So now as we come to an end of these four interesting abstracts on oligometastatic disease, I would like to invite Dr. Deepisa who was senior medical oncologist from Hopal and **S**0 we will be discussing these four abstracts and how it is going to be placed in the treatment paradigm for oligometastatic NSC. So I would also like to invite our panelists, Dr. Kastavthal Patra, Dr. Nikhil Akaliani, Dr. Anupto Snyvall, Dr. Pooja Gupta, Dr. Sobyn Jacob and Dr. Hollis Dessuska. Good evening. So we have around 27 minutes to discuss more so about these four abstracts and we will go a little bit beyond and go into the oligometastatic because there is no other session on oligometastatic. So I took the privilege of taking into that. So these are the panelists, we do not have minutes, he excused himself. So in the next, so first oligometastatic non-small cell will be very much specific, restrict also to non-small cell lung cancer, so that is a thing. So everyone here is a believer in the concept of oligometastatic non-small cell lung cancer, Hollis. So all of you believe in the concept and how many of your patients have really undergone what we have been listening to for the last four abstracts. So how do you choose your patients initially we can go to and then we can refine our things. Kastavthal, from you, you have been, you are a radiation oncologist. So how many of your patients, let us say 100 with metastatic disease because if you look into, I will come to the numbers in a while. So how many of your patients in your hospital are really getting some form of ablative treatment versus or surgery, we may combine both in a NSCL-sesthetic, not colored colinsecting, we have my excuse. Yeah. Yeah. So among all metastases with the advancements in immunotherapia and systemic therapy, I think a good number of 15 to 20% patients are out of those oligometastatic patients. Of course, I represent a particular segment of this thing, population that we see. So in our setting, I would say every month, around three to four patients would be getting local ablative therapy. Okay. And if I take it further, so you have some cut-offs in a institute that it should do something within three, five, ten or two organs per se. Though oligometastases by definition, we'll come to that. So what do you have any criteria for your institution? So three or less is the most ideal, okay, around up to four we enroll, but again, spine, if they're contiguous, I think they're organ or two organs or three organs. There are various criteria, you know, there are various criteria. So you are okay with three, maybe four, but beyond four, you are not happy. Beyond four, we are not happy. Other thing is, you know, single organ, the organ dosimetry makes. So in labor, if all the three lesions are in the same lobe or actual sense of those

things you look at. So those things will have to be looked. Nickle, any different from what cost of a spoken? No, same. Same. The more is like oligometastatic oligo recurrence and oligo-process systems are also forms a significant part in the practice. So one more thing I'll ask my radiation oncologist. So when you look at oligometastatic disease, so you are just thinking of irradiating the metastatic site and how many of your patients, I think that's what we spoke of. Or do you conceptually believe that if I do the metastatic site irradiation, I will be also doing the local, the primary irradiation also of the lung mass. So I hope the question is clear. For NSCLC, we are still not practicing the local lung radiotherapy on the meditator. So, say, if you go through the fall NSCLC. NSCLC. NSCLC. We are only speaking of NSCLC. Okay. So two things are coming up from radiation colleagues before we go into the specifics that they have around, I think 20 percent of the patients look energyable and when thev start choosing they are looking into maybe two or three oligometastatic disease, maybe four. There's no definite cut off. It may vary from patient to patient. But lesser than number, better it is. And none of them are still practicing the thoracic RT as was put up by you. My medon colleagues, any different opinions of what has been spoken till now and with then we'll go on. No, more or less. Okav. So, definition, I'll skip off because I want to discuss what is really pertinent. I totally all of us agree. There's no strict definition as such for oligometastatic. So, the things that is accepted is up to five and maybe two to three organ sites. That's what it is accepted. But you would find even one of the trials have taken beyond 10 metastatic deposits also. So basically there is nothing as a watershed rule that this is what it is and people have made definitions as per their liking. But most of the consensus is about five to seven and two to three organ sites. That's what it is. Any specific organ that is definitely excluded from the oligometastatic definition? We have long brain, we have liver, we have everything. Any organ site which you think is definitely excluded from this? Brain, I quess. Brain is, it is one of the most common oligometastatic. So, two most important organ which are excluded is basically the serosal deposit and second

