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Titel des Beitrags: Aurora kinase inhibition overcomes cetuximab resistance in squamous cell cancer of the head and neck.

Abstract: Squamous cell cancer of the head and neck (SCCHN) is the sixth leading cause for cancer deaths worldwide. Despite extensive knowledge of risk factors and pathogenesis about 50 percent of all patients and essentially every patient with metastatic SCCHN eventually die from this disease. We analyzed the clinical data and performed immunohistochemistry for Epidermal growth factor receptor (EGFR) and Aurora kinase A (Aurora-A) expression in 180 SCCHN patients. Patients characterized by elevated EGFR and elevated Aurora-A protein expression in tumor tissue represent a risk group with poor disease-free and overall survival (EGFR(low)Aurora-A(low) versus EGFR(high)Aurora-A(high), p = 0.024). Treating SCCHN cell lines with a pan-Aurora kinase inhibitor resulted in defective cytokinesis, polyploidy and apoptosis, which was effective irrespective of the EGFR status. Combined Aurora kinase and EGFR targeting using a monoclonal anti-EGFR antibody was more effective compared to single EGFR and Aurora kinase inhibition. Comparing pan-Aurora kinase and Aurora-A targeting hints towards a strong and clinically relevant biological effect mediated via Aurora kinase B. Taken together, our findings characterize a new poor risk group in SCCHN patients defined by elevated EGFR and Aurora-A protein.
expression. Our results demonstrate that combined targeting of EGFR and Aurora kinases represents a therapeutic means to activate cell cycle checkpoints and apoptosis in SCCHN.