Thank you for inviting me here.
So I'll be presenting the five-year update of crown data.
And so we all know that crown is a landmark trial
in Al positive non-smolsel lung cancer patients.
Stays 3B and stage 4 patients were enrolled.
This is the original study design.
And please note that asymptomatic treated or untreated CNS
metastasis patients were allowed to be enrolled.
So they were randomized into law-latinib 100 mg once daily.
That is a standard dose versus chryzotinib
into 250 mg standard dose BD randomized
into one is to one fashion.
And the primary endpoint of crown trial was PFS
by blinded independent central review.
And the secondary end points were PFS
by investigator objective response rate,
intracranial response and OS.
So these are the baseline characteristics.
Please note that 26% of the crown trial patients were,
they had brain metastasis.
So this was the original result got published in 2020 in NEGM.
They showed that the PFS was significantly,
not only better, in fact it was double.
One year PFS rate in chryzotinib was only 39% versus 78%
in law-latinib arm.
And PFS by investigator assessment was also significant.
And so now I'll be presenting the five years follow-up data.
This is a post-doc analysis reported,
updated investigator assessed efficacy outcome, safety
and some biomarker analysis result.
The median follow-up for PFS in law-latinib group was 60 months
and in chryzotinib group it was 55 months.
So this is the crown PFS data after five years follow-up.
Look at the separation of curve, such separation of curve
we usually don't see.
The hazard ratio is jaw-dropping.
It is 0.19.
The PFS median PFS was not reached in favor of law-latinib
versus only 9.1 months in favor of chryzotinib.
At five years, 60% patients were alive
and progression-free in law-latinib arm versus only 8%
in chryzotinib arm.
So PFS by two subgroups, whether they had brain metastasis
or without brain metastasis.
In patients who did not have any brain metastasis
at the time of enrollment, the hazard ratio was 0.24.
The five years PFS rate was 63% in law-latinib group.
Patients who had brain metastasis upfront,
even in those patients, the hazard ratio for PFS
was 0.08, magnificent hazard ratio.
And even in brain-mates patients, the five years PFS rate
and law-latinib arm were 53%.
And actually, it could not be calculated in chryzotinib
because all patients, they progressed in CNS within two years.
What about the response rate?
81% patients in law-latinib had partial response,
objective response, and chryzotinib arm, 63%.
10% patient in law-latinib arm had complete response
and only 2% in chryzotinib.

The duration of response was also prolonged
that response not only higher in number in law-latinib,
but it was durable, not reached in law-latinib
versus only 9.2 months duration of response in chryzotinib.
What about the intracranial response rate?
Confirmed intracranial objective response rate was as high as 60%
in law-latinib arm versus only 11% in chryzotinib arm.
And most of these intracranial response were complete response.
Look at the figure, 49% patients in law-latinib arm,
they had intracranial complete response.
If we look at the data of complete intracranial response
who had measurable brain mets, then the percentage was 58%.
If you compare the other competitor molecule for electinib,
in alex-trial, it was only 38%.
So, time to intracranial progression, not only the response rate
was higher in intracranial, it was durable as well.
So, the median time to intracranial progression,
not reached in law-latinib versus only 16.4 months in chryzotinib.
And again, once again, please note the hazard ratio,
it is jaw dropping, 0.06.
So, law-latinib delayed intracranial progression versus chryzotinib
and there was no intracranial progression events after 36 months.
So, these are the intracranial progression in patients
who had brain mets and who did not have brain mets.
Without brain metastasis, the hazard ratio for intracranial progression
was 0.05.
The patients who did not have any brain metastasis in that arm,
only four patients in law-latinib group patients,
they developed brain metastasis.
And the patients who had brain metastasis upfront,
they are also the hazard ratio for PFS was 0.03.
Such kind of PFS we don't see any clinical trial.
So, what about the efficacy of law-latinib in other important subgroup?
We all know that a EML4-ALC version 3,
that is a poor prognostic version.
So, in that group also, 60 months was the 5 years PFS was 50, 60 months.
And so, that proves that across all the subgroups,
law-latinib was efficient, superior.
Even in the presence of T53 mutation,
the median PFS was 51.6 months.
So, all the patients sample, blood sample was collected
for circulating tumor DNA.
And there was no new ALC mutation on target resistance mutations were noted.
So, that means that law-latinib has a broader activity,
coverage over multiple secondary resistance mechanism on target mutations.
The most of the mutations in law-latinib was because of target activation
of different pathways.
What about adverse events?
My next speaker, Dr. Mirudul Malhotra,
he will be talking on adverse events in detail.
But adverse events related to treatment,
discontinuation was only 5% in law-latinib arm.
So, most of the adverse events, they did not require discontinuation of drug,
supportive medicines, modification of those actually solved most of the problem.
The major grade 3, 4 adverse events in law-latinib arm were hyperclaristrol,
lemias, triglycerides, and rhizine cholesterol and hypertension and weight gain.
So, as you notice that cognitive effect, which all the medical on cloisters are
also concerned,
most of the cognitive effects impairments were grade 1 and grade 2.

Hardly you will see any grade 3 or grade 4 cognitive effects.
So, the 5 year safety summary is consistent with the primary analysis,
no new safety signal and only 5% patients, they discontinue law-latinib due to treatment related adverse events.
And so, and if you modify the dose of law-latinib within 16 weeks,
the first 4 months, how they are doing?
Even in such situations, actually, it does not impact the final outcome.
You will see the curves are not separating widely.
So, in such dose-modified law-latinib patients are also doing well.
So, to summarize, 60% of patients were alive after 5 years.
This is magnificent improvement and such improvement is not seen in any molecular targeted therapy,
not only non-spatial lung cancer, it is even in across all other solid tumors.
92% of patients remain protected from CNS progression with a hazard ratio of 0.06,
and the safety profile was consistent with the preliminary result.
Thank you, everyone.