I now invite for panel discussion the moderator, Dr. Anil Tibdewal.
Thank you everyone.
You would like to have the panelists on the board. I am Dr. Ojani.
I am Dr. Ajay Chobe, Dr. Venkanesha, Dr. Rahul Vahe, Dr. Indraja, and Dr. Vidhu Karga.
Can I have one more edition on collision board?
Dr. Gunshan, who is the Adipa.
Her name is Jelusas.
In my list is not there. Anyway, please come on board.
Dr. Rahul Rai.
Dr. Vidhu Karga, I am Absajjika Longkal.
Thank you.
We have seen all the 407 Absthat, 4 Absthat related to the radiation therapy, and 3 Absthat related
to the pre- or post-akimoredation therapy.
They all had the one, three common aims to improve the locational control because the
locational control is slightly poor. The two-year locational failure rate is approximately
40 to 50 percent in stage three Northmull-Salam cancer.
Overall Savaval is not very good. If you look at the Pacific, five-year overall Savaval is
only 43 percent, which is better but not up to the mark and the reduction in toxicity,
which is mostly related to the radiation as well as the devillumab or the ossimatine.
So, first we will discuss the devillumab arm represented by Dr. Venkatesh.
And he, two or three time mentioned that we will discuss in the panel discussion, we will discuss in the panel discussion.
So, I wanted to, in the background, they mentioned approximately 50 to 30 percent of the patient may not be eligible for the devillumab arm.
But if you see the placebo arm of this particular trial, not much patient has progressed in the placebo arm during the CTRT.
So, what is your opinion on that?
Means they are given, develop in the concurrent setting, but many of the patients in the placebo arm were not progressing doing the chemoredation therapy arm also.
So, that might not be the proper hypothesis for the failure of the trial or what do you think?
Anybody can answer that?
Probably one is timing of randomization, maybe a consensus.
That timing may be the concomitant administration.
Okay.
Dr. Guncha or Dr. Chobbe?
What we saw actually the initial pacific, there were randomization post treatment.
So, we could rule out the patient who were progressing or the patients who were performing well.
But this was not the option in pacific too, because we are initially starting from the beginning.
So, we could not...
So, that was the hypothesis of the trial.
So, you think the hypothesis was wrong?
Because they suggested the synergistic effect of the radiation therapy and immunotherapy.
And we all so boost ourselves for the radiation therapy and immunotherapy to have the synergistic effect.
So, the synergistic effect did not happen in that trial?
So, we did not see this in trials.
So, we cannot say for the trials, other trials would cooperate or negate this finding.

But as of now based on this trial, we can say that it did not have rigid hydrogens.
Okay.
Any opinion, Guncha, apart from this?
No.
Any medical oncologist now opinion?
Why did fail in this particular trial?
The specific to...
Sir, one is the toxicity rate was very high.
So, whether the doses which were required were given or not, that's our concern.
Other...
The discontinuation rate was also high in this... in the CT-RT time.
So, this could be the reason which may have lead to the similar reasons.
Okay.
Now, anybody wants to add it to that particular thing that why the trial has...
Yes, please.
I...
So, in fact, for my...
These reasons, higher dose per message, what is the risk of risk of risk?
Is it very complex?
See, there is this thing, the theoretical is thing.
Yeah.
So, maybe in energy, a U00 rate.
Anyway.
So, in my opinion, there were more discontinuation in the...
In the com...
Comitant chemo-redition therapy phase, as Dr. Venkates has already mentioned, that there were more
discontinuation during the chemo-redition therapy phase, less than four months, was...
was maybe the major factor, more adverse event during the chemo-redition therapy may not be the
radiation induce or develop of induced pneumonitis, but the adverse event, due to the develop
will mainly infection, that might be one of the reasons.
The lack of benefit in the comcomitant phase was probably maybe because of the dose per
fractionation, and another reason which might be there is the irradiation of the lymph node,
which will be happening in the chemo-redition therapy in stage three, North-Malsal, and
Kather.
The one of the major reasons for the... for the benefit of radiation therapy and immunotherapies,
that whenever you give radiation therapy to the tumor cells, there will be release of new
antigen, and they will recruit the cells from the adjacent lymph node.
