So, we will start with a panel discussion without wasting any time. Let me call about
Dr. Ovidpai. Dr. Pritam Kattarya. Ashid, just you.
So, Pritam is outside. Yes. Dr. Vikas Talarajar. Dr. Sangita. I can see Sangita there. And
Dr. Sangita Bishi is also here.
Yeah. Dr. Vijay Patal, going to moderate our session.
So, panel discussion on the same topic.
So, we won't talk about the same topic.
Thank you.
Okay. Because he has already made a case for exon 20. So, at present, how many of you
have seen at least one case of exon 20 insertion? Can I have a raise of hands? There are a
few raise of hands and those are from my colleagues in TmH only. Okay. So, first of all, you
won't catch exon 20 insertion unless you do a comprehensive genomic profiling. Am I
correct? That's right. So, we will start with from Sandeep Nasad Sandeep, I speak
up the mic. Sandeep, when you see lung cancer upfront, how many times you do a comprehensive
genomic profiling?
Sorry, if you are not discussed the financial aspect, I always offer adeno customer in
all the patients.
Sandeep, the cost is not the factor.
Yeah. So, I understand for this discussion, we will keep costs aside of factor because
if cost is a factor, it cannot afford mAvent in m. So, we are talking about those people
only who can afford mAvent in m. So, we would do comprehensive genomic profiling. Now,
Rohan, what do we mean by comprehensive genomic profiling?
So, sir, I believe that in lung cancer, we can consider a panel of 12 to 15 genes as
a reasonable comprehensive genomic profiling.
So, what Rohan told is a creation point of view. Now, when you say comprehensive genomic
profiling and you may get this question in your exams, you are not looking at 100
genes, 72 genes of this. When you see, say the word comprehensive genomic profiling
means you are looking from all directions. You are looking for few genes, you are looking
for amplifications, you are looking for mutations, all sorts of mutations.
Now, many times in the definition of comprehensive genomic profiling, it also comes whether you
are going to get a report of tumor mutation burden.
Now, the tumor mutation burden report cannot come on 12 genes, 70 genes or 80. Reasonably
good sensitivity reports will come only when you are 300 and 400 genes. And that is the
reason why sometimes we will get confused that Cgpm at the Bada gene panel over. That is
for tumor mutation burden, but CgB in itself means that you are looking from all angles,
which means all types of mutations, there is missense, point mutation, translocation,
fusion, translocation, we have a few, we are covering for all of them.
Now, Pritam, now Pritam works in something where in Mumbai what is called as Sogo, which
is South Mumbai. Pritam, when you look at an upfront EGF1 report comes positive.

What
are the factors you look in that report, genomic report?
So, when I get an EGF1 report, I look at what exactly it is, whether this is on 1921 and
so on and other like L8, Fite, R and other mutations which are there. And based on that,
what is the sensitivity to the availability as that is what we are more interested when
you look at the EGF1 report.
Would you look at another notations apart from EGF1?
Yes, so co-mutations I think are important, P53 both for EGF1 and ALK has demonstrated.
Correct.
So, not only you look at the EGF1 type, you also look at the co-mutations type and at
present there is reasonable data for at least for P53 and very sure as we go ahead, we might
get data for other mutations. Now, we would, the panel was for exon 20, we are going not
hardly going to discuss exon 20, but one question. If you get an exon 20 insertion, what do you
do, Sangita?
So, so generally like you said the CGP profile, I usually talk to the pathologist, you know,
to know what the mutation exactly is, if at all if there is some sensitizing in the exon 20.
And then definitely offer them the options of therapy if the cost not fact obviously
discussed the role of amuantibil.
Okay. So, one of the first things you told you that you need to discuss. So, understand there
is not exon 20 insertion is not like there is one insertion, exon 20 is like India. You
would have people from Maharashtra, Bengal, Tamil Nadu. So, exon 20 has a lot many types
of insertion in it. Interestingly, there are few insertion that is one type which I know
is even sensitive to the first generation decay. So, it is important that you discuss
this exon 20 report in your molecular tumumabodes and get an idea whether is this sensitive to
the first generation decay. And if not, add present the data is in much favor of amuantibil.
And that would be an option which you would use.
Sanjay, what is the fear when you use amuantibil?
The first thing I never use, second thing the data shows it is a high time.
Fantastic. So, I know Ashwand and Pithi had raised their hands that is in exon 20 insertion.
What is your fear when you use amuantibil?
Correct. Yes, one?
Correct. So, these are the two more things and we will first see there is no rocket science.
If your patient is affording in today exon 20 insertion after molecular tumumabodes if it is
not sensitive to the first generation decay amuantibil is unfortunate to the opportunity
the only option at present which works. There are options apart from this which are something
called Suno-Vajan inflamutinib but they are not available in India.

