So, I would like to thank the organizers and Prashan for inviting me to this talk.
I think I will quickly review the data.
There were some very specific recommendations and I mean a really small subset of a situation.
So, what we will do is we will see what are tyrosine kinases, we will see what are driver
mutations, see what how do you target driver mutations.
Then we will talk about adjuvant, TKIs, we will talk about non-adjuvant, TKIs and finally,
we will just sum it up with one or two slides I think, which are the most important slides
in the talk.
Tyrosine kinases are basically enzymes which phosphorylide tyrosine residues.
They change the conformational protein, activate proteins and they give a lot of, they start
a lot of events after that which ultimately lead to the malignant phenotype.
They usually activate the tyrosine kinase receptor or they could be non-receptor kinase
but the mutation is activated in enzymes.
And there are inhibitors which can switch off the enzymes and control the cell growth and
which is exactly what tyrosine kinase inhibitor is.
All small molecules are not tyrosine kinases because all the enzymes are not tyrosine kinases
serine kinase also and these are two groups but essentially when we use a general proper
TKI we mean everything but it means need not inhibit tyrosine kinase like B-raf is a actually
serine kinase but the word general word TKI is used for all these drugs which inhibit
kinases okay the T should be because bulk of the kinase are tyrosine kinases okay this
is the thing usually the receptor consists of two parts they come together and the growth
factor binds then it starts a whole lot of second this blue are the second I mean
the translating pathways and finally the metastases angiogenic cell proliferative which are known
which are the features of malignant disease they start.
TKIs are the ones which inhibit the first step that means the receptor to the next step
they inhibit.
Then what's the driver mutation?
Essentially driver mutation is the mutation that drives the cancer and that's the best
way to remember it.
This is a definition by according to NCI but driver mutations have had a big impact on
oncology I mean specifically if you ask me of course CML we know Alk has had a very good
effect on an EJFR we know we get JFR more common but in terms of impact Alk has had a much bigger impact.
NSLC has a lot of driver mutations many are targetable this is the latest and every six
one this changes because more mutations come in you know that unknown part which is 24
is shrinking.
I mean if you have done something like this side about 10 years ago unknown may have been
as high as 50 percent but as more have been discussed I am known as shrinking.

So we are looking at EJFR we are looking Alk in this talk otherwise we are looking at
meds we are looking at ros we are looking at BRAF and RAT and all that but for this talk
we are looking only two mutations EJFR typical mutations which are essentially two mutations
exon 19 exon 21.
Okay when you talk about lung cancer small cell lung cancer has mutations driver mutations
are not targetable PP53 make PI3K is not targetable squamous has targetable mutations
but the percentage is very small and the bulk of the targetable mutations are in non-squamous
histology.
So small cell carcinoma we do not use TKAS so we did that in squamous cell carcinoma in
metastatic setting there is an indication using TKAS but the because the mutations are uncommon
these patients are usually excluded from trials and data is limited so whether we in our pre-volt patient whether we do the questions open probably we do not the guidelines
probably all of them the trials are all rely all non-squamous so what we talking should
we should apply to non-squamous on it.
These are the mutations and these are drugs I am just to give you the number or drug which
are available today and the number is increasing and today we will be talking about two mutations
and three drugs all but in a semi-malic tenor these are three drugs which are using a human setting and new adjuvant setting.
What is new adjuvant?
New adjuvant is before any treatment which we use before the definitive treatment which
can be almost always surgery but things like even is required radiation also is called
new adjuvant the idea is to shrink the disease and idea is to take your micro metastasis
which are the ones which are responsible for treatment failure.
Adjoint is any treatment which is given after definitive treatment and metastatic I mean
the aim is to take care of micro metastasis metastatic is given in in in operative patients
the aim is palaeation prolongation so we are looking at the first two not the third one
here.
In adjuvant setting in case of EGFR the use of adjuvant therapy is well established in
case of ALC it is there there is enough data there is data to show and other mutation the
trials are going on.
New adjuvant setting though they have trials for responses the place is not really established.
To discuss the adjuvant TK I use NSCRC there are four trials basically we are looking at
the Adura trial was asympto NIP radiant and select were a low T NIP and adjuvant was
jefti NIP adjuvant compared is only one which compared a TK against chemotherapy and it
showed the TK has better but jefti NIP we are not using so that the value of the

trial
right now is limited.
The other radiant and select were trials for allotinib radiant was face free trial they
used immunostratic chemistry for detecting EGFR mutation that is not a standard way and
for the entire group the trial was a negative trial but when you took a subset of mutated
patients which is the way we today assess EGFR when you took a subset of mutated patients
the trial was a positive trial.
Select is a face to trial no comparator but it is given very good responses at I mean
two year DFS 88 percent and you can see that okay both these trials used EGFR 1 50 MG OD
I am emphasizing this because though it is not the best treatment it is the only treatment
available to bulk of our patients.
That is the reason I am not trying allotin again again it is not the best treatment if
cost would not a constraint allotinib not the choice but unfortunately ossin mottinib
being being patented is expensive and to take it with three years very expensive I do not
think there are many patients in this country who can afford it but if a fordib will not
issue ossin mottinib gives you almost 80 percent benefit in disease free survival and about
82 percent benefit in CNS disease free survival that is the efficacy.
So the difference between these two is that ossin mottinib improves oss and DFS and the
first generation TK has only improved DFS.
So we believe that some DFS may translate into benefit we believe DFS some benefit is better
than others so allotinib should be used but the choice remains ossin mottinib.
If cost is not a constraint because somebody asked the issue of we are working in public
institution and that is a challenge there.
A new adjoint TK has used there are trials showing good responses there are some data
showing these are patients hardly many mostly rather less than 100 patients today but what
you can see is that they are getting good responses there there is survival which is
33 months 11 months 35 months but the important thing to know is the new adjoint use of TK
as in lung cancer in operative lung cancer is a thing which is under investigation and
that is something probably one should not do.
So I think these are the three most important slides in the entire talk they are very very
congested crowded but the choice was made between comprehensiveness and simplicities
are of your comprehensiveness.
So clinical settings there are 4 clinical settings where we use these with we use TK
as in a operable lung cancer and the first one is completely resected R01B23A and EGFR
19 and EGFR 21 mutation.

