So we move on to the next session which is sponsored by AstraZeneca. It's a panel discussion integrating IO in the management of early lung cancers in both operative and inoperative settings. I would like to request Dr. Smriti ma'am to be the moderator for this session.

I'd like to thank the organizers and AstraZeneca for giving me this opportunity to address this very new entrant into the treatment of early lung cancer. Let me call upon my panelists, Dr. Kumar Prabhash, medical oncologist. You know him very well, so I don't need to introduce. Dr. Minit Shah, medical oncologist. Dr. Virendra Tiwari, surgical oncologist. Dr. Priya.

You know her very well. And Dr. Tondse. So just one medical oncologist and two surgeons, right? Okay. Yeah. So, you know, there's an unmet need that despite surgery and adjuvant therapy, as you see that you go down the stages, 1B to 3B, the five-year survival reduces from about 60% to just around 26%.

which means that we need to do a lot more to improve these results. Now, without much ado, I'll just get into the issue that till now we have been using chemotherapy, but we know that the absolute benefit at five years is around 5%. And I've already shown you what are the five-year survival rates depending on the stages.

Now we have come with the new era where the immunotherapies and also the targeted therapies have made their way into the treatment of early stage lung cancer and have definitely improved the survival. So these are some of the data regarding this, but I won't go into the details, just summarizing that it's around 5% benefit.

So let us come to the case and see how we could integrate the newer therapies. Today, my panel discussion would be on the integration of immunotherapy into early stage lung cancer. So you have a 60 year ex-smoker female, no comorbidities.

And then an incidentally detected lesion in February of 24 during a cataract surgery. And you can see the size of the tumor is 34 by 22 millimeters with the right hyalur lymph node. And that is seen over here. This is the primary tumor and the hyalur lymph node as seen here. So this is what the baseline imaging shows.

Now, coming to the panel, how would you investigate this patient apart from biopsy and histology? So let me first come to the surgeons. Dr. Priya, what would you do in this patient?

Yes, thank you ma'am. So we have done a PET CT scan as you have shown. We have done a biopsy and histology. I would also like to do a mediastinal staging. She has already got a right hyaluronide, it's also T2. And MRI brain is what I would do for this patient. So how would you do the mediastinal staging? I would do an EBUS ma'am. Frankly my institute would prefer an EBUS plus minus EUS.

And the biopsy and histology, I would also send it for the molecular panel after discussing with my medical oncologist. So here I would like to ask the medical oncologist, in early stage lung cancer, what do you do? Which biomarkers do you look for? So Dr. Kumar Prabhas, then Dr. Tonse and Mini Cha. So at this moment, at our center,

end up doing broad molecular profiling. But I need to concede the three of them, which is important in today's time, if the patient can afford everything to decide treatment, that will be EGFR, ALK, and PD-L1. That is something which will be required. If they can afford everything, we can have an argument. If they can't, then what to do? But maybe we can like...

I concur with sir, preferably broad NGS panel or at least a PDL1 and EGFR and ALK testing, these three.

So I completely agree with, so that's what's been routinely advised in all of the trials and EGFR and ALK is the only thing that we need to rule out. But we know that the PCR rates vary between 20, anywhere between 20 to 25%. So we know that one in four do achieve, but we should know that three in four do not achieve. So if possible, a broad panel to know if it's not

EGFR and ALK, then what exactly it is. There may be some other mutation which may confer resistance to immunotherapy and chemotherapy. So we know that ROS, RED may not respond that well to immunotherapies, although they'll be included in the trials, but it's good to know. So if somebody asks you, why have I not got a response while other patient has got, so we need to know some answer. So

by trial wise EGFR and ALK should be ruled out, PD-L1 should be done, but a broad panel testing would be advised. This is for the because there are students. Is there any patient where you will go ahead with surgery without biopsy or FNSE in any situation?

No sir, I don't think we should. So, suppose multiple biopsies are negative then only surgical intervention to get a histology is needed otherwise without biopsy because extent of resection varies a lot. So, size of lesion and the type of disease it makes a difference plus our country is endemic for a lot of other diseases. So, it is better to have a histological diagnosis then only plan for a surgical management accordingly.

