

Good morning. Thank you, organizing committee for inviting to the conference. So my abstract was five-year outcomes of perioperative chemotherapy and immunotherapy in stage three non-small cell lung cancer. So as we all know, lung cancer is the leading cause of cancer-related mortality, and non-small cell lung cancer accounts for 85% of the patients. And 30% of the patients present with resectability upfront.

And as we know, this is the historic data that stage 3 lung cancer, the five-year overall survival is only 36%. We came a long way with significant improvement in both EFS and overall survival with the implementation of immunotherapy and chemotherapy. These are all the trials which are discussed previously. Some approvals are based on only FDA. Some approvals are

from the European organization. So as these are already being discussed previously, so this is a five year update of Nadim Trail. This is a single arm trial.

which has given three cycles of Paclitaxel and Nivolumab followed by surgery. And after surgery, patient received four months of Nivolumab with 40 milligrams twice a week, two weekly, followed by once a four-week, 480 milligrams for eight months. So the

Previously, we had already seen the primary endpoint is progression-free survival at two years. The two-year progression-free survival was 77 percent. Currently, we'll be looking at the five-year survival outcome and the significance of immunotherapy biomarkers like PD-L1, tumor mutation burden, and circulatory tumor DNA.

Coming to the baseline characteristics, the N2 disease contribute to 33% of the patient and multistation constitute to 75% of the patients.

Coming to the follow up, some of the relevant events which happened in the five year follow up. There are five non lung cancer related deaths, four patients who had complete pathological response and one patient in non PCR. Three of these events are due to COVID-19 and one due to pneumonia. One is due to the secondary cancer like pancreatic cancer death. And nine cancer related deaths, three patients who had not been resected had cancer progression related deaths. And other six patients who had resected,

three are of the non-complete pathological response, two in major pathological response, and one in complete pathological response. Coming to the final five-year update, these are the secondary outcomes of the study. The five-year progression free survival is 65 percent, and the five-year overall survival is 69 percent in intention to treat population. Coming to the per protocol population, the five-year overall survival is 78 percent and progression free survival is 75 percent.

Coming to the, if you excluded the five non-lung cancer related deaths, the five-year progression free survival is 75%, and five-year overall survival is 82%.

Coming to the exploratory biomarkers, in this one, we had compared patients who had achieved complete pathological response versus non-complete pathological response. This non-complete pathological response included both major pathological response, that is less than 10% viable tumors and also more than 10% viable tumor. We can see a significant difference in

outcomes, both in terms of progression-free survival and overall survival. The patient who achieved a complete pathological response has a BFS of 60%, 92% compared with 60% for the patient who didn't achieve complete pathological response. Similarly, for overall survival, it is 95% versus 66%.

Coming to the other predictive biomarkers, we can see that there is no significant difference between outcomes for the patient who has PD-L1 positive versus PD-L1 negative. Similarly, there is no significant difference for the patients who had tumor mutation but then high versus low. Coming to the other biomarkers, they had compared with respect to the circulatory tumor DNA at baseline.

for the patients who had mutation allelic frequency of more than 1% versus less than 1%. Patients who had more than 1% mutation allelic frequency at baseline has PFS of 83%.

compared with 48% for patients who had more than 1%. Similarly, for oral survival also, there is a significant difference with respect to the circulatory tumor DNA burden at baseline. More than 1% seems to-- doesn't have done well with respect to the five-year outcomes.

Similarly, for circulatory tumor DNA clearance, clearance by definition means less than 0.1% or undetectable circulatory tumor DNA. So for the patient who had done circulatory tumor DNA clearance have better outcomes in terms of both progression-free survival and overall survival. Coming to the conclusion, as we see, there's a robust clinical benefit of perioperative immunotherapy. This is the study we had the longest follow-up of five years.

This study included only stage 3A resectable non-small cell lung cancer with 5 year progression free survival of 65% and 5 year overall survival of 69%. Historically, the 5 year overall survival for stage 3A non-small lung cancer is 36%.

and there is no signs of late toxicity or treatment related death. And similar to the other immunotherapy trials, particular benefit was seen in patients who achieved complete pathological response

It serves as a good surrogate for overall survival. Another important biomarker is circulatory tumor DNA clearance. After neoadjuvant treatment showed good prediction for progression-free survival and overall survival. This circulatory tumor DNA clearance is particularly important in worse prognosis group like who doesn't achieve pathological complete response.

In patients who achieved pathological complete response, even if the patient doesn't have circulated human DNA clearance, there is no difference in terms of progression-free survival and overall survival. And other important factor is for the patient who doesn't underwent surgery with this therapy, but the patient has cleared circulated human DNA clearance. If the patient is alive at three years, who is alive at three years, till five years follow-up, the patient has not had an event in the follow-up.

and neither PD-L1 percentage or TMB are markers of PFS and overall survival in this exploratory analysis. Coming to the limitations of this study, the sample size is small and similar to the other single arm trials, there is a lack of control arm and these are subgroup analysis. This has to be taken with caution and these are hypotheses generated, generating which can, should be evaluated in the larger clinical trials. Thank you.