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Original article

Clinical and laboratory prognostic factors in patients with metastatic renal cell carcinoma treated with sunitinib and sorafenib after progression on cytokines

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Abstract

Objectives: The aim of this retrospective study was to analyze prognostic factors in patients with metastatic renal cell carcinoma treated with tyrosine kinase inhibitors (TKIs) sunitinib or sorafenib after progression on cytokine therapy.

Materials and methods: A national database of patients treated with targeted agents was used as the data source. A total of 319 patients treated with sunitinib ($n = 181$) or sorafenib ($n = 138$) after progression on cytokine therapy were analyzed.

Results: Prognostic factors significantly associated with poor overall survival in a multivariable Cox model included the time from diagnosis to the start of treatment with TKIs <1 year, increased neutrophil counts, increased lactate dehydrogenase, and Eastern Oncology Cooperative Group performance status 2 or higher. The parameters showing statistically significant association with progression-free survival included time from diagnosis to the beginning of treatment with TKI <1 year, increased lactate dehydrogenase, and Eastern Oncology Cooperative Group performance status 2 or higher. We have also validated the International Metastatic Renal Cell Carcinoma Database Consortium prognostic model in our cohort of patients.

Conclusion: We demonstrate that the International Database Consortium prognostic model performs well for European patients treated with TKIs, including sunitinib or sorafenib, after progression on cytokines and suggest that a reduction from original 6 down to 4 parameters is possible.

Keywords: renal cell carcinoma; prognosis; survival; sunitinib; sorafenib

1. Introduction

Prognostic scores play an important role in the management of patients with metastatic renal cell carcinoma (mRCC). All major randomized trials that established the activity of currently available targeted agents used a prognostic score as one of the principal inclusion or stratification criteria or both. The Memorial Sloan-Kettering Cancer Center (MSKCC) model introduced in 1999 is still widely used with minor modifications [1–3]. More recently, Heng and collaborators from the International Metastatic Renal-Cell Carcinoma Database Consortium (IDC) developed another prognostic model for patients treated with agents targeting the vascular endothelial growth factor pathway [4]. Prognostic models for mRCC that have been accepted for use in the clinical practice are summarized in Table 1.

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Table 1
Major prognostic models for metastatic renal cell carcinoma

Prognostic model	Study	Included parameters
Memorial Sloan-Kettering Cancer Center Model	Motzer et al. [1]	Lactate dehydrogenase Hemoglobin Corrected calcium Performance status Nephrectomy
Memorial Sloan-Kettering Cancer Center Model, modified	Motzer et al. [2]	Lactate dehydrogenase Hemoglobin Corrected calcium Performance status Time from diagnosis to the first dose of IFN-α
Memorial Sloan-Kettering Cancer Center Model for patients progressing on cytokine therapy	Motzer et al. [13]	Hemoglobin Corrected calcium Performance status
Cleveland Clinic Foundation extension	Mekhail et al. [3]	Lactate dehydrogenase Hemoglobin Corrected calcium Time from diagnosis to systemic treatment Prior radiotherapy Number of metastatic sites
French prognostic model for patients progressing on cytokine therapy	Escudier et al. [5]	Serum alkaline phosphatase Lactate dehydrogenase Corrected calcium Number of metastatic locations Time from nephrectomy to metastatic disease
Prognostic nomogram for sunitinib	Motzer et al. [16]	Corrected calcium Number of metastatic locations Hemoglobin Nephrectomy Lung and liver metastases Performance status Platelet count Time from diagnosis to systemic treatment Serum alkaline phosphatase Lactate dehydrogenase
International Database Consortium prognostic model	Heng et al. [4]	Hemoglobin Corrected calcium Performance status Time from diagnosis to systemic treatment Platelet count Neutrophil count

Although the IDC prognostic model has not been used in any major randomized trial, somewhat controversially it forms the basis for patient stratification in the 2012 European Society for Medical Oncology guidelines for mRCC treatment [5].

The present retrospective study has been designed to test the IDC model in a relatively homogeneous cytokine-pretreated population of patients with mRCC treated with targeted therapies including sunitinib (Pfizer) or sorafenib (Bayer) or both. Cytokines may still represent an option in a subgroup of patients and are used widely in resource-poor medical systems [6]. In addition, patients pretreated with cytokines are routinely analyzed together with those treated with first-line targeted agents in mRCC trials [7,8].

2. Materials and methods

2.1. Patients

Patients treated between June 2007 and April 2012 after progressing on cytokine therapy were included in the present registry-based retrospective analysis. RENIS (RENal Information System, http://renis.registry.cz) is a Czech database of patients with mRCC treated with targeted agents in comprehensive cancer centers [9]. Anonymized entries contain detailed standardized data on baseline characteristics, disease course, and therapy. The data is updated biannually. The registry is estimated to cover approximately 90% of the relevant patient population.

The principal inclusion criteria for this study were patients diagnosed with mRCC; pretreatment with cytokines including interferon-α (IFN-α), interleukin-2, or chemo-immunotherapy (with IFN-α or interleukin-2 or both); and subsequent treatment with sunitinib (Pfizer) or sorafenib (Bayer).

Initial evaluation was carried out by physical examination, computed tomography scans, and routine biochemistry. In selected patient, positron emission tomography, magnetic resonance imaging, and bone scans were added according to the clinical situation. The decision whether to treat with sunitinib or sorafenib was made by the attending physician after discussion with the patient. The analysis covered the entire cohort and then separately the subgroups of patients treated with sunitinib or sorafenib. Progression after cytokines and clinical responses to targeted therapies were evaluated using the RECIST 1.0 criteria. Restaging was carried out at least every 4 months.

The study was approved by the institutional board of the Czech cancer registries.

2.2. Statistical analysis

Standard descriptive statistics were used to characterize the sample data set. Overall survival (OS) and progression-free survival (PFS) were the end points of this study. Both outcome measures were calculated from the start of tyrosine kinase inhibitor (TKI) treatment and estimated using the