So, good evening everyone and thank you organizers for giving me this opportunity.
So, today I am going to discuss on unleashing the potential of probiotic fissile bacterium
prosonids to optimize the PD-1 inhibitor efficacy in non-small cell lung cancer treatment.
Coming to the background, if you see in the locally advanced non-small cell lung carcinoma,
the survival rate has been ranged from 13 to 36 percent.
On average for stage 3 non-small cell lung cancer, the 5 year overall survival rate is 30 percent.
We have made a lot of improvements in the treatments and we have incorporated immunotherapy also
in the locally advanced lung carcinoma management.
And in one such Chinese study that is Neo-Tarch, what they have noted was by incorporating immunotherapy
in locally advanced non-small cell lung cancer.
They could achieve the major pathological response of up to 50 percent.
What do you, I mean by major pathological response was, pathological response rate in
more than 90 percent of the cells is called as major pathological response and such rate
was observed in almost 50 percent of the patient.
And there is an even free survival benefit also by adding this immunotherapy in the perioperative setting.
So, again there are multiple studies which have shown that there is an association between
the immunotherapy and the gut microbiota.
There are patients who are responders to the immunotherapy based on what gut microbiota
they have and there are certain patients who are classified as non-responders based on
what gut microbiota they have.
And similarly, depending on the presence of this gut microbiota, there is an altered
incidence of colitis because of the immunotherapy.
So, one such bacterium, today I wanted to discuss is physically bacterium prosonates.
So, first I just wanted to highlight what is the metabolism of like how this probiotic
work and how it will help in the immune system.
So, if you look at this right side walla, the KY and A and 113 A, these are the tryptophan
metabolites.
And when this tryptophan metabolites bind to the AHR complex, it will modify the tumor
micro-environment, it will promote the tumor growth and it will suppress the CD8 T cell
activation.
These are the two points you should remember.
So, when the tryptophan metabolites bind to the AHR complex, it promotes the tumor growth
and it inhibits the CD8 T cell.
So, what we wanted to achieve was to remove this tryptophan metabolites from the tumor.
So, how we can achieve of removing this tryptophan metabolites are the metabolite component of
this facility bacterium prosonates is valeric acid.
And this valeric acid in turn up regulates the run X3 gene and it will in turn causes

the in decreased expression of the interleukin IV induced gene 1, which is the major step
in the catabolism of the tryptophan.
So, with the help of this valeric acid, we can decrease the level of interleukin IV induced gene 1, which in turn decrease or down regulate the catabolism of the tryptophan.
Thereby, there is a decreased availability of the tryptophan metabolites, which in turn
causes the activation of the CD8 T cell.
So, this is the basic metabolic effect of how this facility bacterium prosonates will
help in increasing the efficacy of the PDL1 inhibitors.
So, coming to the methods and methodology, patient has been received knee adjuvant immunotherapy
and chemotherapy and they have classified as responders and non-responders depending
on the presence of major pathological response present or not.
And from these patients, either both from the responders and non-responders, they have
collected the tumor and feces samples and they have underwent the metagenomic sequencing
to study this microbiota.
And what they have noted was all the things which were there in the green represents the
responders.
That means, patient who has achieved the major pathological response and the red one represents
the patients who are non-responders.
That major pathological response was not achieved.
So, if you see this graph, in patient who has achieved major pathological response, the quantity or the ficile bacterium prosonage is enriched in the feces of these responders
when compared to the non-responders.
Similarly, if you see this graph, quantification of this ficile bacterium, it is significantly
higher in the patient who got the major pathological response when compared to the patient who
has not got the major pathological response.
So, in simple terms, patient who are responding to the immunotherapy has got high amount of
this ficile bacterium and patients who are not responding to the immunotherapy has got
less amount of this ficile bacterium.
And similarly, they have that isolated usage of this ficile bacterium alone does not had
slowed down the tumor growth.
But when it has been combined with the PD-1 monoclonal antibody, it enhances the anti-tumor
effect of the PD-L1 monoclonal antibody.
And the basic underlying mechanism was as I described previously, mainly because of the
valoric acid, which is a metabolite of this ficile bacterium, which will inhibit the interleukin
4 induced 1 gene, which in turn decreases the catabolism of tryptophan, thereby decreasing
the availability of the tryptophan metabolites, which in turn causing CD8 T cell activation,
which will help in the activation or potentially increasing the efficacy of immunotherapy.

So, again this is the key result, second result, what they have identified was the metabolite
valoric acid present in this ficile bacterium, it up regulates the run which in turn inhibits
the interleukin 4 induced gene 1.
And because of this interleukin 4 induced gene 1 is less, it inhibits the tryptophan
catabolism, thereby decreasing the tryptophan metabolite products and thereby again causing
increased activation of the CD8 T cell.
So, the conclusion of this study was yes, there is a potential for this ficile bacterium
in enhancing the PD-1 inhibitor efficacy.
And there are implications for personalised non-small cell lung cancer treatment strategies
with special emphasis on importance of identifying specific microbial metabolites.
And thank you.