Original Study

Prescribing Preferences in the First-Line Treatment for Patients With Metastatic Renal Cell Carcinoma in the United States

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Abstract

This study was undertaken to determine, among the various agents available for the first-line treatment of metastatic renal cell cancer, which are the most preferred by US prescribers and why. Our study included 109 board-certified or board-eligible cancer specialists within a diverse mix of practice types. The tyrosine kinase inhibitors of vascular endothelial growth factor, sunitinib and pazopanib, were the most preferred agents. A perception of better tolerability drove treatment decisions for pazopanib, and perceptions regarding efficacy outcomes drove initial sunitinib preference.

Background: Despite existing guidelines for first-line treatment of metastatic renal cell carcinoma (mRCC), prescribing preferences in the United States have not been fully examined. The objectives of this study were to characterize US physicians' preferences and factors influencing first-line mRCC treatment. **Materials and Methods:** A Web-based study presented physicians with hypothetical mRCC patient cases and recorded initial therapy preference and rationale. Descriptive statistics were used to characterize preferred treatment; logistic regression was used to determine patient characteristics associated with therapy changes. Analyses were conducted on pooled responses across cases. Model results were summarized using odds ratios (ORs), 95% confidence intervals, and *P* values for the covariates. **Results:** One hundred nine physicians participated in the study; 96 (88.1%) chose a tyrosine kinase inhibitor as their preferred first-line mRCC treatment (62 [56.9%], sunitinib; 31 [28.4%], pazopanib). Perceived superior overall survival and progression-free survival were top reasons physicians chose sunitinib; enhanced tolerability and efficacy similar to sunitinib were top reasons physicians chose pazopanib. Initial sunitinib prescribers were more likely to change therapy in the presence of comorbid conditions (OR, 2.915; $P = .0068$), poor Eastern Cooperative Oncology Group performance status (OR, 2.368; $P = .0106$), or poor prognostic risk (OR, 3.884; $P = .0224$). This was not seen for initial pazopanib prescribers. **Conclusion:** Sunitinib and pazopanib were the most preferred agents for first-line mRCC treatment. Sunitinib preference was driven by perceptions of efficacy, and pazopanib was preferred for its perceived tolerability and efficacy similar to sunitinib. With varying clinical scenarios, initial pazopanib prescribers were more likely to maintain pazopanib and alter dosing; sunitinib prescribers were more likely to switch therapy.

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Introduction

Renal cell carcinoma (RCC) is the most common form of kidney cancer in the United States, representing 90% of all kidney cancers, and clear-cell histology makes up 70% to 80% of these cases.[1,2] In the United States, the incidence rates for RCC have been gradually increasing since the 1980s,[2] and in 2016, there will be an estimated 62,700 new cases and 14,240 deaths from cancer of the kidney and renal pelvis.[3] Approximately one-third of patients present with metastatic RCC (mRCC) at diagnosis, and an additional 20% to 30% of patients initially treated with curative resection will go on to develop mRCC.[4]

Historically, immunotherapy with cytokines such as interleukin 2 (IL-2) and interferon-alpha (IFN-α) was used for mRCC. However, durable remissions were seen in only 7% to 8% of patients treated with high-dose IL-2 and treatment was accompanied by substantial

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toxicity requiring intensive monitoring and inpatient admission.[1,4] Advances in molecular research on the pathogenesis of RCC have uncovered valuable information on signaling pathways that can be targeted to limit the growth of cancer cells, leading to the approval of at least 7 targeted agents since 2005 for the treatment of mRCC.[4] These approved treatments include bevacizumab, a monoclonal antibody targeting the vascular endothelial growth factor (VEGF) receptor; the 4 tyrosine kinase inhibitors (TKIs) sorafenib, sunitinib, pazopanib, and axitinib, which also target VEGF; and the selective mammalian target of rapamycin (mTOR) inhibitors temsirolimus and everolimus.

mRCC treatment guidelines by the National Comprehensive Cancer Network (NCCN) in the United States and by the European Association of Urology (EAU) in Europe have rapidly evolved to incorporate these approved targeted therapies into their recommendations for first-line therapy for mRCC. The NCCN and EAU list the anti-VEGF therapies sunitinib and pazopanib as options for first-line treatment of mRCC (clear-cell histology), regardless of prognostic risk group. The EAU reserves bevacizumab and IFN-α for use in mRCC patients with favorable to intermediate risk, whereas the NCCN does not make that distinction. Finally, the mTOR inhibitor temsirolimus offers another option for poor-risk patients pursuant to the NCCN and EAU.[5,6]