is the bone marrow involvement. Okav. So, these two are excluded from the oligometastatic definition is something all of us have to remember and this is what it is. So this is what I spoke of the definition. Focal, the focal lefto-minger enhancement also should be accepted. You have to speak into the mic because people would be, these are small domain I agree. But an equal lefto-minger enhancement has to be accepted. So, and medicinal lymph nodes is considered local, regional so that is normally taken up in the little trip is done so that is not done. Superstine, very quick, one minute then we go to specifics. Oligoprogression, oligopurcistent, oligorecurrent. Anyone wants to take it. There is a catch in this. It is not as the English is all about. So, oligoprogression is basically the patient at the base and is having a AMD disease. Patient is on treatment either systemic and plus minus local treatment. Patient was having a stable disease but after a particular time the patient is having only a progression to a limited number of lysin. But the one part is responding to the systemic treatment and the question. So, it is in the same region or new sites? No new sites, so in the same region. So, basically this is what I really wanted and good. This is the basic thing. Most of us believe in, theoretically the English sounds like there should be something as a new region. So, the oligoprogression if you look at and there is a beautiful ASCO recommendations in 2022 on oligometastatic which has been reconfirmed and this is from the ASCO recommendations from the GCO. And if you look at it very clearly you the last part of it something which I want vou to concentrate. Oligoprogression is something that you have a metastatic deposit, you had a response and then there is a loss of response in one of the sites which already had a disease. So, this is something many of us are in the terminology which I felt was appropriate when we are doing this. The oligoposition is something that you are having the activity which is there already and oligo recurrent is something which is more like a metacronous disease the oligo recurrence you could have new sites. So, I hope we are clearing on that part. Then we move on. Rationality all of us know that we conceptually believe that if you have a local RT then probably in the disease we are going to control the sites so that it does not progress through to the different site because there is where the resistance cells will be there which will

metastasize to different sites and the chemotherapy part or system therapy part is very important because they take care of the micrometastasis so that is why you are combining very easv. So, now we come to the case and we will start from the on the site 53 years old man right upper low blung mass smoker 2 level deposits routine investigations within normal limits NSCLC adenocarcinoma no targetable mutations, PDL more than 1 percent anything more required as investigations we can we have to be quick not so no you are happy with this okay we can move on. So, considering the metastatic workup has been completed with MRI brain. This is what you have. Yes sir. MRI brain. Okay fine that is what it is MRI brain. So, basically what I wanted to intent was two things here MRI brain is one of it very well anyone wants to add something to this. So, one more thing is included which I think we do not do in India because of lot of reasons is when you have a liver metastasis MRI liver is sometimes very important specially when you are looking from the conceptuality of oligometastatic disease and radiation oncologist will appreciate it more the MRI brain liver is something that they would require. Do you agree to this part that liver when you want to do an oligometastatic dietary therapy you would be more comfortable with the MR than a PET CT scan and CT scan report. Definitely localisation is much so I think that is what we need to add on to our armamentarium MRI definitely brain is required PET scan and a liver if you are thinking of liver deposits. So, these are the three things which I wanted. So, now we have this case very clear cut stage four we have two different sites which is our liver. So, your treatment options well as we start from you it is eligible for immune checkpoint so chemo plus immune checkpoint. Chemo plus immune checkpoint. Followed by a local treatment. No after my abstract movie. You believed in the concept so this is a two liver site costable. I will still go for local therapy. So, you will start off with a systemic or you will go for a start of a radiotherapy and local treatment. System therapy first. First systemic therapy. So, how long of systemic therapy? Three months. Three months. So, at least of three months of stress therapy and if it is well responding you will then plan for local control. Then that is a local control.

Fine. Cost of any different. Yeah, I will get in the local therapy I would give surgery extreme of it is of extreme importance and the patient should also be evaluated. So, it is post systemic therapy. Post systemic therapy. So, anyone wants to start off with? No, I have a point here. So, if you look at it actually he wanted. Yeah. So, if you are planning to give a radiation or a SBRT to liver then it would be better to do upfront because post systemic therapy it will be difficult to delineate the liver lesion. It may completely disappear also. So, it becomes challenging to treat. The cause. Or at least we need to put a marker in the liver lesions. So, that the delineation while during the SBRT is better. So, it becomes really challenging. So, you would be more comfortable with doing it upfront. The catch is people have will tell you that because there is a disease and there is а 20 to 30 percent chance of progressive disease maybe 15 percent with immune and chemotherapy. So, these patients who progress are not going to do that well. So, why should I put these cases subject them to a local treatment? So, that is what most of us believe in. So, so, so start off with. So, yeah please. So, sir in this situation it is better to take the by FCM coil diligence at that time itself. So, you believe the start with systemic treatments? Yes. They have a good response and then go for a SBRT or a SBRT whatever they feel like. So, you have a point. So, I have two things to ask here and now this actually you presented this abstract and this is the largest numbers in oligobatostatic lung you will find of 220 odd patient the NRG study. And the point with NRG was this was the only bigger trial with immune check points actually. All the trials which had shown a advantage was actually pre immune check point error. Post immune check point error you had two trials NRG and one which is costo presented the booster trial what that was on ablation. And if you look at it the NRG was negative. So, on a negative trial we are so specific on as medons. So, why do you want to practice a local ablation therapy with a negative NRG which you only presented? Sir it is an abstract. It is not been abstract will be dissected. It will be dissected. The reason is at the end I realize that the betterment is more with the

