Good evening and some exciting data from Electinib as well.
So the five year survival data was presented in the SMO-ISHA conference in 2022 and now
we have the seven year OS data.
And this was the Alicia trial which focused on the Asian subset and the 600 milligrams
subgroup.
So the Asian subset in 300 milligrams subgroup is the JALEX whereas the Alicia is the 600
milligrams subgroup.
So we all know about Alkary arrangements.
We have been talking about Alk I think for the full day.
But Alkarynib is approved as first line therapy in patients with advanced Alk positive NSALC
and as an adjuvant treatment for patients with resected Alk positive NSALC that is the
Alina study.
Now in the phase three Alicia trial evaluating the efficacy and safety of Alkarynib versus
chrysotnib in Asian patients, a clinically meaningful improvement in OS with an hazard
ratio of 0.6 was previously seen that is at the five years follow up.
So this is the trial design and here treatment naive patients with an E-COC P-S of 0 to 2.
And the stratification factor was 0 1 versus 2 that is E-COC P-S and whether baseline CNS
meths were present or no.
And it was randomized in a two is to one fashion to Alkarynib and chrysotnib and patients
receive means the two arm is Alkarynib and the one randomization is chrysotnib and the
primary endpoint was investigator associated PFS and the key secondary endpoints was OS
and safety.
And as per this protocol there was no crossover allowed at the time of any event or progression.
So here are the basic the baseline patient demographics and characteristics.
So as we know in any driver mutant positive cancer it is more commonly seen in the young
that is less than 60 more commonly seen in females.
Majority of the patients had a good E-COC P-S. Majority of the patients were non or past smokers.
Most of the patients are almost all of the patients at stage 3 or 4B, 4 disease.
Adenocarcinoma was the most common histology but the most important point to tell is the
presence of CNS meths at baseline was as high as 35%.
And this is the seven year update.
So here we can see that at seven years the median OS for Alkarynib as compared to chrysotnib
was not reached and the stratified hazard ratio was 0.72 and at seven years the OS was 56
percent.
So 56 percent of patients were alive at the end of seven years.
Now this is with baseline CNS metastasis and we knew that 35 percent of patients had CNS
meths at baseline and the median OS and such patients was also 72 months as compared to
46 months with chrysotnib with the stratified, unsatisfied hazard ratio 0.56.
Here is the comparison.

Those with baseline brain meds and those without baseline brain meds.
And those without baseline brain meds the median overall survival was not reached with
either of the arms.
Now regarding post progression anti cancer therapy one very important or concerning factor
was that the number of patients who could actually go on and receive second line treatment and
those who progressed on Alkarynib 70 percent of patients could receive second or subsequent
line of treatment and Lorelatinib was received in 8 percent of patients chrysotnib in 17
percent seridinib in 11 percent but 70 percent of patients could receive second and subsequent
line of treatment.
What about safety?
Now we have seven year follow up we can see that the the grade three or higher adverse
events were seen in 50 percent but leading to treatment discontinuation was seen in 12
percent of patients.
Those reduction in 27 percent and those interruption in 30 percent.
So although there were side effects none of them led to clinically significant treatment
discontinuation, dose reduction or dose interruption.
So this is data from the Alicia trial and seven year follow up and it is the first randomized
trial of an Alkarynib to report a seven year follow up data with Alkarynib 600 milligram
BD there is a clinically meaningful significant OS benefit as compared to chrysotnib and this
is in the Asian subset.
The median OS was not reached with Alkarynib because compared to 80 months with
chrysotnib.
The OS benefit in Alkarynib was seen in patients, those having and those who did not
have baseline brain metastasis.
And despite a longer duration of treatment in the Alkarynib arm there was a similar safety
profile as compared to chrysotnib and no new safety signals.
So this is from the Alicia trial.
Now we go to the second part.
The second part is about interacting in both in Ross 1 positive and NTRK fusion NSCLC.
So we start off with the Ross 1 positive NSCLC in the current indication and the approval
for entrectum is both in the first line NSCLC with or without brain meds.
We know this that it is more common in females, never a non-smokers and the adenocarcinoma
histology and the most common frequency that we see is in 1 to 2 percent of NSCLCs.
But what is the unmet need?
The unmet need lies in those having brain meds.
Up to 40 percent of patients with Ross 1 fusion NSCLC have brain meds at baseline and
with chrysotnib having limited CNS activity there was a big unmet need.
What we can see is with 2 years of follow up if patients are treated on chrysotnib 50
percent of patients will develop brain meds if they did not have a baseline.
Now entrectum was designed to cross the brain barrier and remain in the CNS.

