Thank you for giving me this opportunity to present here.
I think this is one of the toughest title given to me, the application of liquid biopsy
in real world.
So before I get into this, I just want to make sure that why it's important.
See there are a lot of panels we design, we have in the market, but it's important actually
what you have on the panel and how you can detect that, how it has been designed.
That makes it different.
So I think I'll skip this.
See, what we know today about tissue biopsy, there are a lot of issues with tissue and
sometimes it's not available, sometimes it's difficult to do the biopsy and because of
that, we are not able to understand the molecular profiling.
And more importantly now we are talking about the longitudinal monitoring of the disease.
And this was one of the study where they have done CTD and anti-shudrini and it shows
high concordance there.
And if we see the biomarkers in the lung itself and it has been well validated now in the,
I think this is what is very important aspects.
Tumor heterogeneity, we know it very well and if we talk about primary tumor heterogeneity,
what is the difference between the, you know, colonial populations and then when we go to
different metastases with beta, brain, bone or liver and you see the intra metastatic
heterogeneity.
And I think that's where this, you know, this tumor heterogeneity is actually impacting
the success of the tissue biopsy and hopefully the, you know, CTD and a base liquid biopsy
can help us to identify that tumor heterogeneity and more importantly now we see to identify
those resistance signatures out of this.
And second issue is, you know, tumor is evolving, you know, this is the biggest issue.
So what, what we believe that, you know, if you have to treat, successfully treat the
cancer, you have to treat at the speed of the cancer.
And this is one of the study where they have done the comparison between tissue and liquid
within two weeks, within two months and within six, or more than six months.
What you see there is, you know, if tissue is more than six months old, you miss 40% of
the information and possibly the 40% of the information is the ones, you know, which
has evolved, which has occurred and which might lead to the resistance to the treatment.
And a few years ago there was a statement from the ask go even for the patients who are able to undergo a traditional tissue biopsy and liquid biopsy may be safer, quicker,
more convenient and perhaps more informative.
That becomes a very important now here, you know.
So when we talk about the liquid biopsy, we often say, you know, sometimes CTD and these two terminologies are interchangeably used.
But what is the difference between the two, you know, cell-free DNA is the DNA

fragments
coming into the circulation from the normal cells, mostly hematopoietic cells and they
are about 200 base pairs long, you know, in size.
And on the other hand, CTD is a small DNA fragments, about 150 base pairs long coming
into the circulation from the cancer cells and half life is less than two hours.
So what you see the pictorial representation, you know, do dots represent the cell-free
DNA coming from the normal cells.
So on the other hand, you know, green dot represents the CTD coming from the, you know,
tumor cells.
You know, it literally becomes nearly in the haystake.
Thanks to the technology now, we have the ability of, you know, picking a few molecules
of CTD from the background of the cell-free DNA and able to, you know, do the molecular
profile on that.
So when it comes to, you know, you know, liquid biopsy, you know, I just want to look into
the last year, you know, ask go.
If you look at the number of abstracts published in the ASCO last year in various indications
various biomarkers, they were about 370 abstracts.
At decade ago, there were only 10 abstracts in this.
That shows the amount of, you know, research going into the liquid biopsy and, you know,
and showing the promise of this liquid biopsy.
So out of this, you know, this 370 abstracts, 10, you know, were, you know, were from us
once in last year.
And then 10 were this year in the ASCO and we had two abstracts in asthma.
We had four presentations in international sources of liquid biopsy on various biomarkers
and various indications, you know.
But that's on gate.
What does it mean to the on-call just who is practicing in the daily life?
So some of the studies, you know, one of them was, you know, how can we use the liquid
biopsy to monitor the, you know, disease progression or monitor the therapy response.
So this is one of the examples how we are able to identify the, you know, progression
much before it could be captured by pet scanning.
And second was, can we identify the resistance signatures and how they correlate with the
imaging technique?
So some of the study which we have been doing with Dr. Kumar, you know, one of the clinical
end point was, you know, how can we differentiate, you know, what does it mean to the patients?
So if you look at these two results, both progression free survival and overall survival,
patients were stratified at the baseline based on the resistance signatures which were
captured by liquid biopsy.
And we could see if there's a significant difference in the disease outcome.
And what does it mean?

If you look at the CTD and dynamics in responders and non-responders, you know, if you see
that this results here, you know, at, you know, in session during treatment and the last time
point, and you could see the clear trend, you know, CTD and dynamics is clearly telling
us that, you know, how these responders are actually responding to the treatment.
On the other hand, non-responders, how the CTD and dynamics are CTD, load is increasing
there.
Now again, this study was done with Kumar sir, who is here.
And in fact, he has presented last year in, you know, in the presentations.
We are also doing a study on, you know, concordance on tissue and liquid using our, you know,
this proprietary panel of 1080 genes.
So we call it alpha, lung study and targets are about 500 patients.
And hopefully in another two months, we will have complete results.
But in general results, what it shows, you know, when I looked into lung-specific biomarkers,
like what are in there, NCCN guidelines, you know, on the left hand side, you see that,
you know, how we got them and how concordant was there.
On the right hand side, what you see is it's not a sensitivity, it's a detection.
And what is, what is detection, I mean, when you look at those markers, you know, if we
do not have any tissue, we have about 84 percent of detection of those markers.
When you go into the liquid, it's an 86 percent of the, but when you combine that, you know,
that that increase, you know, in earlier present, we have seen it some of, somebody showed that there is a 5 percent difference between liquid and tissue.
But it's in both sides.
When you combine them, it becomes 10 percent and that 10 percent shoots up.
You know, that's what is important.
It may not be, you know, make big difference, but even in one patient, you identify and
that is important because we are talking about precision oncology and even single patient
matters, you know, even if it could be, you know, less than 1 percent.
And there is a guidelines clearly showing that, you know, how when to do tissue biopsy,
when to do liquid biopsy and, you know, it has been discussed earlier, I want to skip
this.
You know, in NCS and guidelines, we have now liquid biopsy is part of that.
Now, what is important in now?
We know that data has shown that there is a sensitivity and specificity.
There is a concordance between tissue and liquid.
Of course, there is also false negative results, what you can see in the liquid biopsy, but
that's what we know today.
If liquid biopsy is negative, that doesn't mean the patient is negative for that.
You know, we have not detected there.
Therefore, you know, we may have to do is tissue biopsy and of course, you know, we are seeing improved that and other important fields.
So, we have seen also, you know, this, how this tissue and plasma, you can see the significant
difference in terms of overall survival.
So, I'm skipping, you know, these because I have only two minutes left.
And there was one study where they had done this, you know, quality of life.