So, what happens is that if you are irradiating all the lymph node, there will not be much
of it in that density of the taint filtering lymphocyte to have the synergistic effect,
that should be there whenever you are combining the immunotherapy and radiation therapy, that
might be one of the reasons, that's why the... if the Pacific too has failed, and also whenever
we do the immunotherapy and radiation therapy, we give at least a gap of some dehydration,
we don't give usually on the same day or on the comcomitant days, while we are giving
the radiation therapy and immunotherapy.

So, that might be one of the reasons, but we know that the Pacific too has failed.
Why haven't they chose the standard of care at the development as a consolidation thing?
Maybe the timing of the trial, because the procedure of the standard of care...
14 and 15, this is around 617, it should have been there.
It should have been there, it should have been there, because they might have done that
the comcomitant versus the consolidation.
So, as we all have received, the adverse event in the Pacific was only 15% here, in the consolidation phase,
but if you see the Pacific too, approximately 26%, it means additional 10% were discontinued,
the treatment.
So, that might be one of the reasons that the trial has failed.
And the summary of adverse event, the radiation immunitis rate was more or less the same,
the great 3 radiation immunitis was almost the same, less than 5 to 10%.
And as already mentioned, the infection or the rate of death in the comcomitant setting was also one of the reason
for the failure of the Pacific too.
But still, so the Pacific one or the Pacific trial, still the standard of care,
so we can continue with the CTRT followed by the dual amount of the maintenance.
Maybe the patient selection, but it is just a subgroup analysis, not the final analysis.
Now, coming to the trial presented by Dr. Atinanjan Basu, I will be not happy with RTOG 017,
we are doing more dose escalation.
RTOG 017 has already mentioned that the dose escalation does not benefit.
Yeah, I agree, sir, because 60-gray, and above 60-gray, we have already established that there is no benefit of escalation.
So, I really don't know why.
Yeah, Dr. Chawe.
So, in spite of giving 60-gray in 30-fraction, the local regional failure is more often present.
So, there is no harm in trying to doge escalation.
At the same time, what we are doing, we are trying to reduce the volume in between,
so that we are trying to achieve the same lung dose or same mainly lung dose,
so that the toxicity is not increased and we are trying to escalate the dose.
So, that can be tried because we have stagnated somewhat, giving 60-gray in 30-fraction,
and local regional failure is still is a problem.
Yeah, okay.
So, what they did in the RTOG 0617 is that they have escalated the dose to the entire volume,
to the entire planning target volume.
So, there will be additional toxicity.
In what they have done in RTOG 1106 is that they have mandated the dose constraint to be the same
for the adaptive lung also.
So, the main lung dose should not cross beyond 20-gray.
In RTOG 0617, it might have crossed, but they have entirely radiated the entire volume.
And if you see, they have did the adaptive, the PET in the mid-treatment.
So, for example, in the fourth week, I want to take the opinion of Dr. Indraja.
Now, what are the problems when you do the mid-treatment the PET CT scan?
What are the problems or the benefits that you can see in the mid-treatment phase of the CTRT?
Yes.
So, usually what is the protocol which is followed in CL lung patients is video

baseline PET.
And the mid-treatment PET is done if the patient has received radiation therapy, at least we should wait for three months for the inflammation to set in.
But if chemotherapy is added, then sometimes we can ask for an early PET, like at around four to six weeks,
to assess the response of chemotherapy, but not for radiation therapy.
Because radiation therapy causes a lot of inflammation, and it is very difficult to differentiate
whether the residual disease is there or not, after the patient has received CTRT.
So, the timing period is very important when you are doing a PET.
For the intention of doing PET is to adapt the volume and not to the response here.
Yes.
So, that is the thing, because this is a negative study, maybe they were not able to differentiate
actually whether the residual disease is there or not, they are just re-radiating the inflammation,
which is setting in.
So, that is the question which needs to be asked, because it is very difficult to differentiate
whether inflammation is there or the residual disease is there, because everything is irradiated in the lung.
But what I would not understand is that even if there is an inflammation, they have not increased the volume,
they have just irradiated a boost, the residual volume, so which was there in the mid-treatment PET CT scan.
So, that is what, if the patient has received radiation therapy, there are no standard cut-offs of SUV,
that above this SUV, you will level it as a residual disease or below this SUV, you will level it as a residual disease,
as an inflammation.
