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Gut microbiota and efficacy of immune-checkpoint inhibitors (ICIs) in patients (pts) with advanced solid tumor: SCRUM-Japan MONSTAR-SCREEN

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Background

MONSTAR-SCREEN is the nationwide cancer genome screening project of prospectively assessing gut microbiota and circulating tumor DNA in 2,000 pts with advanced solid tumor at 31 Japanese institutions. Recently, several studies have showed that gut microbiota modulates efficacy of ICIs across cancer types. Here we report an initial analysis of association between alpha diversity index (ADI) of fecal microbiome and efficacy of ICIs between Sep 2019 and Sep 2020.

Methods

The 16S ribosomal RNA gene sequencing to V3-V4 region was conducted for assessing the ADI, which was represented as an operational taxonomic unit (OTU) score. Objective response rate (ORR) was assessed by RECIST version 1.1 and progression-free survival (PFS) on ICIs was estimated using the Kaplan-Meier method. Microsatellite instability (MSI) and blood tumor mutational burden (bTMB) status were measured by FoundationOneLiquid plus a 1.125Mb bTMB assay at the same time points as the feces collection. In addition, tissue TMB (tTMB) were measured by FoundationOneCDx using pretreatment tissue samples.

Results

A total of 167 pts were included. Most common cancer types were as follows; head and neck cancer (N=43), malignant melanoma (N=26) and gastric cancer (N=25). Of these, 136 (81%) pts received ICI alone, while 31 (19%) did ICI and chemotherapy combination. We determined the optimal cutoff value of 240 by combined sensitivity with specificity for the ORR. The ORR in high OTU (OTU-H > 240, N=52) was 35%, while that with low OTU (OTU-L < 240, N=115) was 17% (p=0.01). In addition, OTU-H pts had a significantly a longer PFS on ICIs than OTU-L (8.6 vs. 2.6 months; hazard ratio, 0.48; 95% CI, 0.30–0.78; p=0.002). Multivariate analyses for the ORR and PFS demonstrated the OTU was the only significant independent factor beyond MSI, bTMB, and tTMB status.

Conclusions

Diversity of gut microbiota by the OTU was significantly associated with higher ORR and longer PFS on ICIs in pts with advanced solid tumor. These results indicated the potential of the OTU as a putative tumor-agnostic biomarker for the efficacy of ICIs beyond MSI, bTMB and tTMB status. Further study with shotgun and single cell metagenome analyses are ongoing.

Legal entity responsible for the study

SCRUM-Japan.

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Disclosure

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