Thank you ma'am. I d also thank the organizers for the opportunity. I will be continuing
where Minith has left off in our quest for prolonging the survival. Our conventional
wisdom has been conservative therapy increases survival. NRGLU002 was a different outcome.
So this is a randomized phase 2, 3 trial of maintenance system therapy versus local conservative therapy plus maintenance system therapy for limited metastatic non-small cell
lung cancer. They have used the word limited metastatic. The definition for oligometastatic
is further adding to the confusion. Background local therapy especially radiation has been
used for pylation. With better systemic therapy, target therapy is immunotherapy and improved
imaging as well as development of SBRT. Interest has increased in using abdative therapy
or that is radiation in this scenario or surgical approaches as local consolidated therapy to
improve oligometastatic and SLG survival. There is a theoretical advantage to local therapies.
Time to first system disease to declare itself, ability to evaluate the response of the disease
to specific systemic therapies. Fewer sites that can be potentially treated and timing
that will limit the development of acquired resistance. We have a large data of prior
randomized studies that have utilized mainly chemotherapy and had shown that local considered
therapy increases the PFS. But none of these trials have incorporated immunotherapy. There
have been single trials of IO, IO plus salvage local therapies that have shown some numerical
benefits in TFS. So what are the methods in energy, multisynthetic trial? This is the
method in the schema. Important is the timing. They included patients with metastatic NSCLC
having completed at least four cycles of courses of first line induction systemic therapy.
They were open to all inductions. They have not satisfied. At least the abstract is not
satisfied. What are the induction therapies used? Restaging studies that reveal no evidence
of progression and limited measure of disease, defined as 0 to 3 discrete, extra clinical
sites. They have not included brain. All of which must be amenable to SBRT radiation without
surgery. So SBRT is one of the prime modalities of consolidated therapies that they have included.
A minimum of one disease site, metastatic or primary needs to be present after first
end induction therapy and treatable with local consolidated therapy. They have satisfied
as squamous versus non-scamous and the continuation maintenance of the systemic therapy as immunotherapy,
cytoxic chemotherapy or other induction regimens of combination.
Arm 1, arm 1 was only systemic maintenance therapy. Arm 2 had SBRT slash radiation or
surgery. The irradiation was followed by maintenance of systemic therapy. The catch

here was that all arm 2 patients, even if treated with surgery, must have one set of
disease treated with radiation. Maybe biased towards a radiation oncologist who were maximum
in the investigator group. If a metastatic site is best treated with hyper fractionated
radiation, this would be permitted if SBRT surgery was not indicated. It enrolled 218
patients from 68 sites. The primary and secondary outcomes, the primary outcome was
PFS defined as modalities of progression or limited metastatic sites after first-line
systemic therapy and OS. OS was more evidence of progression, limited metastatic disease
after first-line systemic therapy. Second objective is quality of life and CTDNA outcomes.
This is the primary hypothesis. The primary hypothesis was that the local considered therapy
increases, improves the PFS in the OS. For the PFS, they considered an improvement in
six month and 12 month rate of PFS at 60 to 75 percent and 12 month from 39 to 57 percent
for hazard ratio of 0.6. For the OS, they looked at a 12 month increase in the OS from
68 to 77 and a 24 month increase in the OS from 47 to 61 with the hazards of 0.6. This
was the Arctic criteria, this was the systemic therapies, maintenance therapies, they have
to start within two weeks of registration. They included the into the gym, Pembroe,
Naivew EP, Atizo. These are the results well matched both arms, male, female, the gender
and ethnicity. Astrology was matched. Now this trial included nearly 90 percent of patients
in both arms who had received maintenance in the therapy. Number of lesions, one to two,
most of the patients were PFS were PS01. Now these were the results of the patients post-induction
therapy that is after four courses of the patient's therapy.
Most of the patients were in stable disease. There were very few complete responses. There
were few partial responses. And the plan for the local system, local conservative therapy, they have not included the number of patients undergoing surgery
in this, in the abstract clearly. But majority of the local considered therapy was for the
primary tumor followed by medicinal nodes. Then there was bone sites in the lung, liver,
spine. This trial had included cranial sites. So this was a PFS, surprising outcomes. One
year PFS rate in the systemic therapy arm was 48 percent. While in the local considered
therapy plus systemic arm was 51, hazards of 0.6. The two-app PFS was not very optimistic,
35 versus 40. This is the OS. The OS was actually detrimental at two years, 58 in the
systemic therapy arm versus 54 in the local considered therapy arm. When you lose, when
you start losing, you look at straws, you want to look at beautiful outcomes, you want
to look at different data, look at the data differently. So this is cumulative

incidence
of time to infield failure. They wanted to see whether there is another way where we
can present the data. So this was death without infield failure as a competing event. They
wanted to look at patients whether immunotherapy or whether the considered therapy contributed
to maybe out of field failure. So even in this, there was no significant advantage of using
a conservative therapy. The second novel outcome criteria that they use was time to
new lesion development. That is death without new lesion development as a competing event.
Even in this, the hazards are crossing unity. Results, toxicity in the systemic maintenance
arm, 11 patients, that is 15 percent and grade 4 and the situation has grade 5 adverse events.
While in the local considered therapy arms, it was 15 percent and 8 percent. And adverse
events related to treatment. For the adverse events, the treatment is definite, probable
and possible. Thus patients with the overall, that is the LCT arm. They had higher toxicities
attributed, attributeable to the treatment. Limitations, it is agnostic to systemic therapy.
No single regimen was followed. Definition of oligometacicist is ambiguous. It was determined
by one cross sectional imaging. No biomarker enrichment was done for at the three month
cut off for starting the treatment. No clear understanding of metastatic disease trajectories.
Previous studies had not randomized patients in IOR. So the take home point here is if
the survival with IO or survival with better targeted therapies is much more. Thus addition
of considered therapy contribute much. So the NRJ LU 002 definitely says that addition
of considered therapy in patients who are now taking immunotherapy might not be the best
way forward. Thank you.