So, we will focus on amuantibil. Now, the issue with amuantibil is amuantibil does lead to a lot of
side effects and these first side effect is infusion reactions. And then let us look at this,
there are multiple data which have been shown and you could see that the all great reactions are
seen in 60 to 40 percent of the patients. The severe reactions are seen in below 10 percent
of the patients and this is one of the thing you are going to counsel your patient that reactions
are apart and pulse flow of this therapy and in the first cycle you are likely to get a reaction
the probability which stands at nearly 60 percent and please when you are demonstrating amuantibil
please keep anti-allergic drugs available with you and at least do a continuous monitoring
of the patient so that if he develops in future reactions you have to tackle them.
Now, what I am going to show you is that most of these reactions happen in the first cycle. So,
this side is dasic he has unfortunately not given anything I am very sure you would have given
and how do you do the first cycle of amuantibil?
So, what we do is we start with the pre-medications. And so we will have to call Dixa and everything and we adjust the rate. So, you know first will be 12.5 then 25 and
graduating to the rate as we do it for a tuxanam. So, very important tip which has been given by Dr.
Pitham first understand that the label itself suggest that the the the dose is very about the
depending on the weight of the patient. Most of our patients are below 80 and the dose is 105
of fg. Now, you dose this patient the first dose on day 1 and day 2 do not try to dose it total
on day 1 you give only 350 mg. If the patient tolerates then you give 750 mg in the day 2.
You give pre-medications. Now, this is something very important if you see the label the label
will set to start from 2450 ml per hour. But practically those who are used will start from
to 12.5 ml per hour because if the patient throws reaction you have a chance to know that in the first cycle itself around out of the 60 percent 54 percent which means 90 percent
of your reactions will happen in the first cycle. Now, another interesting thing about
emuventina is see when we go practically or we give the reaction happens in first 10-15 minutes
the median onset of reaction with emuventina is first 1 hour. So, please do not get over confident in first 30 minutes that the patient is doing well and give assurance to the patient
can be able to get over. Let it be monitored. Now, this is the this mitigation strategy which
was pointed out by Dr. Pritam that you give anti-staminate you give anti-paratic and you
give glucocorticoid to this patients. Now, what are the kinds of reactions which you see and
if you see one of them what to what you need to do?
So, I think very classically you have allergic reactions breathing issues and BP fluctuations etcetera. So, cytokine release like we see with retuxima essentially.

So, this is the chart which tell you that if you have grade 1 and grade 2, obviously like any reaction you hold the reaction, give anti-allergic medications and wait for the reaction to go to grade 1 or grade 0 and then you resume at 50 percent of the infusion rates. Now, if you have a grade 3 then again you can hold it give medications again an resume at if you have a grade 4 then you may have to permanently discontinue emuventina.

Now, this is what I am going to tell you in grade 4 is my personal expense this is not from what the label says. I have treated grade 4 with emuventina after doing classic desensitization over 2LRs and the reason why to select 2LRs is because the product once diluted is is according to label is stable only for 2LRs. Now, this was a genuine problem of how do you see in exon 20 the data from Tata which we published a few years back the median OS was only 4.5 to 5 months was the range.

