- So, good evening everyone. So, I will be discussing regarding this trial Destiny Lung 0 3 part
- 1. So, this is regarding TdXD monotherapy in pre-tweeted HER2 over expressing non-scamous
- NSCLC. So, HER2 over expression that is IHC 3 plus or 2 plus is identified as almost
- 3 to 20 percent of NSCLC tumors and are associated with poor prognosis. So, TdXD is approved
- in several regions such in US and Europe with HER2 positive undecectable in metastatic
- NSCLC and US for previously treated undecectable metastatic HER2 positive solid tumors with
- no alternative therapies. So, the approval of this HER2 positive in HER2 positive solid
- tumors was from Destiny Lung 0 1 cohort 1 A result in which the response rate of TdXD
- was seen in almost 34 percent of patients and in IHC 3 plus the response rate was almost
- 53 percent. So, in Destiny Lung 0 3 it was evaluating regarding the safety and efficacy
- of TdXD based regimen in HER2 over expressing that is IHC 2 and IHC 3 plus NSCLC. So, this
- is the study design this is a phase 1 B multi centric open level dose escalation study of
- $\operatorname{\mathsf{TdXD}}$ in HER2 over expression and a CLC. So, basically there are several parts. So, I
- will be discussing in this part 1 that is TdXD monotherapy and the involvement of this
- arm is complete and the key end point of this monotherapy arm is response rate duration
- of response disease control rate PFS and over a survival and safety and tolerability.
- So, this is regarding patient dispositions. So, 36 patients were enrolled and 33 percent
- of the patient discontinued treatment either because of progression of disease or adverse
- event or patient disease and the median duration of TdXD treatment was 7.2 months and duration
- of follow up was around 15 months. So, coming to regarding the demographics and clinical
- studies the important point is that they have included patients with brain metastasis
- which was seen in 30 percent of patients and when we see the IHC status. So, 2 plus patients
- were there in almost 55 percent of cases. Regarding PDL1 status they have a stratified $\,$
- and the PDL1 less than 1 percent was seen in 33 percent of patients and the prior therapies
- those who received EGFR TKI in the prior therapies were almost 52 percent of patients.
- So, coming to outcome with TdXD the overall response rate was seen in 44.4 percent of
- patient and the disease control rate at 12 weeks was 77.8 months, 77.8 percent. So, median
- duration of response was 11 months that is quite good. This is regarding PFS and OS the
- median PFS was 8.2 months and median OS was again 17.1 months. So, again as good data.
- This is regarding the best percentage change from baseline from the target lesion.

So,

this is the this water for plot. So, when we see the stratification based on the PDL1

status. So, when PDL1 is less than 1 percent those patients did well with TdXD and the

best percentage was magni- magnificent in these group of patients.

This is regarding the exploratory analysis of TdXD response rate and PFS and OS in those

patients who are IHC 2 and IHC 3 plus and those patients who received prior EGFR TKI

and no EGFR TK. So, those patients who are IHC 3 plus did better than in comparison to

IHC 2 plus and those who received EGFR TKI comparatively or numerically better in comparison

to those who have not received EGFR TKI. But PFS and OS was almost similar in both population.

Regarding safety summary, the most common adverse event was nausea, vomiting, fatigue

and the grade 3 and more side effect was mostly anemia and fatigue and the drug risk adverse

event was seen in almost 94 percent of patients while the grade 3 and above adverse event

was seen in 40 percent of patients. The characteristic side effect that is ${\tt ILD}$ which is associated

with TdXD was seen in 2 patients and the drug related left ventricle dysfunction in one

patient only. So, to conclude this destiny lung 0-3 part 1 confirms the clinical benefit

of TdXD monotherapy with a dose of 5.4 milligram per kg body weight. In a pretreated herd

2 positive herd 2 overexpressing IHC 2 plus or IHC 3 plus metastatic NSCLC. Building this $\frac{1}{2}$

destiny lung 0-1 cohort 1A results while the explody analysis showed that the herd $2\ 3$

plus or 2 plus NSCLC or those who received or not received EGFR TKI did better.

see the overall response rate in herd 2 3 plus it was 56 percent and PFS was 6.9 and

OS of 16 months while in 2 plus the response rate was 35 percent PFS 8.2 and OS of 17 months.

While those patients received EGFR TKI the response rate was 68 percent, PFS of 8.2 months OS of 19.6 months and those who not received EGFR TKI the response rate was a

bit lower 17 months 17 percent PFS of 7 months and OS of 14 months. So, these data suggest

that EDXD associated with improved outcome over the second line standard of care in metastatic

herd 2 positive NSCLC and there is no new safety signal where identified and destiny

lung $0\bar{\,}$ 3 is ongoing the part 3 and 4 are assessing the EDXD better treatment in patient

knife treatment knife herd 2 positive metastatic NSCLC. So, this was my last slide. Thank you so much.