The idea of asking this question was primarily for the students. If you read NCCN, you may end up having a certain group of patient where you can skip biopsy, you can go ahead for surgery, but you know from two very prominent surgical oncologists dealing primarily only with lung cancer. In Indian context, usually we don't. We end up having biopsy.

and then move forward in spite of having a small lesion also if it is there. So, it is good to do it before you go ahead. Yeah. So, quickly, you answered this third question that what you need a biopsy and the surgeons have said that if repeated biopsies but they're still at the table, they would try to get the biopsy and prove that it's before proceeding with the procedure.

Now, I want to know from the medical oncologist that do you need PD-L1 in early stage lung cancer for taking decisions on immunotherapy? So, I would like to know that. So, why are you doing the PD-L1? A little loudly. PD-L1 positive report which is more than 50 percent would be very good. We know that it's a

biomarker for response to IO therapy. So, irrespective of the PD-L1 status, we add IO in the new adjuvant setting, but for prognostification and to assess responses, I think I would definitely want a PD-L1. Also, the type of immunotherapy varies, type of checkpoint inhibitor, which I'm going to use depending on the PD-L1 status. How would you do that? So, PD-L1 negative, I would be very comfortable with using nivolumab.

if it is PD-L1 negative. PD-L1 positive, PEMBRO or artesolizumab, both are good enough. So, would the others want to add

For want of time, be brief. So PD-L1 not to decide on treatment. So it will be chemo and IO if it's an eligible patient like 2A to 3B. PD-L1 definitely does have prognostic value. We in fact don't use PD-L1

in early stage to probably guide the choice of IO. But PD-L1 just for prognostic, not to decide on treatment. The treatment plan, if it's to be chemo IO, it will be chemo IO.

Dr. Kumar. So, I think why you require PD-L1 is a bit of a reassurance. I agree with many that you end up giving same treatment, but I'll tell you where it helps you. So, there are times when you are a bit query about giving immunotherapy. There are situations where you say, will immunotherapy end up harming patients? In certain situations, like if you have a, you know,

autoimmune disease or certain situations. Then if you have a PD-L1 of 0 percent and 50 percent, that you may end up deciding. Because there is a data that more the expression, higher the benefit in almost every situation including neoadjuvant setting. That proportionate benefit is different.

But remember that you will end up in situations where you are query about that, do we give or not? And that time, this becomes useful. So, which one would you use? The PDL1 antibody? Platform. Okay. Unfortunately, till recently, we had only 263. And believe me, we used to say, but believe me, it was comfortable situation because DACO is costlier.

and now we have two options. So, we end up with 263 by and large, but I won't mind, I request others, my two colleagues. Generally, we use 22C3 and if there is a panel which has been sent outside, then which is usually 263 is the one which is done. Okay. So,

So, the only thing reassuring is that 22C3 and 263 has good concordance. So, concordance is more than 96, 97 percent. So, the only thing is reassuring, but we've like 263 is what we've been commonly being used at. I agree. We all want 22C3, but if you do others, you are okay that, you know.

So I think the take-home point from this is that it does not come in the decision-making of giving the immunotherapy. It just sort of tells you that, as Dr. Kumar Prabhas said, in difficult situations, whether you'd use, and I think stage two, and if you see the latest 2024 IAS CLC,

recommendations. It was a consensus statement only covering incorporation of immunotherapy in early lung cancer. In the adjuvant setting, where you have not used new adjuvant, then if it is 0%, then they do not advocate

get adjuvant immunotherapy. Also, I think stage two it would be important because this is highly respectable and you don't want patients to progress. So, what do you have to say on that? The stage two. Stage two, today also if you take most of the guideline, they put it that you do surgery and then you think about adjuvant and they write it in case you plan for a new adjuvant. So, that challenge is there.

This is for again for students. Remember those patients stage two becoming un-resectable, that is not the real case. You see that 20 percent patient not going for surgery. These are not those stage one or stage two patients who becomes un-resectable. These are usually higher stage patients

And this number, if you have a median time for surgery in any setting that's around a month, that's overall if you take across the world, unless you have a private setup you can do it tomorrow or day after tomorrow, you will have this number of patients falling through in lung who will be resectable and they don't go on table.