So, if you cannot give an effective therapy it would be difficult for these patients to survive.

Now, emuventina is the only effective treatment in this in this disease at this point of time and reactions were a issue. So, this skipper was a phase 2 design study which was actually to see how we could calm down on the reactions with emuventina.

And what they did was they gave dexamethas on 4 mg, dexamethas on 8 mg they get monty look us and interestingly they even get methotrixet. And this is the phase 2 design where it is actually a Simon's 2 stage design. Now, those of you know about Simon can have a 1 stage design or 2 stage design. Once you recruit few patients and you say if this many patients do not get reaction it is my success and if you get that success you recruit more patients and that is why you say stage 1 they enrolled 6 patient in stage 2 they enrolled 10 patients. So, the total and after that they went for an expansion cohort for 24 patients and the primary endpoint was reactions and these were the secondary endpoints which were been sealed.

Now, what why was the rational for these interventions? Now, I am not going to explain to the rational for dexamethasons neither I am going to explain to the rational for monty look us. The monty look us data specifically came for direct to map those of you who even did multiple well of a node about the data. It has been they even added methotrixet because they saw that in patients where you can inflexymab methotrixet addition in this small doses actually led to a decrease in side effects. Now, what we are seeing here is the initial results which which we are going to see and what we saw with 4 mg is IRR was 5 out of 6 which we saw with 8 mg was IRR of 2 out of 6. What we saw with monty look us was IRR of 3 out of 6 when I say 3 out of 6 when 3 got reaction out of 6. What is the point I am telling you is that if you were going to use dexamethasons that the dose of dexamethasons has to be 8 mg and not 4 mg

because 4 mg clearly
the study shows that it does not work. If you are going to use monty look us it is still
a reasonable but if you could see that it was only dexamethasons which went up to the stage 2 and
so at present we do not have to be very what you would say extra wasn't of trying to use monty
look us to all for methotrixet for air. We can stick with what up the pre-thum told but just to
see that the dexadose is around 8 mg in this and this is what passed the expansion stage.
So this is the prophylactic schedule which if you use where this is very similar to those of
who of us who got trained in the early decade of 2000 when when docile dexamethas was given
when the classic was to give one day prior the patient used to take dexamethasons then it was
very similar to that that the patient takes schedules before and then in clinic you give dose and then
that has reduced the incidence of IRR from 67.4 percent to 22.5 percent.
Now understand in exone 20 at present there is nothing else which works. So it is very important
that we administer this to the patients because many of these patients after going to the horrendous
experience of such reactions may not be willing to take further cycles. So and such simple interventions
in which you could use dexadose 8 mg would able you to give amiventinable exone 20 in such and safely
if no then frankly the patient if he is in June is not going to see the new year and if he is in
near December he may not be able to see the next whatever happens in July or August.
So this is what we need to understand and this is the first thing which I wanted to.
Now I do not know when this comes but you have development of subcuter is abiventinable with
intramunus abiventinable and the reason why I wanted to show you this study is because this study
very interestingly is not looking at OAS, PFS or anything this study actually is actually looking
at non-infinity of subcuter amiventinable and that is the co-primary end point which
are pharmacokinetic study. But even for the pharmacokinetic study interestingly the study has a very
huge number of around 400 patients and what it will lead to it will make sense to look at the
secondary end point analysis of this study also and I will not bore you. What it is showing is
if you give even subcuter it has similar pharmacokinetic properties and even if you give subcut
it has similar efficacy parameters with respect to the response rates progression be survival and with respect to the overall survival if at all it seems to be slightly better than the
IV preparation. Now the interesting thing was in this where when you use a substitute infusion
the rate of at present the discontinuation came down and also the if you look at the
allergic reactions it also came down. Now this is very clearly showing you the rate of allergic

