

EP11.31: Impact of the Gut Microbiome and Diet on Outcomes to first line Immunotherapy based treatment for metastatic Non-Small Cell Lung Cancer (NSCLC) Patients: The PREBIOM Study

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Background

The gut microbiome (GM) can influence immunotherapy response, particularly the abundance of Short-chain Fatty Acid (SCFA) producing bacteria which are strongly related to diet. PREBIOM is a prospective study, where we aim to correlate GM profiles in patients with metastatic Non-Small Cell Lung Cancer (NSCLC) with diet and outcomes to first-line immunotherapy-based treatment.

Methods

We present data on the first thirty-two (32) metastatic NSCLC patients, 28 male and 4 female, median age 71 (range 52-91).
Histology: 14 adenocarcinoma, 10 squamous and 8 other histology.
Stool samples were collected at baseline and during Immunotherapy-based treatment and analysed with 16S rRNA metagenomics sequencing.
The Mediterranean Diet Questionnaire (MDQ) was answered by patients at each sampling point.
26 patients received combination chemotherapy and Pembrolizumab, 5 patients received Pembrolizumab monotherapy, whilst 1 patient received combination chemotherapy and Ipilimumab-Nivolumab.
Spearman's partial correlations of GM with overall survival (OS) and progression-free survival (PFS) were used with MDQ total scores as a covariate.
Only bacteria with >1% mean representation across all samples are reported.

Patient Characteristics

Table 1. Patient Characteristics

	N=32	%
Age- Median (range)	71 (52-91)	
Sex M : F	28 : 4	88% : 12%
Squamous/ Adeno/ NOS	10/ 14/ 7	31% : 44% : 25%

Results

Baseline GM analysis revealed that the genus *Clostridium* IV was associated with improved OS (R=0.41, P=0.019) as well as the species *Akkermansia muciniphila* (R=0.37, P=0.038) and *Dialister invisus* (R=0.39, P=0.029).
D. invisus (R=0.40, P=0.024) and *Bacteroides caccae* (R=0.35, P=0.048) were significantly associated with PFS.

Table 2. Association of baseline bacterial abundance with OS and PFS with mean representation >1%

Level	Organism	Phenotype	Spearman's R	P Value	Mean Representation
Genus	<i>Clostridium</i> IV	OS	0.39	0.027	1.181
Species	<i>Akkermansia muciniphila</i>	OS	0.372	0.039	8.073
Species	<i>Dialister invisus</i>	OS	0.38	0.032	2.902
Species	<i>Dialister invisus</i>	PFS	0.40	0.024	2.902
Species	<i>Bacteroides caccae</i>	PFS	0.35	0.048	1.819

Discussion

The *Clostridium* IV (leptum) group are butyrate producers that contribute to anti-inflammatory processes and support gut epithelium integrity. Similarly, *A. muciniphila* is involved in SCFA production and plays a critical role in host metabolic processes and maintenance of gut epithelium health, whilst *D.invisus* is an SCFA Butyrate producing species which contributes to gut health and immune responses. *B. caccae* is also SCFA producing species involved in the gut barrier integrity and has been associated with response to immunotherapy in other cancer types. The results indicate that GM profiles with SCFA producing gut bacteria were positively associated with improved survival outcomes in immunotherapy treated metastatic NSCLC patients.

Conclusions

This study provides further evidence for the baseline GM profile being correlated to outcomes of patients receiving first-line immunotherapy-based treatment, and the potential of diet to improve outcomes via modulation of the GM and SCFA producing bacteria in patients with metastatic NSCLC.

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