I would also like to invite our chairperson for this session, Dr. Himand Malhotra, who's
a senior medical oncologist and so we'll be sharing the rest of the session.
Thank you very much.
Good morning everybody.
Really impressed the meeting started, dot on time.
So that is a yardstick of a good well-organized meeting.
So happy to invite the next speaker, Dr. Mohit Sharma from Delhi and he'll be talking to
us about the Mariposa study, which is Evoment NIB and Lazart NIB versus Ose Mertonib in
EJFR mutated NSCLC.
So over to you, Mohit.
So good morning everyone.
I thank the organizers, Dr. Nandini and Dr. Ashifu for the invite.
So the first, I have two presentations, back to back.
So the first presentation is AME-Matamap plus Lazart NIB versus Ose Mertonib in the first
line EJFR mutant advanced North
DNA shedding, they're all common in patients in these patients.
So in this study, it was SSD efficacy of the first line AME-Matamap plus Lazart NIB versus
Ose Mertonib among the patients with these high risk features.
So this was the study design.
AME-Matamap, as we all know, is an EJFR med-pyspic antibody with the immune cell directing activity.
Lazart NIB is a seen as penetrant.
A third generation EJFR TKI, TKI, and AME-Matamap plus Lazart NIB, it meaningfully improved the
PFS and duration of response versus Ose Mertonib in Mariposa.
These were the key eligibility criteria, locally advanced or metastatic non-cellin cancer, treatment, NIB for advanced disease, documented EJFR, exon-19, del or L858R, E-COC
PS0 or 1, and asymptomatic brain metastasis, which did not require definitive treatment.
The primary and the patients were randomized to an E-Matamap plus Lazart NIB or Ose Mertonib
AM.
The primary endpoint was PFS and high risk subgroups analyzed for brain meds, levements,
TP53, TP53 commutation, detectable EJFR mutated CTDNA at baseline and without EJFR mutated CTDNA clearance at cycle 3 of day one, that is week nine.
That the diagnostic tests used were CTDNA NGS, which was analyzed with garden 360 and exon-19
deletion and L858R CTDNA and in the blood was analyzed at baseline and cycle 3 day one
with the biodesics, droplet, digital polymerase reaction.
AMI-Vanta map plus Lazart NIB, it reduced the risk of progression ordered by 30% and improved
the median progression fee survival by 7.1 months.
So median follow-up was 22 months.
In the AMI and Lares-Zam, median PFS 23.7 months versus 16.6 months in the Ose Mertonib
as our ratio of 0.7.
In the AMI-Lazarm 41% of the patients they had history of brain meds versus 40% in the
Ose Mertonib arm showed a median PFS of 13 months versus 18.3 months in patients with
the history of brain meds.

So AMI-Vanta map and laser TINIP reduced the risk of progression ordered by 31% in the
subgroup.
In the AMI-Lazarm 50, 15% of the patients had levements at baseline versus 17% in the
Ose M.
Ose showed a median PFS of 11 months and AMI plus left a median PFS of 18.2 months with
the liver metastasis at the baseline.
So AMI and Lares-Zamib reduced the risk of progression of death by 42% in the subgroup.
So this is the patient disposition for the CT-DNA analysis.
The proportion of samples and detection rates were balanced across both the arms and AMI-Vanta
map plus Lazart NIB.
They reduced the risk of progression ordered by 30% over Ose Mertonib in the NGS and DDPCR.
CT-DNA analyzable population indicating that these subgroups were representative of the
intent to treat population.
Approximately 70% of the patients in both the arms had detectable EGFR mutated CT-DNA
at baseline and more patients with detectable CT-DNA had brain and liver metastasis at baseline.
At cycle 3-day 1, detectable EGFR mutated CT-DNA was observed in 15% of these patients
in both the arms.
Ose Mertonib showed a median PFS of 14.8 months in patients with detectable CT-DNA at the
baseline.
AMI-Vanta map plus Lazart NIB reduced the risk of progression ordered by 32% in the subgroup
and consistent results were seen in the subgroup using the CT-DNA NGS assay with the hazard
ratio of 0.71.
We can see here with the detectable baseline CT-DNA AMI plus Laz has a median PFS of 20.3
months versus 14.8 months in the Ose Mertonib arm.
Ose Mertonib showed a median PFS of 9.1 months versus 16.5 months with the AMI-Laz in patients
without cleared EGFR mutation CT-DNA at cycle 3 of day 1.
So AMI-Vanta map and Lazart NIB reduced the risk of progression ordered by 51% in this
subgroup.
These were the baseline demographic and clinical characteristics by the TP-53 commutation
status.
You can see here.
Ose Mertonib showed a median PFS of 12.9 months in patients with the TP-53 commutations
at the baseline.
So AMI-Vanta map and Lazart NIB reduced the risk of progression ordered by 35% in the
subgroup.
The AMI-Laz had a median PFS of 18.2 months in the TP-53 commutation patients versus 12.9
months in the Ose M. While in the wild side TPR, AMI-Laz had 22.1 months of PFAS versus
19.9 months with the OCR.

