original reports abstract

OSSMAR: An Observational Study to Describe the Use of Sunitinib in Real-Life Practice for the Treatment of Metastatic Renal Cell Carcinoma

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PURPOSE Sunitinib offers improved efficacy for patients with metastatic renal cell carcinoma (mRCC). To provide better disease management in the Middle East, we studied its use in mRCC in real-life practice in this region.

MATERIAL AND METHODS Patients diagnosed with mRCC and started on sunitinib between 2006 and 2016 from 10 centers in Africa and the Middle East region were studied in this regional, multicenter, observational, retrospective trial to obtain routine clinical practice data on the usage patterns and outcomes of sunitinib in mRCC in real-life practice.

RESULTS A total of 289 patients were enrolled. Median age at diagnosis was 58.7 years. The patient characteristics were as follows: 73.6% of patients were males; 85.8% had clear-cell renal cell carcinoma (RCC); 97.5% had unilateral RCC; 66.3% had metastatic disease at initial diagnosis; 56.3% received previous treatment for RCC, among which 98.7% had undergone surgery; and 15.2% and 31.4% were classified in the favorable and poor-risk groups (expanded Memorial Sloan Kettering Cancer Center criteria), respectively. On treatment initiation, the mean total sunitinib dose was 48.1 mg, and 87.6% of patients were started on a sunitinib dose of 50 mg. The mean duration of sunitinib treatment was 9.6 months. Overall response rate was 20.8%, with a median duration of 8.2 months. Median time to progression was 5.7 months. Median follow-up time was 7.8 months. By months 12 and 24, 34.3% and 11.4% of patients, respectively, were still alive. Seventy-six patients (60.9%) experienced 314 adverse events. Twenty-three patients (8.0%) experienced 28 serious adverse events. Overall, 83 patients (28.7%) discontinued their sunitinib treatment.

CONCLUSION The results are indicative of the general treatment outcomes of patients with mRCC in the Middle East using sunitinib in routine clinical practice. Reported adverse events are similar to those described in the literature but at lower frequencies.

INTRODUCTION

Renal cell carcinoma (RCC) is the most common type of kidney cancer in adults. It accounts for approximately 3% of adult malignancies and 90%-95% of neoplasms arising from the kidney. This disease is characterized by a lack of early warning signs, diverse clinical manifestations, and resistance to radiation and chemotherapy.[1-3]

Increasingly, renal cell cancers are diagnosed at an earlier stage, and nephron-sparing surgery and thermal ablation are gaining acceptance as a treatment of choice for smaller tumors. Radical nephrectomy is the standard for larger and central tumors.[4]

Before the advent of targeted agents in the management of metastatic renal cell carcinoma (mRCC), available treatment offered low overall response rates (ORRs; approximately 2%-13%), with a median overall survival (OS) of 13.3 months.[5] In recent years, clinical trials have established targeted therapy as the first-line treatment in patients with metastatic disease, offering improved efficacy to patients with mRCC. Although the optimal treatment strategy continues to evolve, 3 antiangiogenic therapies (sunitinib, bevacizumab, and pazopanib), a mammalian target of rapamycin–targeted therapy (temsirolimus), a tyrosine kinase inhibitor (cabozantinib), and a combination of immune checkpoint inhibitors (nivolumab plus ipilimumab) have been approved as front-line agents.[6-10] These agents have largely replaced cytokines in treatment-naive patients. Among them, sunitinib was one of the first to be approved by the European Medicines Agency and US Food and Drug Administration in this setting.[5,11-14]

However, to offer better disease management, we need to understand the use of this product in routine

ASSOCIATED CONTENT

Data Supplement

Author affiliations and support information (if applicable) appear at the end of this article.

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CONTEXT

Key Objective

To understand the use of sunitinib in routine clinical practice and offer better disease management.

Knowledge Generated

The results are indicative of the general treatment outcomes of patients with metastatic renal cell carcinoma (RCC) in the Middle East with sunitinib in routine clinical practice. Reported adverse events are similar to those described in the literature but at lower frequencies.

Relevance

OSSMAR is the first study in the Middle East involving several Arab countries and evaluating the real-time use of sunitinib in the treatment of metastatic RCC. As a result, this study is of primary importance because it allows for a better assessment of the actual effectiveness and practical adverse events of sunitinib in the population in our region.

clinical practice. This trial was therefore designed to address this need to ensure the best use of the product, allowing the maximum benefit to the patient.

