Cancer Psychology & Health Management S.C.C

# A correlation study between gut microbes and immune checkpoint inhibitors in the treatment of non-small cell lung cancer

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## Introduction:

Lung cancer is currently one of the tumors with thehighest morbidity and mortality rates . Immunotherapy revolutionized the way lung cancer is treated. More and more studies reported that gut microbes can affect the efficacy of immunotherapy and immune microenvironment. Here, we conduct a preliminary discussion of the relationship between gut microbes and immune microenvironment and the efficacy of non-small cell lung cancer patients receiving immune chec-kpoint inhibitors.

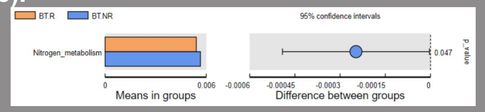
To analyze patients with advanced non-small cell lung cancer who visited the Oncology Department ofthe FifthPeople's Hospital of Chengdu University of Chinese Medicine from December 2020 to June 2021。

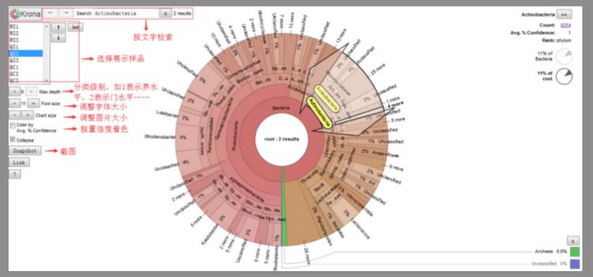
## Methods:

Patients were instructed to use Programmed cell death protein 1(PD-1) inhibitors. Stool samples from patients before and 2-7 days after treatment are then collected. After follow-up, patients were divided into a durable benefit group (R, CR/PR/SD≥ 6 months) and a non-durable benefit group (NR, CR/PR/SD< 6 months) according to iRECIST v1.1. 16S rRNA amplicon sequencing technology was used to detect the gene sequence of intestinal microorganisms. Peripheral blood was collected before and 2-7 days after treatment, and the levels of T lymphocyte subsets and myeloid-derived suppressor cell subsets were measured using flow cytometry.SPSS 25.0 software was used to statistically analyze the changes of immune microenvironment in patients in the non-durable and long-lasting benefitgroups before and after immunotherapy.

## Results:

After Immune checkpoint inhibitors(ICIs) treatment, the Firmiys phylum decreased, the phylum Bacteroides increased, and the proportion of F/B (Firmicutes/Bacteroidetes) decreased. The proportion of F/B in the dur-able benefit group at baseline was higher thanin the non-durable benefit group (P<0.05). The β diversity of the durable benefit group with ICIs was higher than that in the non-durable benefit group (P<0.05). The lasting benefit of ICIs is associated with species enrichment, such as Prevotella, Lachnospiraceae, Clostridiales, etc. (P<0.05).After ICIs treatment, the ratio levels of CD3+%, CD4+% and CD4+/CD8+ in the T lymphocyte subsets were significantly increased, while the ratio levels of CD8+% and Treg/CD4+ decreased significantly (P<0.05).Patients with positive PD-L1 expression in the durable benefit group had higher ratios of CD3+%, CD4+% and CD4+/CD8+ in peripheral blood, and lower levels of CD8+%, Treg/CD4+ ratios and M-MDSC/MDSC and G-MDSC/MDSC ratios (P<0.05). The alpha diversity index was positively correlated with CD3+% and CD4+%, and negatively correlated with Treg and myeloid-derived supp ressor cells (P<0.05).



## Conclusions:

The benefit of ICIs treatment correlated with F/B , alpha diversity, and beta diversity. Some intestinal bacteria in patients were positively and negatively correlated with the treatment benefit of ICIs. The abundance of positively correlated bacteria was higher in the long-lasting benefit group and higher in the non-durable benefit group. Multigrade LEfSe analysis of biomarkers found significant diff-erences (P<0.05) in the increased abundance of Clostridia,Lachnospirales, and Lachnospiraceae after ICIs treatment,which may serve as potential biomarkers for predicting efficacy. ICIs treatment improved T lymphocyte and myeloid-derived suppressor cell function more pronounced in pati-ents with lasting benefit and PD-L1-positive patients, and mproved immune status better.