Carcinoma of unknown primary (CUP): The role of tumor genomic profiling

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CUP is a heterogeneous group of cancers characterized by early metastatic dissemination from an unknown site of origin.1 Overall survival is a dismal 6-12 months and untreated CUP is associated with a 4 week life expectancy.2,3 A 2014 review of the molecular profile of 1806 cases of CUP within the Caris Life Sciences database identified biomarkers with potential therapeutic benefits in over 96% of cases 4 CUP continues to be a diagnostic and treatment challenge and comprehensive genomic profiling may provide therapeutic insight.

Background

Molecular profiles of tumors noted as ‘unknown’ for tumor primary site within the CARIS Life Sciences database were analyzed utilizing CODEai, a platform that integrates real-world clinical information obtained from insurance claims and medical records with genomic data. This real-world cohort consisted of 3,841 tumors 2,137: Adenocarcinoma (ADC) 385: Squamous cell carcinoma (SQ) 1,319: Carcinoma not otherwise specified (NOS).

CUP-ALL: CUP-ADC + CUP-SQ + CUP-NOS

Overall survival (OS) was calculated from time of tissue collection to last contact assessed by Kaplan-Meier estimates.

Study Methods

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Figure 1. Within CUP-ALL, the targeted therapy cohort had a longer mOS of 638 days compared to 374 days in the chemotherapy cohort

Figure 2. Within CUP-ALL, the immunotherapy cohort had a longer mOS of 601 days compared to the chemotherapy cohort with a mOS of 372 days

Figure 3. In CUP-ADC, tumors with KRAS wild type had a longer mOS of 397 days compared to 202 days in tumors with a KRAS mutant variant

Figure 4. In CUP-SQ, tumors positive for PD-L1 had a longer mOS of 769 days compared to 508 days in tumors negative for PD-L1

Conclusion

The findings from this large real-world cohort demonstrate that key molecular alterations have prognostic and predictive roles in CUP. To maximize clinical benefit, prospective studies with various therapeutic classes of cancer treatments exploiting these differences are warranted.

References

