So, I'd like to invite Dr. Lakhan Kashab from Poonanau.
He'll be talking to us about Subtute Ami-Ventenam versus intravenous
in combination with Lazartanib in Refractory JFR mutated in CLC.
So, what are you looking?
Thank you, sir. Good morning, everyone.
So, today I'll be briefly talking about prime results of the Palomathri trial,
which was Subcutaneous Ami-Ventenam versus intravenous Ami-Ventenam,
both in combination with Lazartanib in Refractory,
EGF are mutated at once non-small cell lung cancer.
So, a key takeaway from this trial was that
Subcutaneous administration resulted in a non-inferific casee.
There was a lower rates of infusion related reaction and VT,
and it's more convenient for the patient.
Coming to the study, Ami-Ventenamab, as already discussed,
is an EGF format by-specific antibody with immunoscell directing activity.
However, intravenous ami-Ventenamab is associated with infusion related reaction
to third of the patient, and this requires the first dose to be administered,
protracted in a protected fashion over more than four hours in subsequent
administration over two hours.
So, a patient-centric subcutaneous program was developed,
and a phase two Palomathri study was done to determine a dose,
which is suitable for every two-weekly, three-weekly, and four-weekly schedule.
So, this was for the study then this phase three Palomathri trial,
and it valid the pharmacokinetics and the efficacy and safety of the subcutaneous
formulation.
So, this was the phase three study design.
It included locally advanced or metastatic NSCLC with EGF are exone 19 deletion
or L8, 5, 8-R mutation, who had progressed on ocematinum and chemotherapy,
and had a good performance status.
They were randomized into two arms, open arms included subcutaneous administration
of ami-Ventenamab and the other IV ami-Ventenamab.
The subcutaneous formulation was a fixed dose 1600 mg or in more patient,
who had more than 80 kg of weight, 2240 mg, and it was combined with the
higher-groundase for the better absorption.
While the IV ami-Ventamab, it came in the ami-Ventenamab,
fixed in the formulation of 350 mg and was given 1050 mg in patients less than 80
kg of weight
and 1400 mg more than 80 kg of weight.
Both the patient received less alternative at 240 mg per day.
As this combination is associated with a high risk of venous thromboembolism,
prophylaxis anticongulation was recommended for first four months of the treatment.
There were two co-prime and points which are pharmacokinetic included measurement
of trough concentration of the ami-Ventenamab in both the arm and it was measured
at cycle 2 day 1
or cycle 4 day 1 at the steady-state.
And the second was the AUC from the cycle 2 day 1 to day 15.
Both were tested for knowing priority, secondary and points for overall response
rate.
PFS was tested for superiority, duration of response patient satisfaction,
which was assessed with therapy administration satisfaction survey and safety.
Exploratory end point was overall survival.
So for the statistical point of analysis point of view,
the presumption for the pharmacokinetic end points were that
geometric mean ratio of trough concentration as well as concentration AUC of day 1
to day 15
was presumed to be one between the arm and the non-inferriti margin was 20%
as per the regulatory authorities and the lower bound of this 90%
confidence interval of geometric mean should be more than 80% to prove the non-
inferriti.

Overall response rate was analyzed using logistic regression and non-inferriti if lower bound of 95%
leoporist was more than 60%. PFS was compared with stratified co-oxigration model and there was a
hierarchical statistical testing which first tested for non-inferriti of co-prime and point
then non-inferriti of ORL and superiority of PFS. This is the consort diagram.
Six 35 patients were screened, 418 were randomized equally between the both arms and as we can see
similar number of patient discontinued the treatment in both arms and similar number of
patient or receiving treatment ongoing. Baseline characteristics were well matched.
Off note one third of the patient had history of brain metastasis. This is the pharmacokinetic
endpoint as we can see the trough concentration is similar between the both the group and as well
as the concentration EUC of second cycle day 1 to day 15 it was also similar between the
both group and that resulted in a geometric mean ratio of around 1 and the 90% confidence interval
was well above the non-inferriti margin. So we can also observe in this box plot that the
concentration of the subcutaneous at the trough as well as the EUC was similar as shown in this
diagram. So that showed that the this trend met the non-inferriti criteria of the pharmacokinetics.
Coming to the overall response rate and overall response rate was similar between the two arms
it was 30% objective response rate and disease control rate was around 70 75%.
However duration of response was longer in the subcutaneous administration arm it was 11.2
month versus 8.3 month in IV arm that resulted in 39% of the patient sustaining the response
at the sixth month in subcutaneous arm versus 14% in the IV arm. Similarly progression
fee survival was numerically better in subcutaneous arm versus the IV ami-1 tavamp arm and at six
month 50% patient work for progression fee in subcutaneous arm versus 42% in the intravenous arm.
Overall survival though exploratory end point was better in the subcutaneous arm and the
hazard ratio was 0.62 with the at six month 85% patient surviving in the subcutaneous arm versus
75% in the IV arm. Adverse event was similar between the two arms and these was consistent with the
what was seen in the combination of ami-1 tavamp arm and lazartinib. This continuation rate was
lower in subcutaneous arm 9% versus 12% in the IV arm. Safety profile was also consistent as
the as for the ami-1 tavamp and these were mostly of grade 1 and grade 2.
Importantly infusion related reactions were significantly less it was 13% in subcutaneous arm versus 66% in IV arm that resulted in a 5-fold reduction in the infusion related
reaction and due to the infusion related reaction there was no discontinuation in subcutaneous arm
versus 4 in the intravenous arm. VT was also less in the subcutaneous arm and this was irrespective
of whether the receipt for anti-calculation or not. There was a more convenient administration

with the administration time of 5-0 in subcutaneous arm versus 5-1 and subcutaneous subcutaneous
subsequently 2 hours in IV arm and tummy arm. So to conclude this trial shows that the
subcutaneous formulation is non-fearly efficacy as a lower rate of infusion related reaction
and VT is more convenient to patient with a numerically longer duration of response and
PFS and significant implementing OS. So this thing requires further studies upon these responses
whether the subcutaneous observation or absorption of absorption via lymphatic system enhances
the ami-1 tavamp arm, immunodiliter activity. So it results in a more patient condition
with the lesser infusion related reaction. Thank you. So thank you very much, Lachan.