Integrative kinetics and machine learning modeling for prediction of outcome following immunotherapy in lung cancer

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I will present recent results from COMPO (COMPutational pharmacology and clinical Oncology) aiming at combining mechanistic modeling and machine learning ("mechanistic learning") to integrate longitudinal, multi-modal and high-dimensional data into predictive models of outcome following immunotherapy in non-small cell lung cancer (NSCLC). This will be based on two studies. The first leverages clinical trial data to help in drug development by predicting outcome of late-phase trials (e.g., phase 3) from early data (e.g., phase 2). The second is an integrative analysis of multi-modal deep-level biomarkers (multiplex immunohistochemistry, immune-monitoring, vasculo-monitoring, hematology and biochemistry) collected during the RHU PIONeeR. The results show substantial improvement of the predictive performances of classical markers (PDL1 expression, AUC = 0.64, tumor mutational burden, AUC = 0.65) using a novel kinetics-machine learning (kML) model (AUC = 0.86, c-index = 0.79, test set). The kML model was also able to predict the positive outcome of the phase 3 of the OAK trial (atezolizumab versus docetaxel) using 30 weeks on-study data (model HR = 0.802 (95% CI : 0.655 - 0.907)) while the observed data at this landmark time point was not conclusive (data HR = 1.04 (95% CI : 0.386 - 2.79)).

References :

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[3] Barlesi, F. et al., Benzekry, S. Comprehensive biomarkers (BMs) analysis to predict efficacy of PD1/L1 immune checkpoint inhibitors (ICIs) in combination with chemotherapy : a subgroup analysis of the Precision Immuno-Oncology for advanced Non-Small CEll Lung CancER (PIONeeR) trial. Annals of Oncology, 16 (suppl_1), 2022

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