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Oral Microbiota as a Novel Predictive Biomarker of Response To Immune Checkpoint Inhibitors in Advanced Non-small Cell Lung Cancer Patients

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Abstract : Background: Although immune checkpoint inhibitors (ICIs) have changed the treatment paradigm of non–small cell lung cancer (NSCLC), these drugs fail to elicit durable responses in the majority of NSCLC patients. The gut microbiota, able to regulate immune responsiveness, is emerging as a promising, modifiable target to improve ICIs response rates. Since the oral microbiome has been demonstrated to be the primary source of bacterial microbiota in the lungs, we investigated its composition as a potential predictive biomarker to identify and select patients who could benefit from immunotherapy. Methods: Thirty-five patients with stage IV squamous and non-squamous cell NSCLC eligible for an anti-PD-1/PD-L1 as monotherapy were enrolled. Saliva samples were collected from patients prior to the start of treatment, bacterial DNA was extracted using the QIAamp® DNA Microbiome Kit (QIAGEN) and the 16S rRNA gene was sequenced on a MiSeq sequencing instrument (Illumina). Results: NSCLC patients were dichotomized as “Responders” (partial or complete response) and “Non-Responders” (progressive disease), after 12 weeks of treatment, based on RECIST criteria. A prevalence of the phylum Candidatus Saccharibacteria was found in the 10 responders compared to non-responders (abundance 5% vs 1% respectively; p-value = 1.46 x 10-7; False Discovery Rate (FDR) = 1.02 x 10-6). Moreover, a higher prevalence of Saccharibacteria Genera Incertae Sedis genus (belonging to the Candidatus Saccharibacteria phylum) was observed in "responders" (p-value = 6.01 x 10-7 and FDR = 2.46 x 10-5). Finally, the patients who benefit from immunotherapy showed a significant abundance of TM7 Phylum Sp Oral Clone FR058 strain, member of Saccharibacteria Genera Incertae Sedis genus (p-value = 6.13 x 10-7 and FDR=7.66 x 10-5). Conclusions: These preliminary results showed a significant association between oral microbiota and ICIs response in NSCLC patients. In particular, the higher prevalence of Candidatus Saccharibacteria phylum and TM7 Phylum Sp Oral Clone FR058 strain in responders suggests their potential immunomodulatory role. The study is still ongoing and updated data will be presented at the congress.

Keywords : oral microbiota, immune checkpoint inhibitors, non-small cell lung cancer, predictive biomarker
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