We conducted a regional, multicenter, observational, retrospective study to obtain routine clinical practice data on the usage patterns and outcomes (response rate, time to progression, OS, OS rate, and safety) of sunitinib prescribed for mRCC in real-life practice. We also described the dose intensity and modification in treatment and compared patients' profiles at first treatment administration and at first relapse.

MATERIAL AND METHODS

This was a regional, multicenter, observational retrospective study. A total of 289 patients diagnosed with mRCC and started on sunitinib between June 2006 and June 2016 from 10 centers in the Africa and Middle East region (Lebanon, Tunisia, Morocco, Algeria, Egypt, Kingdom of Saudi Arabia, United Arab Emirates [UAE]) were studied in this product trial. Data were collected between May 2015 and December 2016.

Secondary data pretherapy, during therapy, and post-therapy originated from hospital chart review, relevant medical reports, and workup test results. Data on efficacy and safety were recorded at different time points: at baseline; during treatment at 3 months (± 4 weeks), 6 months (± 4 weeks), and 12 months (± 4 weeks); and at every follow-up once yearly after the last administration of sunitinib until last follow-up, patient death, or data collection cutoff point (December 31, 2016). The efficacy of sunitinib included assessments of the response rate (percentage of patients whose cancer shrank or disappeared after treatment), time to progression (length of time from the start of sunitinib until the disease started to get worse or spread to other parts of the body), and OS (length of time from the start of sunitinib until death or last follow-up). Patients who were lost to follow-up were censored during statistical analysis. The Kaplan-Meier method was used to estimate the number of patients surviving during treatment and after the end of treatment.

Safety was described and based primarily on the proportion of patients with at least 1 adverse event (AE) and at least 1 serious AE (SAE). The emergent AEs (which occurred or worsened after the first study drug intake) were summarized using System Organ Class and preferred terms. Relationship to study drug, seriousness, severity, and action taken, in addition to SAEs, were tabulated.

Descriptive analyses of qualitative variables, patient risk group, relevant medical history or comorbidities, concomitant medications, and patient status were presented as the frequency and percentage in each category, whereas quantitative variables, such as the dose of sunitinib, were summarized using descriptive statistics (number of patients, mean, standard deviation, minimum, and maximum). A significance level of 5% was taken into consideration.

On the basis of Memorial Sloan Kettering Cancer Center (MSKCC) prognostic criteria, the patient risk groups were divided into 3 categories: favorable risk (no poor prognostic factors), intermediate risk, and poor risk (more than 2 poor prognostic factors). Poor prognostic factors included a Karnofsky performance status < 80, time from diagnosis to treatment < 12 months, serum lactate dehydrogenase > 1.5 times the upper limit of normal, corrected serum calcium > 10.0 mg/dL, and hemoglobin less than the lower limit of normal.[15] The model was also expanded to include prior radiotherapy and the number of individual organ metastatic sites (> 2 organs involved). The Karnofsky performance status was divided into 3 categories, < 60, 60-80, and > 80, and entered into the electronic case report form (CRF) at different time points (months 3, 6, and 12).

Available hematology and biochemistry test results were recorded at baseline. During the follow-up, only clinically significant results were recorded in the CRF at month 3, 6, and 12. Hematology tests included hemoglobin, hematocrit, white blood cells, platelet count, and blood protein. Blood chemistry tests include ALT, AST, creatinine, total bilirubin, alkaline phosphatase, glucose, albumin, sodium, and calcium.

Concerning ethical considerations, this study was designed, implemented, and reported in accordance with

TABLE 1. Main Characteristics of the Patients Initiating Sunitinib for First-Line Therapy of mRCC in OSSMAR Study (N = 289)