So this is what leads to a very good intracranial efficacy and response rates.
So what is the update?
The data comes from ALCA that is ALCA, start track 1 and start track 2.
These are the most three most common trials where this data has come from and the primary
end points was response rate and duration of response and secondary end points was the
PFSOS, intracranial activity and safety.
So again patient demographics more commonly seen in the young, more commonly seen in
females, ECOC PAS was good that is 0 and 1 in most patients, most of them were non or
never smokers.
What is important is we have data for both the efficacy, the valuable population, 172
patients and the first line treated population, 67 percent of patients.
Now metastasis to CNS at baseline was seen again over here in 35 percent of patients.
What about efficacy?
The efficacy in all comers, so the response rate is 67 percent, those with baseline CNS
met is 63 percent, those without baseline CNS met is very close to 70 percent and those
in the first line patient population is 68.7 percent and the duration of response for
the overall cohort is 20 months and for the first line treated population it is 35.6
months.
What about the survival?
We have both median PFS and OS data.
In the all comers that is the ITT population it was 16.8 months median PFS and in the first
line treated population is 17.7 months.
What about median OS?
It is 44 months for those in the ITT and 47 months for those who were treated with first
line entrechnum.
Very important what about CNS activity?
The intracranial response rates were as high as 50 percent in the ITT and those treated
with first line 60 percent of patients and the median duration of response for those who
were having brain meds at baseline was 12.9 months and the median intracranial PFS was
15.6 months in first line treatment patients.
Now we have already talked about this.
The response rates and the survival let's go on to safety.
The most frequent treatment related adverse events were dysgusia, weight gain, dizziness,
constipation and diarrhea but what is important to know again that although the most common
treatment related adverse events great three or higher was seen in 43 percent the number
of adverse events that actually led to discontinuation, interruption or permanent reduction or permanent
discontinuation was actually less.
So the final conclusion is that there is durable overall and intracranial response regardless
of the baseline CNS status and this is the summary in one slide in the ITT

population.
This is the summary in the first line treated population that is first line metastatic or
locally advanced ROS positive NSCLC treated upfront of first line with entrechnum.
What about ntrk fusion positive NSCLC and we present the updated data.
So here we can see we will directly go on to the response rates in ntrk.
So the objective response rates in the ITT was 32 percent and in those with baseline
meds was 60 percent and those without baseline CNS metastasis was 64 percent but what about
the duration of response.
So the duration of response the median is 27.3 months and 29 months in those with baseline
CNS meds and 27.1 months in those without baseline CNS meds.
What about the PFS and OS data the median PFS is 28 months and the median OS is 41.5
months.
So we spoke about efficacy and this is time to intracranial progression.
So here we can see that the curves are almost flat or almost straight in those who are having
CNS meds and time to intracranial progression.
So there is a good intracranial control.
So the intracranial objective response rate was 64 percent and we can see complete responses
in as high as 50 percent patients.
The intracranial duration of response the median was 55 months and the intracranial PFS was
very good at 32.7 months.
So what is the conclusion for ntrk positive NSCLC.
So this was the updated data and ntrk demonstrated clinically meaningful overall survival and
intracranial efficacy with the manageable safety profile in those who are ntrk fusion
positive NSCLC at a 26.3 month follow up.
Here the response rates are as high as 62.7 percent and the duration of response is 27.3
months.
Intraactive did demonstrate durable responses in patients with ntrk fusion positive NSCLC
irrespective of baseline brain meds and this confirms the high level of activity of ntrk nib in the brain.
The safety profile of ntrk nib was consistent with previously reported data.
The data in this updated analysis supports the use of ntrk nib as a first line treatment
option in these patients irrespective of brain meds.
Further investigation will be needed to increase the understanding of the prognosis of patients
in this rare population and what are their long term outcomes.
Thank you.