A Cross-Sectional Investigation of Fatigue, Mucositis, Hand-Foot Syndrome and Dysgeusia in Advanced Renal Cell Carcinoma Treatment: Final Results From the FAMOUS Study

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Abstract

Treatment of metastatic renal cell carcinoma can be associated with adverse symptoms. The perception of fatigue, mucositis, hand-foot syndrome, and dysgeusia, and quality of life (QOL) was assessed in 63 oncologists and their patients receiving first-line treatment. Physicians underestimated the severity of the symptoms and the severity correlated with a lower QOL. A consistent assessment of symptoms in routine practice might improve QOL, adherence to treatment, and outcome.

Background: The management of symptoms associated with treatment of metastatic renal cell carcinoma (mRCC) is crucial to ensure treatment adherence and outcome. The perception of symptoms can vary between the treating physician and patient, leading to assumptions and subsequent changes in treatment, potentially affecting treatment effectiveness. The aim of the present cross-sectional study was to evaluate the perception of the common symptoms of fatigue, mucositis, hand-foot syndrome, and dysgeusia in patients with mRCC receiving systemic therapies in routine practice. **Patients and Methods:** German patients receiving first-line systemic treatment for mRCC and their physicians were independently queried about the incidence and severity of fatigue, mucositis, hand-foot syndrome, and dysgeusia. Patients also completed the Functional Assessment of Cancer Therapy—General questionnaire to assess their quality of life (QOL). The effect of the 4 symptoms on QOL was analyzed using linear regression modeling. **Results:** A total of 63 matching questionnaires were completed by both physicians and patients with first-line treatment. The incidence and severity of symptoms differed between the patients and physicians. Patients rated the severity of symptoms significantly higher than did the physicians. A greater severity of symptoms correlated with a lower QOL. In multivariate regression analysis, fatigue adversely affected overall QOL. **Conclusion:** Physicians underestimated the severity of common symptoms in patients with mRCC. The incorporation of patient-reported outcome measures into routine practice might increase awareness of patients' overall QOL and thereby potentially improve treatment adherence. A thorough evaluation of fatigue, its potential underlying causes, and active measures to manage fatigue could potentially improve patients' QOL.

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Introduction

Renal cell carcinoma (RCC) accounts for approximately 4% of adult malignancies and has the highest mortality rate of all urologic tumours.[1] About 25% to 33% of patients with RCC present with advanced disease, and 20% to 40% of patients diagnosed with localized disease will subsequently develop metastases.[2] About 40% of patients with RCC will die of the disease.[1]

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With the approval of multiple targeted systemic therapies, the treatment options for metastatic RCC (mRCC) have dramatically changed in the past decade and have considerably improved the prognosis for patients undergoing palliative treatment. With the variety of available options, the sequencing substances has become a treatment reality. However, there is growing evidence that maintenance of a chosen treatment (if likely to be effective on the tumor) remains important and possibly beneficial. With that, in addition to the risk factors and comorbidities, the expected effect on quality of life (QOL) has gained importance when deciding on the treatment a patient should receive. Thus, the better management of side effects through the improved use of concurrent medications as well as dose modifications, and variation in treatment schedules has increased the compliance of patients and has, consequentially, led to an increased treatment duration. The results from the PISCES study suggested that fatigue is one of the crucial side effects that affect patients' preference when given the choice.[3]

The perception and assessment of the various aspects concerning this area can differ between healthcare workers, the treating physician, and the patient.[4,5] Physicians appear to underestimate the pain and to rate emotional problems higher than do the patients.[4] This variation in the perception of side effects can lead to wrong assumptions and subsequent dose modifications and/or treatment changes, affecting treatment effectiveness. Patient-reported outcomes have been increasing in importance[6] and can serve as a useful indicator for physicians to facilitate the choice of treatment.[7] It has, therefore, been recommended that assessment of patient-reported symptom monitoring and management should be undertaken when using targeted agents.[8]

