Squamous-cell carcinoma variant histology (SCC-VH) in muscle-invasive bladder cancer (MI BC): a comprehensive clinical, genomic and therapeutic assessment from multiple datasets


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Abstract: 258997

**BACKGROUND**

Analyses on the URI/RISC database were performed by grouping variant histologies into 6 categories, where pure and mixed cases of each histological variant were respectively combined. In our study, we included all MIBC patients who received neoadjuvant chemotherapy (NAC) and pathologic complete response (pT0) on final pathologic examination, as well as including cN0 and cisplatin-only treated patients. The Foundation Medicine (FM) assay was the only histological variant associated with worse CSS compared to UC, when only NAC-treated patients were considered, even after multivariable adjustment (HR: 2.1, 95%CI: 1.1–4.2, p=0.03). We aimed to examine the genomic landscape of SCC, and to examine the efficacy of NAC in this disease, and present results for SCC-VH cases from PURE-01, a trial of pembrolizumab in the neoadjuvant setting.

**STUDY FLOW-CHART**

**STATISTICAL ANALYSIS**

Analyses on the URI/RISC database were performed by grouping variant histologies into 6 categories, where pure and mixed cases of each histological variant were respectively combined. Furthermore, we analyzed data by separating pure from mixed cases of each variant histology. Two histological subgroups were tested as independent predictors. For example, SCC was analyzed combining pure and mixed cases, and also as pure SCC and UC with SCC component, separately. The primary study endpoint was the cancer-specific survival (CSS), which was analyzed across different histological variants and according to treatment delivery. Here, UC was used as reference category while all other histological variants were compared with it.

**RESULTS**

The secondary endpoint was the histopathological downstaging, which was defined as a pathologic nodal stage (pN) that was at least one stage lower than the pre-NAC clinical stage. When no variation in the pN stage occurred, we used the above-mentioned criteria using the tumors over (pre-NAC, CT and PT), Kaplan-Meier method was used for estimation of CSS, both defined as the period of survival from BC. Kaplan-Meier and Cox regression models were used to analyze the effect of NAC, and supportive subgroup analyses were run. Within the FM data, hybrid capture-based IGP of 37 patients with squamous-cell carcinoma patients were examined. The probe set was generated for SCC patients (Figure 4). Finally, clinical-relevant gene frequency was reported according to UC and SCC histologies with associated 95% CI. All statistical tests were two-sided with a level of significance set at p<0.05. Analyses were performed using the R 8.0 software environment for statistical computing and graphics.

**CONCLUSIONS**

- SCC was the variant histology exhibited the lowest effect of neoadjuvant chemotherapy in terms of activity and CSS.
- Genomic profiling revealed opportunities for targeted immunotherapy.
- Genomic correlates of SCC chemotherapy resistance warrant further investigation.
- Finally, data coming from the PURE-01 study show an unprecedented benefit of neoadjuvant immunotherapy on SCC.

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