So, that is the thing, so it is difficult, and so you have to wait for, from my point of view,
you have to wait for three months for the inflammation to set it, and at three months, if the patient is showing
our lot of residual uptake, then you can say that the patient is non-responder,
and if the PET is not showing uptake, then you can say that the patient has responded to radiation therapy.
How to take the we cannot talk about the active engine or the gas map?
In the nature, this is not response assessment, this is during the treatment of PET scan has happening,
we do not expect any response at that point.
We want to actually consolidate only to present PET area, which is showing an SUV more to that area to a higher dose.
So, will there be a problem for this?
Yes, yes, definitely.
If you see the freedom from local regional progression, the adaptive arm and the control arm, they did not show any difference.
So, that means whenever we are adopting the volume, we are not increasing the local rapid clearance rate.
So, in a way, that is not there, but what the trial was trying to prove is that whenever we are eraditing the boost,
we are giving the boost to the residual volume, your local failure rate should have come down, which has not come down.
Sir, I have a comment to make here.
Yes, please.
I can. So, they adapted mid-treatment, that is they did not complete the 60-gre, is what I understand.
So, adapting mid-treatment, we might have missed the clinical target volume that might have not shown uptake on the PET,

and we have consolidated the volume even less.
If you see the left-hand side of the figure, they have kept the CTV as it is.
So, the CTV will be the same.
It is only the residual gross tumour volume that they have boosted up to a dose of 80-gre approximately, any way.
Because they have analyzed in their supplement also, they have given that SUV peak, they have analyzed very well.
They have taken baseline, they have taken mid-treatment, divided by the metabolic tumour volume.
Then why the challenge? Even I am surprised by reading this, that they should have been some more benefit,
if you have done everything properly, instead rather even toxicity is more in adaptive, though not statistically significant,
but for percentage wise it is more.
What is SUV max?
So, SUV max, we will just elaborate the parameters.
So, these are quantitative parameters which are calculated.
So, basically, FPG is injected and SUV max is standardized uptake value and it is a maximum.
So, it is basically a quantitative unit of FPG.
So, when peak we are talking about, so we get an image of FPG, and if we are putting a region of interest on,
say particular a primary human, and if you want to get an SUV max, then at that region of interest,
what is the maximum quantity of SUV we are getting, that is SUV max.
And if you want to calculate the rest of the voxels also, and you are taking into account that activity also,
then it is called SUV peak.
So, it is basically you are taking the whole region and not the focus which is showing maximum uptake.
So, that is the difference between SUV max and the SUV peak.
How do you do that?
Yeah, metabolic tumour volume is basically a software generation.
So, we have a software and we put a region of interest.
It is a three-dimensional region of interest is put and you can correct it and there is a threshold is set.
So, if you want a SUV max 2.5, so it will take all the voxels in which that you are showing more SUV compared to 2.5 times the SUV.
That will take.
So, that is the metabolic tumour volume is calculated.
Any idea of what did they take in that up to all of this, that the SUV max or any SUV peak or what is that?
Peak and MTV.
Peak and a peak and MTV.
There is something called TLG also.
Yes, TLG is nothing but the value multiplied by the metabolic tumour volume by SUV mean, then it is you give the TLG.
That is total lesion glycolis.
So, all these you get from software, right?
Yes, yes, we can get it from software.
As we have already seen, the central freedom from local regional population is not much difference as the trial has expected.
And the toxicity of the protocol is physically a great 3 RT plus your lung toxicity is also less than 10%.
So, which were both in the comparable.
So, for me, the RTOG 617 has already closed the debate that dose escalation might not be helpful and this trial has further strengthened.
The rational that dose escalation might not benefit in reducing the low-corrhizional failure rates.

So, in a message that I will say that dose escalation, the local control does not increase dose escalation, whether it is increasing the toxicity,
might not be, there is no significant increase in toxicity.
Dose escalation, whether it is leading to the survival improvement, no increase in survival.
So, I think dose escalation might not help in improving the low-corrhizional control.
We need to look beyond the dose escalation.
What are the positive points about RTOG 10106 is only to as per my understanding.
The adapting tumor volume did not increase the local recurrence rate.
We have it out whether we will adapt the tumor volume, then we might miss the tumor that we are going to boost or that we are going to radiate.
So, adapting the tumor volume did not increase the local recurrence rate, that is the first thing.
