So, this is the primary results published in JCO the sometime back of the RTOG 1106 with
ECHOG Acryne 6697 trial.
It is a phase 2 trial of mid treatment individualized PET CT based adaptive dose escalation for
stage 3 and SLC.
So, what is their purpose?
They followed the old RTOG 0617 protocol of a dose escalation with a twist in it.
We will come to that where what they have done in this CTRT they utilized the mid treatment
FDG PET.
The aim was a dose escalation and the method they utilized is an adaptive radiation.
So, this is the schema standard dose radiation at 2-gray per fraction with the PET evaluation
would be around 4 weeks versus a bit accelerated 2.2-gray per fractions, evaluate the PET and
we will come to that what are the parameters.
They neither continue the same or continue the adaptive new plan.
So, let us go back to bit of the background.
We know first the RTOG 0617 published in Landsat 2015 a phase 3 2 into 2 factorial design for
unreceptible stage 3.
They tried 2-dose protocol 60 and escalated 74 with or without situ-tuximab in addition
to their concurrent PAC-LICARBO plus consolidation with an primary endpoint of overall survival.
No benefit by dose escalation, no benefit by adding situ-tuximab, more deaths and esophagitis
by increasing the dose.
So, it is kind of not taken up well and it is one of the very negative trial.
In the 5 years result is same with a median falloff of 5.1 years, more esophagitis this
which is actually 3 to 4 times more in the experimental arm.
So, it proven that the standard remains a 60-gray radiation with concurrent chemo for the stage
3.
The 2 years data in the control arm is kind of similar to pacific data because by the time
the pacific data started coming out.
So, people have tried doing whether the technology matters.
So, a secondary analysis of IMARTI with a median good follow-up, 47 percent of the original trial had IMARTI but no difference in survival with 3D CRT.
Of course, less of pneumonitis reduce hard dose and this kind of given that V 20 is better
achieved can be an indicator for radiation pneumonitis.
By this time the pacific trial is published.
So, even after the 5 year data of quite impressive, more or less the stage is treated
by chemo radiation followed by a consolidation.
Now, why this trial came up?
There are phase 2 data before that.
There are 2 important phase 2 data.
One treated about 66 patients, stage 3 and SLC post 40-gray utilization of PET to a dose up to 66-gray, 30 to 35 percent volume reduction by this adaptive and a better wear
coverage.
The other one more impressive from the same author of this current data published in

JAMA with 42 patients and they also selected poor KPS and poor PFT patients.
So, this indicated why maybe sorry their adaptive played a role.
So, their adaptive is after 45-gray and a similar kind of escalation completing in 30
fractions up to even 86-gray and had concurrent chemo as well and consolidation.
So, what the current one did, they utilized baseline PET as usual as also a mid treatment
PET and followed an ACS standard utilizing the same machine and machine parameters.
The PET registration protocol is from their 0-5-1-5 study published before.
They also utilized 4-D CT-based simulation in select cases preferably IMARTI-IGRT.
They documented a metabolic tumor volume from the PET, followed standard dose prescriptions,
no elective nodal coverage.
The adaptive PET would come around 18 fraction which will be 36-gray for the standard, arm
and 39.6-gray for the experimental one.
Try to keep the mean long dose of the whole plan less than 20, long V20 less than 35
and esophagus D-max less than 74.
So, this work in the documented in their trial.
So, their primary therapeutic endpoint is freedom from loco-regional failures or progressions
and which is a centrally reviewed thing, no failure in the PTV primary or the node.
The primary imaging endpoint is change in the SUV peak from the baseline to the mid-treatment
PET and they try to correlate this with an FFLV.
So, these are the key features among all the features which is more or less well-balanced
in either arm.
So, major due to the patients are adenocarcinoma, major T-S-3A.
Most of them, about 60% are tumor-sized in either arm less than 5 centimeter.
Former smoker or current smoker are predominant in their trial.
So, what's the result?
The adaptive RT causes a 56% reduction in the metabolic tumor volume.
However, the median mean long dose which is more or less similar in either so as the
hard dose, so as the great to esophagitis.
In fact, adaptive had more great to esophagitis and these parameters you can see from the table
as well.
Once they applied this in their alive and progression free survival and also freedom
from low-corregional progressions, the curves are overlapping so it did not translate into
any clinically endpoint-based benefits.
So, what they concluded?
As we started with these four points following the RTOG0617 dose escalation, is it feasible
by a mid-treatment PET and adaptive planning?
Just if we check feasible, yes, it is feasible.
What they utilize to be a mid-treatment, mid-CTRT-based, FDG-PAGE, is it effective?
It is kind of effective, I will come to it.
Their aim was a dose escalation which they have safely been able to deliver also with
acceptable toxicities and the method they use in adaptive RT for that.
But it has translated no benefit in freedom from local progressions between the standard
dose chemo radiation versus adaptive and there has to be additional data on these SUV peak

and metabolic tumor volumes correlating with the freedom from local progressions because
we all know the inherent challenges of a mid-radiation treatment PET-CT and documenting
these parameters.
So, I have put my take home that the dose escalation still remains controversial, since
a long back it is almost 10 years now from the RTOG0617 and it is still controversial.
The mid-treatment PET have added further more controversy due to the inherent changes of
radiation and the assessment of these PET parameters while somebody is on chemo radiation.
The only favorable factor is the toxicity remains similar even after doing a dose escalation
in this and this may not be in tune to the current standard of care in stage 3 and SLC
once the specific data has matured.
So, what should we do?
Maybe beyond PET adaptive radiation try to do proton-based, try to do SBRT with the lung
primary and sequential to mediational what the LU008 is doing and probably some MR guided
role if we try to really assess some beyond the biological parameters predictive factors
for adaptive radiation.
As of now, this is from authors, there is no recommendation for going for phase 3 for
this current trial.
So, I end, thank you and Merry Christmas.