Thank you organizers for the invitation.
And I would like to discuss this world conference on lung cancer paper on Phase 3 trial on
SF189,
and there are many potent second and third generation alkenibutans like electinib, brigartinib, lollatinib, seratinib.
They are prone to resistance and palindromia and they still develop and that includes CNS
progression, that leads to CNS progression, which is a major cause of illness and death.
So, SAF 189, that is 480, is a highly potent brain-perinterating next generation alken
and Ross 1 inhibitor, dual inhibitor and has demonstrated promising clinical efficacy in
Phase 2 studies.
So it was an interim analysis which was reported called the remark study in this conference.
So the eligibility of this study was locally advanced or metastatic alkenib positive lung
cancers which were treatment of ECOC 0 to 2 and it was further stratified into 0 to 0 or 1 ECOC PS or 2 and whether or not CNS metastasis was present.
So, foratinib was given in the doses of 1-6-MG QID and every 21-day cycle and cresotinib was
as the usual dose to 50-MGPD.
So the primary endpoint was assessment of PFS, objective response rate, the time to progression,
time to response and the overall survival and safety and also the pharmacokinetics and IRC
associated intra cranial efficiency as well as the quality of life.
So, the patients were screened around 330 to patients were screened, a few of them failed
screening and patients were randomized to around 272 to 75 and the 481 arm got around
139 and cresotinib around 136 and there were disease progression noted in the 481 arm
as well of 18 patients and death of 4 patients and intolerance of 5 patients, withdrawal
by patient 5 and patients' decision to withdraw the stop the drug was in 4 and in cresotinib
arm pretty much disease progression was higher of 60, death in 1, intolerance in 4 and withdrawal
by patient of 11 and so in both the groups the demographically it was more or less equally
distributed and the significance was that in the 481 arm almost 36 patients versus 20
patients in the cresotinib arm were above 65 years and gender wise and racial wise it
was both same and the majority of the patients in both the arms almost at around 99% 95 to
99% of the patients in both the arms were non-smokers.
So, ecop PFS, majority of the patients were ecop PFS 0 to 1 and the disease status was
majority of the patients were disease stage 4.
CNST metastasis was present in almost in equally around 28% of the patients in the 481 arm and the cresotinib arm had 37% of the patients.
So, coming to the primary end point of PFS assessment so the 481 did not yet reach the
PFS value whereas in the cresotinib arm it was around 13.93 months and it was a significant

PFS the PFS was statistically very significant and with a good hazard ratio of 0.23 and the
secondary end point was the time to progression which was again in cresotinib it was around
19 months and again 481 was quite useful in this aspect also which had a hazard ratio
of 0.04 and again P value was quite significant.
The secondary end point overall survival was around in the cresotinib arm it was around
2 years 24 months and again the significant hazard ratio was the hazard ratio was around
0.6 favoring the 481 arm but the statistically it was not significant with the P value of
0.07.
So, systemic and intracranial objective response rates was almost you know the in the 481
arm it was 92% whereas in the cresotinib arm it was 80% and the overall response the patients
with intracranial overall response was you know almost 100% in the 481 arm and cresotinib
arm had 50%.
So, the safety summary was that the 481 was well tolerated without any major grade 3
toxicities the treatment related adverse events was observed in both the arms almost equal
but there was the cresotinib arm had significant treatment related adverse events of hyperglycemia
hypertension and prolongation of QTC.
So, grade 3 treatment related adverse events occurred in 37% of patients of cresotinib
compared to 55.6 patients with cresotinib and common grade 3 adverse events for 481
was hyperglycemia hypertension and prolonged QTC and there were no interstitial lung disease
or visual loss or hallucinations observed in the 481 arm as compared to the cresotinib arm.
So, conclusions the remark study made its primary endpoint demonstrating a statistically significant
and clinically meaningful improvement in PFS in ACTK and AF NSCLC in interim analysis
with a significant P value and the hazard ratio of 0.23.
It also showed significantly improved improvement of CNS efficacy versus cresotinib and with
a hazard ratio of 0.04 again statistically very significant and it also showed an improvement
in overall survival versus cresotinib with a median loss of not reached versus around
24, 9 months 24.94 which was although not statistically significant but it had a good
hazard ratio of 0.6 favoring the foratinib arm.
So, safety profile of foratinib was as well as expected without any new findings and these
data have verified that for atinib is a new treatment option for advanced ALP positive
NSCLC patients.
So, with this I conclude my talk.
Thanks.