analytics partner to over 90 global clients, including 15 of the top 20 large Pharma.