So, and that is one of the things to remember in neoadjuvant setting that the data which gets criticized for this 15-20% patient not going on table is not because of neoadjuvant. These are various other reasons you will have it which may not go on table. So, stage 2, if you plan, it's okay. But what madam is trying to convey, stage 2, doubtful, you think immunotherapy may or may not be given, no.

better send the patient on the table and then see the patient later on what you want to give an argument. But in case, if you have a stage three, you need to push that these patients are systemic disease better to give new argument. But if someone chooses other way around,

I won't debate with the person. Because you have a natural, it's called natural for chemotherapy, which was far inferior than what we have chemo plus immunotherapy. And there are a whole lot of stage one patient into that. In fact, that was the criticism for the trial. And if you take new adjuvant and adjuvant, that was compared. There was no difference between the two arm, suggesting that stage one and two may not become un-resectable in these times, in majority of the time.

So I absolutely agree with that. So if you see any new agent immunotherapy trial, there is another arm with new agent chemotherapy. So if you see dropout rate in chemotherapy compared to chemo plus IO, there is no statistically significant difference. There is a dropout in chemotherapy arm also. So whenever you start a treatment, any treatment that gives you idea about the disease biology and which is very important.

So, it is not because of IO factor alone. Whatever treatment you have started, if there is a two month or three month of treatment going on, you are bound to lose some patient.

I think that is what has happened in your new adjuvant immunotherapy trials also. So that's the important point. The new adjuvant therapy helps you to actually identify the biologically aggressive disease where even if you were to do upfront surgery, these patients might do badly later on. The PET CT confirmed what was shown on the CT. The MRI brain showed no meds. And it was, of course, an adenocarcinoma.

EGFR and ALK negative and PD-L1 40%. Now, I just want to know, the surgeon, you know, after all, EGFR, ALK does take at least minimum two weeks. So, in your practice, have the patients accepted that waiting period of maybe two to two and a half weeks to get this report before putting them on chemoimmunotherapy?

That depends a lot on the counseling, ma'am. Honestly, if it's a good MDT which has been conducted and if the patient and caregivers have been explained the entire situation. I have seen at least 60 to 70 percent of the patients are okay to wait. In a place like institute like TMS, they have no option anyways but to wait. So, it's all right. But in private setup, I think that if it's a proper MDT and a proper counseling has been done, they are ready to wait.

And if not then yeah very honestly stage 2 is still upfront surgery. So if the patients are not willing to wait or they are going to do a shopping and rather may land up on the wrong side of the treatment it's fair enough to go in and operate those patients. So here you know the patient had the hilar lymph node was positive but rest of the nodes were negative on EBUS.

And now I want to come to the surgeons again. The prerequisite now, you decided to do surgery on a patient. So about this showing how the pulmonary functions are. So what are the values at which you take the cutoff?

So, in your initial slide only you had mentioned two points. One is that patient was a smoker with 10 pack here, another thing bilateral emphysematous changes. Yeah, mild but it was there. Yeah. So, in imaging that you had put, I could see a little bit of ILD kind of changes over the right lower lobe basal area. And DLCO, if you see it is 46 percent.

and it was a low five segment will go. So, predicted post-operative value in this case is going to be slightly lower than 40 percent. If you see ACCP and other guideline, they say 30 percent cut off, but in Indian setup what we have seen less than 40 percent they fall into high risk. So, this is what we need to be very well aware of that is pulmonary functions are not very adequate for a surgical management.

Dr. Priya? Yeah, so along with these two, the DL still takes 46%. She's got a reasonable six-minute walk test. I would see her effort tolerance overall. We'll do a room air ABG also. If there are facilities which are there and she's affording, we'll do a CPET.

that is again if it's possible if not and if uh i mean it's not available everywhere then uh taking that due risk i don't think she's going to her emphysema is going to improve but yeah if she starts on some new adjuvant therapy then we have time for pre-habilitation

If not, then it's borderline. Might just be able to do it. But you would still think that this patient could be eligible for surgery? Yes, yes, it is. If patient is not willing for... Eligible for surgery. So these are the important tests to be done beforehand. Now, coming to what is the stage of the disease? Anybody? Quick. Any one of you? I won't ask all of you. This is a... We said between...

3 and 5 cm tumor and a hilar node positive on the ipsilateral side. So what would be the stage? 1B2. Yeah. So this is 2B. So what are the treatment options you would consider here? Like, surgeons, would you like to do upfront surgery?

