Thank you so much. We only know that CTDME is very well accepted in lung cancer management
today. The very first biomarker in CTDME is 4790M to monitor to know whether there is
an early relapse or sorry resistance mechanism of resistance to first-line TKI. And where
do we have application of liquid biopsies today? There is no application of liquid biopsy
for tumor diagnosis. It is only there as a porn for prognostication and disease monitoring.
And that is a very important information that Leon should know that it is not there for
diagnosis. And of course it will be helping not just in advanced stage disease patients
where you can look at a MARDI. It can also be used to see as a periodic follow up as you
see in early treatment responses. Now how do we check that by looking at the rotational
profile? CTDME is also very fragile but today we have fixative solutions which are very similar
to formulant fixation which gives extents the half-life of CTDME. And CTDME has been very well
approved across multiple guidelines in terms of where it can be used as a testing when the
tissue testing is not possible. There is insufficient tissue and the patient is not
fit for going for another tissue biopsy. Or even when you do more tissue biopsy there is a very
high risk of death for the patient. These are the three scenarios well. CTDME has been used.
And from one of the studies back in 2018 with Dr. Anadha Madam and Kumar said we had
200 patients out of which 30 patients were not eligible to go for a tissue biopsy. They
came very bad condition. And in that small lot of 30 patients also we saw some 30%
EJFR positivity. So that clearly demonstrates that when there is a crisis you can use the
liquid biopsy CTDME testing for looking at biomarkers. Of course you require a strong diagnosis pathologist
without pathologist. I cannot take forward any diagnosis. However for looking at the therapy
options you can use CTDME. And this is a study coming from one country on toruos perspective.
I think we will get something from India also very soon. Like what each hospital or a center
will have their own experience in terms of this. And where do we look at where did all
these start? It is all started because there is tumor heterogeneity. So when you do a biopsy
you are not able to. So everything for the pathologist I is a malignant cell but not all malignant
cells carry all tumor containing mutations. Therefore when you do a biopsy you are limited to
the location where you capture the mutants. So when you do a CTDME you are able to get the
holistic picture of the disease not just from the location where you look at the biopsy but also
when the DNA bleeds into circulation. So intra tumor and inter tumor heterogeneity is one of the
main achievements that you get with CTRME. So there on liquid biopsy has an

application in today's clinic.
We all know but I am just going to. So particularly in metastatic condition as well as given recommendation
that you can use a combined profiling to get a better understanding of the disease.
So tissue testing with liquid biopsy for all metastatic patients definitely gives some kind
of a value add. Of course new adjuvant treatment followed by that. How is the treatment impact?
Does it really reduce the disease burden or not? Based on what you get as biomarker at the initial
brain sleep, you can use that for surveillance monitoring or after surgery and again when the
tumor comes back you can again look at it and then follow up. So this is just a small data from our lab
where we have two different panels. The idea is you know we have to be cost effective at the same time.
If there is a situation where we are looking at adding expensive drugs are we missing something
in the patient or not in such a scenario we cannot limit ourselves to in the same guideline
biomarkers or well established mechanisms of resistance. We might want to look at those genes
which have relevance documented in small and chemical studies or anecdotal case studies.
So this is a over experience on looking at a thousand two hundred gene panel on 52 cases where we did
combine liquid biopsy and solid biopsy together. In these patients we have found that there is a
clonal you know hydrogen 90. We were able to pick up some important biomarkers in the liquid
which you were unable to pick up in the tissue biopsy that is adding value to either therapy
decisions or problem stickation. I won't go into details in the interest of time but what the take home message here is
in broader panels also you have a significant value word that comes in when you do a liquid biopsy
profiling along with tissue biopsy and this is just a small data on the top mutated genes.
You see that more than 90% of the time in advanced lung cancer patients whatever mutations you
see in tissue you also see in liquid biopsy nearly 90% of the time. So 10% of the time you may not
pick up those mutations that you got in either of them picked up in the other and this is a small
panel. So this is a cost-effective panel where you are just looking at NCC and relevant biomarkers
plus tumor agnostic biomarkers and plus some markers which can give you information about the
small cell transformation and other critical information that is required for treatment
decisions. Even in small panels you when you do a tissue plus liquid biopsy together you definitely
see a significant value word in terms of suppose there is a driver mutation in exam 19 at sorry exam 21
at L858 and then you also have a VUL at L850 but that is also somatic. It is very close to the
active side pocket the doctor must be thinking that you know why is the TK not giving full response
because there is a neighboring somatic mutation that will impact the drug binding

efficacy.
So this is where broad you know or rather a comprehensive understanding of the gene becomes
important we need we should not limit ourselves only to the very characterized hot spot mutations
and this number is coming to nearly 15% in lung cancers many times.
So these are two cases where just to demonstrate how heterogeneity plays a very important role.
This is a case of lung cancer patient diagnosed in 21 December and initially
tissue perhaps we did not have enough material and then we read the op sheet and we got this is
actually a case from the image only and then she was raw, so impossible treated and then
when we went ahead and looked at the tissue plus liquid biopsy at the time of disease progression
we found that the raw spen fusion was detected in both tissue and liquid.
However that kinase domain mutation which is the mechanism of resistance was you know was detected
only in liquid but it was not detected in that biopsy specimen. So if this liquid was not done
with the tissue when they did the rib biopsy the information would have been missing and we
would have been scratching it's what would be the primary mechanism of resistance, you know secondary mechanism of resistance that happened in this patient.
Now because of this information the second generation in third-generation alkyne but a rossin inhibitors could be given to the patient sorry.
This is another case of combined you know liquid and tissue biopsy profiling.
So these are the take-home messages as I said you know we can look at the you know second
and third-generation inhibitors when you have mutations in the kinase domain
or let a neighbor reprotect a neighbor. Now this is another case of lung cancer she presented with you know all this I am in the interest of time I'm not going into a lot of
details here okay she's diagnosed lung cancer what happened the tissue was insufficient and the
doctor did not want to wait they said okay let me just quickly do a liquid biopsy in parallel.
In liquid biopsy there was a rossin positive and they went ahead starting treatment.
Six months later she completely there was a remission of that lesion and after two months more than that
then she slowly started developing more in the mediastinum and then the doctor this time
decided to go for a combo. I just wanted to bring out here when they did the combo we found
an L85A r previously it was a rossin fusion and so this particular L85A r was present in both
tissue and the liquid biopsy. So this initially the tissue which was inadequate they had a perycadial
effusion cell block which they gave it to us at the time of relapse. We found this mutation only
in that perycadial effusion cell block. So this clearly explains that that whatever new driver
mutations we are identifying at times it might be localized to certain locations in the human body
but later on it might be getting into circulation thank you.