The FAtigue, Mucositis, Hand-FOot-Syndrome, and DysgeUSia (FAMOUS) study explored physicians' and patients' assessment of the frequent symptoms of fatigue, mucositis, hand-foot syndrome, and dysgeusia in real-life patients undergoing systemic treatment for mRCC in routine practice. We present data on the assessment of fatigue, mucositis, hand-foot syndrome, and dysgeusia for patients receiving first-line treatment of mRCC. Comprehensive results on the incidence and severity of fatigue for all patients were published previously.[9]

Patients and Methods

More than 100 study sites (German office-based oncologists and uro-oncologists) have been recruiting patients for the multicenter, prospective, noninterventional clinical mRCC registry since December 2007. The project was reviewed by a local ethics committee and is registered in the ClinicalTrials.gov registry (NCT00610012). To date, > 1200 patients have been recruited. The registry recruits unselected adult patients with mRCC at the start of first-line treatment and collects data on medical history, all systemic therapies, and other information during the course of disease. All patients provide written informed consent. For the integrated, cross-sectional FAMOUS study, questionnaires were sent to physicians engaged in this registry and treating patients at the time of the survey.[9] After completion of the physician's questionnaire, a separate questionnaire was sent to the matching patient. This 2-step process ensured that physicians were not aware of the patient's answers at questionnaire completion. During the final analysis, we examined whether the time difference between the patients and physicians completing the questionnaires affected the study results.

The physician questionnaire asked for an evaluation of the incidence and severity of fatigue, mucositis, hand-foot-syndrome, and dysgeusia using a 6-point Likert scale, with 0 indicating the symptom was not present and 5 indicating the symptom was as bad as one can imagine. The patient questionnaire contained the same questions regarding symptom assessment. Both questionnaires were validated for clarity and comprehensibility. The patient questionnaire was complemented by the Functional Assessment of Chronic Illness Therapy—Fatigue (FACIT-F) questionnaire to assess health-related QOL.[10,11] The FACIT-F measurement system contains the Functional Assessment of Cancer Therapy—General (FACT-G) questionnaire and a symptom-specific subscale for fatigue based on a 13-item questionnaire. Both use a 5-point Likert scale to assess single items. The FACT-G score consists of 28 items in 4 domains, allowing calculation of 4 subscale scores addressing physical well-being, social well-being, emotional well-being, functional well-being, and a global score representing overall health-related QOL.[10] The FACIT-F subscale score describes the symptom burden from fatigue, with the lower values representing greater fatigue (score range, 0 to 52). If items were missing for < 50% of a subscale, the remaining item responses were prorated using the mean of the answers provided for that subscale.[11]

The analyses were descriptive in terms of the frequencies within the variables. By convention, $P \leq .05$ indicates significance. Differences between samples were analyzed for continuous variables using the t test and categorical variables using Fisher's exact test. All P values are 2-sided.

A linear regression model was used to determine the effect of the 4 symptoms on QOL (FACT-G score). Goodness of fit was measured using a likelihood-based pseudo r^2. Pearson correlation analyses were performed to identify the associations between the symptoms and dimensions of QOL. In addition, Pearson correlation analyses were performed to investigate the associations between the patient's and physician's reports on the severity of symptoms. This was done for all patients and the time difference between physician's and patient's completion of the questionnaire was taken into account.

In the present study, "systemic treatment" was defined as systemic anticancer treatment using immunomodulatory agents, chemotherapeutic agents, signal transduction inhibitors, or monoclonal antibodies.

Results

Questionnaires and Patient Characteristics

A total of 271 questionnaires were sent to 71 study sites participating in the RCC Registry at the time of this survey, and 167 questionnaires (62%) were returned. All 167 patients were contacted, and 98 (59%) returned the patient questionnaire. Thus, 98 questionnaires were returned by both the treating physician and the corresponding patient. At questionnaire completion, 63 patients (64%) were receiving first-line treatment and were included in the present analysis. The patient characteristics are listed in Table 1. The median age at the start of treatment was 72 years, and 71% of patients were men. At the start of first-line treatment, the Karnofsky score was ≥ 80% for most of the patients (82.5%). Only 1 patient was of high risk according to the prognostic criteria of the Memorial Sloan Kettering Cancer Center (MSKCC score). Almost one half of the patients had at