Maybe a few years back I would have probably argued for that very strongly. But now I think it's very operative. Chemo immunotherapy is also coming in with the agent trial. So it can be either of the four. I think marks should be given for all four, but it depends on the MDT. So my take is that if patient is fit for immunotherapy in his treatment protocol anywhere, then I will prefer new agent.

because it is highly known positive to be and he is going to benefit with that. That will give us also little bit of down staging. So I will prefer neoadjuvant chemo plus immuno if patient is fit. And we get time for prehabilitation which is very important for her surgically. So the medical oncologist, do you agree with the options that the surgeons have chosen?

Preoperative chemoimmunotherapy I would consider in this patient because smoker PD-L1 is positive and stage 2B. So you know that the overall survival at 5 years is not high in these people. So giving a neoadjuvant chemoimmunotherapy would definitely improve the EFS and

So I want to ask the other medical oncologist. What is now suppose the surgeon says I leave it to you whether you want me to do surgery then you want to give adjuvant immuno because the PDL one is 40% or you would want to do it the other way. So how do you select this? So I strongly favor for new adjuvant chemo I or hands down.

for a number of reasons. That is, tumor being in situ has a good modulation of the immunotherapy for the responses to, that is chemo, that is one.

Tolerance of the patient to initial cycles of chemotherapy is much better as compared to post-surgery receiving adjuvant. So we know that the number of patients completing adjuvant is lesser as compared to those who receive neoadjuvant. Thirdly, they know that their definitive treatment at a surgery is not done. So compliance rates are higher for the neoadjuvant setting. Fourthly, there is an option that we know that PCR is number one, a good prognostic factor, good prognostic indicator.

And fifth, completing adjuvant will be one year of treatment. So there can be a second counseling if there is a patient achieving PCR and there is financial issues. So there can be a counseling of yes versus no to adjuvant. So there are a number of proponents for new adjuvant.

So I think all the medical oncologists would opt for a new adjuvant rather than this and I think one of the important rationale for new adjuvant immunotherapy is that you have a tumor in C2 and that's why there are new antigens which are produced by the action of the chemo on that and that leads to a heightened effect of the immunotherapy whereas in the adjuvant setting

you don't have the tumor, so the new antigen load would be low. So that is one of the important facts about this. So we have already addressed this. Can I add, madam? What has been said, we have heard, but if your surgical colleagues choose the other way around, don't get him wrong. That is also one way of doing it. So madam is suggesting that both ways of doing is fine, that you do upfront surgery, then you give adjuvant,

chemotherapy, menotherapy and other way is that you give new argument chemo immuno and then go ahead with surgery with tilt towards by the time you pass out and all you'll see more and more will be new argument rather than argument. So even in the consensus statement they kept as a stage two non-consensus recommendation for new adjuvant chemo that's why I chose a stage two disease patient

Whereas for stage three, there are no such debates. So, it's straightforward, you would use a neoadjuvant chemoemine. So, this is how the- Just adding a line, we are colleagues together and at our center, there's a TMH, we end up doing surgery followed by adjuvant today also. So, it's a slowly changing process. Stage three has moved on, but stage two still we do. Yeah. So, this is how the whole molecule, I mean the-

tumor board, multi-speciality tumor board. So you need all components to come to a decision on this. And this I've already addressed why newer adjuvant therapy is preferred. And this is the latest AGM trial where durvalumab with chemotherapy was compared to placebo with chemotherapy. And then after surgery, the durvalumab was given for 12 cycles. So this is, as you can see, of course, that

those patients they were all resectable stage 2A, 3B according to the AGCC 8. Now even when I show you a slide of all the trials, it will just to show the results but you cannot compare head on because some have used AGCC 7, some have used AGCC 8 and then some of the exclusion criteria.

it's only to get a flavor about the results. So you can see that most of them had an N2 disease, like 49%, as you can see on this side, had N2 disease. And of course, if you look at the staging, then about 47% was stage 3A, and PD-L1 expression was seen between, I mean, evenly distributed in all those subgroups.

groups. Then of course if you look at the treatment summary, so this is the modified intention to treat. That means you exclude later on EGFR and ALK positive patients, so it's called modified. Now you can see those who underwent surgery were almost equal in both the arms. And the adjuvant phase also you can see that

they were still ongoing, almost 65% of the patients. And R0 resection rate was very high, like 94% on the durvalumab arm and 91% on the placebo arm. So that's very important. And completed surgery in almost equal number of patients. So why I'm trying to bring out this slide and also...

this EFS has been proved to be significantly better with the chemo-immuno versus the placebo arm. Then of course, across all the subgroup analysis, this benefit was seen. So that is also important.

