So for next panel discussion, our panelists are Dr. Sombana Throy from Kolkata TMC, Dr.
Yeshvan Kashchev from Balco Medical Center, Ripur, Dr. Devanshya from Mumbai, Dr. Pitham
Khataria from Mumbai and Dr. Chandrikanth M.V. from NH Kolkata.
Shall we start? Dr. Pitham, Dr. Devanshya. Dr. Devanshya is in here. So Dr. Chandrikanth,
you will take over her questions, yeah. Okay, so let's have a discussion. Good morning
everybody. So I will be talking about the abstracts that were discussed right now. We
have already had a very nice panel discussion on Adriatic. I will skip through it. We will
talk about it but I think we will just summarize it, I think because we have all done that
recently and then we will go on to the other abstracts, right.
So quickly Dr. Sombana, your comments about the Adriatic study design, like a quick recap
for those people who are not there in the morning when we are at the panel.
Hello, so Adriatic is a newer one with the dual volume, consolidation dual map. If we
look at the great data for the pacific and even the pacificate, now the small cell with
a limited stage of CTRT and PCI is also allowed. So we have looked at the PFS and OS, there
is look it is very lucrative for the, although the third almost data is not mature enough,
but still PCI was allowed. We do not know the additional benefit of carboplating in comparison
to the cisplating the PFS curve and OS curve. So those who are receiving carboplating definitely
well better than the cisplating though the cause is not known.
They will be coming.
But definitely dual volume map consolidation is a good study and reality for us and we
have to look at the more mature data in the third amals.
Right, exactly. So the third am data is here to come, although there was a protocol amendment
in 2020 where they stopped the crooting patients under the tremelium map trial and I did not,
I could not find out why they stopped doing that. I do not, it was anybody here part of
the Adriatic study, no, at that time. Okay, all right. So to summarize this is an unmet
need. We have discussed this in the morning where we treat limited stage disease also
as a kind of a, we considered it as a systemic disease because we do see relapses and we
see them in maximum 24 months. Hence, and that is also another question to the panelists.
Why did they arbitrarily take two years instead of one years in pacific you did, you know,
you give immunotherapy for one year. So.
Yeah, that is also an unanswered question for us that two years was as three as we do not know.
So here we're giving the immunotherapy longer which will have implications when it comes to
maybe monitoring the patient in terms of toxicity. Secondly, like we mentioned before,

a PCI was permitted as per discretion. Dr. Chandakhan, would you just quickly summarize this slide in terms of what we discussed in the morning as well. Yeah. Right, so it's a very designed study. It had the flexibility of giving both cisplatin and cubaplatin even twice a day. Radiation was allowed. PCI was allowed, you know, interesting is half of them did omit PCI. The reason why they omitted PCI is these patients in the Adriatic study, in the limited stage, are living longer than the pacific trial. So small cell is looking better in terms of the absolute OS when compared to non-small cell. So if you can avoid PCI, especially in those elderly who have the risk of cognitive decline, it's reasonable. But as we were discussing, you know, you need to do proper surveillance for the brain metastasis if you avoid PCI. So that flexibility of avoiding PCI in the immunotherapy era is there and the randomized trials have done at nearly 50% of patients. Right. Two more points. One, the radiation must have commenced no later than the end of cycle two of chemotherapy. And thirdly, the patients had to be randomized within 42 days. So these are two important points just like pacific. They had to be randomized early with regard to radiation. So basically we're looking at a very nicely good patients upset with a good performance status. And those who are able to tolerate their initial treatment very well without any significant toxicities. So that's where I would stop here. With regard to the baseline characteristics, they are well matched. And as we know, 90% are smokers. And stage one to three, as limited, they have taken. In early stage, surgery, very early stage, they underwent surgery also, but they were not taken in this trial. So they were well matched. Okay. And we've already spoken about cisplatin and carboplatin. Almost 35% patients did get carboplatin in this arm. And nearly half of them did not receive PCI.

If you look at the time from randomization, till randomization from end of CTRT, around 58% patients were randomized after 28 days. Almost, I would say to the tune of half.

