Comprehensive multiparametric biomarker analysis of 199 anal squamous cell carcinomas

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Abstract

Background: Anal squamous cell carcinoma (AASCC) is a rare, HPV-associated malignancy accounting for 2.4% of digestive system cancers. In most cases, these malignancies are detected in the early stages and successfully managed with chemoradiation. Uncommonly, these cancers recur or present with metastases. In this setting, cisplatin and 5-fluorouracil represent the only endorsed regimen. Favorable case reports in the medical literature indicate success with targeted bispecific antibody therapy; however, little is known on what other therapies may be of clinical benefit. The purpose of this study is to identify other novel, potential targets and therapeutic options for this disease, utilizing a multiparametric approach.

Methods: In total, 199 anal squamous cell carcinoma specimens were tested via a multiparametric profiling service (Crisi Life Sciences, Phoenix, AZ) consisting of gene sequencing (Sanger or next generation sequencing [NGS]), protein expression (immunohistochemistry [IHC] and gene amplification (FISH) service (Caris Life Sciences, Phoenix, AZ). Six cases were documented as positive for HPV or HIV; status was not provided on the remaining 193.

Results: Key results are shown in the table below, as percent/two cases. AASCC: Analytic squamous cell carcinoma. 

![Results Table](image)

Conclusion: Multiparameter tumor profiling identified a low incidence of gene mutations. Protein expression aberrations identified potential treatment options for resistant disease, such as topoisomerase inhibitors and taxanes. Mutations in PIK3CA, Akt1, and FBXW7 indicate potential for targeting the PI3 kinase pathway. Although other mutations were rare, many were also called in the context of a multiplatform assay, suggesting that additional downstream targets may need to be considered for these patients. Our findings show novel therapies which could be considered when designing clinical trials. EGFR and HER2, while not the most common variants detected, may still derive benefit from targeted therapy. These findings expand the list of therapeutic options and support the potential for multiparametric profiling to provide valuable information in the clinical setting.

References