Characteristic	Value	Clear Cell (n = 217)	Mixed	Nonclear Cell (n = 33)	*P*
Age at diagnosis (years)					
No. of patients	262	197		33	.001
Mean ± SD	56.3 ± 14.0	57.1 ± 13.1		48.5 ± 16.3	
Median (min-max)	58.7 (16.1-91.2)	59.1 (16.1-91.2)		46.6 (23.3-79.9)	
Age at treatment baseline (years)					
No. of patients	281	215		33	< .001
Mean ± SD	57.2 ± 13.8	57.9 ± 12.8		48.9 ± 16.5	
Median (min-max)	59.4 (17.6-91.2)	59.7 (17.6-91.2)		46.8 (23.3-80.2)	
Sex					
No. of patients	280	214		33	.235
Male	206 (73.6)	165 (77.1)		21 (63.6)	
Female	74 (26.4)	49 (22.9)		12 (36.4)	
Country					
No. of patients	289	217		33	.001
Egypt	72 (24.9)	57 (26.3)		12 (36.4)	
Lebanon	71 (24.6)	53 (24.4)		1 (3.0)	
KSA	66 (22.8)	37 (17.1)		14 (42.4)	
UAE	27 (9.3)	25 (11.5)		1 (3.0)	
Tunisia	20 (6.9)	17 (7.8)		0 (0.0)	
Morocco	18 (6.2)	18 (8.3)		0 (0.0)	
Algeria	15 (5.2)	10 (4.6)		5 (15.2)	
Pathology					—
No. of patients	253	217 (85.8)	3 (1.2)	33 (13.0)	
Location					
No. of patients	243	203		23	.674
Unilateral	237 (97.5)	197 (97.0)		23 (100.0)	
Bilateral	6 (2.5)	6 (3.0)		0 (0.0)	
Stage of RCC at initial diagnosis					
No. of patients	264	208		30	.008
Stage 1	15 (5.7)	15 (7.2)		0 (0.0)	
Stage 2	32 (12.1)	29 (13.9)		3 (10.0)	
Stage 3	42 (15.9)	33 (15.9)		6 (20.0)	
Stage 4 (mRCC)	175 (66.3)	131 (63.0)		21 (63.6)	
Metastatic site					
Lung	170 (58.8)	131 (66.5)		19 (57.6)	.871
Lymph nodes	98 (33.9)	68 (34.5)		20 (60.6)	.002
Bone	81 (28.0)	60 (30.5)		12 (36.4)	.532
Liver	56 (19.4)	39 (19.8)		11 (33.3)	.106
Visceral	31 (10.7)	15 (7.6)		7 (21.2)	—
Brain	20 (6.9)	15 (7.6)		2 (6.1)	.999
Local recurrence	19 (6.6)	16 (8.1)		2 (6.1)	—
Adrenal cyst	18 (6.2)	15 (7.6)		1 (3.0)	.736

(Continued on following page)

TABLE 1. Main Characteristics of the Patients Initiating Sunitinib for First-Line Therapy of mRCC in OSSMAR Study (N = 289) (Continued)

Characteristic	Value	Clear Cell (n = 217)	Mixed	Nonclear Cell (n = 33)	*P*
Sunitinib as first-line therapy					
No. of patients	154	101		13	.999
Yes	152 (98.7)	99 (98.0)		13 (100.0)	
No	2 (1.3)	2 (2.0)		0 (0.0)	
Previous treatment of RCC or mRCC					
If yes, chemotherapy*					
No. of patients	279	216		33	.121
Yes	157 (56.3)	118 (54.6)		24 (72.7)	
No	122 (43.7)	98 (45.4)		9 (27.3)	
No. of patients	154	101		13	
Yes	2 (1.3)	2 (2.0)		0 (0.0)	.999
No	152 (98.7)	99 (98.0)		13 (100.0)	
If yes, surgery					
No. of patients	154	117		23	.455
Yes	152 (98.7)	115 (98.3)		23 (100.0)	
No	2 (1.3)	2 (1.7)		0 (0.0)	
Type of surgery					
No. of patients	151	114		23	.87
Partial nephrectomy	40 (26.5)	25 (21.9)		6 (26.1)	
Radical nephrectomy	111 (73.5)	89 (78.1)		17 (73.9)	
Patient risk group (expanded MSKCC criteria)					
No. of patients	264	205		32	.029
Favorable	40 (15.2)	35 (17.1)		2 (6.3)	
Intermediate	141 (53.4)	112 (54.6)		13 (40.6)	
Poor	83 (31.4)	58 (28.3)		17 (53.1)	
Patient risk group (MSKCC criteria)					
No. of patients	264	210		15	.634
Favorable	92 (34.8)	74 (35.2)		8 (53.3)	
Intermediate	142 (53.8)	110 (52.4)		6 (40.0)	
Poor	30 (11.4)	26 (12.4)		1 (6.7)	

NOTE. Data are No. (%) unless otherwise indicated.

