Testing a Novel Irreversible Anti-EGFR Drug for Head and Neck Cancer Treatment.

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Introduction. The epidermal growth factor receptor (EGFR) is a member of the ErbB family of receptor tyrosine kinases and is frequently overexpressed in head and neck squamous cell carcinomas (HNSCC). Cetuximab (Erbitux) was the first chimeric monoclonal therapy approved by FDA for HNSCC patients; however the response rates are low due to existence of resistance to those kinds of reversible inhibitors. Thus, novel irreversible inhibitors have emerged has a promise to overcome this problem. In the present work we aimed to test the efficacy of AST 1306, a novel ErbB family (EGFR and ErbB2) irreversible inhibitor in a panel of HNSCC cell lines.

Material and Methods. Seven HNSCC cell lines was used to test the efficacy of AST1306 in comparison to cetuximab by using cell viability assays (MTS). The inhibitory effect in the activation of EGFR and intracellular signaling pathways was assessed by western blot.

Results and Discussion. In the viability assays we found that the cell lines tested depicted different sensibilities to the inhibitors, being the SCC25 and SCC4 the most responsive to cetuximab and AST1306, respectively. In general the cell lines were more sensitive to the irreversible inhibitor AST1306 when compared to cetuximab, even that ones that were completely resistant to cetuximab. We observed that AST1306 was a potent inhibitor of EGFR phosphorylation and of the MAPK and AKT pathways when compared to cetuximab.

Conclusions. Altogether these findings suggest that the pharmacological efficacy of anti-EGFR therapy is greater with irreversible inhibitors when compared to the reversible inhibitor cetuximab. Further studies are needed to explore the action way of AST1306 and his efficacy in vivo in head and neck cancer.

Keyword: Anti-EGFR, AST1306, Cetuximab, Head and Neck tumors.