

Chapter-6: Summary

Every individual is unique and that implies on cancer too in terms of their genome complexity. The concept of personalized therapy comes from here. It is a well known fact that cancer patients with the same histological grade and clinical stage may respond differently to the common therapeutic regime. Therefore, predicting response to neo adjuvant chemotherapy is of immense clinical value in cancer management where we could able to tailor made the treatment modality for better clinical outcome in different cancers including esophageal squamous cell carcinoma.

Among the 108 ESCC patients who underwent neo adjuvant chemotherapy (NACT), we found those who weren't smokers lived longer. This was found true with female patients also who lived longer than their male counterpart. Other habits like use of alcohol, pan, and tobacco chewing except areca nut use couldn't correlate with response to chemotherapy. Follow up duration was found longer in non pan users. In most of the studied patients, we reported normal serum biochemical values, which indicate good performance status, better capacity to tolerate neo adjuvant chemotherapy and low possibilities of metastases.

ALDH1 over expression was found correlating with poor response to neo adjuvant chemotherapy whereas p16 over expression was found correlating with the better response in the same group of the ESCC patients. HER2 over expression in ESCC didn't show any impact on predicting treatment response but showed significant correlation with ALDH1 positivity. Majority of HER2 positive ESCC tumors were reported as aneuploids and had low S phase fraction. Significant percentage of diploid tumors had high S phase fraction and responded to neo adjuvant chemotherapy.

A model for response assessment of the treatment modality in esophageal squamous cell carcinoma is developed and proposed based on the findings of this study. We propose assessing tumor, node and performance status clinically, and testing ALDH1, p16 through immunohistochemistry, and analyzing ploidy status with S phase fraction through flow cytometer upfront in ESCC patient.

If the ESCC patient's tumor reported higher tumor and node status, poor performance status, ALDH1 over-expression, p16 negative status, aneuploid and low S phase fraction, they would most likely respond poor to neo adjuvant chemotherapy and therefore NACT has to be followed by surgery and other targeted therapy (to eliminate cancer stem cells) in this group of patients.

If the ESCC patient's cancer reported low tumor and negative node status, good performance status, ALDH1 negative, p16 positive, diploid with high S phase fraction, it may indicate good response against NACT and in this group of patient's, radiation could be added along with the chemotherapy as chemo-radiation, where surgery could be avoided since cancer stem cells which are known to reseed the tumor couldn't be found.

In conclusion, ALDH1 can have a role as biomarker in predicting response to neo adjuvant chemotherapy in ESCC patients. p16 could predict responder among those who underwent neo adjuvant chemotherapy. The association between ALDH1 and HER2 and their cumulative impact on the clinical course of ESCC requires further evaluation in larger patient population. More cancer stem cell marker on larger ESCC patients number need to be investigated in future to propose definite NACT response assessment model. This proposed model for response assessment against neo adjuvant chemotherapy for esophageal squamous cell carcinoma patients may be validated over a large number of patients of other parts of the country too in the future study that would help the findings of current research to move from the realm of the lab to the clinics.