Abbreviations: KSA, Kingdom of Saudi Arabia; max, maximum; min, minimum; mRCC, metastatic clear-cell renal carcinoma; MSKCC, Memorial Sloan Kettering Cancer Center; RCC, clear-cell renal cell carcinoma; SD, standard deviation; UAE, United Arab Emirates.

*One patient received 6 cycles of interferon and 4 cycles of sorafenib; the other patient received gemcitabine and doxorubicin.

the International Conference on Harmonisation Harmonised Tripartite Guidelines for Good Clinical Practice, with applicable local regulations and with the ethical principles laid down in the Declaration of Helsinki. The final protocol and the final version of the informed consent form were approved by the institutional review board of the Hôtel-Dieu de France University Hospital in Lebanon and Egyptian Ministry of Health and Population's Research Ethics Committee before proceeding with the data collection.

The investigator at each site ensured that living patients included in the study were given full and adequate oral and written information about the nature, purpose, and possible risks and benefits of the study. The living patients' signed and dated informed consent forms were obtained before collecting any patient data specifically for the study. If the patient could not write, his or her legal representative/guardian signed the dated informed consent.

RESULTS

Patients

A total of 289 patients were enrolled in this study, of whom 206 (73.6%) were males and 74 (26.4%) were females. Median age of the patients was 58.7 years (range,

16.1-91.2 years) at diagnosis and 59.4 years (range, 17.6-91.2 years) at treatment baseline. Seventy-one (24.6%), 66 (22.8%), 27 (9.3%), 72 (24.9%), 15 (5.2%), 20 (6.9%), and 18 (6.2%) patients were enrolled in Lebanon, Saudi Arabia, UAE, Egypt, Algeria, Tunisia, and Morocco, respectively. The most reported comorbidities at baseline were hypertension in 59 patients (20.4%), anemia in 43 patients (14.9%), and diabetes in 34 patients (11.8%).

A total of 253 patients (87.5%) had an available pathologic diagnosis for their RCC. Of the 253 patients, the majority (85.8%) had clear-cell RCC, whereas 33 (13.0%) had nonclear-cell RCC, and the remaining (1.2%) had mixed-type RCC.

Of the 289 patients, the majority (97.5%) had unilateral RCC. At initial diagnosis, 15 patients (5.7%) had stage I disease, 32 (12.1%) had stage II disease, 42 (15.9%) had stage III disease, and 175 (66.3%) had metastatic disease. The majority of patients had lung metastasis (n = 170; 58.8%), 98 patients (33.9%) had lymph node metastasis, 81 (28.0%) had bone metastasis, and 56 (19.4%) had liver metastasis.

A total of 157 patients (56.3%) had received previous treatment of RCC (in metastatic or nonmetastatic stages). Among those, 2 patients (1.3%) had received chemotherapy, and 152 patients (98.7%) had undergone surgery.

Using the expanded MSKCC criteria, 40 patients (15.2%) were classified in the favorable-risk group, 141 (53.4%) were classified in the intermediate-risk group, and 83 (31.4%) were classified in the poor-risk group. According to the standard MSKCC criteria, 92 patients (34.8%) were classified in the favorable-risk group, 142 (53.8%) were classified in the intermediate-risk group, and 30 (11.4%) were classified in the poor-risk group. These results are listed in Table 1.

On treatment initiation, the mean total sunitinib dose was 48.1 ± 7.1 mg. Nine patients (3.2%) were started on a sunitinib dose of 25 mg, 26 (9.2%) were started on 37.5 mg, and 248 (87.6%) were started on 50 mg. The mean duration of sunitinib treatment was 9.6 ± 12.1 months (Table 2).

Effectiveness

Efficacy of sunitinib treatment was assessed on the basis of response rates at months 3, 6, and 12 of treatment (Data Supplement). The ORR was 20.8%. Ten patients (3.5%) had a complete response, 50 (17.3%) had a partial response, 76 (26.3%) had stable disease, 56 (19.4%) had progressive disease, and 97 (33.6%) had undetermined response. Median duration of ORR was 8.2 months (95% CI, 2.2 to 64.4 months).