Even with these published guidelines, however, there is limited evidence on physician preferences for first-line treatment and rationale for their choice. Ryan[7] assessed prescribing preferences among US-based medical oncologists for second-line therapy in mRCC patients; however, to our knowledge, no study has provided information on the current prescribing preferences, physician beliefs, and factors associated with their choice of first-line treatment in mRCC.[7] Therefore, in this study we aimed to further understand current prescribing preferences in the management of mRCC patients in the United States and to ascertain which specific patient factors influence the choice of treatment as first-line therapy, specifically risk status, adverse events (AEs), comorbidities, performance status (PS), and age at diagnosis.

Materials and Methods

To assess US physicians' treatment preferences for first-line mRCC and the factors influencing those decisions, a 60-minute, Web-based survey was created that presented study participants with a series of varying hypothetical first-line mRCC patient cases and asked for a prescribing decision and rationale for that treatment option.

Study Population

Study participants were recruited from the Network for Oncology Communication and Research (NOCR) database, a proprietary research database composed of approximately 3000 physicians specializing in medical oncology, hematology oncology, and urology in the United States. The NOCR is a representative sample of board-certified and board-eligible cancer specialists with a diverse mix of practice type, age, and gender. A sponsor-blinded e-mail invitation was sent to the candidate medical oncologists, which described the study in generic terms.

Because this study was largely descriptive in nature, the primary goal of determining an appropriate sample size was to ensure that the results would have reasonable precision around reported treatment preferences. On the basis of the estimated 16,500 US cancer specialists, a sample size of 100 physicians was determined to provide precision within $\pm$4% to $\pm$10% of any treatment choice at a 95% confidence interval (CI), depending on the level of consensus among physicians for given treatment choice(s). Therefore, assuming an 80% response rate, 125 physicians were recruited from the NOCR.

The eligibility criteria for clinician participation, collected via a screening questionnaire sent to potential participants, included: (1) board certification (or eligibility) in medical oncology, hematology oncology, or urology; (2) 3 to 35 years of clinical experience outside of training; (3) practicing in either a community- or hospital-based (nonacademic) setting in the United States; (4) spends $\geq$70% of their time in direct patient care; (5) is currently treating or is the chief prescriber of chemotherapy for 4 or more mRCC patients per year; and (6) is not currently a paid consultant, including for research, for a pharmaceutical manufacturer or brand, health care company, or government agency.

Physicians were excluded from enrollment if they worked outside of the United States, were affiliated with a government health care entity, or received compensation as a paid consultant for a pharmaceutical manufacturer, health care company, or government agency.

Data Collection

The study was hosted using Xcenda's proprietary Virtual Tumor Cases platform (Xcenda, Palm Harbor, FL, USA). Virtual Tumor Cases is designed to present clinicians with a series of customized, hypothetical patient case scenarios developed with input from a medical oncologist, and through a combination of questions and exposure to supporting diagnostic information, probes study participants on how they would treat a specific hypothetical patient.

The double-blinded study was piloted by telephone with 5 qualified clinicians to ensure that the tool was well understood and that the online study could be completed within the allotted time frame. Results from the pilot interviews were excluded from the final analysis. Physician responses were collected between August 21 and October 9, 2014.

Study Design

Before reviewing any hypothetical patient case scenarios, we collected baseline data on cancer specialists' treatment of first-line mRCC. Specifically, physicians' overall first-line, preferred drug therapy was identified (referred to as their "preferred initial choice of first-line mRCC therapy"), and data on the 2 most important factors influencing preference for that therapy were captured. Additionally, physicians indicated whether they were likely to prescribe their overall preferred first-line therapy according to the dose and schedule as in the label or if they would use an alternative dose and/or schedule (and the rationale for such a decision).

Study participants were then presented with 8 hypothetical patient cases with varying clinical characteristics (Table 1) and asked to provide the same prescribing intent information and influencing factors as previously described. Additional information was provided for 3 of the 8 base cases to determine how the presence of AEs, level of physical activity, or other clinical characteristics might affect physicians' treatment strategy. The AE for the first of these 3 cases