Now, again if you see the difference in the PCR rates, that is very important. That was highlighted by the medical oncologist that you get a PCR rate which is significantly better than just chemo. So, you can see it's almost a 13 percent difference. If you look at the major pathologic response, the difference is almost 21 percent. So, downstaging and pathologic complete response rates very important.

And look at the number of studies which are going on and that is why the medical oncologists find it more and more difficult to select which treatment. And the reason is this table. If you can see, no doubt in the Checkmate 770, there was PCR rates were higher, but it's around the same. As I said, you can't do cross-trial comparisons. And if you look at the

EFS in all they were positive so they're significantly better. Overall survival data you have only for Pembroke-Luzon map and that shows that significantly better and all the others are trending towards the same results. So how do you choose an IO? So you have clearly said that there is no sure way of choosing. I think anything you would want to add to this?

So even the NCCN guidelines mentions the same drugs like Pembro, Nivo, Durvalumab along with chemotherapy and then you have two Chinese entrants also, which of course we don't have access to. Then of course

we have addressed this question that how do you decide whether it should be new adjuvant or adjuvant? I think this will come only in stage two. Stage three, I think we are very clear that we would go for the new adjuvant setting. So, um,

Again, it's a multidisciplinary team and this patient received four cycles of chemo with Dervolimab and the response was assessed after four cycles. What do you do in your practice? When do you assess for response? Anybody? Just one person, anyone take. After four cycles. We have only three minutes. After four cycles and we do a PET-CT scan. Yeah. So, this is what was seen post. You can see the response here.

Now, how would you reassess like CT or PET-CT? Quick, anybody. At our institute, we do a PET-CT. Yeah. Now, anybody else? Now, what are the pitfalls of imaging after chemoimmunotherapy? Anybody?

You have to be very careful about the pitfalls. Yeah. So, I think so what madam is trying to suggest that you may find something new because of pet being there and immunotherapy being there and other parties, it underestimates the response of what you see in the scan and when you see a pathology wise, there's a fair amount of discordance and if you see major pathological response, they don't match with what you see as a partial response as far as the resist is concerned.

So one of the things is sometimes you see additional nodes and actually this is just the infiltration by the lymphocytes. So Dr. Priya and the other surgeons, would you again do an EBUS in this situation? So that is one pitfall of staging with PET-CCT post chemo plus IO. So one thing is that if the node is on the same side,

like on the right mediastinal 2 or 4 R area and it is resectable, patient has already received neoadjuvant chemoimmuno, I am comfortable going ahead with surgery because that is the node which is anyway going to come out. But suppose there is an avid node over the other side of

mediastinum or contractile hilar, in that case I would like to repeat my invasive mediastinal staging either EBUS or mediastinoscopy.

And to prove that that is not a diseased node, it is just because of treatment. And if it is negative, then only there is worth attempting surgery in such cases. So ma'am, a little bit of-- we would like to actually go on a different path here. That is theoretically possible in an institute like DMH. But in practical scenario, it is very difficult to have a patient with invasive mediastinal staging and then goes ahead for four cycles, chemoimmunode, then again goes for invasive mediastinal staging.

It's either cost effective nor resource. So if the primary has responded and if there is a node on the opposite side either, I'll take it with a pinch of salt. Maybe discuss with my radiologist as to what was it before and now. If patient can afford and they are willing, fair enough. But beyond theoretical, I will have to be a little practical in the private setup when it comes to post-immunotherapy staging now.

Now this slide already covered what were the surgical, how many patients underwent equal in both arms. But what is important is reasons for not undergoing surgery, progression of disease was about 6.8% and similar on both the arms. And deaths if you see is only around 1.4% on either arm. So I think attrition rate, as I said, though it is written around 20% total if you look at it,

And now about the surgery, were any concerns that you all have about the surgery? As you can see over here, that minimally invasive surgery was possible in almost similar numbers in both the arms.

And if you look at the type of surgery, then lobectomy was possible in almost 80% of the patients in both arms and very few patients needed pneumonectomy. So what do you have to say? Yes, ma'am. So pneumonectomy, if we are going to lead a pneumonectomy, it's actually quite a sad situation and that would be a no-no to begin with.

