Next session is a sponsored session by Pfizer.
I invite Dr. Akhil Kapoor sir for Marayar Sita Mottay, the session.
I also involved the panelists, Dr. Chandrokan sir.
Dr. Sathric, Dr. Tharajan was, Dr. Minit Shah.
Minit, my, Minit.
Shall I say requesting you to be in the panel as well, if isable?
There was a non-sponsored session before and, yeah, yeah.
So, the session which was preceding this, that was a last session.
In that non-sponsored session, that has already been shown and was discussed that Lola at NIB has definitely an edge over multiple other TKs, so that's not a doubt.
I think that makes our job much easier because when in a non-sponsored discussion, it has already been shown that what is going to be the best possible TK, it becomes easier for us.
Minit, your comment on this itself.
I think it leaves us with a very competent first-line treatment choice.
Usually we have doubts and discussions as to this is because of this and the other choice is because of this.
But I think it's set the field apart.
So with the data both promising in terms of activity, intra-kennel efficacy and safety,
I think it has set the field a little bit apart.
I think with the time which is coming, I think there is no requirement of panel discussion also for such a specific drug for L
because we know presently the best possible TK is this and there is no doubt about it.
If this is not feasible due to cost and other things, then how to go, that needs to be discussed.
But other things, I don't think there is a science which is lacking anywhere and there is a separate discussion required in terms of this.
That's not most any different.
I was just searching, you know,
Alka G1202 R mutation resistant to normal adenive right?
Yes.
And more sensitive to your tener.
So you should look into the mutation pattern also, which is more 2, 3, 3, 3, no?
G1202, just Google.
Just Google.
Okay.
So I think the thought process should be if the patient comes to you, which are the patients which you will not be giving L
latenib.
You know, that is the question what comes to you.
The choice is L
latenib.
But is there anything where you cannot give it and that usually happens, you know, when the, in an oncology institute, it's a different story.
But, you know, in a community medicine, when you're practicing community oncology, it happens that the patient is not going to do it.
It happens that the patient with brain medicine, L positive is already radiated when the patient comes to you.
I mean, that is a scenario where you think twice before starting L
latenib as a first line treatment.
So, Jadir Khan, sir.
There is a situation in the EJFR.
For example, patient was started on immunotherapy outside and the patient later came positive to be EJFR.
So it's the same thing which was we dealing with previously.
So we were using to start first line TKIs and then shifting to ocema t after two to three months.

Something like that will be applicable here.
What do you suggest patient has been given brain radiation and now immediately you don't want to start load at him.
Something like that will be applicable.
Right.
So there should be a bit of RT wash period.
But, you know, in a disease like L positive lung cancer, the aim is we do not want to do it.
We do not want on target mutation to develop.
Means I want to inhibit all the domains of ALK.
Only with that I will be able to attain the longest PFS.
And number two, I do not want the brain to be touched by cancer.
These are the two things because the moment there is brain met, whatever you do, you do SRS, you do surgery, there is going to be residual problem.
And number two, the moment there is progression, whatever next line of therapy you give, you will not be able to salvage it.
So the key is to give the best treatment in the front line because the PFS one is the one that decides the whole story and make sure the patient, if there is brain met, meditate away with a TKI, if there is no brain met, do not allow the patient to develop metastasis.
Because if you start the similar low latin in the subsequent lines, like third line, second line and beyond post, first or second generation,
TKI, you would have, you would have what is called compound mutations.
You will have G120 to R as Dr. Tara was saying.
So when you have compound mutations, even then this low latin may not work.
So therefore in oncology, the thing is if you have the best drug, do not keep in your pocket, give it to the patient, give the best PFS one because that is the one that decides the long term thing.
And make sure the brain is not touched by cancer. I think this holds good for all cancers and especially lung cancer.
So it is very, very clear that we want to avoid any resistant mutations, especially compound mutations to which most of the TKI's are not sensitive.
So what happens? We are now looking actually towards fourth generation LTK also because since low latin is being utilized so much,
there will be some mutations which are developing to which most of the TKI's are not sensitive. We do not have anything left after giving a low latin.
