At the outset, I would like to thank organizers for giving me an opportunity to present this
study at this venue.
Today, I will be discussing about updated efficacy and safety and biomarker analysis in
the patient with TRK fusion in the lung cancer who were treated with larotectinib, which
was presented by Jessica Linen World WCLC 2024.
So to introduce TRK-Jinfugins around cogenic driver mutations, these are recently known.
What we say it is rare in common cancers, while it is common in rare cancers like infantile
fibrous archomas or mammary, secretary, gland tumors.
And like in common cancers like lung cancer or colon cancer, incidence is very low.
Any lung cancer rate is estimated to be 0.2%.
So why it is important to test for this gene fusion is we have a targeted agent available
with it.
The first one was the Enterectinib and the second one is the Lirotectinib, which Enterectinib
is active against NTRK as well as ROS1, which is available in India.
Lirotectinib is the first in its class, which is highly selective, which is Pantarkey inhibitor
like TRK-1, 2, 3, all were inhibited by this.
It is CNS active and highly potent inhibitor for this efficacy.
So now we reported as efficacy and safety data along with the biomarker analysis of this
lung cancer treated with Lirotectinib with additional 12 month follow-up endpoints.
So it had included one patient from phase one of lung cancer from the advanced solid
tumor basket and 31 patients from phase two trial, where the data cut-off was done at
20 July, 2023.
The dose of Lirotectinib was used 100 mg BID.
The primary endpoints were overall response rates.
The secondary endpoints were duration of response, PFS overall survival, safety and the exploratory
endpoints was genomic analysis.
So baseline characteristic in patients with TRK-Fugin positive lung cancer.
So median age was 55 years.
If we look at the fusion, NTRK-Fugin was seen in 24 patients, where NTRK-3 fusion is seen in 8 patients.
If we look at across the tumor histology, so 30 patients were of adenosine, one patient
was of a TPL carcinoid and one patient of neuroendocrine tumor.
There were 12 patients out of 32 who had known CNS metastasis at the baseline.
Most of the patient had received prior therapies, likely in the form of surgery, radiotherapy,
or immunotherapy, with variable responses to prior systemic therapy.
Now we look at the actual efficacy.
So overall response rate was 66% for all patients.
And if we look at the patients with CNS metastasis, the overall response rate was 67%, which
is equally good.
And there was a median time to response for all patients was 1.8 months.
So these drugs first act early and act well, even at the CNS.
If we look at the magnitude of response in below-set graph, the magnitude of response
is also good in these patients.

Now we look at the duration of the response.
The median duration of the response was 34 months.
A progression-free survival was 28 months and there were 34% of patients at 4 years who were without progression.
Overall survival median was 33 months and there were 38% of patients were alive at the
end of the 48 months.
So this is biomarker data where they have tested CT, DNA, and tissue sample, both at
the baseline and at the progression for different other mutations.
Some mutations were in the NTRK-gin tyrosine kinase domain mutations and there were some
mutations at the baseline in the N-rasine T53 mutation.
We made them resistant for NTRK targeted therapy.
There were some acquired mutation during the therapies like some T53 mutations, some K-ras
mutations, and even some acquired mutations in the tyrosine kinase domain of NTRK receptor
and that made them resistant for the further therapy.
We look at the adverse effects.
So this is fairly well tolerated drug.
There were side effects where predominantly grade 1 and grade 2, grade 3, 4 were reported
only in 9 patients, of which only one patient has to discontinue treatment because of race,
lever function tests like AST, ALT, and gamma-dultermal transverse.
But there was no reported treatment-related death.
So to conclude, LAR TETNIP continues to demonstrate rapid durable responses with extended survival
benefit with favorable safety profile with good action at the CNS metastasis.
The results support the systematic use of NGS to detect NTRK-gin fusions.
Even a CT-DNA-GS analysis can be used to detect NTRK-gin fusions.
If negative results, then it should be followed with the tissue-based NGS.
In a subset of patients who had acquired mutations and that were identified in revealed alteration
in TRK, kinase domain mutation or TP53 mutation or KRAS mutations who had supported poor prognostic
markers.
In a nutshell, in patients with TRK fusion lung cancer with LAR TETNIP, 66% of response
rates, 34 months of median duration of response, 22 months of median progression free survival,
39 months of median overall survival.
Thank you.