reactions. Now let me come back to ROHIT. Now ROHIT we know that you use subcuter to use DEXA
incidence comes down. Another important thing which goes with ami-mentinab is venous thromboembolases and what do you do in your patients who are going to receive ami-mentinab
about venous thromboembolases and profile axis. So I think so I think the trial also profile
actinacuagulation was given in the initial phase of the trial I think we should consider that
because that is a significant. Correct. So please understand when you are going to use ami-mentinab
and if you are going to use the regimen of ami-mentinab pemid tracillin carboplatin classically say that it is not a tree drug regimen it is actually a four drug regimen the
four drug is anticoagulant. You need to give anticoagulant to these patients because if you
see if you do not give profile actinacuagulation one out of your four patients with ami-mentinab
is going to land up with BTV. So venous thromboembolism is important and you need to
give profile axis for the same and with that we will come to now Sangita.
The next thing which actually happens which is again I do not have slides for that is
rash and paranachia. Those of you which you have given ami-mentinab will know that reaction can
get managed BTV gets managed paranachia and rash and edema over the foot which are because of the
med related side effects they are very difficult in the patient quality of life hamper. So what
do you do in your practice for the same? You should be interrupt the cycles. So Sangita says I interrupt
the cycles okay this patient also is happy I am also in that. I mean see rash is something
very difficult but then if they are non-itchy rash and if the patient does not have the discomfort
then we always continue but if there is causing a lot of discomfort we definitely interrupt.
So that is correct if it is grade 3 or grade 4 it calls it. I do not have a slide set that is
in re-angi of infidel my request forward to give on that slide set of rash management and all.
There are good mitigation strategies which have come with respect to profile actically giving
antibiotics. Profile actically and I would request them to share with you all and if they can share
with me I will put in the group so that you all can have that. You want to talk about that?
There are cocoon trials so we are going the trial is going on cocoon trial where we compared
the proactive skin management versus the reactive skin management and where we gave the profile
actically antibiotics topical antibiotic for initial few days and then the systemic antibiotic
especially the tetra-cycline group of antibiotic and then the moisturizer and the chlorhexidine
gel for the hair rash and we are expecting that all the dermatological toxicity will be much lower
with amoebentumab with the proactive skin management. So since the data is not out yet and we are

expecting the data in ELCC next year so that is why I said he has MNC policies I do not have any
of those policies so I was previewed to some of the interim analysis which have been shown and did
actually look good in which giving chlorhexidine shampoos for the specialist. It is like giving
doxie for those that look at the patients. It looks like we used to basically like cetuxima
we did it here. Something very similar to the step protocol which was developed with cetuxima
very similar lines it is got getting developed which actually if you see that it is very difficult
if you have a patient on long term on amoebentina which they go to get pustules in the
scalp and in fact they cannot even do shampoo. I remember one of my patients whenever you
used to shampoo you used to do the cbc in accident tell me they come at a hemoglobin drop
over here because a long term scalp gets get some tans it is even it gets infected and the
quality of life with the patient gets bad because it stains very the order is not good. So these
are these are things which impact the quality of life of the patient the paranoid eye here is
the impact patients cannot walk the for this get swollen. So it is important that we have because
see in exon 20 now we do not have any options. So we need to see that how best we can give
amoebentina if in this and any prophylactic thing which prevents this is great. Now with that
we have some time left and let me take an opinion from the house. So what is your standard today for
EGF for exon 20. Standard is what is already the guideline but then on a routine practice
I do not think even 10% of my patients are affording for it.
Then we are not talking about non-effolding patients.
Then it is definitely chemo vata mevantima. So you want to give amoebentina blazer tineptovolio patients.
Chemo vata mevantima. No I am not anyone exon 20 now. Exon 20 over the last four minutes we talk
about afferent patient. EGF for right. Sorry let me make that. We are talking about EGF for TKS
sensitive mutations and commonest of them will be EGF for 90.
So we are switching on from the wasimartinib to this amoebentina blazer tineptovolio
How comfortable you are something to make the switch?
Oceomartinib will be the first choice.
He is very clear oceomartinib will be the third choice.
So probably flora 2 now with the oceomartinib plus pam clackinin.
So yeah I think the flora 2 trial.
So one other thing which we need to understand is that oceomartinib alone may not be the
best option for most of our patients especially if they can tolerate chemo vata therapy.
Either it can be the flora 2 or once laser tineptovolio it may be amoebentina blazer tineptovolio
So after the progression of oceomartinib what is there?
So I think the element of my place.
So that my cozeta.

