

Thank you for the opportunity. As discussed by Dr. Basusar, we are not satisfied with our chemo radiation approaches and we are trying to either dose escalate or do something to increase the efficacy of our chemo radiation. This is one attempt as he mentioned LU008 where they try to treat with two modern modalities of radiation. One is SBRT and another is chemo radiation to different volumes. This was presented in Astro this year. So, principal investigator is Dr. Charles Simone. So, the hypothesis is for locally advanced non-small cell carcinoma concurrent chemo radiation followed by dose mop, dose mop, local control remains poor despite of all efforts. So, there is a possibility of combining SBRT with chemo radiation to the node SBRT to the primary tumor. So, this chemo radiation approach is being replaced with conventionally fractionated radical therapy with SBRT to primary tumor. It is hypothesized that it will be well tolerated and will improve the local control. So, this is a representative case example. This study was done as a phase 2 study. This is a phase 2 study. So, how the volumes would be? So, we know that there is a primary tumor and there are mediastinal or high lymph nodes. Usually what we do is we treat both with chemo radiations combined, but here they have tried treating primary tumor with SBRT and nodes with the chemo radiation. But how it has changed the scenario? It has reduced the lung volumes receiving certain doses like 40 grade, 20 grade, 10 grade. As you can see it is 44 percent reduction, 29 percent reduction and 8 percent reduction. So, this phase 2 study was done and the study results were published in 2013. So, here 55 patients of locally advanced lung cancer non-small cell were subjected to single arm study where SBRT followed by concurrent chemo radiation to the nodes were done and subsequent treatment was common. So, the one year PFS was 62 percent which was better than the results of historical results of concurrent chemo radiation trials and one year PFS receiving lower volume was better than the specific trial. Median OS was encouraging 40.8 months and most of the failures were distant failures not the local failures. Toxicity were under control and were not very grave they were better. So, this phase 2 study was designed in such a way that only single arm study was done and, but the phase 3 study was planned on the basis of results of phase 2 and it was a randomized study where there were 2 arms one is control arm and one is experimental arm. Control arm is the usual what we do in our usual practice chemo radiation 60 grade into grade perfection followed by the our protocol as immunotherapy. In the experimental arm they combined SBRT with concurrent chemo radiation as we all know

SBRT we have to give a BED of more than 100 gray then only it will be effective. So, the doses for SBRT were either 54 gray 3 fractions or 50 gray 4 fraction depending on the location and in both peripheral lesions tumors and if the disease was central or it was close to the nodal disease then 50 gray 5 fractions. Then radiation to the higher or mediastinal source was same as our previous practice like 60 gray 30 fractions and chemo concurrent chemo was planned as per our usual practice like metformin or docetaxel or in adenocarcinoma splat in pemetrexate and maintenance dose volume up as indicated or if not indicated then 2 cycles of paclitaxel based chemotherapy. So, the inclusion criteria was it should be documented histological proof of non small cell and stage 2 and stage 3 which are medically inoperable or refuse surgery who are candidate for chemo radiation identified primary tumor and at least 1 nodal metastasis. So, no previous disease they allowed the neodymium chemotherapy up to 4 cycles. Primary tumor should be less than 7 centimeter because we are giving SBRT is more than 18 year performance status of 0 to 2. Tumors which were close to the nodal disease less than 2 centimeter were excluded and priority in this region was subjected to the physician choice. So, the primary objective was to compare overall survival and progression free survival. There were many secondary objectives like response rate, local control, pattern of failure, changes in pulmonary function, quality of life, toxicities and prognostic value of baseline physical activity on the other parameters and there were some exploratory objectives like collecting the biopsy specimens for future analysis and regional lung ventilation and those thresholds on the toxicities. So, statistically this is a hybrid superiority/infinity design in which this study arm will be considered not better only if it is proved to be inferior and it is expected to increase the 5 year overall survival from 38 percent to 48 percent and it is expected to increase the 2 year PFS from 41 percent to 53 percent and 4 year PFS from 31 to 44 percent. So, already the trial has started approval and it is the sample size is around 450 patients and there will be interim analysis based on the PFS and OS whether it is going right or wrong it might be stopped in between and it will be doing a approval in 4.7 years and there will be pretreatment analysis for every 3 years in both arms at every center. So, currently what is published is that it has already started and as of now 30 patients have been accrued and 266 sites have been opened for accrual and this the good part of this is there is no lab or PFT cut off no city chest MRI brain lab time windows no exclusion for any actionable mutations and it allows

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2 patients also and we hope that this may change the standard of caring in operable locally advanced nasopharyngeal carcinoma. It might improve local control PFS and OS and as we are moving towards high precision radiotherapy this might be helpful because we have the tool of SBRT it was tried as a boost to CTRT but it failed because of toxicity's but now with this method we can apply both together. Thank you.  
Thank you.  
Thank you.