771P - **Correlation of gut microbiome composition with checkpoint inhibitor induced severe immune-related adverse events**

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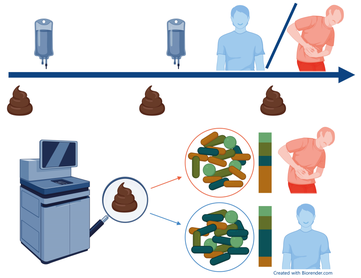
Immune checkpoint inhibition (ICI) has proven to be a major breakthrough in cancer treatment but often causes severe immune-related adverse events (irAEs). While gut microbiome composition has been associated with ICI efficacy, its role in irAE development is uncertain.

Objective was to assess the role of **gut microbiome** composition during **checkpoint inhibition** in **severe immune-related adverse event** occurrence.



Using 16S rRNA gene sequencing (V3-V4 region), differences in gut microbiome composition were assessed between patients with and without severe irAEs.

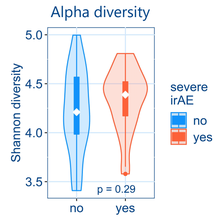
Cancer patients treated with first-line combined CTLA-4 plus PD-1 blockade (cICI; n=54) or anti-PD-(L)1 monotherapy (n=132) were included.
There were no differences in gut microbiome composition at baseline between the two treatment groups.
Further analyses were stratified by treatment regimen and sampling time point.

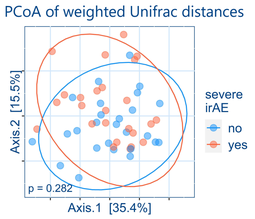
Baseline characteristics of **cICI** treated patients

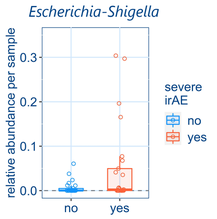
	Without severe irAE (n=26)	With severe irAE (n=25)
Age (years)*	65 (53-72)	61 (51-67)
Male seks	18 (69%)	15 (60%)
Tumour type		
Melanoma	13 (50%)	21 (84%)
RCC	12 (46%)	3 (12%)
WHO performance status		
0	15 (58%)	9 (36%)
≥1	10 (38%)	16 (64%)
Antibiotic use before start ICI	2 (8%)	2 (8%)
Steroid use before start ICI	2 (8%)	6 (24%)

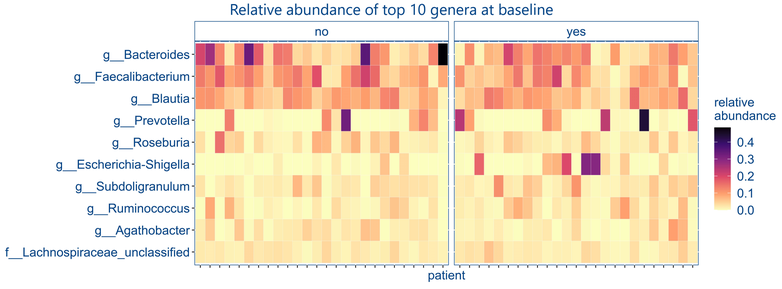
*median (Q1-Q3); WHO: World Health Organisation

Baseline analyses of **cICI** treated patients



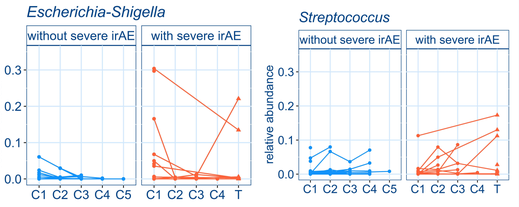






Among cICI treated patients, no significant differences in alpha (within sample) diversity or beta (between sample) diversity were observed at baseline between patients with and without severe irAEs. Out of 25 patients with severe irAEs during cICI treatment, 4 patients had high relative abundance (>10%) of *Escherichia-Shigella*.

Longitudinal analyses of **cICI** treated patients



At cICI-induced severe irAE onset, high relative abundance (>10%) of *Escherichia-Shigella*, *Streptococcus* or both were seen in 4/9 patients (44%), while no patient without severe irAE had such high relative abundances at any time point.

Similar differences in gut microbiome were not seen in **anti-PD-(L)1** treated patients with or without severe irAE at any time point.

High relative abundances of **pro-inflammatory genera** *Escherichia-Shigella* or *Streptococcus* **before and during ICI** treatment were **associated with severe irAE** onset in cICI treated patients, but not in anti-PD-(L)1 treated patients.

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