719   **Poster Session**

The Lung Immune Prognostic Index (LIPI) stratifies prognostic groups and correlates with gut microbiota (GM) in patients with advanced renal cell carcinoma (RCC).

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Background: The LIPI score has been reported as an independent prognostic factor in RCC patients treated with immune checkpoint inhibitors (ICI) or tyrosine kinase inhibitors (TKI). Here, we aimed to correlate LIPI score and GM composition in patients with RCC. **Methods:** We prospectively collected fecal samples of all comers RCC patients who started a 1st or beyond line therapy (standard or clinical trial) in the NCT0457446 at Gustave Roussy. Neutrophil to lymphocyte ratio (dNLR) and lactate dehydrogenase (LDH) were obtained from routine blood tests. Shot gun metagenomic sequencing (MGS) data were analyzed by multivariate and pair-wise/fold ratio. Clinical benefit ratio (CBR, complete response + partial response + stable disease, RECIST1.1) and overall survival (OS, from treatment start) were evaluated. Multivariate analysis (MVA) for OS included age, gender, therapy line, IMDC, histology, hypoalbuminemia. **Results:** From February 2016 to July 2021, 160 patients were screened and 102 were included. Median age was 61 years (22-89), patients were mostly males (75%) and clear cell histology (90%). Patients were treated in 1st (15%), 2nd (53%) and beyond (32%) lines. Treated with ICI monotherapy (65%), followed by TKI or mTOR (20%) and ICI combination (19%). IMDC was 32% good (G), 54% intermediate (I) and 14% poor (P) and LIPI was 69% G, 25% I and 6% P. Median OS was 42.9, 17.7 and 8.3 months in patients with LIPI G, I and P, respectively (p<0.0001). Among IMDC risk groups, IMDC G + LIPI G had better OS compared to other subgroups (p=0.017), and those with IMDC P + LIPI P had the worse OS. Overall, LIPI G had higher rates of CBR than I+P LIPI (74% vs 50%; p=0.0158). At MVA, LIPI was independently associated with OS (HR 6.25, 2.02-24.34; p=0.0187). Overall, *Parabacteroides merdae* and *Veillonella parvula* were enriched in LIPI I+P, while LIPI G harbored *Faecalibacterium prausnitzii*. In patients treated with ICI monotherapy, LIPI I+P were enriched with *Bacteroides spp* (*P. merdae*, *Phocaeicola vulgatus*), and LIPI G had an overrepresentation of *Ruminococcaceae unclass* bacterium. **Conclusions:** We report the first MGS study correlating LIPI score and GM composition in RCC patients. LIPI score correlates with clinical outcomes (OS and CBR) and helped to better-stratified IMDC risk groups. Patients LIPI G harbor health-related commensals, while I and P groups are associated with harmful ones. LIPI score could represent a clinically relevant score to stratify mRCC patients. Clinical trial information: NCT04567446. Research Sponsor: RHU Lumière and Gustave Roussy Foundation.