So, Minit, do you want to show some focus on fourth generation TKI's, L2TK's?
So till the time the data is well enough and it beats the current low latin standard, I think the standards are set quite high with the third generation TKI.
So the fourth generation has to, I think, better inter-kaline penetrance and the resistance mechanisms which develop probably should be delayed or impaired.
So I think I just want to stress upon what's servicing. So we usually don't talk about that cohort of patients who has servicing may be low latin potentially ineligible, ineligible.
So what about patients with familial hypercholesterolemia or hypertrichlicitymia?
Or what about patients who are already on mood stabilizers for mood disorders, schizophrenia? So I think more than the RT where I don't have a clear-cut data to show that why I shouldn't give low latin.
But what about these patients who are predisposed from before? Any changes?
So this is very important and relevant question which I wanted to come at and Minit has already highlighted that point.
Apart from radiation, these two other situations where we are somewhat concerned.
Familial hypertrichlicitymia, whether you can give low latin or not, if you are planning any other LTKI, whether you are losing something or not.
So these are the important scenarios. Familial hypertrichlicitymia, I think if it is well under control with the rosova statin, we can still give low latin.
And we had a patient, since we were doing genetic testing in a lot of patients, we had some interest in this particular aspect.
And SGPGI is doing testing for genetic component of hypertrichlicitymia.

The patient had a testing done and the familial hypertrichlicitymia.
The patient was started on low latin. Thankfully, she is doing well on 40 milligram of rosova statin.
So rosova statin was in higher dose than the routine doses.
Another situation which you highlighted.
So patient or mood stabilizer, whether we are able to give low latin or not. This is another scenario.
So sir, we were discussing and highlighting. Since we are so much convinced about the low latinib data, now there is no point in discussing when to give low latin. The point is discussion when not to give low latinib. So we changed the panel accordingly and we were discussing about that.
So patient who is on mood stabilizer, are you comfortable in starting low latinib or would you offer other TKs? What is your suggestion sir?
One patient where it is a troublesome having mood disorders.
But far uncommon then you will have few things. There are some episodes will be there.
But where I had to really get troubled and stop, it does happen. So if the patient is already on mood stabilizer, then to start this situation have not faced.
So this is important if someone is on mood stabilizer. But when that happens, it is really disturbing.
Because by the time patient starts responding, patient is good and inherently you feel kind of somehow you want to continue the treatment.
After that giving mood stabilizer, that also have not done. That patient, we stopped it and we changed the treatment if I remember correctly.
But yes, I agree with you. This is one drug which you will like somehow to give it. You will say if you are starting it, somehow you will try to manage side effects and see that patient continues the treatment.
Anyone, you are or anyone else's experience?
Anybody has in special situation? We have faced some situation already. Patient on mood stabilizer was three drugs from the psychiatry department of BHU.
And then patient was affordable for every treatment. Patient had taken opinion from MSKCC as well.
The patient came for opinion. Since patient had seen multiple publications on ALK from me and Kumar sir.
So the patient asked me, and the patient asked whether you want to discuss with sir also. So I had a small discussion with sir as well.
So this patient we did not opt to start on a law latin. This is the only situation I think is where we do not want to.
We are not very comfortable in starting law latin.
We may end up in future once we are more comfortable we may end up.
So we are a 30 year old lady whose presentation was altered behavior.
So MRI CT done there is nothing. And then ATTT taken there is no response.
And then someone did an MRI and there is a meningial uptake.
And they did a cell block and liquid and it came as ALK in that.
So for that patient was said on Lola. So patient was in CUN almost 3 and a half years.
So I mean just a bleptom meningial disease can also be an ALK present here in their lymph nodes.
And they were sort of reactive reporter. So that is such rare presentations.
So make sure you are not treating a brain problem due to ALK when you are.
And the reason why there is bit of psychological disturbance due to Lola is a bit of NDRK pathway.
That is a probable reason why you have the psychological disturbances.
So bit of NDRK pathway is also little bit inhibited by Lola latin.
So the good thing about Lola latin is that it is penetrating brain so much that there is less transfer of developing further brain metastasis.
And disease control in the brain is much important.
