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Abstract Title: Artificial intelligence to improve selection for NSCLC patients treated with immunotherapy

Authors:

Arsela Prelaj, Medical Oncology Department, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy

Mattia

Boeri, Tumor Genomics Unit, Department of Research, Fondazione IRCCS Istituto Nazionale Tumori, Milan,

Italy

Alessandro

Robuschi, Department of Electronics, Information, and Bioengineering, Polytechnic University of Milan, Milan,

Italy

Claudia Proto, Medical Oncology Department, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy

Giuseppe Lo Russo, Medical Oncology Department, Fondazione IRCCS Istituto Nazionale Tumori, Milan,

Italy

Roberto Ferrara, Medical Oncology Department, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy

Giulia Galli, Medical Oncology Department, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy

Alessandro De Toma, Medical Oncology Department, Fondazione IRCCS Istituto Nazionale Tumori, Milan,

Italy

Marta Brambilla, Medical Oncology Department, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy

Mario Occhipinti, Medical Oncology Department, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy

Sara Manglaviti, Medical Oncology Department, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy

Alice Labianca, Medical Oncology Department, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy

Teresa Beninato, Medical Oncology Department, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy

Marta Bini, Medical Oncology Department, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy

Mavis

Mensah, Tumor Genomics Unit, Department of Research, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan,

Italy

Monica Ganzinelli, Medical Oncology Department, Fondazione IRCCS Istituto Nazionale Tumori, Milan,

Italy

Nicoletta Zilembo, Medical Oncology Department, Fondazione IRCCS Istituto Nazionale Tumori, Milan,

Italy

Filippo de Braud, Medical Oncology Department, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy

Gabriella

Sozzi, Tumor Genomics Unit, Department of Research, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan,

Italy

Marcello

Restelli, Department of Electronics, Information, and Bioengineering, Polytechnic University of Milan, Milan,

Italy

Alessandra

Pedrocchi, Department of Electronics, Information, and Bioengineering, Polytechnic University of Milan, Milan,

Italy

Marina Chiara

Garassino, Medical Oncology Department, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy

Francesco

Trovo, Department of Electronics, Information, and Bioengineering, Polytechnic University of Milan, Milan,

Italy

Presenting Author:

Arsela Prelaj, Fondazione IRCCS Istituto Nazionale TumoriFondazion, Milan, Italy

Email: arsela.prelaj@istitutotumori.mi.it

Abstract Body:

IntroductionIn advanced Non-Small Cell Lung Cancer (aNSCLC), Programmed Death Ligand 1 (PD-L1) remains the only used biomarker to candidate patients (pts) to immunotherapy (IO) even if its predictive accuracy is not satisfactory. Indeed, given the complex dynamics underlying the cross-talk between the tumor and its microenvironment, it is unlikely that a single biomarker could be able to profile prediction with high precision. Artificial Intelligence (AI) and machine learning (ML) are techniques able to analyze and interpret big data, which cope with this complexity. The present study aims at using AI tools to improve response and efficacy prediction in aNSCLC pts treated with IO. **Methods**A classification task to determine if a pt is likely to benefit from IO was formulated using complete clinical data, PD-L1, histology, molecular data, and the blood microRNA signature classifier (MSC), which include 24 different microRNAs. Pts were divided into responders (R), who obtained a partial response or stable disease as best response, and non-R, who experienced progressive disease. A forward feature selection technique based on the Akaike Information Criterion was used to extract a specific subset of the pts data, being the most informative ones for the task. To develop the final predictive model, different ML methods have been tested: K-nearest neighbors, Logistic Regression, Kernel Support Vector Machines, Feedforward Neural Network, and Random Forest. **Results** Of 164 enrolled pts, 73 (44.5%) were R and 91 (55.5%) non-R. At data cut-off (Nov 2020), median Overall Survival (mOS) was 10.1 (95%IC 7.0 - 13.2) months (m). mOS for R pts was 38.5 m (95%IC 23.9 - 53.1) vs 3.8 m

(95%IC 2.8 - 4.7) of non-R, p<0.001. Overall, the best model was the Logistic Regression and included 5 features (3 clinical, 1 tissue and 1 blood features): ECOG performance status, IO-line of therapy, the neutrophil-to-lymphocyte ratio (NLR), the MSC test and PD-L1 with the following corresponding parameters w= (0.692, 0.718, 1.058, 0.566, -0.471), respectively. The intercept of the model is w_0 = 0.467, and the model achieves a 75% accuracy, computed using a leave-one-out approach. PD-L1 alone has an accuracy of 65%. We also evaluated the accuracy of the models excluding PD-L1 (74% accuracy), MSC (73% accuracy), and excluding both PD-L1 and MSC considering only clinical features (71% accuracy). **Conclusions**The results suggest that the data integration provided by AI techniques is a powerful tool to improve personalized selection of pts candidates to IO. In particular, the model shows that higher ECOG, NLR value, IO-line, and MSC test level correlate negatively while higher PD-L1 correlates positively with the response. The model confirms PD-L1 and MSC as relevant biomarkers to improve the accuracy of pts response. Considering the difference in survival among R and non-R groups, these results suggest that the model can also be used to indirectly predict OS.

Category: Clinical Implementation of Machine Learning Models in Oncology

Keyword 1: Artificial Intelligence
Keyword 2: Lung Cancer
Keyword 3: Immunotherapy

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