Case study

Lung Adenocarcinoma - Non small cell lung cancer

(LUAD-NSCLC)



nova DISCOVERY

The challenge

Janssen sought a validated *in silico* disease model of non-small cell lung cancer (NSCLC) tumors with common treatment-resistant mutations, enabling control arms with virtual patients, where in-person controls are unethical.

The solution

NOVA's *in silico* model of NSCLC tumors harboring treatment-resistant epidermal growth factor receptor (EGFR) mutations, validated using two independent data-sets, allowed accurate simulation of disease progression after standard therapy. It also predicted patient response according to tumor mutation profile.

Disease background

Lung cancer is the second most prevalent cancer and the most common cause of cancer deaths worldwide, according to the World Health Organization. NSCLC makes up the majority of lung cancer cases. About a third of NSCLC patients have mutations in the epidermal growth factor receptor, a signalling protein involved in cell growth and division. Some of these patients benefit from EGFR-targeting drugs like first-generation EGFR tyrosine kinase inhibitors (TKIs). But patients with a particular type of EGFR mutation called exon 20 insertions (5 to 12% of EGFR and NSCLC patients) don't respond to EGFR-targeting therapies, leaving chemotherapy as their only option.

Janssen was seeking:

- A validated disease model predicting disease trajectory and time-to-progression in patients with EGFR-positive exon 20 mutations who had received EGFR-targeting tyrosine kinase inhibitor treatment
- An ethical route to creating virtual control arms in NSCLC trials
- A deeper understanding of how tumor growth and mutation status evolve over time, informing patient selection for clinical trials

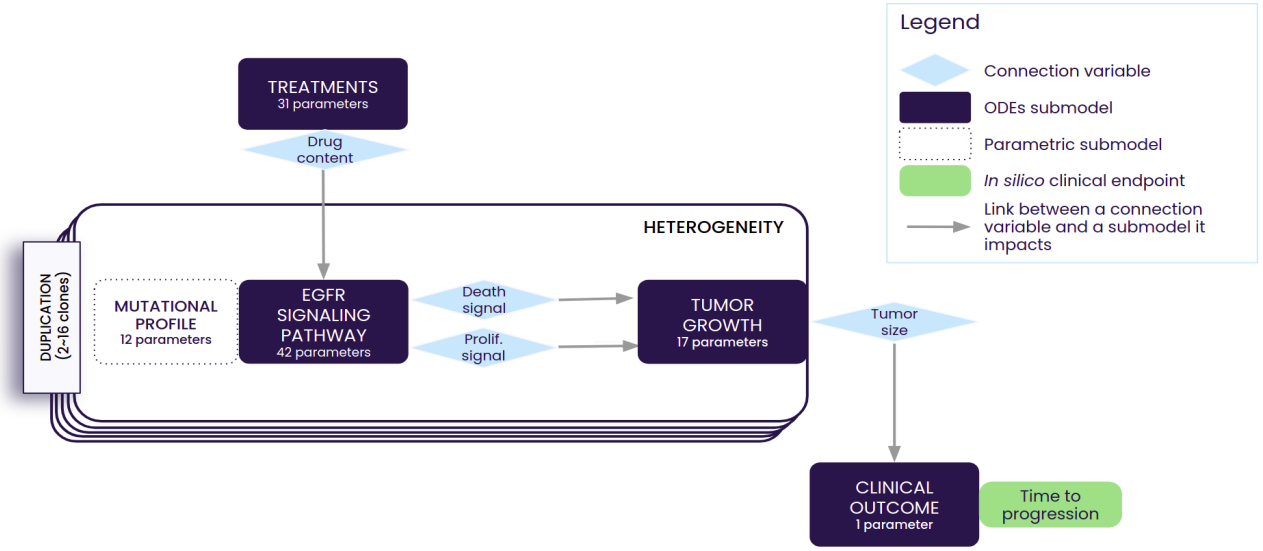
Recruiting patients for a control (placebo) study arm for potentially life-saving therapies is ethically challenging. *In silico* modeling allows sponsors to predict the clinical outcome of a control arm, enabling more accurate assessment of treatment effect. There is no limit on the size or duration of an in silico trial, and researchers can explore the effects of different treatment regimens and combinations on a variety of tumor mutation types and patient profiles.

How NOVA approached the challenge

NOVA built an *in silico* model of EGFR-positive NSCLC, using publicly-available data and the JINKO* platform, a state of the art clinical trial simulation cloud-based SaaS solution. The model was successfully validated using two separate, independent lung cancer data-sets. It was also benchmarked to an alternative, Bayesian NSCLC model (Nagase *et al.*, 2020) built using real patient data; both models generated similar results.

Janssen and NOVA were thus able to confidently simulate the natural course of disease among patients with EGFR-positive NSCLC, following standard treatment. By modeling the growth trajectories of tumors that carry different sets of driver mutations among 9 mutations (including 4 EGFR-positive mutations) and the associated clinical endpoints, they were also able to better understand disease progression in particular patient subgroups.

Illustration of the NSCLC Model



The model was validated using the Lux-Lung 7 dataset (Paz-Ares et al. 2017).

The outcomes

This *in silico* approach enables more informed clinical trial decisions, and more cost-effective R&D. It allows researchers to test relevant hypotheses as early as possible, and overcome some of the challenges of testing targeted therapies, including:

- powering clinical trials, as we are able to simulate them with an unlimited number of patients
- limiting ethical and practical difficulties of running control arms: modeling digital twins for each patient enrolled in a clinical trial effectively creates a synthetic control arm.

More about our JINKO clinical trial simulation platform

JINKO is a complete solution for trial simulation & design optimization

Combining the powers of data science, biology and medicine, JINKO is the first collaborative trial simulation platform capable of predicting the clinical outcomes of trials carried out in human subjects. JINKO models diseases and treatments, using unlimited numbers of virtual patients, to accurately inform the design of in-person trials.

JINKO offers users:

- ➔ Simulation outputs with multiple viewing filters (e.g. stratified by patient type)
- ➔ User-friendly interface for trialists, pharmacologists and other R&D functions to collaborate seamlessly, reinforced by confident mapping of Knowledge to Computational Model
- ➔ Cross-company curated knowledge base to capitalize on past research and stay up-to-date on latest science and publications
- ➔ Fully documented and auditable content (white-box)
- ➔ A means of strengthening internal communication and fostering cross-functional workflows

The platform's content, design and capabilities accelerate the impact of simulation technology on clinical research, helping ensure scientific knowledge is translated as rapidly as possible into clinical benefit.

More about NOVA

Novadiscovery (NOVA) is a leading health tech company using in silico clinical trials to predict drug efficacy and optimize clinical trial development. Our computational models of disease and treatment, based on the latest scientific knowledge and data, help biotech and pharma companies generate digital evidence to take more informed R&D decisions. These help lower risk, reduce costs, and accelerate time-lines.

Come visit our website: https://www.novadiscovery.com/