So coming to Dr. Ashvant again, is that your standard practice giving cisplatin or carboplatin? One, what do you give usually in limited stage? We give it a basis. And in very elderly patient or neurotoxicity or nephrotoxicity, then our cardiac issues, then we give carboplatin. Okay. And what about BD dosing of RT? We prefer twice daily. Routine OD doses. So as Dr. Chandakanth had mentioned earlier in the panel, there are concerns with toxicity with the BD dosing. The trials did not, so there seemed to be an initial overall survival benefit, which did not come out to be true later on. The dictum is that between BD and OD, most likely they're the same. Definitely more toxicities with BD dosing of RT and isophagitis specifically is difficult to handle. And you can't really dose reduce

or delay much
in terms of toxicities. So we've already discussed about 58% patients randomized and
a small word on prophylactic cranial irradiation that the paradigm seems to be changing. So the
baseline characteristics are reflecting that, that you're using a broader based patient population,
something like what we've seen a real world setting, albide, with very good performance
status and a very nicely selected population. So as we know, the median PFS was 16.6 versus
9.2, which was very good. And the overall survival was an unprecedented, there was a 2022 month
difference in the overall survival. At 36 months, it was 56.5 and 47.6 respectively between the two
arms. So that's a good 10% benefit. So I think we'll take one by one starting from Dr. Pritam.
What is your take on this result, practice changing?
I think that 46% versus, you know, so overall survival in the development of my bomb was, I mean,
the combination of was 20, 68% versus 58.5 is a good one. I think in a small cell, I don't think we could get much better than this. And obviously the third arm results are still
pending. But I think this is a practice changing and I think we should inculcary now.
So we'll be including a day of practice come Monday, right? And that goes for Dr. Somnath.
Yes, for Adiatic? Yeah, definitely. But as we mentioned morning, we discussed in, you look at the three years, there is more number of censoring at the rate of three years. So that
is also crux of this study. Look at the data for also the PCI, but this is not PCI, I do not know
if we omit the PCI, how these censoring events occurs in the three years. That is one question,
but definitely it is a good practice changing definitely. Our practice, Nimonath is, we have
seen more frequent with Duroalluma. So though trial data said that they are very much comparable,
but still with Duroalluma, risk of Nimonath is more. But it is a practice changing.
The only thing that would be interesting to see is when you combine both Duroand Tremi.
What would be the incidence of Nimonath is and other things because we are much afraid of the
CTLF for individuals. And so I think that will sort of put more sort of understanding how the
post radiation toxicity because of two IOs will make.
Right. Dr. Shandlakan?
Yeah, it is practice changing. Any increment in small cell lung cancer is a big welcome.
And small cell living longer than non-small cell and limited stage is fantastic.
And very important is we usually avoid carboplatin, but if you have used carboplatin,
the carboplatin subgroup has lived longer than the cisplatin subgroup. And the benefit of
Duroy is much better than the carboplatin subgroup. So this is something that is new.
You know, we expect cisplatin guys to live longer, but here's carboplatin is living longer.
Also, the benefit of Duroy is more in the carboplatin. So that is something which

was
which we did not really see in the extensive stage trial. So this is something new that has
cropped up in the subset analysis. But would you change your practice based on that?
No. The real question is would you start giving carboplatin to everybody in limited stage?
Right. So at least I'm not guilty if you have carboplatin.
Anyone in limited stage, we need to have a watch on the marrow toxicity because good amount of marrow is involved if you're giving radiation. So that is the thing.
And it's just a subset analysis. So I think we need more data. We need a slightly longer follow-up.
And but it's reassuring that even if you give carboplatin, you're not really going to,
you know, worsen patient outcomes. You're not compromising with the patient outcomes.
So the subgroup analysis was not powered. And that's my take on it as well.
Okay. Coming to Dr. Devanshree is not here. Dr. Pritham coming to the BD radius. So this is
basically as post hoc subgroup analysis that was presented in SMO. So we've picked out those
three specific subgroups that they used. If you look at the data for those patients who receive
BD radiation versus OD radiation, again, the three-year OS rates were higher with the BD
radiation dose, 65.8 versus then the OD radiation. So again, would you consider making this a standard
practice or you know to increase outcomes further or would you take this with a pinch of salt?
So again, we'll have to choose our patient wisely because when you give a BD dosing,
there's a risk of toxicity that would always be there if you look in a practical term. So
if the patient is young, we could attempt that because we should not get compromised in terms of
using chemotherapy. You know, sometimes we would be ending up only getting one modality of treatment.
That should not happen. So we have to choose our patient wisely. If the patient is fit enough
without any morbidities, we can definitely attempt to be reducing. Okay. So in terms of time, I will
go through this next very quickly. Point I would like to make is that there were differences in
the patients that they took. So they took better patients who receive PCI more often
and convinced RT more than 28 days later, which might account for this change. The other thing
is that Adriatic was not designed to define the benefit of these strategies, right? It was just
shows that regardless of whatever radiation you do, there is a survival benefit. And the same goes
for the PCI, yes, and the PCI, no subgroups. There was some different PCI people who received PCI did
seem to do better. But again, they were younger, had a better performance status, hence maybe a better OS indoor volume map. So maybe it's just the patient population. Again,
the trial is not designed to reflect this. We have trials which are working on that to tell us
whether PCI is beneficial in limited stage and extensive stage disease or not. So