Median time to progression in the patient population was 5.7 months (95% CI, 4.9 to 6.5 months; Fig 1A). On the basis of the expanded MSKCC prognostic criteria, time to progression was also calculated in different patient risk groups. The median time to progression was 10.2 months (95% CI, 8.3 to 12.1 months) in the favorable-risk group, 5.7 months (95% CI, 4.3 to 7.0 months) in the intermediate-risk group, and 5.0 months (95% CI, 3.9 to 6.1months) in the poor-risk group (Fig 1B). On the basis of the MSKCC prognostic criteria (excluding prior radiotherapy and the number of individual organ metastatic sites), the median time to progression was 8.8 months (95% CI, 5.9 to 11.6 months) in the favorable-risk group, 5.0 months (95% CI, 4.1 to 5.9 months) in the intermediate-risk group, and 4.8 months (95% CI, 1.6 to 7.9 months) in the poor-risk group.

OS was calculated for patients who were started on sunitinib between 2006 and 2015 (Fig 2A). Median follow-up time was 7.8 months.

Among the 289 patients included in the study, 34 (11.8%) had died, 156 (54.0%) were lost to follow-up, and 99 (34.3%) were still alive by month 12. By month 24, 41 patients (14.2%) had died, 215 (74.4%) were lost to follow-up, and 33 (11.4%) were still alive. By month 60, 44 patients (15.2%) had died, 236 (81.7%) were lost to follow-up, and only 9 (3.1%) were still alive.

On the basis of the expanded MSKCC prognostic criteria, the percentage of patients alive at 12 and 24 months was 47.5% and 20.0%, respectively, in the favorable-risk group, with a median of 11.9 months (95% CI, 11.0 to 12.8 months). In the intermediate-risk group, 37.6% and 12.1% of patients were alive, respectively, with a median of 8.6 months (95% CI, 6.2 to 11.0 months); in the poor-risk group, 21.7% and 4.8% of patients were alive, respectively,

TABLE 2. Descriptive Analysis for Sunitinib Treatment at Baseline (N = 289)

Treatment at Baseline	Value
Total sunitinib dose (mg)	
No. of patients	283
Mean ± SD	48.1 ± 7.1
Min-max	25-50
Patients receiving sunitinib dose (mg)	
No. of patients	283
25	9 (3.2)
37.5	26 (9.2)
50	248 (87.6)
Sunitinib treatment duration (months)	
No. of patients	278
Mean ± SD	9.6 ± 12.1
Median	5.8
Min-max	0-88.9

NOTE. Data are No. (%) unless otherwise indicated.

Abbreviations: max, maximum; min, minimum; SD, standard deviation.