immunotherapy than with the local therapy. Good. So, the difference was in the OS also. So, this is the basically what is happening is what I want to make out is. So, what if you have a powerful systemic therapy it overtakes the radiotherapy effect. So, if you have most of the EGFR TKI trials which you will showing has the first generation. So, when the Ocimatum comes in will the benefit hold is the question we have to ask our cell because that these trials which I am which we are showing this all these three trials are pre immune checkpoint error and based on this only the NRG came in and when NRG comes in and we find it to a negative trial. So, it need more better selection of patients at the end of three months that this patient will go for a patient. So, what do you propose with the knowledge we have? No or anyone wants to come. Maybe we should, when ICAs are used as you said this is a negative transfer ICI we should not add of now and LCT is what I was with my milli the present at the next time. What you told us there are two to three issues with adding LCT after ICI the index. As a moderator I am just putting both the things and I will tell you what I feel like. Immunotherapy the cells which are induced. So, sir you are very convinced that with the immune checkpoint you will not use. You have an already a negative trial. You are good friends with the radiation oncologist in your hospital. No, no. That is evident from your answer. At the point I want to highlight we should not forget the toxicity part as well because whatever we are combining. Let us look at the efficacy and then we come to toxicity. Yes sir. If there is no efficacy then toxicity part goes away. I agree when you combine there will be a toxicity additional for every trial for every combination also. Is there a efficacy is what we are discussing here. Sir we do not have any good data with local treatment fit. You have something to say? Say, sir because we do not have any positive data. With two levements with big trial energy negative with addition of immune checkpoint and whatever addition we had was prior to immune checkpoint. So, would you today when the patient responded so well to an immune checkpoint chemo would you consider SBRT or RRT? Yes. Yes. Because. Okay. So, most of us consider. So, even in favor of local therapy the trials as you showed are saber comets, gumets and

those overall the data what I feel is treating oligometristic site. The conceptually told. Conceptually evidence is something data is evolving but conceptually told. Any new thoughts or say we move on. Okay. So, basically. Sir sir. Please. Sir sir. We had minutes data of CTDNA fall. So, maybe those patients were the rapid fallicity they may be if have a nomogram. And then of three months of induction. Those patients who don't have a rapid CTDNA fall they can be taken up for. So, we are coming to something with the trial short and I think a minute presented that trial and I will show that that could be a way to go forward. That's not a one trial. There's actually one more presentation that was there as a publication that has come up last year. I'll come to that CTDNA could be the way to go forward. The point that is coming through is once you do a local treatment you do a CTDNA and it is negative. Then it makes sense to go ahead and treat this patient and these are the patients who are going to do well with the local ablative therapy. And this is not one study actually two study which I could pick up on as either presented or published and both telling you the same thing. So, this could be one way of saving patients from radiotherapy and choosing patients. So, okay. We will come to that. I have a more basic question and I want all of us because I also was not very close to the keen when I still like what this abstract presentations. I looked into how many of these trials had radical RT to the thorax and please the energy had radical RT to the thorax and the metastatic site and look at the iron gas study the gomase everything what we always quote. Every trial has a radical RT to the primary site plus the metastatic site. So, question is even you showed with EGFR positive patients the primary radiotherapy to the thorax has actually put up a OS and a PFS benefit. So, with this data coming in why as a group and radiation oncular specially have not pushed for doing a primary RT radiotherapy to the thorax. Any one of the two can come in because both of you committed that you do not do it. So, I took your answers first actually. We will skip our data and leave our log code. So, I hope you are getting because I also was very clear and when I see trials more and more and all of you need to go back and see these majority of the trials 80 out of 100 have RT to the primary and it makes sense because if you are leaving the primary of the more of this resistance mutations are going to come in and there could be massive progressions.

