Comprehensive profiling of renal medullary and collecting duct carcinomas

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Background: Renal medullary carcinoma (RMC) is an aggressive malignancy affecting predominantly young African Americans with sickle cell trait (SCT) or disease (SCD), whereas a pathologically similar collecting duct carcinoma (CDC) affects patients without sickle cell trait. Clinical responses to chemotherapy and IL-2 in RMC/CDC are poor and novel therapies are needed.

Methods: Patients with RMC (ages 13-85 y.o., all male) and 15 patients (ages 26-74 y.o., if M > 13 y.o.) with collecting duct carcinoma (CDC) were studied. Expression of PD-L1 was evaluated with two monoclonal antibodies (SP142 and SP263) and tumor infiltrating lymphocytes (TIL) were evaluated for PD1 expression (MRQ-22 antibody) using immunohistochemistry (IHC). Additional studies included ALK rearrangement (SP57783 antibody), gene expression (break translocate after IHC), next generation sequencing (NGS), and microsatellite instability (MSI).

Results: Cancer cell PD-L1 expression above the threshold (2+, ≥10%) was seen in 12/22 (72.7%) cases. Most specimens analyzed were from male patients, with African-Americans comprising the majority of confirmed RMC (77.8%, 7/9). Four of the AA profiled had the sickle cell trait, two had documented sickle cell disease, and one had no sickle cell disease. ALK rearrangement (IHC) was negative in all cases. However, ALK rearrangement (FISH) was detected in one patient (RMC#4). MSI (Fragment Analysis) was performed when enough tissue was available.

Using the aforementioned antibodies, PD-L1 IHC antibody clones SP142 (Ventana) and SP263 (Dako) were used for scoring. Staining intensity was either negative (0%), 1+ (weak), 2+ (fair), or 3+ (strong). Percent values corresponds to 0 (absent), 1+ (weak), 2+ (fair), or 3+ (strong). Positive values were used to indicate tumor cell staining of RMC increased (as seen in CDC). Table 1 – Demographic information on RMC and CDC specimens. Most patients were male, with African Americans comprising the majority of confirmed RMC (77.8%, 7/9). Four of the AA profiled had the sickle cell trait, two had documented sickle cell disease, and one had no sickle cell disease. Although no ALK rearrangement was detected by IHC, ALK rearrangement was detected by FISH in one patient (RMC#4).

Conclusions: RMC and CDC strongly express PD-L1 in the majority of cases (12/22, 72.7%). PD-L1 expression above the threshold (≥2+, ≥5%) was seen in 10/12 (83.3%) cases. Positive PD-L1 expression across the majority of RMC and CDC appears to be an FDA-approved therapeutic target, with promising clinical responses reported. The absence of MSI in these cancers indicates a different mechanism of disease progression and treatment strategies may be needed for these patients. A multiplatform approach can identify various potential targets in these orphan diseases.

Additional data will be presented in Figure 1. Additional data will be presented in Figure 2.

Figure 1 – PD-L1 by IHC in RMC and CDC using SP142 antibody. Shown on the left are images of a patient with RMC including H&E (A), PD-1 at 20X (B), PD-L1 SP142 at 20X (C), PD-L1 SP142 at 40X (D), and PD-L1 SP263 at 20X (E).

Figure 2 – Renal medullary carcinoma (RMC) Immunohistochemical images. Shown on the left are images of a patient with RMC including H&E (A), PD-1 at 20X (B), PD-L1 SP142 at 20X (C), and PD-L1 SP263 at 20X (D).

Table 1 – Demographic information on RMC and CDC specimens. Most specimens analyzed were from male patients, with African-Americans comprising the majority of confirmed RMC (77.8%, 7/9). Four of the AA profiled had the sickle cell trait, two had documented sickle cell disease, and one had no sickle cell disease.

Table 2 – Concomitance between PD-L1 IHC antibody clones. Eighteen RMC and CDC specimens were also stained with the SP263 antibody for comparison with the SP142 antibody. Scores are shown in the figure on the left. Scoring was either positive or negative using the aforementioned threshold. Staining intensity was either 0 (absent), 1+ (weak), 2+ (fair), or 3+ (strong). Positive values were used to indicate tumor cell staining of RMC increased (as seen in CDC). A concordance analysis showed 94.4% (57/60) agreement. The sole discordant case RMC#2 had inconsistent cytoplasmic staining using SP142 antibody.

References