But if we get to have access to four generation drug which is going to be developed is under development.

Again we will be very much concerned whether it is having much higher neurological toxicity.
So we all want to see higher generation drugs but whether that will solve the problem or not
because we do not want to reduce further quality of life as well.
If there is higher neurological toxicity I think most of us will not be agreeing to utilizing first line drug
which has higher neurological toxicity than Lola latin.
With Lola latin we have now become comfortable because we have now some experience.
Thankfully we started to have in second line a lot of patients had compassionate access drug which the data was published by Amit
and we had discussed this yesterday as well.
And this is the area we want to understand.
Again the problem is that 20% patients will develop brain metastasis despite seeing a spindle in second line drugs.
So this was the usual paradigm.
We started with serotonin.
So serotonin is mostly out when it is not being utilized through access program but if the patient is affordable cost of
chryso and serotonin are nearly similar most of the time we start with serotonin if third generation is not feasible.
And then what we see?
20% patients are serotonin are developing significant progression in the brain that is causing a significant patient's percentage of the patients to
drop out.
So 25% of the positive patient do not receive available next line therapy.
That is the most important problem.
And we have seen this in our own data set which was published in JTO actually.
The 441 patients data set of L positive which was published from Tata Memorial clearly showed that a significant proportion of the
patients cannot receive second LTK also.
Though it has been discussed in multiple other symposiums that as a forgiving disease you can use next generation but what I feel is
that always if the patient progresses in the brain the problem is that the patient's quality of life will be so much deteriorated that
you will think whether you should treat or should call the day off.
Taritan, do you agree with the same?
Yeah.
Completely.
I got the brain mass related.
I'll make the right.
Yeah.
So all these data sets are already clear.
The response is crown data that already we have 5 years data between available.
So we want to just come to the very rapid discussions.
At 60 months median follow up median PFS was still not reached with law alert and this was just 8% with a
crosotene.
So this is about the PFS.
I would request you to highlight the situations of concomitant mutations again.
This is very relevant in EGFR has been discussed multiple times in which scenarios of concomitant mutations and the
variance of ALK you'd be thinking that these patients are going to have poor prognosis and poorer outcomes.
The crown data was really excellent but the only scenarios which where the crown data reached the median one was the
median three.
So we all know that variant one, two and three does have a prognostic impact and variant three was the one where

actually reached the median of 53 months.
Another very troublesome scenario is TP53 but it's important to know that all TP53 mutations are not the same.
It's important to know whether it's in the DNA binding domain, not in the DNA binding domain.
So just the mere presence and waff of TP53 is not important.
It's important to talk with the MTB team and the molecular oncology and see how much of an impact it has won.
It's been the data is there of TP53 but a number of other concomitant mutations also have an impact as we've seen in
EGFR there is CTNNB1, we have SMAD4, we have service talking about MTAP and also all of these concomitant mutations do play an impact
and we should have two as a bifurcation.
Presence or absence of TP53 or presence or absence of any concomitant mutation and we'll see that that cohort also does make an impact.
So, yes that's about it.
I would like to comment on the variant. Do you think having knowledge of variant will be useful when you are utilizing the treatment in ALG?
If we are now giving lower latin A upfront to most of the patients, so I don't think earlier when we were using then the variants were more useful.
And if a patient is borderline patient is doubtful whether I should start with lower latin or some other TK due to cost constraint.
In which variant you will be more pro towards utilizing lower latin A?
So, I think the three is well known that is the variant.
Because variant three is known to have poor prognosis and with variant three the median PFL with the chryseo-tin A comes down to just six months or even less.
So, that is the most important that patients who are even on drugs like electin A.
And some patients you see they are progressing within four or six months of starting treatment.
Most likely these were variant three which were not previously tested properly or this detail was not available.
Because most of the time labs report as an ALG fusion and we don't ask for the type of variant.
But thankfully in the can make centers like the image we are now clearly reporting the variants as well.
I think that was, so the concern this is useful information for problem-sticating and choice, some choice in the TK as well.
Very important, so one of the first experiences of Lola for me was chryseo-tin A.
Three months progression, ALG positive by IHC and negative by fish.