But for lobectomy and whether it may not differentiate between minimal invasive versus open, I would be very open to open in the initial few years because we don't have the numbers as what they have sometimes in very large volume institutes of minimal invasive. So there has been what I have encountered is more fibrosis, more perinatal fibrosis. So I am quite open to open early for such cases. No.

No, I agree with Priya. Do we stop or we have two, three minutes more? Dr. Kumar Prabhas, do we stop? One minute. Okay. Yeah. So, be quick. So, I agree with Priya. So, higher the response, more the desmoplastic changes, especially along the node. So, in such cases, if patient has responded very well, we also prefer open surgery. But it has not happened like that lobectomy has got converted to pneumoectomy or...

has become inoperable because of those sticky node. It is difficult, challenging, but doable, but we prefer open. So again, you see in all the stages very high R0 resection rates. That is also important. So what would you do after a PCR? Would you stop the immuno because all the trials continued the immuno irrespective. Anybody quick?

Usually, we'll continue but in case you have to stop, this is one group which you can stop. You can stop in other group also taking another trial as an example. But yes, by and large people consider that giving some more time immunotherapy after surgery where there's no PCR is a better way of. I think so. That is another benefit of starting with new adjuvant.

Yes, that is true. The two slides I skipped just showed that even the N2 nodes did as well as the others. So that was the important thing. Now, this patient underwent mediastinoscopy and lobectomy, and there was a complete pathologic response is being continued on adjuvant IO.

And this is the ASCO recommendations. You know, you have the new adjuvant immunotherapy here, chemoimmunotherapy as one of the options. But of course, there are circumstances where you would use only chemotherapy.

There are circumstances where you go directly for surgery. So that we have already discussed and that's why you need a multidisciplinary this. So I think with this we end. The second case was only if the patient is totally unresectable. So what is the mode of treatment? If unresectable, it would

At today's time, the first thing we do, we send to Anil. He's our senior additional oncologist. The patient is fit for radiotherapy or not, that's the key. If fit and able to deliver radiotherapy with systemic therapy, that should be the goal. And then think about adjuvant subsequently. And in case, our colleagues suggest that it's not possible,

Then also we say, try to do something, give systemic therapy, and then the tumor comes down, again gets evaluated by him, can we give RT or not in these group of patients, and then subsequently to continue systemic therapy. So, unresetable, one is CT-RT. If not possible, remember, that becomes a palliative approach, but

But you may be able to get some patients who can do good with the RT when you select it appropriately. And after chemo radiation, what would you do? Chemo radiation, what we do in today's time is that if you have mutation-positive patient, be careful. EGFR, you have very good data. Please give it. If mutation negative, especially the driver ones, I'm not saying all mutations, don't take Keras into it.

then give immunotherapy to this patient. Durvalumab has very good data. You have some other drugs also, but primarily in Indian context, it is the Durvalumab where you have the best data possible. The problem is that if you have ALK positive, then what you do? That answer I don't have directly today. Indirectly, you have data from Alina. When you do surgery, what happens to the patient? At this moment, we debate a lot.

But we end up not giving. So, I think this was the second case we received the value map. So, I think we have covered everything, resectable as well as unresectable, and how we would incorporate the new trends into our treatment paradigm. So, I think with this, I would like to thank the panelists and also the audience. If there are any questions, you're free to ask.

Thank you, ma'am. One comment is that we have an adjuvant trial of Durvalumab versus Durva plus Rumnavalumab that is ongoing at multiple sites in India. So I think we should promote it and let the patients receive the best possible treatment which is available. So that's a message that if trials are available, we should promote it so that the appropriate patients can get the best possible treatment.

Just a last 30-second comment. So we were talking about the iffy nature in stage 2. So there is a clear-cut recommendation in stage 3. But in stage 2, okay, we can go for surgery followed by the other approach. So in breast cancer, if we take as an analogy, we've reduced it down to 2 cm.

So like HER2 and TNBC, if it's as low as 2 centimeters or above, we have to give neoadjuvant. So we don't fear the disease progression at the end of it, but we've understood slowly that the PCR of 60-65% does have prognostic value. So gradually over the year, even in lung, I think the concept and

importance of PCR will be learned and even in stage 2, the neoadjuvant concept will come. Yeah, I will continue the discussion, but there is a lot to it. Yeah, so I think with that, we'll conclude. Thank you very much.

Thank you. Thank you, ma'am, for that excellent panel discussion and bringing out all the relevant points.