Original Study

Outcomes of Patients With Metastatic Renal Cell Carcinoma and End-Stage Renal Disease Receiving Dialysis and Targeted Therapies: A Single Institution Experience

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Abstract

Data are limited regarding outcomes in patients with end-stage renal disease (ESRD) and metastatic renal cell carcinoma (mRCC) receiving targeted therapy. We retrospectively identified patients with mRCC and ESRD treated at the University of Texas M.D. Anderson Cancer Center from 2002 to 2012. Fourteen patients were identified with a median number of targeted therapies (TTs) per patient of 3 (range, 1-4). Outcomes in patients with mRCC and ESRD were similar to those reported in patients with normal kidney function.

Introduction: Limited data are available regarding patients with renal cell carcinoma and ESRD treated with TTs. The objective of this study was to explore the tolerability and safety of TT in patients with mRCC and ESRD. **Patients and Methods:** We retrospectively identified patients with mRCC and ESRD treated at the University of Texas M.D. Anderson Cancer Center from 2002 to 2012. Patient characteristics including demographic, histology, treatment, and adverse events are reported. Duration of treatment (TOT) was determined from date of drug initiation to discontinuation. Overall survival (OS) was determined from initiation of TT to death. Statistics are descriptive. **Results:** Fourteen patients were identified. Ten patients had clear-cell histology and 4 had papillary histology. The median number of TTs per patient was 3 (range, 1-4) with median TOT of 28 months for all TTs. Eighty-eight percent of all toxicities were Grade 1 to 2; no Grade 4 toxicities were noted. Treatment discontinuations included 3 patients treated with sorafenib due to hand-foot syndrome, intolerable fatigue, and squamous cell skin cancer development; 2 patients treated with pazopanib due to intolerable fatigue and increased transaminase levels; and 1 patient treated with everolimus due to pneumonitis. Eight patients died from progressive disease. Median OS from initiation of TT was 28.5 months and 35 months from time of diagnosis. **Conclusion:** Toxicities were mild to moderate and consistent with those reported in previous studies. TTs appear to be safe, well tolerated and produce antitumor response in patients with mRCC and ESRD receiving dialysis.

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Introduction

In 2013, an estimated 65,000 people in the United States will be diagnosed with renal cell carcinoma (RCC) and 14,000 will die from the disease.[1] Approximately 30% of patients present with metastatic disease at the time of diagnosis and 20% to 30% develop recurrent metastatic disease after nephrectomy. Overall, the prognosis for patients with metastatic disease is poor, with an estimated 5-year survival of 10%.[2]

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Improved understanding of the biology and underlying pathogenesis of RCC has led to the development of molecularly targeted therapies (TTs). Currently, 7 TTs are approved by the US Food and Drug Administration for the treatment of metastatic RCC (mRCC): sorafenib, sunitinib, pazopanib, axitinib, bevacizumab, temsirolimus, and everolimus. TTs have largely supplanted cytokine-based therapies in the treatment of patients with mRCC because of their greater tolerability, ease of administration, and improved outcomes.

End-stage renal disease (ESRD) is prevalent in the United States with an estimated dialysis population of 430,000 patients.[3] Compared with the general population, the incidence of RCC might be higher in the ESRD population, the underlying biology might be different, and the clinical and pathological features might be more favorable.[4] Patients with ESRD are often excluded from prospective clinical trials because of their altered pharmacokinetics.

Limited data are available regarding patients with RCC and ESRD treated with TTs. The objectives of our retrospective study were to investigate the safety and efficacy of TTs in patients with mRCC and ESRD.

Patients and Methods

After institutional review board approval, we retrospectively reviewed the institutional electronic health records of patients with mRCC who were seen at the University of Texas M.D. Anderson Cancer Center (MDACC) from 2002 to 2012. Patients 18 years of age or older who were treated with TTs (sorafenib, sunitinib, pazopanib, bevacizumab, temsirolimus, or everolimus) and underwent renal replacement therapy with hemodialysis (HD) or peritoneal dialysis because of ESRD were included.

Data collected at baseline included demographic characteristics (age, race, sex); medical history; Memorial Sloan Kettering Cancer Center (MSKCC) prognostic variables[5]; and data regarding nephrectomy status, previous therapies, duration of ESRD, mode and duration of dialysis, renal transplantation status, tumor stage and grade, histological subtype of tumor, last available MDACC follow-up, information about adverse drug events (AEs), and date of death.