And then we gave PEM, carbopem maintenance for one year and then progression.
And then we did a rebuyopsy and sent for a comprehensive genomic profile.
There IHC was positive, NGS variant three mutation.
And now it's almost three and a half years, Lola progressed.
So that is how it is important.
So variant three at times, IHC was positive but your conventional fish may not pick it up.
So we need to be careful before we decide on this.
So variant three is important.
That's the importance of getting a good quality NGS at the baseline itself.
People ask you are 50% when I quote the data that 45% patients or team at YANSI are easier for positive.
So the need of doing NGS, I think this was a very relevant question which a patient actually asked me.
I told the patient, up KNGS, EJFR, exone, PENTI, and IIA, or EJFR most horn mutation,
HVATA, KIHAMARASO patients from Petaliska, EJFR, BOSTI VATA.
The patient which has a NGS QIA, OSNAP, VATA, KIITPC, ROTA, VOTA, VOTA, VOTA, FASTA, REPORBIA.
The patient asked, this is the importance which is difficult to communicate to the

patient,
but yes, we need to know about concomitant mutations.
We need to know about various other probabilistic factors.
If the NGS is being done at the same time, we know that we can get knowledge of various other things at the same time,
which we discuss about STK, KEEP, and if the tri-vore notation is negative.
So this is the importance of having a good quality NGS at the baseline.
This is a one-time investment, but very useful for the patient.
So don't back out of it, even if your 50% patients are EJFR, L-POSTI.
So this is the intracranial progression data.
I think this is very, very relevant.
Shall I just try to highlight this data and how much is this of relevance?
So I think I can't see the HR, but HR is zero point.
So that's what I'm saying.
I'm not able to see the HR.
So that is the data.
I mean, hardly anybody is going to get progressed in the brain.
And one of my friends actually had an alc positive lung cancer and he progressed in two years.
So the issue was like Dr. Ula's, Bhattra said, 30% of the patients are anyway going to progress in two years.
But also important is to know the compliance, because when I really went into deep into it, the compliance was not there.
So I mean, like you always blame that the disease has progressed, but also important to know the compliance of the drug.
So compliance tends to be poor in TKI mostly due to cost issues.
So that is very important that we are counseling the patient about the TKI.
We should ask them to continue at the proper doses at us wise.
If it is requiring dose reduction due to toxicity, it is fine.
There is already data if you are reducing due to toxicity, it is fine.
But whether the dose reduction is like for example, patients starting in the alternate day to reduce the cost, whether that is as effective as we don't know.
There are some studies which will be upcoming for that also, but that is very relevant question and we will see it later.
Okay, sometimes the real challenge is also quite effective because the one patient of mine was on lower latrine for six month.
The six month patient was in, the patient was responding.
He was getting from ESI, but he was still out of pocket.
So he went, I wrote for the two months of the lower latrine.
It took only one month and then went for some let do, Baba's let do and came for two month after that.
Sir, please check my city scheme.
Yes, it is now controlled still.
Well, I have left the lower latrine and I am taking let do.
And after two month again came and then the disease was progress.
So he asked me to write it again, but it is not possible to write in ESI again because if the disease has progress, then I asked, do you have medicine?
So he told me that he is having medicine for one month and he took that and after that patient was again responding and I restarted and now patient is coming till now.
And he was the first of my patients of lower latinib.
Now four years are going on.
So that's when the patient is not compliant or has stopped treatment, then most of the time he challenge helps.
That is a very important point which has been brought about.
Dr. Satriyak, you have discussed again your comment regarding a situation.
Sometimes we use to think lower latin will be best if the patient has baseline brain metastasis.
When the patient doesn't have baseline brain metastasis, still is it useful or you

can go away with second generation TKs?
No, even without brain metastasis, if we see the results lower latinib is still useful and it should be the first priority.
Because patients will progress in the brain.
They will progress in the brain.
So a message for the students specifically.
Patients with or without brain metastasis lower latinib remains the drug of choice with the available data because it is relevant in both the settings irrespective of presence of brain-land brain.
And if we see the intracranial response rates, this is very relevant because we were discussing about the sto-tactic radiation.
