Good afternoon to all.
Thank you, organizers for this wonderful opportunity.
So in the next seven minutes or so, I'll try to review this very interesting study.
The study title inspired.
So the complete study title, European Alkib versus Krizotnib in ALK, TK, Nave, Locally
Advanced Metastatic ALK, Pause to Non-Smancer Lung Cancer, intermittent and interim analysis
of a randomized open-level phase three study.
So from the study title itself, there are at least three problems.
One is very difficult to pronounce drug.
Second is comparison is done with a probably outdated drug Krizotnib.
And third, it's an intermittent analysis.
For the completion of the review within the next seven minutes, I'll call this drug as
Erupline, not Erupline Alkib.
So this drug is a new generation oral TKI that is effective both systemic as well as
CNS, ALK, Pause to Non-Smancer Lung Cancer.
In the pre-clinical studies, it has shown a effect against wild type as well as mutated
ALK gene.
So in the phase one, in the treatment name as well as pre-treated population, it has shown
impressive oral response rates.
As you can see in the ALK name, the oral response rates was 81% in the dose escalation and
nearly 80% in the dose expansion.
And pre-exposed, the response rates dropped down to 40% to 45%.
So this led to a phase two study, which was interlexed study in which about one part six
patients with the Krizotnib progressive disease were exposed to Erupline, an ITMG-1's daily
21-day cycle with a seven-day leading phase of 60MG-1's daily.
And in this phase two study, there was a response rates of nearly 70% and PFS of nearly 20 months.
And with those patients with intra-linear disease, the response rates was nearly 64%.
So with this data, there was a regulatory approval in China for those patients for second
line use of Erupline post-Krizotnib failure.
And this is now the phase three trial.
And you can see it's a multi-center randomized open-label phase three study conducted across
40 hospitals in China.
And previously, it was treatment-name alone, but it was amended to include those patients
who have received one line of prayer chemotherapy to increase the, accelerate the enrollment.
Second patients were receiving the Erupline at 180MG-1's daily with a seven-day leading
period of 60MG-1's daily, or the standard dose of Krizotnib, which is 250MG-2's daily.
The seven-day leading period was given to mitigate some of the risk of early onset pulmonary
toxicities, which was observed in the phase one study.
And more importantly, crossover to Erupline was not allowed after Krizotnib failure.
The primary endpoint was PFS, which is assessed by independent radiological

committee.
And secondary endpoints include PFS by investigator, overall response rate, duration of response,
intracranial, overall response rate, and time to CNS progression, overall survival and safety.
And the stratification factors include PFS, previous chemotherapist regimen, baseline
CNS metastasis, and radio therapy to the CNS metastasis.
Coming to the statistical analysis, a target sample size of 292, 146 in each group, calculated
annual dropout could be approximately 5% enrollment period of 16 months, only possible in China.
In 1.2, PFS events were required to provide a statistical power of 80% to detect a hazard
ratio of 0.66, which means that it can increase the study drug could increase the PFS from
11 months in Krizotnib to 16.5 months in the Erupline.
Intramanalysis, which is what we are discussing today, is planned after 70% of the PFS events.
Most of the survival endpoints are calculated by Kaplan-Meyer method, and Cox's proportional
hazard regression model was used to estimate hazard ratios and 95% cross confidence intervals.
efficacy was evaluated in the intensity population.
So, this is a study disposition.
Again, from September 2019 to December 2020, hardly a one-year period, they have recruited
292 patients across 40 hospitals in China.
And as you can see, most of the baseline characteristics are well matched between the two groups.
Importantly, CNS metastasis was seen in 26% in Erupline, and about 30% in the Krizotnib.
And prior chemotherapy exposure was seen in near-labored, 17% of the patients.
So coming to the primary endpoint, at the time of this analysis, this interim analysis,
a total of 145 PFS events have occurred.
36% of the patients in Erupline and nearly 62% in the Krizotnib.
And the primary endpoint of PFS by independent radiological committee was significantly longer
with Erupline at around 27.7 months compared to 14.6 months with Krizotnib hazard ratio
0.34, which was statistically significant.
And two-year estimates of PFS was also better with Erupline at 61% versus 25% with Krizotnib.
And if you look at the forest plot, we get a general impression that most of the subgroups
have benefited with the experimental drug.
Some of the subgroups where the confidence-to-install median crosses the median are those patients
who are more than 65 years of age, those who had clinical stage 3 disease at enrollment,
at enrollment, and those patients who had previously exposed to chemotherapy.
Again, numbers are small and this study was not power to find the absolute differences
between those groups.
Again, the secondary endpoint of PFS as per investigator was also longer among those patients
who are being exposed to Erupline.
Coming to the other secondary endpoint of objective response rates, as you can see,

objective response rates was nearly 90% in both the groups.
But the median duration of response was significantly longer in Erupline at around 27 months compared
to 13 months in the Erupline.
Coming to the CNS responses, those with measurable disease, the Erupline had 91% CNS response
compared to 60% with Krizotnib.
Coming to the all CNS disease, the objective response rates were 57% in the Erupline compared
to about 25% in the Krizotnib.
Again we can see in the right side column, we have two capillomia curves.
We can see in the top one, those patients with baseline CNS metastasis, in the bottom
one, those with those CNS metastasis, the hazard ratio in those with meds are 0.24.
And those with those metastasis is 0.36.
In fact, the addition of Erupline, basically use of Erupline has mitigated some of the
negative prognostic effect of the CNS metastasis.
So overall surveyable data is immature and median was not, was not estimated either group.
24-hour overall surveyable rate is around 85% for either group.
Coming to the CFT very quickly, the median duration of exposure to drug was 24 months
with Erupline compared to 12 months for the Krizotnib, despite higher exposure.
The grade 3 grade for toxicities were pretty much similar between both groups at around
50%.
And those toxicities which are more common in Erupline compared to that of Krizotnib include
lipid dysfunctions, rash, hypertension and abnormal liver function.
And the most common grade 3 toxicities in Erupline included hypertension at 9.1% and
abnormal hepatic function at 9.1%.
ILD was seen in about 5% in both groups.
Serious treatment related adverse effects similar in between both groups 10-15% discontinuations
were much more, discontinuations are similar around 5%, but those interruptions were much
more common in the Erupline in the Krizotnib at 30%.
So in conclusion, it's an interminal analysis that had shown that Erupline is superior to
Krizotnib with respect to the primary endpoint of IRC-SSPFS.
And this improvement was irrespective of baseline venous metastasis.
Other secondary endpoints also favored efficacy with Erupline and tumor responses were much
more durable at 27 months with Erupline compared to about 13 months with Krizotnib.
And again, it has much more effective in controlling and preventing CNS metastasis.
At 18 months, the cumulative incidence of CNS metastasis was only 3.2% per Erupline and
more than 4 times at 12.2% per the Krizotnib.
Always data is immature.
Some of the shortcomings or some of the limitations of the study is that it is exclusively done
in China.
They have recruited nearly 290 patients within 16 months period and it is not possible in
the rest of the world.
Again, the comparator arm is Krizotnib which is probably something that is substandard

or not very standard in 2024.
Again, it's an open-label study design that is done because of the differential dosing
of the experimental drug as well as the Krizotnib.
So with that, I will conclude my brief review of this trial.
Thank you very much.