

Good afternoon everybody. Thank you for the opportunity. I'm going to discuss this *Akkermansia*, a *Muciporales* based multi genomic profile in advanced non-small cell lung cancer.

As we had discussed, we were discussing earlier, PD-L1 is not a very good marker for the response of immunotherapy. So, there has been research to study the microbiota for this setting.

*Akkermansia* is a human intestinal symbiotic. That is, I've been isolated from human feces.

It is a gram negative anaerobe that is mucin layer degrading bacterium. It constitutes about 3% of total microbiota of healthy adult. Metagenomic data has shown that it has inverse correlation between abundance of *Akkermansia* and disease such as inflammatory bowel disease, obesity and diabetes. Alteration and gut microbiota, this dysbiosis are capable of inducing abnormal immune response in gut associated lymphatic tissue and that these alterations can compromise the systemic immune response. And this is the immune response that is responsible for treatment for response to immunotherapy. Stool *Akkermansia* is associated with immunotherapy clinical benefit. An *Akkermansia* is associated with acute lymphatic tissue and acute lymphatic tissue. The acute lymphatic tissue is associated with acute lymphatic tissue. The acute lymphatic tissue is associated with acute lymphatic tissue. So, AKK level in stool is generally a proxy for this, this dysbiosis in, in, in, in the gut. How can we explain AKK loss in stool? So, patient with NSCLC, that one, that one I'm able to affront immunotherapy with chemotherapy one and role between June 2020 and March 2024 in this study. So, the stool sample was collected at baseline and after two cycle of immunotherapy. And in this study, the genome, quantitative genomic study was done from stool and from plasma antibody levels were, were studied and subsequently response to immunotherapy was, was studied in this setting. So, the matter that was used was, was topo score. It is a rapid, rapid tool was that, that is able to, uh, stratify patient individually. It, based on 92, shotgun metagenomic sequencing across, across the malignancy. It was developed in, in, in, in NSCLC, RC, C, C, u, u, u, u, thymic cancer, melanoma and see, uh, colorectal cancer. Uh, in, in, according to this, this, this study, the U dysbiosis, that means, ideal gut flora should contain, uh, Lactobacillaceae family, Oscillospira family, polyamine and tiptoe, tiptofin pathway.

In this virus, dysbiosis gut, that there is, uh, enrichment of enterocloster genus, streptococcal genus, uh, Veillonella genus, and lactobacilli family. Topo, uh, topo score represent first easy to use and cause effective tool. That is capable of detecting intestinal,

this, dysbiosis associated with longer OS and, uh, OS after immunotherapy across the cancer. Higher, uh, this, this study also checked the NT, AKK, IGG title. So this, uh, higher title was associated with this gut dysbiosis and was then, uh, tend to loss of AKK in intestinal, uh, residency. So this, in serum, uh, uh, the, uh, the NT, AKK, IGG, anti body, well, test test in the study. And it result that, that commensal specific human immune response in multivariate analysis. Uh, so it, the conclusion was the higher, IGG, anti AKK level correlate with worst survival. Uh, so, uh, the hazard ratio was 7.84 with confidence interval between 2.2, 2.04 to 30.2 with p value of 0.03. So the patient who had NT, uh, NT, AKK, IGG, they'd worse with immunotherapy. This was through in, uh, in, this was, this is also, uh, uh, uh, subsequently the T's is basically the AKK specific IGG, IH1 and IH17 immune response that is found up to 20% of cases are delayed areas for clinical benefit to immune, immune therapy. The patient with a positive results shows poor PFS, uh, in, uh, in both a patient when compared to interferon gamma and interleukin 17. So in conclusion, RK minutia species and immune response directed against them are surrogate marker for this, uh, gut this biases stool, RK minutia, mulsi, uh, pilia prevalence and relative awareness has prognostic value in, uh, ICA treatment in first line and second line NSCLC. Immune response targeting a clinical relevant and immunogenic commercial such as RK minutia lead to bacteria elimination and can be deteriorated in NSCLC. Now there is subsequent phase one phase two trial also going on in the authors. Thank you.