If you are having a mutation outside these mutations then I do not think this discussion
applies because the select trial I think the select trial had about 3 patients which are
outside of 100 and the option is osmative ATMG per day for 3 years 80 percent reduction
relapse rate and 82 percent reduction in CNS relapse.
Allotenib is the other option if you do not have access or if you kind of osmative not
an option then allotenib is the option.
Importantly also to remember is that if you have there are people who have EGFR positive
and PDL1 positive both cannot be used.
Then you use the sequence PDL1 osmatinib the toxilung toxicity goes up dramatically.
So this one condition where you do not use both and if the PDL levels are more than 1
percent with EGFR mutation you use the EGFR drug not the PDL1.
Superior Salka stumors the data is indirect.
If you can if they get operable after chemo radiation surgery and chemotherapy if given
you use osmot limit.
And finally for all positive tumors who are more than 4 centimeters involved lymph nodes
all involved nodes use electinid 600 milli twice a day for 2 years.
You expect the benefit of PFS is 76 percent and CNS progression benefit of 78 percent.
So I think this summarizes what you what TKI was the current practices of TKI in operable
lung cancer.
I think that's.
Thanks.
Thanks a lot.
Yeah so we make if you can open the session for Q&A.
Hello pretty comprehensive presentations.
Most of my questions are already answered because I already had a question key why the you know
the immunotherapy trials had excluded EGFR positive patients.
But what if the EGFR positive patients are given immunotherapy do they does it work or
has been tried.
I mean if you're giving EGFR PFS osmot limit yeah then that works out but I don't know
why would you do it.
And secondly it would be so you could say that if you relapse after one year what will you
do possibly use immunotherapy.
Okay anyways we'll have to rebip the end the cascade starts again and another question
was have you ever you know come across a situation where we have to give TKI on humanitarian
grounds where the patient doesn't have money but it's a female non-smoker at no carcinoma
and you have to give something to her and you cannot tolerate any conventional chemotherapy.
I do in practice I have given without even a patient in this patient at diagnosis civil
and diplomatic patients I given the drug in seven days she responded by the time report

it's been done and these are early days when that time days to do fish and the report is
going to take forever to come but I have done that and this lady went home she I'm going
through a little bit I said take this and go and I give Jeff Renee she responded and would
you recommend it with you know in today's time would you.
Today scenario at least get a fish for EGFR again I'm telling you in this country practice
why is even alkyl out of outer region yes because in that course gone I mean these guys
are going on to let you know that when that was top man actually in the drug they had
so for most people in this country the only option in TKI is Jeff Teneb or alloteneb or
Afetenem now it's available okay and if you are going to that go that way then do a fish
for EGFR why do you want to complicate things all right and so financially considering
do you recommend alkyl or a crosotative for alpositations.
Any questions comments from the audience for Dr. Rhea any comments so you know I mean
can you just you know you said you did a comprehensive slide but you know in a simple manner so
what's your take I mean how do you decide post operatively somebody's gone for a you
know surgery with a curative intent and is EGFR positive.
See I think what will happen most situations that they will not go for a sub-op
okay and in metastasistic we know that these drugs are better than chemotherapy so I suppose
one would choose an EGFR even if it's alloteneb or chemotherapy but the answer is indirect
they know that.
Okay thanks so the chances of recurrence after surgery you know you have suppose you have
two arms you know one gets a loteneb yeah other one doesn't get a loteneb we don't talk about ocematodem so what's the chance of recurrences.
Some cells coming out there so 39% reduction in recurrence.
39% recurrence.
That's what coming to.
Perfect thanks thanks a lot.
Thank you yeah sorry.
Hi my question to Rhea.
Like involvement of immunotherapy it was observed that those patients who develop lung cancer
and on treatment those who contracted the infection they have a longer survival contrary
to those who didn't so this how the immunotherapy was evolved so does there is any data or is
any support that patient who develop infection who on an immunotherapy have prolonged survival.
In fact patients who were patients receiving immunotherapy and the squamous cell carcinoma
group they were more prone to getting post obstructive pneumonia because of the nature
of you know centrally located tumors and another study showed that because of the T cell up
regulation there were more chances of these patients getting a CMV reactivation and that

leading to iris so there are no studies as of now showing that you know patients on immunotherapy
getting infection have a better survival.
Okay because it was in other way round.
It evolved like that way.
So as a question again to her is there any because there are multiple factors which can
you know cause the pneumonitis is there any risk stratification score or predictor of
post-ICN pneumonitis?
No.
No.
I think we have to.
Anybody who can answer because there are a lot of factors you know it gets confusing
for a surgeon it's going to be after four factors I am done.
So if the patients are having pre-existing autoimmune condition and if they are trying
to give their immunotherapist or suppose those patients don't have an active autoimmune
disease like RA or something previously RA was there.
This patient may be at risk of delimininitis that's the only thing but I don't think there's
any other way of finding that this patient will be pre-disposed to a you know pneumonitis
here.
I think we just need to cover extensively in the history as of now.
Okay thanks a lot.
Thank you very much.
Thank you very much.
Thank you very much.
Thank you very much.
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