And many of the time that we see we have a larger volume and we are not able to deliver the concomitant chemo-redition therapy.
So, this trial might help us in using the adaptive treatment volume so that we can proceed with the definitive chemo intent in our addition therapy.
So, this is the trial that the energy LU008 which might be the answer of the not so potential candidate for definitive CTR, your concomitant CTRTA.
Whenever the patient is not eligible for CTRTA, we do the sequential sort of chemo-redition therapy and more or less the results are slightly better than the palliation but not the concom...
We will not conquer with the concomitant chemo-redition therapy.
So, Guncha and Dr. Chobbe, in your opinion and your practice, how many patients you are not able to deliver the concomitant chemo-redition therapy only because of the volume that the tumor encompasses?
Out of 10 patients, how many do you think that?
So, out of 10, sir, if we have such kind of situation where the volumes are too large, we either go for a sequential or we go for sequential.
So, maybe around 2 to 3 patients out of 10?
Sir, approximately 20 to 30 percent.
Not a job, eh?
So, I think it is one or two patients out of 10 which we feel is this kind of scenario.
So, what is the protocol as such, we go for a NACT and the volume strings and then we consider for CTRT.
Otherwise, the patients tolerate it but sometimes the patient have a neutropineia post-3, 4 cycles of chemotherapy.
That is the only toxicity we find.
Most of the patients tolerate NACT followed by CTRT.
I want to bring my surgeons and my medical oncology friends.
So, in such scenario where you have, for example, multi-station N2 and a destructible primary, you know that the perioperative immuno-check 1 inhibitor followed by the surgical assessment is also coming in a big way.
And this is the trial that the energy eluteobaziroid where you have the volume which is large for the CTRT but they are trying to do the heavy artist so that the volume becomes less and it is more precise.
And concomitant chemotherapy after the SBRT.
Do you think that the surgery will have a slightly better role as compared to this particular tarskema in having the multi-station N2 node?
So, in multi-station N2 node it is very important to know which station is prominent in that patient.
So, if it is like on the, say, resectable kind of thing and it is not bulky tumor.
So, yes, if the patient is fit and it has been like every parameters of the patient is okay, then surgery is one of the option but yes, to declare finally for the surgery to take the patient for surgery, we have to give them an option like if it is a bulky nodal disease or a multi-station with a bulky,
then yes, we should go for other modalities like for the chemo radiation or

radiation like pre-operative chemo therapy and then see the reassessment response.
Before going directly to the surgery.
Okay. The question was for resectable primary and multi-station N2.
These are the resectable primary, less than 7 centimeter.
With multi-station N2.
Yeah, so these are referred for the chemo radiation therapy so I assume that they are either bulky or they are multi-station N2.
So, sir, when we are planning for pre-operative or pre-op, I mean, new agent chemo immunotherapy, we need to understand that there will be patient which will not respond with, even with this drug also.
And when this is N2, which is a multi-station, this is technically unresectable even after this surgery and very less chance that it will respond.
So, it is difficult for two plans for this.
I am not very helpful.
I am not very hopeful about the trial that the energy alluded to it.
In having the multi-station N2, they are just trying to reduce the incidence of the pneumonitis, maybe that might be one of the reasons that they are doing the study.
Because whenever you have a large bulky primary and a multi-station N2, say for example, two R-station, four R and a high-low low low primary, we usually do not have a problem with the upper low, the middle low primary with the mediational nodal environment.
Only with the low low, the volume increases, so the chances of pneumonitis increases.
So, maybe your administration of the development in the consolidation setting might not happen when you have radillogically or clinical evidence or not.
So, that might be the reason that this particular trial may be helpful in our clinical practice.
Apart from that, I do not think that whenever you have an upper low primary, we out of 10, 9 out of 10 times, we are able to deliver the CTRT with the OIR constant with a normal limit.
Can I agree with you? The biggest challenge of this is in our setting also, neither it is going to save time because the SBRT itself will take time.
It is not a treatment which can be started in two days. So, that will take its own time from planning and delivery.
Then the long course, as usual of chemoridation, the time it takes. So, probably the consolidation we are dealing.
And yes, I agree with good quality, I am not to plan hardly we face challenge in long in meeting of the constraint.
