Circulating KIM-1 is a minimally invasive biomarker correlated with treatment response to nivolumab in patients with metastatic renal cell carcinoma


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**Background:** There are currently no circulating biomarkers used for clinical monitoring of clear cell renal cell carcinoma (ccRCC). Such a biomarker could facilitate individualized treatment decisions and minimize exposure to ineffective therapies. Prior studies have suggested that circulating KIM-1 is a potential minimally invasive biomarker for ccRCC, but the utility of KIM-1 for identifying early response to nivolumab therapy is not known.

**Methods:** CheckMate-009 was a prospective trial investigating nivolumab (every 3 weeks at 0.3, 2, or 10 mg/kg) in patients with metastatic clear cell RCC. We measured serum KIM-1 at baseline and after 3 weeks of treatment (prior to cycle 2) using a custom sandwich immunonassay using the R-PLEX platform. Human KIM-1 antibody (R&D systems, #AF1750) was used to prepare biotin conjugated antibodies and detection antibodies. The assay lowest limit of detection for KIM-1 was 4.88 pg/mL. We assessed the association between early changes in serum KIM-1 and treatment related clinical outcomes.

**Results:** Clinical data and serum KIM-1 was analyzed in 54 patients. KIM-1 was high in all patients at baseline (median serum KIM-1 5913 pg/mL, IQR 2137-25101 pg/mL). 25 patients (48%) had a decrease in KIM-1 at 3 weeks after a single dose of nivolumab. Decrease in KIM-1 at 3 weeks was associated with improved PFS (univariable HR 0.26, 95% CI 0.13-0.52; multivariable HR 0.22, 95% CI 0.097-0.50 after adjustment for sex, prior nephrectomy, nivolumab dose, and IMDC risk factors).

**Conclusions:** Serum KIM-1 is elevated in patients with metastatic ccRCC and is associated with clinical outcomes. Among patients treated with nivolumab in the CheckMate-009 trial, early decrease in KIM-1 from baseline to 3 weeks was predictive for PFS.

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