So, I will be presenting an study which was presented in WCLC this year.
This sounds to be quite interesting study because if this clicks very well, probably
many of our patients will be going on to this kind of a therapy.
So, this therapy basically is for the KRS G12C mutant in first line.
So, this is something what we always wanted and probably this is a ray of hope.
And this specific study focuses on the efficacy and safety of a new molecule, Almonarase.
This is a second generation KRS inhibitor with combination of immunotherapy that is Pembrolizumab plus chemotherapy.
So, this is like three therapies together a typical maximum combination what we can give in the first line.
So, basic background comes from the understanding that chemo immunotherapy is used in first
line NCLC patients, especially patients who are having a negative molecular markers like
EJFR alk and they are also low and negative on the PDL1 expression or the tumor burden
is quite high and we need a good urgent control or a faster response rates.
So, these are the patients where we want in combination of chemotherapy and get maximum
response.
So, we have also seen combination working well as in florid 2, in patients who are EJFR
mutant combining Osmotenium plus chemotherapy and in some studies where even Jeff D. Niverse
combined with chemotherapy.
So, this combination of targeted therapy plus chemotherapy represent a very excellent opportunity
in first line because most of the studies which are available for KRS are for second
line and beyond.
So, if this is something which has good potential and a good number of patients as we know good
number of patients do have KRS.
So, background comes from this study the response rates where the second generation ulmanar acid was used and they had an excellent overall response rate of 77 percent.
So, this was a favorable response with combination as a monotherapy and then in combination
with tamboural uzumab.
And later this was taken up into the phase 1 phase 2 study where they wanted to decide
the dose 50 milligram or 100 milligram.
You can see there is a part A, B, C, D, E and G and what we will be focusing today is
the part B, 9 where there is a combination of this second generation kerosene emitter
with immunotherapy pembro plus chemo.
So, this is what is the study what we are going to understand and this is a small cohort
21 patients.
It took all patients who were treatment naive, PDL1 anything from 0 to 100 percent.
It does allow most of the trial now new trials in lung are allowing one or sometime even
two chemotherapy cycles because we know that this agent this engines reports do come after
2, 3 or sometime even 4 weeks later.
So, practically when patient is symptomatic we do not want to wait.

In fact, patients or patients related to do not want to wait and we do give therapy.
So, these are very fair practical thing where they exempt giving one or two cycles it is
ok.
And if patient has progressed like prior adjuvant or new adjuvant therapy then at least there
should be a 6 month gap.
So, they did have 2 analysis dosages 50 milligram and 100 milligram twice daily and other things
will not discuss here.
So, we will directly come to the baseline patients here as you can see more than 90 percent patients
were having either PDL1 low or negative.
So, these are patients who are having less than 50 percent of the PDL1 and 43 percent.
So, almost close to half the patients did receive one cycle of chemotherapy plus immunotherapy
combination prior to the enrollment.
Coming to the safety profile of this combination patients did have anemia good lot number of
patients almost half of them.
Some grade some grade of anemia but luckily the grade 3 and above were less than 5 percent.
Coming to the other hematological toxicities like neutrophil count, neutropenia, thrombocytopenia,
leukopenia they were also seen in almost one fourth of the patient.
And these were each of them if we go for the individual drug the ulmonar acid was the only
one which had 5 percent discontinuation rate because of its own side effects others are
almost 10 percent.
So, this is a spider plot and the response rate and you can see that the objective response
rate was 50 percent.
So, half the patients are going to respond in a very nice way and if we go for the disease
control rate so including the stable disease it is close to 85 percent.
So, that is a good response in first line as we expect in the first line good response
in the first line.
And if we see the median duration of therapy it was 4.5 month and almost three fourth of
the patient did remain on therapy at the time of data cut off.
So, what we conclude from this that this combination of second generation Keras inhibitor G12C inhibitor
with Pembro and chemo can be a potential first line treatment in this kind of subset of patients.
The manageable the safety profile is quite manageable.
We know how to monitor the hematological toxicities and how to manage the cytopenias
and preliminary efficacy is quite promising with OR of 50 percent and CBR of almost 85
percent and this is a big chunk almost 90 percent plus patients who are going to be having
a PDL1 lower negativity.
So, beyond this what they want to do is a phase 3 study which is again looking after looking
for the global registration and once we have that probably this will open the door

for
open the door for next this kind of niche area where we want to do something in the first line.
So, this is something called as a sunray 01 phase 3 study where the combination either
with 50 or 100 milligram and pembrolyzumab dose optimization the safety lead in part B
will be the combination of all the 4 agents dose after the dose conformation they will
be randomized to receive either combination of Keras inhibitor plus immunotherapy or immunotherapy
alone or the combination with or without the anti Keras.
So, I will stop here and hopefully in next 2 years or so we will have the results for
this and probably we will have we will open the door for Keras inhibitors also.
Thank you. Thank you for the patient listening.
Thank you.
Bhavisham.