



Cellworks Singula™ TRI Predicts Personalized Treatment Outcomes for Esophageal Adenocarcinoma Patients Beyond Standard Clinical Factors

myCare-004 Study Finds Cellworks Personalized Therapy Biosimulation Provides Superior OS, DFS and TRG Predictions for GEA Patients

CHICAGO, June 6, 2022 – Cellworks Group, Inc., a world leader in Personalized Medicine in the key therapeutic areas of Oncology and Immunology, today announced results from the myCare-004 study, which demonstrate that the Cellworks Singula™ Therapy Response Index (TRI) is highly predictive of Overall Survival (OS), Disease-Free Survival (DFS) and Mandard-tumor regression grade (TRG) for gastroesophageal adenocarcinoma (GEA) patients. In this retrospective study, Singula™ TRI provided additional predictive information for OS and DFS beyond patient age, patient gender and physician-prescribed treatment.

The results from the myCare-004 clinical study were featured in a poster session as part of the 2022 ASCO Annual Meeting during the Gastrointestinal Cancer – Gastroesophageal Pancreatic and Hepatobiliary Track and available online as Abstract 4064.

“This study confirmed that there are many dysregulated signaling pathways responsible for hallmark behaviors of cancer and variable drug response in gastroesophageal adenocarcinoma patients,” said Dr. Elizabeth Smyth, Cambridge University Hospitals NHS Foundation Trust and Co-Principal Investigator of the myCare-004 clinical study. “Cellworks personalized therapy biosimulation enables us to utilize a patient’s comprehensive next generation sequencing (NGS) results and understand the downstream molecular effects of specific drugs on cell signaling to predict how each patient will respond to therapies prior to treatment. The next step is to evaluate whether biosimulation-informed therapy selection can be used prospectively to improve the survival of GEA patients.”

“Gaining a better understanding of the molecular determinants of gastroesophageal adenocarcinoma is key to improving therapy response rates for GEA patients,” Dr. Rebecca Fitzgerald, MD, Professor of Cancer Prevention at the University of Cambridge; Director of the CRUK Cambridge Centre Early Detection Institute; and Co-Principal Investigator of the myCare-004 clinical study. “There are limited treatment options for this cancer type and we look forward to testing the Cellworks personalized therapy predictions in a prospective trial.”

The Cellworks Biosimulation Platform simulates how a patient's personalized genomic disease model will respond to therapies prior to treatment and identifies novel drug combinations for treatment-refractory patients. The platform is powered by the groundbreaking Cellworks Computational Omics Biology Model (CBM), a network of 7,000+ human genes, 30,000+ molecular species and 100+ signaling pathways. As part of the biosimulation process, personalized disease models are created for each patient using their cytogenetic and molecular data as input to the Cellworks CBM. The Cellworks platform analyzes the impact of specific therapies on the patient's personalized disease model and generates a Singula™ biosimulation report with Therapy Response Index (TRI) scores from 0 to 100 that predict the efficacy of specific chemotherapies.

myCare-004 Clinical Study

Background

In this study, the Cellworks Singula™ Therapy Response Index (TRI) was used to prospectively predict the Overall Survival (OS), Disease Free Survival (DFS) and Mandard-tumor regression grade (TRG) in a retrospective cohort of gastroesophageal adenocarcinoma patients from the UK OCCAMS consortium. 271 GEA patients were selected who had pre-chemo treated biopsies with 50x whole genome sequencing. 234 patients were male and 30 female with a median age of 65.6 years. Within the study population, there were 35 T2, 215 T3, 70 N0, 126 N1, 62 N2 and 266 M0. Patients were prescribed chemotherapy treatments according to UK clinical guidelines.

Methods

A mechanistic model created for each patient using comprehensive genomic inputs biosimulated downstream molecular effects of cell signaling and drugs for a patient's personalized *in silico* disease model. Random sampling stratified by clinical factors was used to split the data into independent training (N=140) and validation (N=131) subsets. Multivariable Cox Proportional Hazard (PH) and Proportional Odds models were used to predict survival and pathological response as a function of the pre-defined Therapy Response Index (TRI) and clinical thresholds compared with standard clinical factors.

Results

Cellworks Personalized Therapy Biosimulation found that 99% of the patients' tumors had deficiency in DNA repair genes. Other pathways included amplification of multi-drug resistance pumps, TP53 mutations and aberrations of the PI3K/AKT pathway genes. Cellworks Singula™ Therapy Response Index (TRI) provided additional predictive information for OS and DFS beyond physician prescribed treatment and standard clinical factors. TRI was also predictive of TRG in univariate analysis. TRI scores were generated for 82 alternate therapies for each patient, enabling selection of optimal therapies with estimates of improvements in median OS and DFS compared to standard care (SC).

Conclusions

The study found that Cellworks Singula™ TRI was predictive of Overall Survival (OS), Disease-Free Survival (DFS) and Mandard-tumor regression grade (TRG) beyond clinical factors in this cohort of gastroesophageal adenocarcinoma (GEA) patients. These positive results suggest the utility of biosimulation-informed therapy selection to improve survival of GEA patients.

About Cellworks Group

Cellworks Group, Inc. is a world leader in Personalized Medicine in the key therapeutic areas of Oncology and Immunology. Using innovative multi-omics modeling, computational biosimulation and Artificial Intelligence heuristics, Cellworks predicts the most efficacious therapies for patients. The Cellworks unique biosimulation platform is a unified representation of biological knowledge curated from heterogeneous datasets and applied to finding cures. Backed by UnitedHealth Group, Sequoia Capital, Agilent and Artiman, Cellworks has the world's strongest trans-disciplinary team of molecular biologists, cellular pathway modelers and software technologists working toward a common goal – attacking serious diseases to improve the lives of patients. The company is based in South San Francisco, California and has a research and development facility in Bangalore, India. For more information, visit www.cellworks.life and follow us on Twitter @cellworkslife.

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