



GENEGO SERVICES GROUP

GOOD RESPONSE BIOMARKERS
SECURE SUCCESS OF PHASE III TRIAL



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FORMULATION OF GOOD RESPONDER SIGNATURE FOR PATIENT STRATIFICATION

CLIENT

A top 10 global pharmaceutical company.

CHALLENGE

The client needed to select a cohort of good responders for their drug candidate for Phase III trial following Phase II results that showed the drug response rate was heterogeneous among patients. Expression data was collected during the trial with the goal of explaining the differences and formulating an expression “gene signature” to qualify good responders. Using several statistical methods of data analysis, the company’s scientists created the “signature”; but its performance on a broader set of patients was uncertain and unpredictable. As “gene signature” performance is known to be highly dependent on biology of “end point” and statistical methods¹, the company sought expert advice, from GeneGo, a Thomson Reuters business, known for their unparalleled knowledge of pathway-based feature selection and methods of quantitative functional analysis.

CONSULTING COURSE OF ACTION

First, GeneGo applied its two proprietary network topology methods of identifying and prioritizing of key genes regulating differential expression, i.e. interactome overconnectivity analysis and “hidden node” algorithm.

Next, differentially expressed genes and the “gene signature” formulated by the client were subjected to concurrent pathway

analysis guided by the identified key genes. This analysis revealed the most significant biological pathways and protein networks affected in patients with a good response to the treatment. Concurrent visualization of the four subset of genes (key genes identified by two methods, entire differentially expressed profile, and company’s signature) on the signaling pathways helped to understand the mechanism behind the signature, improve its composition and build a “causal network” to be tested as a multi-variant biomarker.

OUTCOMES

Through collaboration with GeneGo, the client produced a biomarker signature which included minimal number of genes for the best characterization of the good responder phenotype based on the statistical parameters of methods applied in the study.

The expression biomarker signature identified in this study is currently being validated in clinic in the scope of a Phase III trial. IP for the signature remains solely with the client.

REFERENCE

- ¹ Shi W. et al. A comprehensive survey of common practices for the development and validation of microarray-based predictive models. *Nat Biotechnol.* 2010, 8, 827-38. 30



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