You know, what you see, it's, you know, when you do the liquid biopsy, you have improved
quality of life parameters as well.
And there are, these are multiple studies where they have done the, you know, meta-analysis
to understand that the actionable alterations found in tissue and liquid biopsy, how it
is improving there as well.
And you know, this, I found this very interesting, you know, does molecular result timing matters.
And in fact, this is what is here.
If patients who have been treated after report comes, that's the A group.
And in the B group in the patients treated before report comes and then switch to TKIS
and then C group is when, you know, patient has been already treated with chemotherapy
and then not switch to the TKIS.
And you can see there's an overall survival, you know, benefit if you get liquid biopsy
earlier and treat according to that.
So, I think we were just discussing about that, you know, how it becomes important liquid
biopsy.
So, we have a lot of negative patients and we have captured P-10 mutation which leads
to actually resistance to the immunotherapy because, you know, it induced that environment
like Ido1, P-D-L1, expression tumor, regulate with cells and therefore, it becomes very
important.
And it's not only that, you know, as earlier speakers spoke about that, you know, combination
of tumor mutation burden with P-D-L1.
Similarly, I say, you know, combination of, you know, genome instability, including tumor
mutation burden, genome wide, HRD, you know, loss of heterozygosis and P-D-L1 can improve
the, you know, prognostic impact of these biomarkers.
And of course, you know, when we talk about the genomics, it becomes important, you know,
a variant of onion clinical significance and the interpretation becomes the key.
Like in this case, this was a dual EGF or positive patient who has progress on FATNIV
and shown resistance TKIS, what was the reason and what we found is met and PET3 mutation
which were variant of onion clinical significance.
When you look at the close proximity of those two mutations, you know, met particularly
where it was very close to exam 14 mutation has a similar, you know, biological molecular
impact, the report.
It is the reason for that leading to the resistance TKIS and combination approach is better there.
And another case was, you know, it was an actually history of breast cancer and second
primary of adenocorsion of lung.
And when we got the report and we found EGF or mutation and the doctor is a question,
it's EGF or negative because they have already done this test.

When we asked the report and we looked into there because it was a hotspot testing. That's why it becomes important.
You know, when we do the hotspot testing, we need to know, you know, if that particular
mutation is covered or not.
And I also want to highlight just another 30 seconds.
Liquid biopsy beyond blood, you know, we know there are other body fuels including sly Y, CSF, you know, urine, etcetera.
And they play important role and how that increase the, you know, sensitivity of the
liquid biopsy, just one case here, you know, it is increased in sensitivity.
It was, you know, non-submersal lung cancer was known for EGF or positive.
And you know, in the blood we found, I think it was negative.
But when you see in the CSF, we found it's a 19 deletion with VAFF, you know, 92 percent
heart to amplification 21 copies, T53 VAFF of 87 percent.
So this is where it becomes important.
When we discuss this with the doctor, his question was why blood is negative, why CSF
is positive.
And we did a homework and we went ahead and what was the reason for this was, you know,
when you have this parallel kind of space of the brain involved, shedding do happen into the blood.
When meningal space of the brain is involved, the shedding happens into the CSF.
And then we came to know that, you know, this patient has a leperminal gel disease and that's
the reason.
And the second question was whether we should be treated with ossimatinu or trastrozumab,
you know.
At the end, you know, we know that these are two pathways active and therefore both has
to be targeted and this patient was put on ossimatinu with intrathetical trastrozumab.
And this test was done in the May until today, patients were doing very well and, you know, this is why it is important.
And we know there are multiple challenges and we most of the time talk about, it costs
is one of the challenges, this was one of the study.
Of course, it is about 27 percent.
But if you combine others, which is awareness, access, simple quality time, that is actually
more than 50 percent, you know, that is the time, you know, this becomes important, you
know.
Lecker biopsy reduced the time.
It also gives us opportunity to analyze the tissue, which is not possible and samples,
which is not possible on tissue, but we can do on the liquid biopsy.
So, with this, you know, I understand that, you know, we often give the bias to the tissue
considering that is a gold standard.
What I see today is, you know, that tissue, which is gold, considered gold standard has
become old and the liquid is the new solid and bias should be given towards the choice
of doing this comprehensive testing based on the understanding of tumor biology, tumor

evolution, tumor heterogeneity.
With this, thank you so much.