We were discussing about other modalities of the radiation and the patient is asymptomatic without much edema.
So to answer what is your comment and how do you first consider your radiation oncologist, then consider patient.
So I personally believe if someone is going to live for 3-4 years, 5 years, radiation should be avoided in all situations.
So if a patient is not grossly symptomatic, even with mild edema, you start the patient and Lola and do an imaging after one month
and make sure that it is not progressing.
So these patients are going to live long and WBRT is a big big no when you are giving Lola.
Unless it is a very gross disease.
The moment you give radiation, there are toxicities.
He will keep on needing Dixa and he is going to live long.
That is for sure.
So radiation oncologist Sathas tells us that we will not give WBRT, we will give SBRT only.
What is?
Even if SBRT, there is going to be some neurodiphesit or whatever.
So actually in our MDT now the uniform unanimous decision is to delay RT, whether it is SRS, SBRT or WBRT, because now the concept of driver mutant positive and a good brain penetration with the TKI is well accepted in the MDT.
So we all, even though our radiation oncologists are primed that if it is EJFR or ALK and if we are able to deliver the TKI, then we will delay the RT.
As long as the patient is not symptomatic.
So what is your concern with SRS?
So no absolute concern.
The only thing is we all know that WBRT, the side effects are developing at the end of one and a half to two years, the side effects are developing in terms of cognitive decline.
We do not know when it will start for SRS.
So although SRS is highly specific as what Dr. Chandrkantu saying, maybe we will see it five years or six years, some like necrosis, long term necrosis area.
So necrosis is very, very troublesome. When it develops, it will not develop in all patients.
It will develop one in ten patients who have received SRS, but that will make you suffer so much that the patients will have a tough time managing radiation necrosis.
We have utilized lotus devasizumaph or radiation necrosis with ALK, with all that ongoing.
Some patients had some benefit for radiation necrosis, but it is a difficult challenge that a patient is diseases well controlled, but a patient is suffering because of the radiation necrosis.
So that is why we are very concerned. So this is a very important message to our budding medical oncologist that have a discussion with your colleagues.
When you are discussing it and ask your addition colleagues, what are the expected toxicities?
Your addition oncology colleagues and other colleagues should be able to tell the

toxicities and whether it is going to hamper the quality of life of the patients. And whether it is that treatment will actually be helpful or not in the long term. If you are using drugs like low alert, it becomes much less useful to have given SBIT in such settings.
But if a situation is not able to be started on low alert, like most of the patients are able to receive grizzot in due to support program, then it is fine to utilize radiation, correct?
So this is the subgroup analysis. Poor domestic biomarkers we have discussed variant 3 and 3B. A good point is that for with P53, again I will request Shalesser to highlight the P53 mutant outcomes with low alert in M.
I think the outcome with P53 is, we all know that it is a poor diagnostic marker. So presence of P53 is going to have a poor prognosis.
So a good point is that even with P53 mutation, many had highlighted a useful point. Many P53 mutations are different.
We are usually collating all P53 into one subgroup, but that is not correct. Some P53 mutations are not so bad, but most are bad.
And P53 mutant, the expected PFS with electinum is 18 months, that is the subgroup analysis. And with P53 mutation, the low alert in the PFS is 51 months.
So that is no comparison. And there is no doubt in poor prognosis subgroups you are utilizing low alert in it.
And we always check that is why P53 commutation, which is a very, very important aspect.
And we strive to give low alerting by some other mechanisms if the patient has P53 commutation.
So coming to the safety and efficacy, we had very initial discussion because safety is the only concern actually, because everybody is convinced about efficacy.
The safety was the main concern, but now I think with the valuable experience and everything, we are becoming much and more and more comfortable about the safety part of this.
And as it was being discussed by Velasad in his previous panel, the patient has some difficulties, disturbances.
First you should have detailed counseling to the family members, close family members.
Spouse is looking together. The spouse will be the first person who will notice some changes, because patient himself or herself will not be able to note that because these are subtle changes.
And these will be noticed first by Spouse. And what we have, we have written in our counseling brochure that is stopped for some time and report to the hospital, either by mail or come to the hospital.
