P096 Prognostic factors in the use of immune checkpoint inhibitors for metastatic renal cell carcinoma

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Introduction & Objectives: There are still few reports on prognostic factors in patients with renal cell cancer (RCC), who are treated with immune checkpoint inhibitors. We investigated prognostic factors for unresectable or metastatic RCC patients treated with anti-PD-1 antibodies.

Materials & Methods: Forty-three patients with unresectable/metastatic RCC were enrolled between January 2018 and October 2021. Fifteen patients were treated with anti-PD-1 and anti-CTLA4 antibodies, 5 were treated with anti-PD-1 and tyrosine kinase inhibitor (TKI), and 23 were treated with anti-PD-1 antibody alone.Blood samples were drawn before the start of treatment, and 77 soluble factors in plasma were analyzed by multiplexed bead array. The patients were dichotomized into high and low groups by the median values of each factor. Overall survival (OS) and progression-free survival (PFS) were statistically analyzed using the Kaplan-Meier method and the COX proportional hazards model, with $P<0.05$ being considered significant.

Results: Median PFS was 196 days (9-1291 days) and median OS was 358 days (31-1332 days). Significant differences in both PFS and OS were observed in MMP1 (Matrix Metalloproteinase-1; OS, p=0.008; PFS, p<0.001), IL-1b (OS, p=0.016; PFS, p=0.021), TNFR1 (Tumor Necrosis Factor receptor-1; OS, p=0.012; PFS, p=0.017), and IL-6 (OS, p<0.001; PFS, p=0.004). On multivariate analysis with these factors, IL6 showed a significant difference in OS (HR 23.876, 95% CI 3.426~166.386, p=0.001), while MMP1 showed a significant difference in PFS (HR 5.305, 95% CI 1.648~17.082, p=0.005). In addition, OS and PFS were examined in the subgroup treated with or without anti-PD-1 and anti-CTLA4 antibodies. In both subgroups, significant differences were observed in IL6 for OS and MMP1 for PFS. Other factors, including IL-1b and TNFR1, showed significant differences in the anti-PD-1 antibody alone subgroup, but not in the combination therapy subgroup.

Conclusions: Multivariate analysis detected MMP1 and IL6 as prognostic factors for PFS and OS, respectively. MMP1 is the most highly expressed stromal collagenase that degrades fibrous collagen. Overexpression of MMP1 is associated with tumor invasion and metastasis and is involved in the development of lung cancer. Therefore, it also seemed to be involved in tumor invasion and metastasis in RCC. IL6 is known to induce the expression of SOCS3 (suppressor of cytokine signaling-3), a negative regulator of cytokine signaling in RCC. Since IL6 suppression may modulate tumor immunity and prolong prognosis, combination therapy with immune checkpoint inhibitors and anti-IL6 antibodies may be promising. In addition, our results showed that treatment with anti-PD-1 antibody therapy may prolong OS and PFS.