any concerns
about safety, Dr. Somnath? We've discussed pneumonitis. Yeah, safety concern. Pneumonitis is one of the
more concern as the volume of is all of us post-CTRT, this is pneumonitis. Apart from this,
there is some cumulative toxicity carry from the carboplatinosis, splatin-based regimen like
myelosuppression can. But it is not, it is manageable. I think where most concern is
and pneumonitis. So we monitor patients closely. We look at follow-up them thoroughly with
legato, immune mediated toxicities. Bi-enlarge did not seem to be very challenging in this study.
We'll follow-up as for protocol and those patients where we're not giving PCI, we need to
do a good monitoring in terms of CNS metastasis. Again, I'll skip this part. We can discuss this
later. Okay, so this is something which was very interesting. I think Dr. Alok is not there.
I generally just looked at guidelines while I was making this. Is there any role of adding this
in those patients who are not fulfilling the strict trial criteria? Like sometimes we have
patients who have a poor PS, we don't really start in the second cycle. We start in the third cycle,
sometimes we give sequential radiation. So there's no data here, but guidelines recommended,
so which I found very interesting. I would like your comment on this.
If you look into the separation of PFS of the OS curves that happening little later on, so
immediate defect does not happen. I think even if a patient comes at three months, I think it's
okay to give the role of that. Yeah, so I think we would probably want to give,
especially if their performance status improves and we feel they're good candidates.
I think we leave that. We've seen that the combination works better, but the point is that
the earlier the diagnosis, the better it is. And of course, there might be some molecular
differences between limited stage and extensive stage and the added effect of radiation.
So we need more data on that. Conclusions, yes, to Adriatic. We do need longer follow-up and
Ramalamamab data. We can use either regimens of radiation, can use PCI, cannot use PCI, but
we need to monitor if we don't use PCI. Carbosis, we need further data as of now cisplatin,
but yes, we can give carbon-platin also. And we would want real-world data,
especially with regard to patients where we started late, later than 42 days, and those
with a slightly poor PFS, and in whom we gave sequential RTE. Coming to beat SE study design,
Dr. Alokizan here, we've already discussed this earlier. So basically, the trial added
bevacissumab to the combination of atoposide and platinum and atisosome, atisosomeab.
Keeping into account the similar findings in the IM-150 criteria. The point I would like to note
is that data patients with no contraindications for bevuse, and it's very