Maybe V5 to some extent, but rest all are mostly met up. So, other than their best end point would have been rate of pneumonitis.
I am particularly excited about this. Is that a six-met trial? Yes, please.
Do the escalation for the primary? Yes, VD for the primary is increasing. So, you can, is the same thing.
The dole escalation for the primary is equal.
Already you have a mid-season node, it has crossed. So, when we do for stage 1, stage 2, N0, SBRT, the intent is your visible disease is that.
Here the disease has already gone to mid-estion and echelon. So, even if increasing the primary, it is like seed soil theory and accepting that fact that, okay, I increase the primary dose.
So, probably it will not seed further. So, in the interest of time, I would like to move further in the panel.
How many of our radiation oncologist and medical oncologist has asked for the e-bus?
So, before doing the CTRT, because if the patient is having multi-station N2, say for example, pay positive.
So, this trial is showing there the discordant in approximately one-third of the patient.
How many patients do you ask for an e-bus whenever the patient is referred for CTRT?

So, but the situation is because most of our patients in Indian scenario, some nodes made a channel could be either TB or some infection inflammation will be there.
But this is done in such a setting where PET is negative in e-bus. So, that is, I do not know, it might not be applicable for our...
It might not be applicable for our... Yes, sir, exactly. It might not be applicable in our situation.
So, if you change the radiation therapy planning volume as well as everything, approximately 10 or 20 percent of the patient has undergone the surgery also, whenever they were downstaging.
So, why are we not doing the e-bus for each and every patient whenever we have a nodal station positive on PET?
So, what is the sensitivity or negative... Yeah, so...
The specificity of the PET city.
So, in that manner, we are very clear. So, we have published the DMH data, which says that the sensitivity of PET is around 83, 84 percent.
Specificity is relatively very low, around 60 percent, because lot of granular matter nodes and the infectious nodes we get.
And every time we get a call about...
May mean non-small cell lung cancer, what is your opinion about mediational nodes?
So, it is very difficult in Indian scenario to comment that it is an involved node and whether it is a granular matter node.
But the negative predictive value of PET is very high. It is around 85 percent.
So, what we usually recommend if PET is positive, obviously that the nodes are involved, then you can avoid doing a futile mediastanoscopies.
But if PET is negative, then in centrally located tumors and in more than T2 stage tumors, you should be doing a mediastanoscopy, even if the PET is negative.
That's what DMH data also says.
I want to add Dr. Panita here. So, this particular trial has shown that whenever there is a PET, local lymph node metastasis,
there is approximately one third, means more than 35 percent discordant between the PET CD and whenever we do the E-bus.
So, this will have a very important change in management whenever you have, for example, if the node is positive on the PET,
but it is down stage and the patient is eligible for surgery.
And whenever the PET is positive and the lymph node, say for example, at 2R is positive and 2L is also positive coming on the E-bus.
It will change the radiation therapy planning parameters.
So, we should do E-bus in all the curative, in all the curative, in all the curative, in all the normal cell lung cancer.
We should promote to do the E-bus because it is changing the treatment in approximately one third patient.
I know I totally agree and this is quite stunning data.
So, I think absolutely we need to start incorporating it.
The question is, are we able to do this in all patients?
So, that is number one. I think, you know, we always keep discussing this when PET came, we always say, you know, do limited PET or don't do this.
The idea is that you are changing everything for that patient is going to take a huge amount of treatment.
So, if you have the ability to actually decide exactly where the disease is and how extensive it is,
and you can tailor the radical therapy for that patient.
Whatever you do is worth it, right?
So, the question is how are we going to get that for all our patients?
I think absolutely.
Absolutely. It will be an accessibility of E-bus.
Yeah.
Please.
Please, please follow up with PET CT-BIS protocol.

And please, I will try to predict the phenolar C-BIS.
Your mic is off, I guess.
We do PET CT in all our lung cases.
And based on negative predictive value, what she has said, K85% negative predictive value.
So, if our nuclear medicine colleague says that there is a high chance of it being positive,
or then we go ahead with it.
And if there is a suspicious node, maybe the size or the ability is not there, then we go for E-bus.
So, ideally, we would like to have both, but because of logistic and the patient volume, we might not do it in all cases.
But we utilize a judiciously.
So, we prefer PET CT-based planning.
But in cases which are doubtful, we still go for E-bus.
