



SPEECH INFORMATION (For Conference Program Book)

Topic	The Potential Role of Gut Microbiota and Metabolites in HCC Immunotherapy
Abstract	<p>Combination immunotherapy with immune checkpoint inhibitors (ICIs) has become a standard first-line treatment for unresectable hepatocellular carcinoma (HCC). However, durable clinical benefit is achieved in only a subset of patients, underscoring the need for reliable biomarkers to predict treatment response and survival. Emerging evidence indicates that the gut microbiota and its derived metabolites play a critical role in shaping systemic immunity and modulating the efficacy of cancer immunotherapy. In this presentation, I will overview the findings from prospective translational studies investigating the gut microbiota–metabolite–immune axis in patients with HCC receiving ICI-based therapies. By integrating fecal microbiome profiling, targeted metabolomic analyses, and detailed clinical outcome data, we examined associations between microbial features, tumor response, progression-free survival, and overall survival. Our data demonstrate that gut microbiota composition differs substantially between viral hepatitis–related HCC and metabolic dysfunction–associated steatotic liver disease (MASLD) related HCC. Patients with MASLD-HCC show enrichment of potentially pro-inflammatory taxa and lower baseline levels of short-chain fatty acids and secondary bile acids. Despite these compositional differences, a shared metabolic signature emerged across etiologies: higher levels of microbiota-derived metabolites, particularly fecal acetate, were consistently associated with durable tumor response and improved survival following combination immunotherapy. Multivariate analyses confirmed fecal acetate as an independent predictor of clinical outcomes, suggesting that microbial functional output may be more clinically relevant than specific bacterial taxa. These findings highlight the gut microbiota–metabolite–immune axis as a promising source of noninvasive biomarkers and potential therapeutic targets, offering new opportunities to advance precision immunotherapy in HCC.</p>