So, what do you think of? So, tomorrow you will go into rethink about a strategy for oligometastatic energy. So, like in prostate radiation even in oligometastatic site. Yeah, prostate and primary site has come in. Palma study was a varied group of patients it was not only NSCLC. Palma had various of course. So, it is all developing concept you have a point there. So, you have a point there I mean if in prostate why not in NSCLC? No, you have evidence also and the other positive trials have done that. So, I am going to skip this because we have spoken about it. This is the trial which cost took may put through but mind you this was not radiation. Although he is a radiation oncologist was given to him it is ablation is cryotherapy and thermal ablation and with immunotherapy. So, I wanted to this trial with immunotherapy although it is an interim analysis because the full recruitment has not happened. The next criticism for me is the unknown patients are 30 percent. I do not know EGF or positive patients could be there and will you give immunotherapy to these patients is something which I am very skeptical. So, unknown mutations is something I am skeptical when I look at immunotherapy. I would not preferably give immunotherapy for unknown mutation. So, I need to have a very specific. So, that is the criticism for this but also done this is one with immune checkpoints is showing advantage in contrast to the energy. But here it is not radiation it is ablation. We will move on we have 5 to 6 minutes. This is the NSCLC same case I have just twisted it to exon 19 positive. PDL 1 more than 1 I do not think it matters. I will skip the metastatic work up site. So, what would be your treatment of choice for this and I also want to please commit first and then I will come to the next one. So, TK. You will go for TK. So, which TK at this point? Ocematinib. Ocematinib. So, you are going to go for ocematinib. At any point do you feel you will be going for us local ablative, local consultative therapy. I do not have any evidence right now to put a like to go ahead with the local ablative consolidation therapy. So, I will continue on EGF or TK. Ardho no kavak karnabarigabar. He is not. He is also not good with his radiations I am telling you. So, you will go with TK alone and go on doing it. You are not going to consider a local consultative therapy. No. No. Please. Sir, also good with the ocematinib alone. The third generation TK.

Yeah. But some clinical scenarios are we should have seen in the clinical practice. The patient is on ocematinib for the one year and after the one year. So, 6 months you did the PET scan. It is showing a excellent response. The SUVs come down from 16 to 2.5. There is a decrease. One is doing a complementary response. The other is liver mats is showing a decrease SUV. What are going to do with that case? 6 months post ocematinib. Sir, I will continue ocematinib. You will also continue ocematinib. Oc or oce plus pam carbo or pam carbo jeff. So, you are not also going to send it to radiation on carbo. Sir, because the data what we have is first generation and ocematinib we have third generation. So, it might not hold that data. It might not hold. Oles? Same ocematinib, sir. Put them out of the cells. Oc, say or would you consider this also as 6 months because it is only limited very good response you would consider something as ablation. No. So, if the patient has taken jeffitinib with chemotherapy because it was vanitas patient, would you do that after 6 months? Yes. In that situation, I will consider. So, again jeff will be given with chemo's. That is ok. You have done four cycles chemo's over. The patient did not tolerate chemotherapy. Your own single is in jeffitinib. Response is as good. So, you will then consider or not consider. So, basically you are telling if the first there is a ticker, I will consider if the third there is a ticker, I will not consider. Is there any data set for you to tell no at this point for not to consider? Sir, there is a trial where you after giving you a ticker. If the CTDN is negative, then you can actually discontinue and ticker also. So, there you can avoid. Do you do that? No, no, no. It is a evolving data set. The not-star trial which is looking at OSIMAT-TEN-HIP is actually ongoing. We do not have the data set. So, point I want to put up because lack of time is at this point with OSIMAT-TEN-HIP, the data set is lacking. It is not, it does not, we do not go the advantage or there is a disadvantage. With FOGEN-TKI, we do know there is advantage. So, that is where it should be. The point which I wanted today, if you have OSIMAT-TEN-HIP, let us say your TUMO board agreed to do a system ablation radiotherapy.

Would you stop your TKI during your radiotherapy or would you continue your TKI during radiotherapy? All the medouts. Stop. So, how long before and how long after? Two weeks. Two weeks? Two weeks. Before. So, you will stop. Okay. You will continue. Continue. Continue. I would continue. Since now we have data for microgrid or bioglyce, binoculars, bioglyce. We are doing radiotherapy. No, because this is more common than what you would use it. So, we need to be clear on should I continue TKI in this or not. If the radiation is not affected long, we have risk of luminatous. Okay. So, there are two concepts here. Because now we all believe that thorax, thorax, arty should be given and trials are now up going. But point which I wanted most of us believe that the cold belief was that and when it trials allowed to stop TKI's for three weeks actually, around that period, radiotherapy and mainly it is for thorax because of the toxicity of iodine. But there is now evidence to contrary that it really does not matter. So, you can do both ways but be careful that normally the lot of centre will stop it for some time. And that is what it is and that is why many times surgery is also preferred because it did not need to stop when you can really operate it. So, I will just move on. This is the trial which I... So, actually if it is brain-based, we need to stop it. The boat is supposed to move island. You have to stop. It has to stop the right. So, yeah. Because the neuro-toxicity also has... There is no hard, overwhelming evidence but that is the normal practice which I wanted to point out. So, there is normally people stop. So, if someone... people do not stop, it is nothing as a medical negligence. But yes, there is data more to stop than not to. That is what I really wanted to point out. Because we want to say something. So, no, in the previous case, we should also dissect out whether there has been a complete response, metabolic response on PET or what to do with patients who have not had a complete metabolic response at the oligometro-stitix site as well as the primary site. So, we were talking about all comers. We did not dissect out.. So, do you believe that if there is a complete response, you will not go for a... SABAR? Complete response. Complete response. So, if there is not a complete response, definitely a local ability of therapy