interesting, that they
did not take a great many patients, even patients who were on anti-platelets. They did not take
those patients into the trial. So again, a very select patient population. The PFS was
positive. The hazard ratio was good, but Dr. Shantakant, I'd like your comments on this.
Would you call this PFS clinically significant, and would you like to see the OS data here?
Right, so it's small cell. We won't do this. So just the initial PFS may not translate,
and that's what has happened in this. Yes, so that's what's happened. The PFS was hardly
1.3, 1.4 months, and if you look at the second intermose analysis, it wasn't significant.
So the placebo arm also overperformed, but that might be because of the patient population
that we were seeing. It was mostly a trial limited to Japanese and Chinese patients,
and there was some other, you know, the less brain metastases and again platinum might have
made a difference. Coming to safeties, there were no significant differences in safety between
the addition of mevacissumab and the other, but then they did choose a very select patient criteria.
So as of now, no role. There is no special subset where there might be efficacious. We can wait
for the third intermose analysis, but I think the panel agrees with me on this. Would you want to
add mevacissumab to the existing regimen right now? No, no, no. Okay, so we are unanimous on that.
Okay, coming to this third abstract, edibbrellimab plus chemotherapine sequential thoracic radio
therapy as first line therapy. So what they did was they used, this is a Chinese trial,
where they took edibbrellimab, which is also PDL1 inhibitor, and combined it with EPEC similar to
Caspion and IM power. And then those patients who were responding,
oh, I'm out of time. Okay, those patients who were responding, they received thoracic radiation,
and those patients seemed to do better. The median OS was 22.9 months as opposed to the other trials.
So Dr. Preetam, a quick take on this trial. Yeah, I think the OS is good, but if you look at the
toxicities, which are concerning, pneumonitis of 36 percent and grade 3 grade 4 events also,
62 percent. So I'll be a little more careful and waiting for the
phase-state trial, it had to really put a light on that. So patients, Dr. Zhanzakan,
patients who are not, who have responded, would you want to add thoracic radiation?
No, so I mean if it's extra thoracic disease is less and only thoracic disease is there,
and they have responded, I mean radiation is really done well, I think this is in the IO era,
you know, even in the IO. So this is the USO. Yes, there is a Chinese IO that's there.
Yeah, so Chinese IO is done. So we have some significant data even in the IO era. I think we
should add thoracic, arty, thoracic limited responding disease. And that is what

the guidelines also
say that if there is responding disease, you can consider adding radiation. 30 degrees and 10
fractions is the consensus. Uh-huh, coming to the last abstract, which is Delphi 301. So
I'll talk to Dr. Yeshwanth about this. So there is an unmet need, according to you for study. Yes,
Yeshwanth, there is unmet need because second line we have chemo option, but most of our patient
do worse. And so there is definite unmet need. And this drug looks very promising. And
in next year as Akil said that generics are also coming. Okay, yes. So they took a very
nice patient population where there were platinum refractory, they received, it was a very heavily
pre-tated patient population and we don't have much to offer these patients. So there is an unmet need,
nearly 91% of them had received brain directed therapy also. So median OS was 15.2 months and
OS was regardless. And this is an important point of whether you, it was a fraction of refractory
disease more than 90 days versus less than 90 days. And there were good responses overall,
overall response rate was also good. So coming to the brain metastasis data,
Dr. Ashwand. Yeah. There also this drug has it, this drug has done well.
Yes. So that is another unmet need that it seems to be fulfilling that those patients
who had brain metastasis, there seem to be some intracranial disease control.
And with regard to toxicity as well as efficacy, there was not much difference.
Like Dr. Monica told that there are grade one, grade two toxicity, CRS were more,
but other toxicity was not much. So this looks promising.
Right. Okay. Some more, do we have time? Can we talk a little about the toxicities? Because
that is something that I am a little concerned about. Dr. Shandra Khan quickly like in like 30
seconds. It's a bite. You know, it's nice to see bites coming even in the
solid human space. So CRS is what that we need to be cautious about.
Anything specific that you would do for these patients and would you find challenging
with regard to this? Or do you think it's easily manageable in the clinics?
I think you should be a little cautious, you know. If for CRS we need to admit and be careful in
the first infusion at least. Yeah. Dr. Preetum. Yeah, I agree with him. I think we have to be
careful about the CRS part of it and you know, they're taking care of. So you look at you know,
specialist centers where you know, the I see facility and everything is there to take care of it.
And as Dr. Monica mentioned, they used the 1MG dose earlier to decrease the incidence.
It's pretty much like what we do in Ami Vantamab. Right? We do a lot of pre-medication. We keep
the patient for an extra day. This trial used in patient monitoring for almost 72 hours initially
to look for these toxicities. They did use steroids. But the good thing is they were mostly grade 1
and grade 2. I would say we definitely need further data. The study seems very, very promising. Good
PFS, good OS. There is an unbit need which this is satisfying. But we would love to

have a phase 3
trial and basically learn how to manage these toxicities and see if we can do something like
the subcutaneous Ami Vantamab like where we can try to minimize these toxicities by using different
methods. All right. Thank you.