UniSR	**Progetto proposto in applicazione del D.M. 351 del 9/4/2022 Corso di Dottorato di Ricerca Internazionale in Medicina Molecolare**

PROGETTO

DoS: Prof. Stefano Cascinu

Titolo: AI-HOPE Lung cancer: building a predictive tool for metastatic lung cancer

Curriculum: Immunologia e Oncologia di Base e Applicate

Link alla propria pagina personale sul sito OSR/UniSR
https://www.unisr.it/docenti/c/cascinu-stefano

Descrizione del progetto (*Numero di caratteri inclusi spazi*: 2.000-3.000):

In the last decade, the treatment of metastatic lung cancer has been in constant evolution, thanks to the approval of innovative therapies such as immunotherapy and molecular target therapy. Basing on molecular selection criteria and pathological anatomy (such as the immunohistochemical determination of the expression of PD-L1), it is now possible to differentiate the subpopulations of patients that are supposed to benefit from a specific treatment. The value of PD-L1 is in fact used as a predictor of response to first-line immunotherapy (with a cut-off of 50%), while the determination of some target genes (EGFR, ALK, ROS1, KRAS, BRAF, but also RET, MET, NTRK) guide the choice towards gene-specific tyrosine kinase inhibitors (1).
Despite the development of these precision therapies, there still is a proportion of patients who do not benefit from the identified best treatment and experience early disease progression. This percentage varies greatly among treatments, ranging from 3-10% with the main target-therapies such as anti-EGFR or anti-ALK (2, 3) to 30% in real-life first-line immunotherapy studies (4). Early progression forces clinicians and patients towards a therapeutic change, but sometimes it might anticipate performance status deterioration, not permissive for further oncological therapies, or even the patient's early death (5).
Several studies have suggested factors that could potentially play a negative predictive role in response to immunotherapy, with a special focus on molecular characterization and tumour microenvironment (6). Some other trials have studied the role of metabolic and radiological features at baseline, with great help coming from radiomics techniques (7).
On the other side, little is known about oncogene-driven tumours, although some machine-learning models have demonstrated preliminary efficacy in identifying predictive factors (8).
The goal of our project is building a predictive response algorithm for patients with metastatic lung cancer, exploiting an artificial intelligence platform created in collaboration with Microsoft. It will collect patient information from all areas (clinical, laboratory, radiological, pathological) and analyse them as a whole, following the lead of HSR AI-SCORE project (artificial intelligence for prognostic classification of patients with COVID19 pneumonia).

Periodo di studio e ricerca presso in Impresa /Centri di ricerca / Pubbliche Amministrazione

Il periodo è obbligatorio per 3 tipologie di dottorati (sono esclusi quelli di ricerca PNRR) per un periodo minimo di 6 mesi ad un massino di 12

Il dottorando svolgerà il periodo OBBLIGATORIO presso _____
mesi

Periodo di studio e ricerca all'estero

Il periodo è obbligatorio per 4 tipologie di dottorati per un periodo minimo di 6 mesi ad un massino di 18

Il dottorando svolgerà il periodo OBBLIGATORIO per n. 6 mesi

Skill da acquisire dal dottorando (*Numero di caratteri inclusi spazi*: max 600):

The PhD student will deepen his / her knowledge of clinical, radiological and pathological anatomy predictive factors, interacting with different professional figures. From a technical point of view, he / she will lead the working team, coordinating doctors, computer scientists and data scientists. He / she will be in charge of facilitating the data extraction process, helping them in the understanding of business' needs and checking manually the work done. He / she will also acquire notions of machine learning and mathematical models, learning how to critically analyse the results.

Referenze (max. 15)

1. Metastatic Non-Small-Cell Lung Cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up, Ann Oncol (2018) 29 (suppl 4): iv192–iv237, https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer
2. Osimertinib in Untreated EGFR-Mutated Advanced Non–Small-Cell Lung Cancer, Soria et al, N Engl J Med 2018; 378:113-125
3. Alectinib versus Crizotinib in Untreated ALK-Positive Non–Small-Cell Lung Cancer, Peters et al, N Engl J Med 2017; 377:829-838
4. First-line pembrolizumab for non-small cell lung cancer patients with PD-L1 ≥50% in a multicenter real-life cohort: The PEMBREIZH study, Amrane et al, Cancer Medicine April 2020; 2309-2316
5. Clarification of Definitions of Hyperprogressive Disease During Immunotherapy for Non-Small Cell Lung Cancer, Kas et al, JAMA Oncol 2020 Jul 1;6(7):1039-1046
6. Predictors of Response, Progression-Free Survival, and Overall Survival in Patients With Lung Cancer Treated With Immune Checkpoint Inhibitors, Memmott et al, JTO July 2021, Pages 1086-1098
7. ^{18}F-FDG Pet Parameters and Radiomics Features Analysis in Advanced NSCLC Treated with Immunotherapy as Predictors of Therapy Response and Survival, Polverari et al, Cancers (Basel) 2020 May 5;12(5):1163
8. Development and Validation of a Machine Learning Model to Explore Tyrosine Kinase Inhibitor Response in Patients With Stage IV EGFR Variant-Positive Non-Small Cell Lung Cancer, Song et al, JAMA Netw Open 2020 Dec 1;3(12):e2030442.