should be given. If there is not, if there is a complete response, that's a... My point to contrary is that most of the times that you do biopsy from this socalled computer response, 17 out of 100, you will find a residual disease. So, I don't think there is any data set as per the PET scan report. This is the two trials we have to go through. This... the first one is the first-gen TKI. The second one is ongoing. The first one, the first-gen TKI is a positive trial on the PFS and OS. So, this is what I am going to stop. The CTDNA part is very clear. I think this is a second data set which I wanted to show you on CTDNA and which just shows... The Govindan group has done it and this again shows you that if CTDNA is negative, pre-RT, post-systemic therapy, these patients do extremely well. So, this could be a way how we can actually do it. I am going to skip this because of lack of time. Just one more last thing because this is important, one minute only. Brain meds, where will you do SRS? Until what number of brain meds are you going to do to SRS? And when would you let your surgeons also come in? Quickly and then we stop. So, surgical role is for a single large med with a significant perilisional edema. Mass effect or edema. I generally do a SRS till around 3 to 4 minutes. So, SRS before is acceptable. That is what it is. Surgery, if it is very... it has edema more than 3 centimeters where you do not have a biopsy, where you need tissue. That is where surgery really helps. That differentiation we have to make. So, I... and post-surgery, there is data set that if you do a radiotherapy, the SRS part of the post-surgery was... observation was SRS was WBRT. The OS is similar, but that the locariginal recurrences are much lesser. So, I will stop here to conclude that oligometrist disease is highly complex and heterogeneous state of disease. Number of meds, organs, we all know that confusion still persists. Do you have trials which have gone up to even 10 meds or more? Evidence is mainly faced to retrospective phase 3 evidence is evolving. It is the need of the hour. It is... but the usual concept is start the system therapy, reassess after 3 months. And then if required, you can go on to 6 to 12 months, but at that point you have to start going on. And please, all this cases need to come to a MDT before and even after. It is not that a medon alone decides every case. And we are not probably converting bad into good. Only thing is we are only consolidating the good patients into doing better. CTDNA is something which I am very impressed with. This could be the way we could probably start choosing our patients, especially whom will benefit and probably what... minute told. If the patient has a prolonged response to the first line treatment, these patients are probably going to do well with a local ablative therapy. Eagerly betting for the phase 3 results, brain max. This is something which I have already spoken, SRS 3 to 4. Big lesion more than 3 to 4, where indeed a biopsy where there is a lot of perectumeral edema,

you should be doing surgery. That is where it should be preferred. In a biomarker, addictive NSCLC, the third generation PKIs are definitely going to increase the survival and should be a part of the armamentarium. Thank you. Thank you all. Thank you. May I just make one last comment. So in TMH, we are running two separate phase 3 randomized trials on the same, wherein one is the EGFR or ALT mutated and the other is non-river mutated oligometastatic setting, wherein we are treating the oligometastatic site with radiation at upfront or after 3 to 4 cycles of standard systemic therapy or 3 to 4 months of TKI, followed by response assessment and we are randomizing at that time whether the patient will receive local consolidation, RT to the primary or not. So you may be answering both of these. But what I meant to say is that data, whatever you have is merely looking at both the things. Yes. So that is what we are trying to incorporate. You are going to do it on a more better systematic way so that we can answer. Thank you. One wrote it. Thank you. Thank you. All the panelists, thank you organizers for calling here. Thank you. Thank you. Thank you for the great discussion and thank you to all the panelists. We move on to the next session, which is a panel discussion on choosing the right therapy for Undisectable Stage 3 NSCLC. This is a session sponsored by AstraZeneca. I would like to invite our moderator, Dr. Weibav Choudhry, who is a medical oncologist from.