Good afternoon everyone and thank you organizing committee and Akhilse for giving me for this
opportunity.
So I am going to present this important abstract which basically had compared the low dose
Pembrodism map with standard dose Pembrodism map.
This abstract was published in Espo Congress Barcelona 2024.
So basically this is very close topic to me because when I was in TMH Sanadasi, me and
Akhilse.
This topic already got approval from the ethical committee in TMH Mumbai and we were
trying to get it clear in TMH Vananasi as well.
So this is a declaration of the interest the sponsor ship details.
So as we all know that Pembrodism map in the metastatic knowledge model lung cancer, it
has proven a miracle in those patients having a driver mutation negative.
We have a lot of studies which has proven that it has a durable responses, it has a good
overall survival benefit.
But if we will sit in the real clinical scenario, what we see that the annual cost of even
with the patient assisted program, the Pembrod usually cost around 11 lakhs annual the finances
cost to the patient and without the Pembrod program, the cost of the each cycle is around
4.3 lakhs.
So this is very difficult to get retried to the patient and as we also know that only
one third of the patient usually get achieved with this Pembrodism map that response date
with the Pembrodism is usually varies from 20% to 60% and this basically depend on multiple
factor.
The patient age, comorbidity is the PDL1 status.
The toxicity matters and also this is a very important chart we can see in our right side.
This is basically a pharmacokinetic and pharmacodynamic chart of the Pembrodism map which it was seen
in the phase 1 trial that the linear correlation of the Pembrodism usually start with 0.3 mg
per kg.
And it achieved a plateau at doses around 2 mg per kg.
So initial the FDA approval came basically with the doses 2 mg per kg but later the company
came with the fixed doses schedule with 200 mg with 3 weekly and 400 mg with 6 weekly.
So that was basically being practiced in the most of the clinical trials and we are practicing
in the clinical scenarios.
So the basically the background for this abstract is basically the dosing and the patient selection.
This is still a matter of the discussion.
So this was a basic hypothesis behind this study.
So here this study had compared the standard dose Pembrod 150 to 200 mg every 3 weekly
or 400 mg every 6 weekly and compared with the 300 mg 6 weekly and 100 mg every 3 weekly.
So primary objective of this study to basically establish the not infinity of the

low dose
Pembrodism map with the standard dose Pembrodism map.
The secondary outcome was basically to develop the biomarkers which can predict the immunotherapy
treatment response.
So this is basically an open level non-infinity trial and all the patient with non-small cell
lung cancer who are eligible for the Pembrod based treatment they were included in the study.
So it was a pre-planned decision before starting the study that interim analysis has to be
performed after the first 250 patient and who will be forward for the year of the one around
one year and they have considered as a 10% difference between the overall survival in
those patients whether to decide this study has to be continued or need to be stopped.
So this is a design of the dedication trial.
The patient would randomize into the two arm the first is a standard dose Pembrod which
included the 400 mg every 6 weekly, 150 mg 3 weekly or 200 mg every 3 weekly and other
is study arm was a Pembrod where they have used a reduced dose that is 300 mg every 6 weekly and 100 mg every 3 weekly.
The patient inclusion criteria all the patient eligible for the Pembrodism map based treatment
the type of the treatment given Pembrodism have alone or in combination with the platinum
doublet.
The stratification criteria they have used is a smoking PEL1 status the EECOC PAS01 versus
2 they have taken the cut off of 10% whether to continuation of this study or to discontinuation
in the study.
So total 256 patient data were included in the interim analysis 123 patient in this standard dose arm and 133 patient in the reduced dose arm.
In the standard dose arm 8 patient received the dose 150 mg every 3 weekly and 115 patient
received 400 mg every 6 weekly.
In reduced dose arm out of 133 patient 5 patient received the 100 mg every 3 weekly and 128 patient received the Pembrodosis 300 mg every 6 weekly.
And Pembrodism map was administered along with the chemo therapies around 49.2% of the patient.
So this is basically the baseline characteristic which were comparable between the both arm
the standard dose and the reduced dose.
The EECOC performance status of 0 or 1 was present more than 80% of the patient.
The PEL1 less than 50% population was seen in around 62% patient in standard dose and
60% in the reduced dose.
And more than 50% patient population was present in 38% in the standard dose and 41% in the
reduced dose.
So this is basically the chemo immunotherapy was given in patient population having PEL1
status less than 50% in around 96% in the both arm and in PEL1 more than 50% population
chemo immunotherapy was given around 30% of the patient in the both arm.
The median cumulative dose of the Pembrod was 1600 mg in the standard dose and 1200

mg in the reduced dose arm.
The patient who are still on the treatment after the burn year the patient population
is around 34% in the standard dose and 28% in the reduced dose arm.
The reason if you will see the progressive disease it was seen in the 38% patient population
in the both arm.
The adverse events was the reason of the end of the treatment is around 8% population
in standard dose and 10% in the reduced dose arm.
And the death of the patient was around 11% in standard dose and 11% in reduced dose arm.
If you will see the result in arm A the one year overall survival was basically comparable
between the both arm.
It was around 53.4% in the reduced dose and the 56.6% in the standard dose arm.
The median was also around 15.9 month in the reduced dose and 13.1 month in the standard
dose and the P value is not statistically significant.
And also the median PFS was comparable between the both arm.
There is a capelin mirror analysis here we can easily see there is a no separation between
the overall survival curve and the PFS curve between the both the standard dose and the
reduced dose arm.
So in conclusion the one year survival difference of 2.7% they have found in the interim analysis
which was within the 10% cut off criteria.
So this was basically the decision for continuing then close in criteria for the patient.
The still the multiple trials are going in the dosing duration and the personal treatment
personalization of the treatment which are still under research and beneath the more data
to define that.
And if you will see the all the cross trial comparison we can't do but still the in the
keynote 189 trial the one year OS with the PEMRO 200 MG it was around 70% and the median
OS was 22 months higher than in the dedication trial.
The one year OS was found only the 58 and the 17 the median months in the median OS.
So we still need the full paper and the full results of this trial and we will also wait
for our institutional data also which will be I think completed in the few years.
Thank you.
Thank you for this very important paper.
I will request comments from many of the members.
I'm giving since there are a lot of students here I request you to sensitize the students
about the dosing of immunotherapy because we have done low dose immunotherapital in head cancer now we are doing trials of PEMRO, Lotus PEMRO and lung cancer just works on
dosing.
Yeah, so this is a very important study.
We know that the dose that has been approved not just for immunotherapy but for many of
the targeted drugs as well is probably higher than what is actually required for efficacy.

So but what is that magic number?
What is too low?
What is optimal?
And there's no way to tell from a single study.
So similar to us as we are studying 50, this studied 100 maybe 50 years too low maybe 50
years more than what we require.
We don't know.
So you know the way to do it is we require a lot of money and a lot of resources which
is not possible.
So this is the best that we have but absolutely I think the take home message is that a lower
dose than what is approved is efficacious and if your patient I mean if your patient can
afford it great I mean if they have insurance and if they have coverage great but if they
do not do not deny them by not offering them a lower dose because we have quite a few
data now and this is a randomized study which is giving you some kind of confidence that
a lower than approved dose is similarly efficacious than a full dose.
And this is of course not the full end result of the study but this gives us confidence.
Rightly looking at the curves it doesn't look like there's going to be a whole wide separation.
So I think take home messages please offer your patients the drugs that are available
that is affordable in whatever abilities that they have.
I think most of us are already practicing this thing the 100 mg we are already giving
it but we need a more clarity of the data so that we can promote it as well.
Thank you.
Thank you Dr. Pooja.