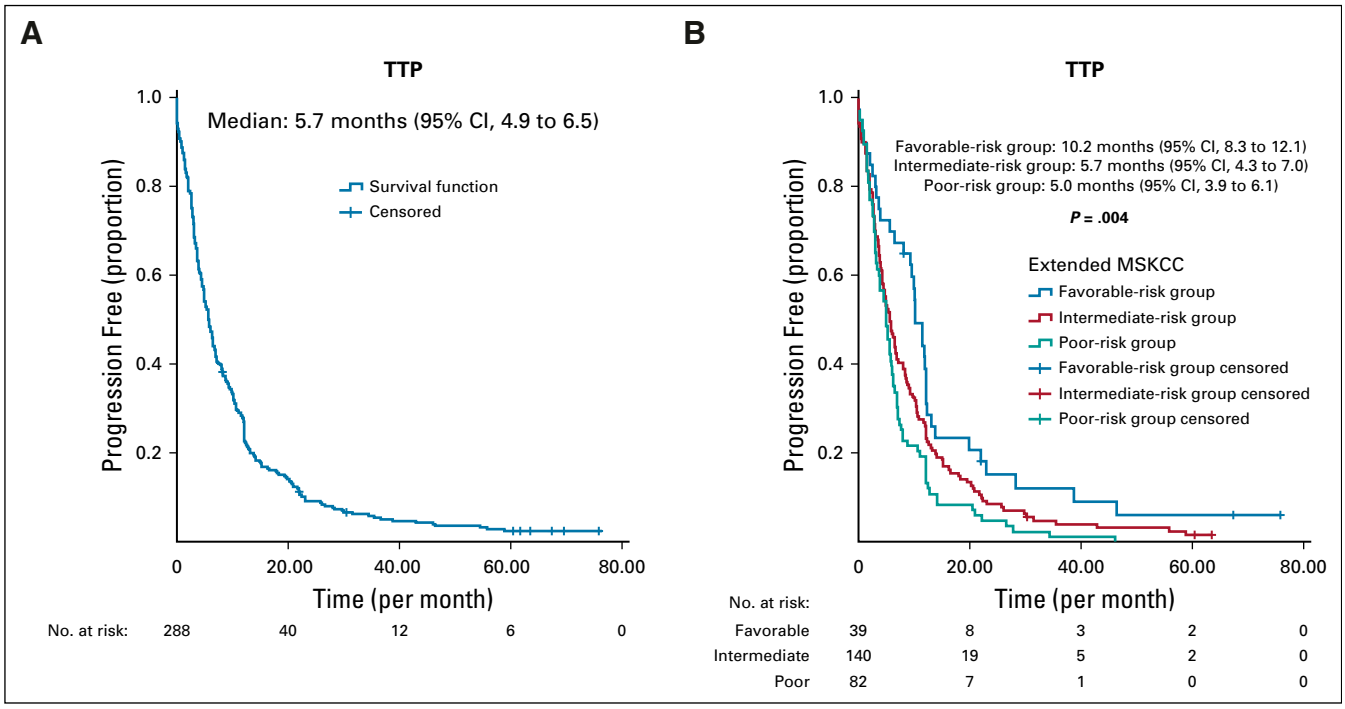

FIG 1. (A) Kaplan-Meier curve for time to progression (TTP). (B) Kaplan-Meier curves for TTP in different patient risk groups on the basis of expanded Memorial Sloan Kettering Cancer Center (MSKCC) criteria.

with a median of 6.2 months (95% CI, 4.8 to 7.6 months; Fig 2B).

On the basis of the MSKCC prognostic criteria (excluding prior radiotherapy and the number of individual organ metastatic sites), the percentage of patients alive at 12 and 24 months was 44.6% and 15.2%, respectively, in the favorable-risk group, with a median of 10.5 months (95% CI, 7.6 to 13.4 months). The percentage was 31.7% and 9.2%, respectively, in the intermediate-risk group, with a median of 7.0 months (95% CI, 5.4 to 8.6 months) and 13.3% and 6.7%, respectively, in the poor-risk group, with a median of 6.3 months (95% CI, 2.4 to 10.2 months).

Safety

One hundred seventy-six patients (60.9%) experienced 314 AEs during the observation period. Twenty-three patients (8.0%) experienced 28 SAEs.

Among AEs with a frequency of > 3%, mucosal inflammation was detected in 20 patients (6.9%), diarrhea was detected in 15 patients (5.2%), and vomiting was detected in 14 patients (4.8%). Hypertension was found in 12 patients (4.2%). Anemia and thrombocytopenia were detected in 12 patients (4.2%) and 10 patients (3.5%), respectively.

The mean hemoglobin level was low over the study period, as was the mean hematocrit level. The mean WBC count decreased from 7.6 ± 3.5 (10^9/L) at baseline to 5.9 ± 2.7 (10^9/L) at month 12. The mean platelet count fluctuated during the study but remained within the normal range. Mean ALT and AST levels were within the normal range over study visits. Mean bilirubin levels decreased from baseline to month 3, reaching normal range. Creatinine levels decreased slightly, from 1.4 ± 1.4 mg/dL at baseline to 1.2 ± 0.9 mg/dL at month 12. The mean alkaline phosphatase level decreased throughout the study, reaching 115.2 ± 88.0 U/L at month 12 (upper normal). Albumin levels remained stable throughout the study. Mean blood glucose levels increased at every time point, reaching 130.8 ± 45.8 mg/dL at month 12. Mean sodium and calcium levels remained within the normal range throughout the study. Karnofsky performance status scores were generally similar at all assessments. All details are listed in the Data Supplement.

Treatment Modalities

Overall, 83 patients (28.7%) discontinued their sunitinib treatment. Among these 83 patients, 21 (25.3%) discontinued by month 3, 35 (42.2%) discontinued between months 3 and 6, and 27 (32.5%) discontinued between months 6 and 12 of the observation period. The main reason for temporary discontinuation of sunitinib was AEs. Other reasons were disease progression and financial issues (Table 3).

By month 3, 28 patients (13.5%) had their sunitinib dose changed. Between months 3 and 6 of the observation period, 14 patients (15.1%) had their sunitinib dose changed.

