

Significant incidence of Braf p.V600E mutations in esophageal cancer sets the stage for potential use of tyrosine kinase inhibitors.

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Introduction Diagnosis of esophageal cancer varies from locally advanced to metastatic at presentation. Most of these patients are cachectic at presentation and physically not suitable for radical tri-modality treatment as per the CROSS trial. Hence, the prognosis of esophageal cancer remains guarded. Presently, tyrosine kinase inhibitors (TKI) are successfully used in treating melanoma, non-small cell lung cancer, and possibly for treating esophageal cancer. Allele Specific Multiplex Sequencing (ASMS) detects somatic mutations in samples with low mutant copies and in the presence of overwhelming wild type. Hence, we have re-evaluated and are reporting the findings of the incidence of Braf p.V600E mutation in esophageal cancer using ASMS.

Methodology DNA was extracted from 40 formalin fixed paraffin embedded tumor tissue (FFPE) samples that were collected from patients with squamous-cell carcinoma of the esophagus. The Braf p.V600E/K mutations were analyzed using ASMS. All positive results were confirmed by bi-directional ASMS. The results were correlated with patients' demographic and pathological data.

Results Overall incidence of Braf p.V600E was 92.5% and was present in all stages (IB, IIB, IIIA, IIIB, IIIC and IV) of esophageal cancer. There was no difference in the incidence of Braf p.V600E between patients who smoke, consume alcohol, chew betel or any combination, and those who do not. There was also no gender difference in the incidence of Braf p.V600E.

Conclusions Braf p.V600E is a pivotal driver mutation in the MAPK pathway. Firstly, the data show incidence of Braf. p.V600E is higher than that reported in the literature. The results pave way for further follow up studies for possible use of TKI targeted chemotherapies. Secondly, incidence of Braf p.V600E mutations could be independent of known cancer etiology (e.g. smoking, consumption of alcohol, chewing betel)