Despite their unprecedented results in various cancers, predictors of clinical benefit and strategies to safely enhance immune checkpoint inhibitors (ICB) efficacy are urgently needed. Preclinical studies have highlighted that immune-based therapies rely upon the composition of the gut microbiota to exert their bioactivity. We evaluated the impact of microbiota in cancer patients treated with ICB. We showed in patients with advanced non-small-cell lung cancer (NSCLC), renal cell carcinoma (RCC) and urothelial cancer treated with anti-PD-1/PD-L1 mAb that antibiotic (ATB) prescription before ICB had a deleterious impact on clinical outcomes. Subsequently, using metagenomic analyses we demonstrated that commensal bacteria *Akkermansia muciniphila* was found to be strongly associated with favorable objective response rate and longer PFS. To validate the relevance of these clinical findings, we brought up two major lines of evidence. First, we demonstrated that in NSCLC patients, the presence of specific IFNγ+ memory CD4+ and CD8+ T cells toward *A. muciniphila* predicted a longer PFS. Secondly, fecal microbiota transplantation (FMT) was performed using patient feces to recolonize germ-free or ATB-treated mice in two tumor models. We demonstrated that manipulation of gut microbiota could increase ICB efficacy. The discovery of immunogenic bacteria capable to predict and increase clinical benefit of ICB will help for the development of novel biomarker tools and a future therapeutic concept, whereby treatment of cancer can be improved by the modulation of gut microbiota.