Adverse events were graded according to the Common Terminology Criteria for Adverse Events, version 4.0. Duration of treatment (TOT) was defined as the time elapsed between the initiation of TT and the discontinuation of that TT for any reason. Overall survival (OS) was defined as the time from initiation of TT or time of diagnosis to time of death from any cause. Response was objectively accessed by the treating providers. Patient characteristics were summarized using median and range for continuous variables and frequency and percentage for categorical variables.

Results

Patient Characteristics

Fourteen patients with mRCC met our inclusion criteria. The baseline patient characteristics are summarized in Table 1. The population's median age was 57 years, and 50% were male. Eighty-six percent of patients had a nephrectomy, all before the initiation of any TT. Two patients (14%) had Karnofsky Performance Status scores < 80, and 21% had favorable risk, 50% had intermediate risk, and 29% had poor risk disease per MSKCC criteria.[5] The median number of metastatic sites was 4 (range, 1-9). Three patients (21%) had a Charlson Comorbidity Index score of 8, 6 patients (38%) had a score of 9, and 5 patients (36%) had a score of 10. No patients had received transplants or immunosuppression before or at the time of TT initiation.

Patient Outcomes and Safety

The median number of TTs received was 3 (range, 1-4) with median overall TOT of 27 months for sequential TT and 28 months for sequential therapies including TT, chemotherapy, and cytokines. The percentage of patients who received each TT and their median TOT are summarized in Table 2. Median TOT of 8 months was noted in 4 patients treated with chemotherapy, and 3 months median TOT in 3 patients treated with cytokine therapy (interleukin-2, interferon-α). The objective response rate to all TTs according to treating physician evaluation was 31%. The RCC histology, sequence of TT, and total TOT for each patient are presented in Table 3. At last follow-up, 8 patients (57%) had died with a median OS of 28.5 months (range, 3-65 months).

Targeted therapies were discontinued 6 times (16%) because of AEs. Hand-foot syndrome, intolerable fatigue, and squamous cell skin cancer caused 3 patients to discontinue sorafenib; intolerable fatigue and increased transaminases in 2 patients led to discontinuation of pazopanib; and 1 patient discontinued everolimus because of pneumonitis. Most AEs were Grade 1 or 2. Although serious AEs were uncommon, those reported during TT treatment included myocardial infarction, congestive heart failure, and pancreatitis. Common AEs reported by patients are shown in Table 4.

Three patients received an intravenous (I.V.) dosage of 10 mg/kg of bevacizumab every 2 weeks. All 3 patients were treated on Fridays after receiving dialysis earlier that day to maximize drug bioavailability. No dose reductions were noted in our study.

Seven patients were treated with sorafenib. Two patients received 400 mg orally twice per day (b.i.d.), with 1 patient requiring dose reduction to 600 mg once per day because of toxicity. Three patients received 600 mg daily dosing, with no dose reductions reported. One patient received 200 mg b.i.d. dosing, but the dosage was reduced to 200 mg b.i.d. administered Monday through Friday because of AEs. One patient was treated with 100 mg daily of sorafenib, with no dosage reduction reported.

Eight patients were treated with sunitinib. All 8 patients were treated on a 4-week on, 2-week off regimen. No dosage reductions were reported. Three patients were treated with 50 mg daily, 4 with 37.5 mg daily, and 1 with 12.5 mg daily.

Three patients were treated with temsirolimus. No dosage reductions were reported. All 3 patients were treated with 25 mg I.V. weekly on Fridays after receiving dialysis earlier that day to maximize drug bioavailability.

Seven patients were treated with everolimus. All 7 were treated with 10 mg daily, with one dosage reduction to 5 mg daily because of AEs.

Nine patients received pazopanib. Five patients were treated with 800 mg daily, with 2 dosage reductions—1 to 400 mg/d and 1 to 600 mg/d—because of AEs. Four patients were treated with 600 mg daily, with all 4 patients requiring dosage reductions to 400 mg daily because of AEs.

No significant interruptions to treatment with TT were reported in the 14 patients examined in this study.