**Influence of angiotensin system inhibitors and HMG-CoA reductase inhibitors on outcome of targeted therapy in patients with metastatic renal cell carcinoma**

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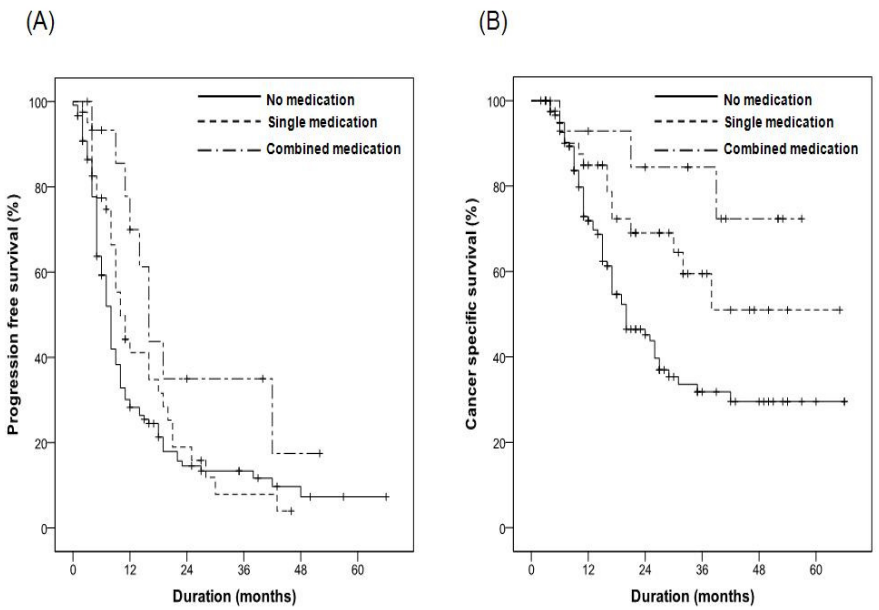
**INTRODUCTION & OBJECTIVES:** There is increasing interest in chronically used medications that may influence the risk for developing or progression of cancer. We aimed to study the effect of angiotensin system inhibitors and HMG-CoA reductase inhibitors on outcome of targeted therapy in patients with metastatic renal cell carcinoma.

**MATERIAL & METHODS:** Between December 2005 and December 2010, 178 patients with histologically confirmed metastatic renal cell carcinoma were treated with targeted agents. According to exposure to angiotensin system inhibitors, HMG-CoA reductase inhibitors or combination of these drugs, patients were divided into 3 groups; group 1 (no medication, n=121, 68.0%), groups 2 (single use of angiotensin system inhibitors or HMG-CoA reductase inhibitors, n=41, 23.0%), and groups 3 (combined use of angiotensin system inhibitors and HMG-CoA reductase inhibitors, n=16, 9.0%). The effect of exposure to these medications on objective response, progression-free survival, and cancer-specific survival was evaluated with adjustment for known confounding risk factors.

Figure 1. Kaplan-Meier analysis for (A) progression free survival and (B) overall survival of patients treated with targeted therapy according to the medication.




**RESULTS:** The groups were balanced regarding known clinicopathologic prognostic factors except body mass index (23.1 vs. 23.4 vs. 25.8 kg/m$^2$, p=0.001). Objective response rates in 3 groups were 82.9, 86.8, and 100.0% at first imaging evaluation within the first 3 months, respectively (p=0.222). 3-year

progression-free survival (13.3 vs. 7.9 vs. 35.0%, p=0.033) and cancer-specific survival (29.5 vs. 51.0 vs. 72.4%, p=0.003) was significantly different according to the medication group (Figure). In Cox proportional hazards models, single use of angiotensin system inhibitors or HMG-CoA reductase inhibitors (HR 0.430, 95% CI 0.217-0.853, p=0.016), and combined use of angiotensin system inhibitors and HMG-CoA reductase inhibitors (HR 0.303, 95% CI 0.094-0.978, p=0.046) were significantly associated with cancer-specific mortality.

**CONCLUSIONS:** Angiotensin system inhibitors and HMG-CoA reductase inhibitors improved the outcome of targeted therapy in metastatic renal cell carcinoma in this study. Combined use of angiotensin system inhibitors and HMG-CoA reductase inhibitors was associated with a lower risk for cancer-specific mortalitythan when these agents were used alone.