Current Practices in the Management of Adverse Events Associated With Targeted Therapies for Advanced Renal Cell Carcinoma: A National Survey of Oncologists

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Abstract

Current practices and attitudes of oncologists in the management of adverse events (AEs) from targeted therapies in renal cell carcinoma (RCC) patients are poorly understood. To address this issue, we analyzed survey responses of 101 oncologists. Results suggest that many patients with RCC require dose modifications/discontinuation because of targeted therapy–related AEs and that nononcologists are frequently consulted to manage these events.

Background: Oncologists treating patients with targeted therapies encounter adverse events (AEs) that pose management challenges, lead to dosing inconsistencies, and impact patient quality of life. Oncologists' practices and attitudes in the management of targeted therapy–related AEs in patients with renal cell carcinoma (RCC) are poorly understood. We sought to identify unmet needs associated with AE management and understand oncologists' treatment optimization strategies. **Methods:** A 24-item online survey was administered in August 2012 to 119 US oncologists treating patients with advanced RCC. The survey solicited responses regarding demographics, practice settings, AE management practice patterns and beliefs, treatment barriers, and patient education. **Results:** Respondents indicated that between 25% and 50% of patients require dose modification/discontinuation because of AEs. The greatest barrier to optimizing treatment for RCC is the unpredictability of patient responses to treatment (43%). Most respondents (78%) discuss AE management with patients, but only a minority of them proactively reach out to patients (46%). Most practitioners (70%) refer patients to nononcology specialists when faced with unfamiliar AEs, although finding interested physicians (43%) and time constraints (40%) were the most commonly cited barriers to consulting with other specialties. **Conclusion:** Results suggest that many patients require dose modification/discontinuation because of AEs and that nononcologists are a frequently utilized resource to manage these events. There is a need for predictive drug toxicity markers to establish counseling and prevention, along with opportunities for increased education on supportive care techniques to maintain health-related quality of life and consistent dosing.

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Introduction

Targeted therapies are emerging as a viable treatment option in the management of advanced renal cell carcinoma (RCC). Molecules critical to the growth and survival of cancer cells, such as the vascular endothelial growth factor (VEGF) or its receptor (VEGFR) and the mammalian target of rapamycin (mTOR), which are all implicated in the pathogenesis of RCC, are being increasingly exploited as primary drug targets. These agents can delay time to

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disease progression and have shown improved progression-free survival in phase II/III clinical trials,[1,2] with many promising drugs in the pipeline. To date, the anti-VEGF monoclonal antibody bevacizumab (in combination with interferon alfa), the VEGFR inhibitors sorafenib, sunitinib, pazopanib, and axitinib, and the mammalian target of rapamycin inhibitors temsirolimus and everolimus have received regulatory approval in the treatment of advanced RCC.[3,4]

Although the target specificity of these newer therapies circumvents some of the systemic adverse effects associated with conventional chemotherapy, accumulating clinical experience and the unique adverse events (AEs) being reported[5] warrant attention. This is important to maintain dose intensity of anticancer regimens and enhance patient quality of life. Several authors have addressed the clinical and management aspects of treatment-related AEs in cancer patients who are now living longer because of targeted therapies.[5-7] There is, however, a lack of evidence-based treatment strategies and consensus among health care providers regarding the management of AEs, which would require significant collaboration between centers and supportive care specialists. In addition, the rapid pace of development of these innovative oncologic therapies, and a paucity of supportive care specialists familiar with this niche therapeutic area, are all hindering the constitution of effective AE management strategies.

Understanding current clinical practices is important to assess potential knowledge gaps and can permit the optimization of existing treatment strategies to improve patient care and the design of effective educational efforts. Only a few studies have explored the prevailing clinical scenario in the management of AEs, with EGFR inhibitors having received most attention,[8-10] and none with therapies used in patients with RCC. This study reports the results of a national survey of oncologists, which was conducted to identify unmet needs associated with the management of patients treated with targeted cancer therapies for advanced RCC and to gain a better understanding of oncologists' perceptions and comprehensive care strategies used with these treatments.

Materials and Methods

Survey Development

A structured questionnaire was developed in collaboration with a panel of experts (MEL, ME, AC, and PC), Pfizer Inc, and Sermo. The self-administered survey was tested and refined based on the feedback received regarding readability, usability, clarity, and randomization of questions. The finalized survey consisted of a 24-item questionnaire with 1 or multiple options to choose from, as applicable. The first 5 supplementary questions (QS1-QS5) were related to the practice demographics and the rest (Q1-Q19) pertained to clinical practices; the complete questionnaire is available as supplementary material (see Supplemental Appendix 1 in the online version). Pfizer Inc. provided the funding for survey development, administration, data collection, and analysis.

Survey Administration and Participant Characteristics

The online survey was administered to 119 participants between August 29 and August 30, 2012. The responders consisted of institution-based and community-based practicing oncologists and hematologists involved in the primary management or active monitoring, or both, of patients with RCC treated with targeted therapies. Responders were not provided any remuneration. The data were collected and captured in an Excel (Microsoft, Redmond, WA) database and subsequently retrieved for statistical analysis.

Statistical Analysis

Descriptive statistics were used to analyze participants' responses. The Pearson χ^2 test, Fisher exact test, and independent samples t test (2-tailed) with equal variance were used to compare institution-based and community-based providers. Statistical significance was considered at $P < .05$. All statistical analyses were performed using Stata/SE, version 12.0 (StataCorp LC, College Station, TX).

Results

Response Rate, Clinical Demographics, and Practice Setting

Of the 119 responders, 101 institution-based (n = 26) and community-based (n = 75) physicians completed the survey (Table 1). Institution-based respondents had more patients with RCC (QS3), although community physicians managed more patients with RCC and metastatic disease (QS4). Institution-based physicians practiced at an academic medical center or affiliated teaching hospital. Community practice settings included private practices (solo or group) or community cancer centers, hospitals, or clinics (QS2). Geographically, practice locations were distributed relatively evenly (QS1).

Management of AEs: Practice Patterns and Opinions

Most respondents initiate patient discussions at the start of treatment to ensure understanding of AEs (Q3); institution-based doctors were more likely to strongly agree that well-informed patients comply with treatment ($P = .018$) (Q4). Yet only 43% of physicians followed a comprehensive care plan to provide patient support, and just 46% followed up to ensure AEs were managed (Q3) (Table 2).

The most commonly used resources for patient education in AE management included the respondent's own institution, pharmaceutical websites, sales representatives, and advocacy organizations (Q5). Institution-based physicians more often turned to their own institution ($P = .021$), whereas community-based physicians tended to use information from sales representatives or advocacy organizations (Q5). Although 55% of respondents agreed that patients who are knowledgeable about AEs are more likely to comply with treatment (Q4), only 32% of physicians strongly agreed that their practice takes extra measures to educate/support patients (Q2) (Table 3).

For effective AE management, 75% used a comprehensive care team (Q6), and nearly all found this beneficial (Q12). Most agreed that adjusting therapy dosing based on patient needs/safety, rather than switching therapy, can achieve optimal outcomes (Q13). More than half of respondents stated that fewer than 25% of their patients changed/discontinued treatment because of AEs. Forty-six percent stated that AEs caused 25% to 50% of their patients to discontinue treatment (Q14).

Medical uncertainties were identified as the greatest treatment barrier (Q1). Among other barriers, institution-based respondents most often cited lack of physician education, whereas community