***PTEN*-R130\*-HNSC**

***Gene Function and clinical relevance*:** The *PTEN* gene encodes for the tumor suppressor protein, PTEN, which is a dual protein and lipid phosphatase. As a lipid phosphatase, it converts PIP3 to PIP2 and as a protein phosphatase; it dephosphorylates tyrosine, serine and threonine-phosphorylated proteins. The lipid phosphatase activity is critical for its function as a tumor suppressor protein as it inhibits the PI3K-AKT-mTOR signaling pathway. Somatic inactivating mutations and deletions in the *PTEN* gene are associated with multiple cancers including uterine (21%), prostate (19-22%), glioblastoma (32%), lung (2-4%) and breast (9-10%) cancers (TCGA, provisional, PMID:28481359)

***Alteration and Frequency***: The p.Arg130\* (p.R130\*) alteration in *PTEN* results in a premature truncation of the PTEN protein at amino acid 130 of 403, within the phosphatase tensin-type domain. The R130\* results in loss of function of PTEN constitutes about 7% of *PTEN* altered head and neck cancers (PMID:28481359, TCGA, provisional). *PTEN* alterations are common in HPV-negative head and neck cancers (PMID:25631445).

***Prognostic Implications***: Loss of Heterozygosity(LOH) on chromosome 10, in the *PTEN* locus and loss of PTEN expression correlate with invasive and poorly differentiated carcinomas, lymph node metastases and poor prognosis of head and neck squamous cell carcinomas (PMID: 22413021).

***Therapeutic Implications***: There are no FDA approved or NCCN compendium recommended therapies selectively targeting *PTEN* R130\* alteration in head and neck squamous cell carcinomas.

In a phase II study, a head and neck squamous cell carcinoma patient with harboring a *PTEN* R130Q mutation exhibited a partial response on treatment with the combination of the mTOR inhibitor, **Temsirolimus**, **Carboplatin** and **Paclitaxel** (PMID: 28961834).

In a preclinical study, *PTEN* mutant head and neck squamous cell carcinoma cell lines were less sensitive or resistant to inhibition by **Taselisib**, a PI3K- α β δ Δ λ isoform-specific inhibitor in a cell proliferation assay *in vitro* (PMID: 26589432)

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