So in the PFAS for patients with all these high risk features, it favors AMI-Vanta map
plus Lazart NIB.
So to conclude, the high risk features they occur commonly in the first line EGFR mutated
exon 19-del or 8-5-way tar, non-small cell cancer which carry a poor prognosis with a
median PFS of 9.1 to 14.8 months on Ose Mertonib.
AMI-Vanta map plus Lazart NIB, it significantly improved the median PFS versus Ose Mertonib
in these high subgroups which we have already discussed.
And among the corresponding subgroups without high risk features, AMI-Vanta map plus Lazart
NIB showed a consistent PFS benefit over Ose Mertonib.
So AMI-Vanta map plus Lazart NIB, it produces superior outcomes in patients with and without
high risk features and represents a promising new standard of care for EGFR-muted advanced
non-small cell and cancer.
I guess it has already approved in US for the first line.
So this is the second presentation which was presented recently at SMO Barcelona in 2024.
This is mechanisms of acquired resistance to first line AMI-Vanta map plus Lazart NIB
versus Ose Mertonib in patients with EGFR-muted advanced non-small and lung cancer.
And this is an early analysis from the Phase III Mariposa study.
We all know progression on Ose Mertonib is nearly inevitable due to acquired resistance
that can be diverse and polytronyly.
The most common EGFR TKI resistance mechanisms are EGFR and MET alterations.
AMI-Vanta map a multi-targeted EGFR met by specific antibody with immune cell-directed
activity targets EGFR and MET-BATE resistance upfront with the potential to alter the spectrum
of acquired resistance.
And AMI-Vanta map plus Lazart NIB it significantly improved the PFS versus Ose Mertonib in the
Phase III Mariposa study which we have just discussed.
And this is now approved in the US for the first line treatment of EGFR-muted non-small
and cancer.
In this study it is reported the acquired resistance mechanisms for patients with disease progression
on first line AMI-Vanta map plus Lazart NIB versus Ose Mertonib.
The Mariposa study design which we have already discussed.
The CT DNA analysis or total of 858 patients with treatment NIB EGFR-muted exon-19 deletion
or L858R locally advanced or metastatic non-small cell and cancer.
They were evenly randomized to receive AMI-Vanta map plus Lazart NIB or Ose Mertonib.
The paired blood samples were collected at baseline and end of treatment for analysis
of detectable circulating tumor DNA by next generation sequencing garden 360.
All P values were nominal and end of treatment it was defined as disease progression or treatment
discontinuation or within 90 days of discontinuation.
From Met and EGFR based resistance mechanisms AMI-Vanta map plus Lazart NIB it significantly
reduced the incidence of acquired met amplification and EGFR resistance mutations

versus Ose Mertonib.
The acquired met amplification were 3-fold lower and EGFR resistance mutations they were 8-fold lower for AMI-Vanta map plus Lazart NIB versus Ose Mertonib.
There was no statistically significant differences were seen between arm for the other resistance
mechanisms such as her 2 amplification or RAS, RAF path phase, PI3, K cell, CIP.
AMI-Vanta map plus Lazart NIB did not meaningful increase other molecular escape pathways and
had a low rate of TP53 RB1 loss that was associated with small cell lung cancer transformation.
There was no clear resistance mechanisms were detected in 86% percent of the patients for
Ose Mertonib and 68% of the patients for AMI-Vanta map plus Lazart NIB.
And among patients with the known resistance mechanism Ose Mertonib had a more heterogeneous
mutation landscape than AMI-Vanta map plus Lazart NIB.
So complex resistance was defined as having two or more resistance pathway alterations
detected by the CT DNA.
So Ose Mertonib had a higher frequency of complex resistance than AMI-Vanta map plus Lazart NIB.
So Ose Mertonib had 42.6% while AMI-Vanta map plus Lazart NIB had 27.8% resistance in
more than two resistance pathways.
So lower rates of exon 19 deletion or L858 are was detected in CT DNA seen in AMI-Vanta
map plus Lazart NIB versus end of treatment.
This is the this we can see at the baseline and see here the at the end of the treatment.
So AMI-Vanta map plus Lazart NIB had a deeper and more sustained EG for inhibition than
Ose Mertonib.
So using CT DNA NGS analysis AMI-Vanta map plus Lazart NIB significantly reduced the
incidence of metamplifications and EG for resistance alterations versus Ose Mertonib
the burnt amplification 4.4% versus 13.6% with a p value of 0.017 and EG for resistance
mutations 0.9% versus 7.9% and no significant differences were observed among met and EG
for independent resistance mechanisms between the arms.
AMI plus last had a low rate of TP53 RB1 loss and Ose Mertonib had a higher frequency
of complex resistance than AMI-Vanta map plus Lazart NIB.
So AMI-Vanta map plus Lazart NIB's multi targeted EG for met approach it narrowed the spectrum
and reduce the complexity of acquired resistance versus Ose Mertonib.
Thank you so much for your patient listening.
Thank you very much Moniz.
We will have the discussions at the end of all the presentations.