Comparison of SCC to HPV-positive cervical cancer and small cell cancers of other organs

Results, Gene sequencing

Table 2. Gene mutations/alterations. Mutations were found in 11 of 52 cases tested (21%) across the two platforms at Caris Life Sciences and MD Anderson.

Results, Immunohistochemistry (IHC)

Table 3 - Specific gene mutations. Representative mutations detected at Caris Life Sciences with corresponding protein changes are shown. The number of times detected is in parentheses.

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Abstract #5601

Objectives: Small cell cervical cancer (SCC) is an extremely rare and aggressive form of cervical cancer, accounting for only 1% of all cervical cancer cases, or ~150 cases/year. 70% of patients will recur, even when diagnosed with early stage disease and there are few therapeutic options in this setting. We evaluated tumor samples obtained from a large repository to determine prevalent targetable molecular aberrations in these rare tumors.

Methods: Seventy-eight SCC samples were profiled, 53 of those on a commercial multiplatform, including a combination of gene sequencing (Sanger or NGS, up to 47 genes), amplification (CISH or FISH), and protein expression (IHC).

Results: Top2A (85%) and TOP101 (55%) had high overexpression, while ERCC1 had low expression (11%) in SCC samples. SCC tumors had higher protein expression of cKIT (28% vs. HPV+ CC 3%, p<0.05). HER2 amplification was identified in 4.5% of SCC and 8% of HPV+ CC. EGRF amplification was not seen in SCC but was identified in 11% of HPV+ CC. Gene sequencing identified higher mutation rates for TP53 (23%) and KRAS (18%) in SCC compared to HPV+ CC (10% and 10%, respectively) but lower rates of PIK3CA (15% vs. 26%). Comparatively, small cell lung cancers had mutations in TP53 in 57% of cases and in KRAS in 3% of cases. NGS evaluation of 51 cases also identified 3 GNAS and RB1 mutations (6%), 2 CTNNB1 and SMAD4 mutations (4%), and single gene mutations in BRCA1, P105, MET, APC, ATM, HNF1A, and FBXW7 (2% each).

Conclusions: Multiplex tumor profiling identified high expression of TOP2A and TOP101, protein expression of cKit, and sensitivity to etoposide and topotecan.

The high protein overexpression of drug pumps (i.e. BCRP and MRP1) highlight the difficulty in treating this disease.

Lack of PD-L1 tumor-infiltrating lymphocytes suggests that immune-related monotherapies targeting the programmed death (PD) pathway may have limited utility in treating SCC.

SCC has distinct differences from HPV+ cervical cancer, which may inform treatment options; differences include significantly higher protein expression of cKit and PD but lower expression of ER, higher rates of TP53 and KRAS mutations, and significantly lower rates of 

Although from different origins, SCC shares more similarity to SCLC as evidenced by similar frequencies of RB1 mutations; differences, however, include EGFR and HER2 amplification rates.

Potential druggable mutations include AKT1, KRAS, PIK3CA, and PTEN.

Use of a specific biomarker profile may result in a positive outcome, as shown in the case study. Based on the 18% incidence of KRAS mutations in the population profiled, the RAS/MAF pathway may be an area of targeted focus.

References