So, resource limitations.
So, I just would like to comment, because the seismic data is a Australian-based study.
But in India, even if the PET is positive, and if the size, so if we get an uptake, then we go and see the radiological features of the node.
Whether there is loss of fatigue, whether it is taking contrast, or it's looking a well-defined node.
But so, in Indian scenarios, even if the node is there and it is less than one centimeter and showing uptake,
then at that time, we are in a very doubtful situation, whether it is actually a infectious node or a metastatic node.
That radiological criteria also needs to be considered, especially in Asia and India, where the TPS prevalent and the other granular metastasis are prevalent.
So, I think we need to promote more and more E-bus.
Yes.
So, this is the trial for the radiation immunitis to reduce the incidence of the toxicity, that is the radiation immunitis.
And in approximately 10 to 15 percent of the patient in real world, the patient has more than or equal to grade 3 radiation in this immunitis.
So, this is a very good trial, but I don't think so that the results are really matching to all the other literature.
Guncha, you have presented this. So, you take on this, because the rate of the incidence of grade 3 immunitis is slightly higher, not slightly, if much higher, than whatever has been reported in all the randomized controlled trials.
Yes. So, I think the number of smokers and preexisting comorbidities could have been a factor which has led to a slightly higher incidence of radiation immunitis in this particular study.
But I agree that in the rest of the entire cohort, approximately 5 to 10 percent is what we see even in our clinics as grade 3 or more radiation immunitis.
So, I have a lot to chop behind your please.
Yes, but then also, I mean, this is a very simple intervention that can still be done, even if it's in 5 to 10 percent of the patients, so that we can reduce the incidence.
Okay. Can I comment here? Yes, please.
If we compare the other trials, please can we go back to that? Sorry.
The problem is that all those trials were industry sponsored very well selected patients, and this is an investigator initiated study.
So, I think investigator initiated study are more real world situations. So, I don't think we get so low immunitis in the real world setting as 3 percent only.
That is my take, in this point.
So, most are pacific, laura pacific to all these astrosinecus, phosphatrials. They are bound to select very selected patients who are very very fit, likely to have less toxicity in both arms.
So, that is one of the point which is worth the discussion.

In this rest of the time, we can discuss this later, but I have a slightly different opinion.
But now, coming to the last two, the laura and the poll star study.
So, very good result, very good PFS result. The timing is you can give the osmatine both the homo, homo, lertinib.
Until the time of disease progression, the PFS is 39, although, or the 31 in the poll star. You can see that.
The only thing is that do we, the medical oncologist's friend, should we do the biomarker testing for all curative or for all non-smolcell lung cancer because we have the data for the all.
So, in all the non-smolcell lung cancer patients, yes sir.
You will recommend EGFR only or L-calsor or the NGS for all the patients because there is data for the all-calsor which is coming up.
So, EGFR and L-cals are usually done if we are planning so.
Okay. Okay. Yeah. If positive, we will consult for osmatine, or there is any role for the first generation or the second generation also because a lot of our patient, Dr. Manita, group has only published that only less than 5 to 10% of the patients are really
affordable for osmatine, or the image equivalent in a beta. So, what is the real impact of this particular trials in our world scenario?
So, sir, the first and second generation drugs are not tried in this setting, poor CT and D setting.
But if you want to extrapolate from poor surgical setting, adjuvant setting, they have shown PFS benefit only. There is no always benefit with those drugs.
Osmatine has shown both. So, if patient is affordable, yes, osmatine would be the first choice.
But for other, we need to discuss with patient because this drug will continue further.
Okay. So, how long was it?
Yeah. Till the time of this progression or you want to do circulating tumor DNA and then you want to do...
For now, it is still...
For now, it is still progression.
Till the time of progression. Okay. So, in the interest of the time, we should consider, I guess we should consider for at least EGFR, L-cals, PDL1 for all the curative as well as the metastatic non-calsor lung cancer.
And we have NGS for metastatic non-calsor lung cancer.
And we should... The data for both the PFS for the Chinese osmatine, although Amo, Latinia and the osmatine are really good.
And we hope that they convert into the overall survival benefit.
So, with this, I would like to thank all my panelists and the organizing team for giving me the opportunity. Thank you very much.
Thank you. Thank you, Arbenas, for having us.
Thank you, everyone.