

Cellworks Biosimulation Identifies which NSCLC Patients will Benefit from Combining Chemotherapy with Immunotherapy

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New study validates Cellworks predictions of chemotherapy benefits in real-world NSCLC patients, guiding treatment decisions beyond PD-L1 status

SAN DIEGO--(BUSINESS WIRE)-- **Cellworks Group Inc.**, a leader in Personalized Therapy Decision Support and Precision Drug Development, today announced results from a study, where Cellworks' biosimulation platform accurately predicted overall survival (OS) and chemotherapy benefit in two real-world non-small cell lung cancer (NSCLC) patients cohorts. The study showcases Cellworks' ability to advance personalized cancer treatment by identifying NSCLC patients most likely to benefit from combining immunotherapy and chemotherapy, regardless of their PD-L1 levels, thereby optimizing treatment strategies and improving patient outcomes.

Results of the study were presented on September 10, 2024 in an oral session (MA09.06) titled, '**Use of Biosimulation to Predict Chemotherapy Benefit in Patients with Metastatic NSCLC Being Treated with Immunotherapy**', by **Dr. Mark Klein, MD**, Staff Physician at the Hematology/Oncology Section at the Minneapolis VA Healthcare System and an Associate Professor of Medicine in the Division of Hematology, Oncology, and Transplantation at the University of Minnesota; and a Principal Investigator for the study. The presentation was part of the IASLC 2024 World Conference on Lung Cancer hosted by the International Association for the Study of Lung Cancer in San Diego, California.

"A majority of patients with advanced NSCLC do not have a targetable mutation and rely largely on PD-L1 status to guide treatment decisions – however, no reliable biomarkers currently exist to identify patients who would benefit from the addition of chemotherapy," said **Dr. Charu Aggarwal, MD, MPH**, Professor of Medicine, University of

Pennsylvania, Associate Director, PC3I and Director, Program in Precision Oncology Innovation, Penn Center for Cancer Care Innovation; and a Principal Investigator for the study. “This study highlights the potential of utilizing the Cellworks Computational Biology Model (CBM) and Therapy Response Index (TRI) to predict chemotherapy benefits for NSCLC patients. Cellworks biosimulation approach marks a promising step forward in refining and improving NSCLC treatment strategies.”

“While PD-L1 has been the standard biomarker for selecting NSCLC patients for immunotherapy, it is not predictive of chemotherapy benefit,” said **Dr. Michael Castro**, Cellworks Chief Medical Officer. “This study shows that by using a tumor’s genomic profile and Cellworks personalized therapy biosimulation to understand signaling pathway dysregulation and drug response, we can better predict which NSCLC patients may benefit from chemotherapy and which patients will not. Biosimulation has the potential to refine patient management for NSCLC patients above and beyond generalized guidelines using PD-L1 only and advance the precision oncology mission of getting the right treatment to the right patient.”

Study Design

The Cellworks TRI algorithm was trained on a real-world retrospective cohort of 553 NSCLC patients from the U.S. Veterans Health Administration (VHA) who had undergone tissue-based comprehensive genomic profiling conducted by Foundation Medicine. The TRI, Cellworks CBM and clinical thresholds were locked and prospectively validated in an independent set of 710 advanced NSCLC front-line patients obtained from the Flatiron Health-Foundation Medicine NSCLC clinico-genomic database (FH-FMI CGDB). Biosimulation was performed using the Cellworks CBM, which predicts changes in key biomarker concentrations and hallmark cancer phenotypes, triggered by genomic aberrations and therapeutic intervention. The hallmark phenotypes were combined using statistical and machine learning methods to generate the TRI, which was trained to predict outcomes.

Study Results

The Cellworks TRI was significantly associated with OS above and beyond other clinical factors, including PD-L1 levels ($p = 0.036$). Patients in the high TRI group (≥ 32) showed no benefit to the addition of chemotherapy. In contrast, patients in the low TRI group (< 32) received an estimated incremental benefit in median OS of approximately 3 months with the addition of chemotherapy and immunotherapy.

The Cellworks Platform

The Cellworks Platform biosimulates the impact of specific drug compounds on an individual patient or class of patients using their multi-omic profile. Multi-omic data from an individual patient or cohort is used as input to the in silico Cellworks Computational Biology Model (CBM) to generate a personalized or cohort-specific disease model.

The CBM is a highly curated mechanistic network of 6,000+ human genes, 30,000 molecular species and 600,000 molecular interactions. This model along with associated drug models are used to biosimulate the impact of specific compounds or combinations of drugs on the patient or cohort and produce therapy response predictions, which are statistically modeled to produce a qualitative Therapy Response Index (TRI) score, scaled from 0 (unfavorable outcome) to 100 (favorable outcome) for a specific therapy. The Cellworks CBM has been tested and applied against various clinical datasets with results provided in over 125 presentations and publications with global collaborators.

About Cellworks Group

Cellworks Group, Inc. is a leader in Personalized Therapy Decision Support and Precision Drug Development. The Cellworks Platform predicts therapy response for individual patients and patient cohorts using a breakthrough Computational Biology Model (CBM) and biosimulation technology. Backed by Artiman Ventures, Bering Capital, Sequoia Capital, UnitedHealth Group and Agilent Ventures, Cellworks has the world's strongest trans-disciplinary team of molecular biologists, cellular pathway modelers and software engineers working toward a common goal – attacking serious diseases to improve the lives of patients. The company is based in South San Francisco, California with a CLIA-certified computational laboratory in Franklin, Tennessee and a research and development facility in Bangalore, India. For more information, visit www.cellworks.life.

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