So pam has already planned that if the patient would progress on oceomartinib and this and hence
deserving amoebentina for the later lines of that.
We used to do when when oce came you checked first and keep oceomartinib and then we
eventually switched on to oceomartinib.
But I think chemo vatae KAI we have been using and we are confident in managing side effects
and all that.
So probably I think.
So probably until later tineptovolio become a reasonable result also because of the perturbity
of neuropathy and has side effect related issues and we become comfortable.
Chemo vatae KAI might remain the option for most of patients who are reporting.
Now let me throw this to and let me ask Roushab.
Roushab if you have a patient of exon 19 and who has a p53 deletion?
So exon 19 with a p53.
What will you offer?
Funds is not an issue that is why you did it from garden.
Lazer tineptovolio.
So please understand that today if your patients financial concerns are not then that do not make decisions only on looking at the EGA part.
Please also look at the co-mutation button.
Question to the panelist and let me ask.
Pitham if you have a patient who has multiple brain mitts and he will see saying that finance
is not an issue with me.
Would you want to put the patient on OC plus chemo or you want to put the patient on
M.A.M.M.M.M.M.T. in a plus laser tineptovolio.
I want to represent the other tineptovolio.
That would be one sub-surd of patients with the.
Very yeah.
And this question again and I would want the J&J people to act.
M.A.M.M.M.M.M.M.M.M.
is a large molecule but we have been privy to data which show that
M.A.M.M.M.M.M.M.M.M.M.
also in patient with brain mitts has activity and how do you explain that?
So the possible explanation is the immune made use of M.A.M.M.M.T.
so it has been shown in the data that M.A.M.M.M.M.M.
activates natural colars cells as well as the macrophages and through antibody dependent cytotoxicity and the irritatinglla Tr Former
it is the possible mechanism since it does not process the blood brain barrier.
So same as that of immunotherapy, what has been seen with immunotherapists.
So actually that was one of the question my patient who had brain medicine asked me,
you are giving me an exone 20 aminoparid does not cause the blood-driven barrier.
But thankfully by that time in the SMO last year you had presented the data of aminatin
amin brain medicine already.
So does anyone have any questions?
Related to exone 20 related to EGFR, Afro-in relative aminatin aminat, laser-tenab.
If not, so I think to summarize this discussion it is very clear that in exone 20 insertion
at present aminatin aminat is the only option which gives a survival benefit to the patient
and a respectful progression fee survival.
Now and hence we need to know how to manage this drug properly.
Infusion related reaction, 70 we taken care of, VTV profile xities, profile xities

estimate
given and you need to be proactive with the pattern of pattern IKEA management and even
with the management of the skin ration, skin rationed this patient.
Now if you have an afferent EGFR, you have multiple options but with if you have especially
a co-mutation on what we call the high-risk disease today, flow rate 2 option or aminatin
people laser-tenab when laser-tenab becomes available in India, would be the good options
to go but if your patient definitely has brain medicine, aminatin people laser-tenab, in
our afferent patient seems to be a much better option even than the flow rate 2 option.
With that I think it is our time.
I thank the panelists for the good interaction and the Jainte people for answering our queries.
Thank you.
Thank you Vijay from whatever we understood was great.