That is what we do consult over patients. And when we see that within 48 to our 2-3 days, that is 2-3 days, the effect again starts to wane off.
And the most important part is that these toxicities will develop much and much more in younger patients.
That is important because any of you, in your, the sheet that you attach for patient counseling, do you consider doing MMSA at baseline for these low latin patients?
It is advisable, it is advisable as beneath the strength to highlight because these are subtle changes.
And the patient is already suffering from a diagnosis of cancer. So the changes, mood changes are due to the drug or due to some psychological disturbance due to diagnosis of cancer per se. That is very important because we have seen patients of cresotin have also having mood disturbances, but that is not due to cresotin, that is because of the diagnosis of the cancer.
So that is an important concern and this is a very valid suggestion. We should have a baseline MMSA if feasible so that you have a ready
to compare when the patient has some of this disturbance. So that is a very valid comment. So the concern, any comment on this baseline MMSA?
I totally agree, you know, you need to be knowing whether the patient has baseline issue or whether it is developing over a period of time. That is an objective way

of assessing it.
And rest other toxicities of low latin are mostly paper toxicities which we have discussed and covered multiple times.
Rosova statin and phenofibrate are very commonly utilized. Atova statin is a no-no because of interaction with low latin. So that is an important message.
Atova statin is to be avoided when you are treating low latin have induced hypertradyl acidemia, but Rosova statin is the preferred one.
You can start with 10 mg and it is correct up to 20 mg. Most patients will do well with 20 mg.
So my patient asked, you know, after 6 months, my cholesterol is so high, will I die of heart disease? So there is data that the cardiovascular mortality is not much even if there is cholesterol. So it is fine, it is not that bad cholesterol.
And the point is that if there is uncontrolled cholesterol, the effects start to develop in hurt and vessels after 15 to 20 years. We are yet to see so longer follow.
So what will happen after 15 to 20 years? If the patients are able to survive to that duration, then it will come into mechanism.
And then you...
Somebody who already has, I think, a little bit in here there.
If you are not able to control it, then it becomes an issue. But if you are able to utilize Rosova statin and is it in the most of the time it is well under control.
So that is why it is called paper toxicity.
Another problem, fatigue and edema.
This...
Tarajan was any comment on edema management with lower or lower levels or other met inhibitors also. Both have similar side effects.
What am I doing in my op eddies usually whenever the...
Even any patient of any disease is coming, we are checking weight. That is the practice from the TMH op eddies.
We are taking weight of every patient and that's why we are monitoring the lower level of the patients also.
And if there is a weight gain or there is a pedal edema, we are adding like a lacy lefthon half-tablet in the morning only.
And that is more than sufficient to control it.
And some weight is your therapy will also have.
So utilizing drug, utilizing some life-changing parameters and then utilizing lacyl lefthon is very useful.
So let's come to one of the cases because we have covered all the toxicity part.
This is one of the real cases treated at TMH Varansi.
64 year lady shortness of 3 months, PS2 at the baseline.
Pet city swinger, large mass, right lung mass.
Adino cars rumour, PDL-126, NGS was awaited. NGS later came as to variant 2, which is a rare variant actually.
And this was E28-20 fusion.
And this patient was started on Lohr-Lartnib and you can see the responses.
And these are the further responses at 6 months.
This patient is on 100 milligram Lohr-Lartnib and remains in near Sierra from nearly 4 years of therapy.
So this was one of the initial patients which was started on Lohr-Lartnib when I moved to Varansi after Mumbai.
And the patient has on managed, happened to repeat, he is there.
But Rose was at in 10 mgs being utilized and patient is doing well.
So it's very clear. There's no doubt about that.
Lohr-Lartnib is the standard of care treatment.
And it remains the standard of care.
There are some pros and cons which needs to be identified and covered and discussed with the patient.
And you need to learn how to manage the toxicity.
You don't need to blame the drug toxicity.

It is, onus is onus to manage the toxicity well and discuss with the colleagues who are having higher experience of managing the toxicity so that the patient can get the benefit of the best possible treatment.
With this I would like to end here. Thank you for the presentation.