Eighteen patients (7.9% of alive patients) had their sunitinib treatment temporarily discontinued by month 3. Reasons

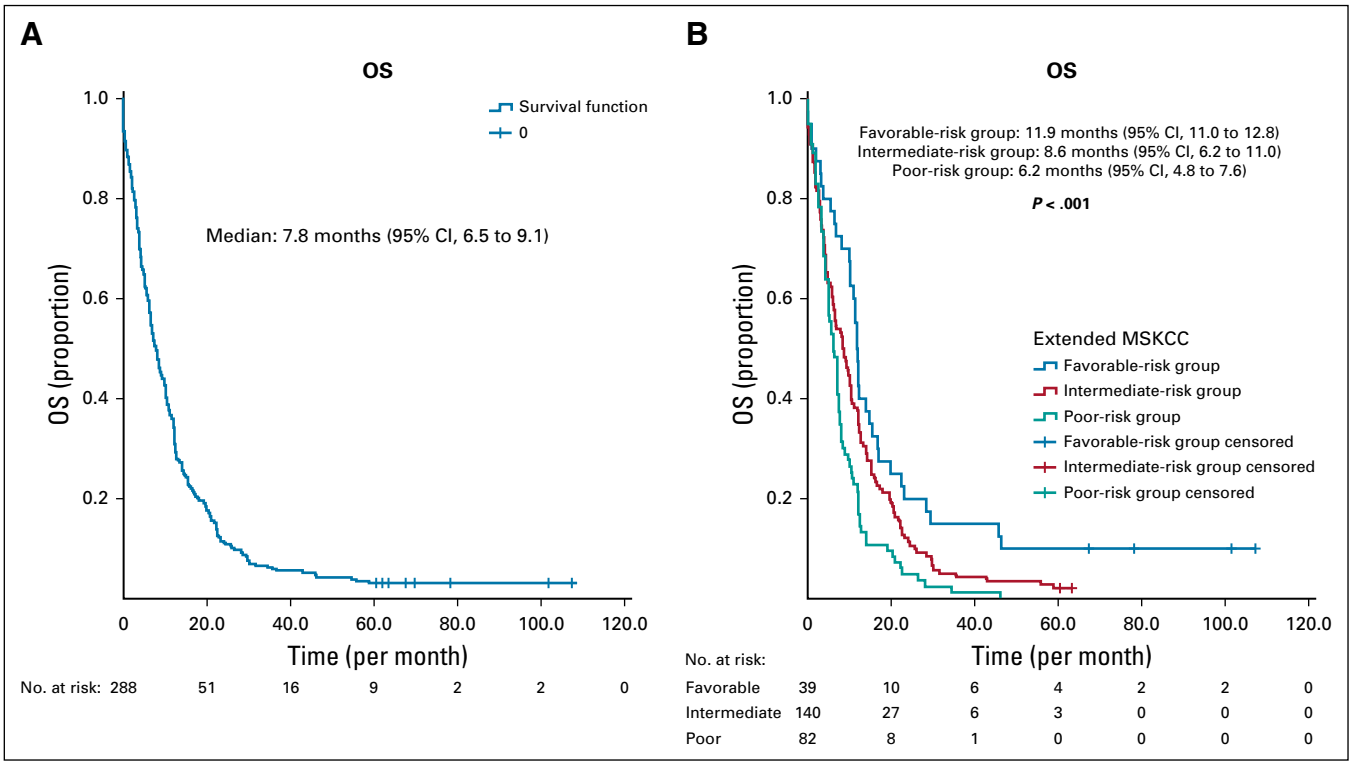

FIG 2. (A) Kaplan-Meier curve for overall survival (OS) for patients who started receiving sunitinib between 2006 and 2015. (B) Kaplan-Meier curves for OS for patients who started receiving sunitinib between 2006 and 2015 in different patient risk groups on the basis of expanded Memorial Sloan Kettering Cancer Center criteria ($P < .001$).

for discontinuation included disease progression in 1 patient, the occurrence of AEs in 13 patients, poor tolerance in 1 patient, insurance problems in 1 patient, and financial reasons in 2 patients. Twelve patients (7.0% of alive patients) had their sunitinib treatment temporarily discontinued between months 3 and 6. Reasons for discontinuation included the occurrence of AEs in 8 patients, poor tolerance in 1 patient, insurance problems in 1 patient, and financial reasons in 2 patients. Three patients (3.0% of alive patients) had their sunitinib treatment temporarily discontinued between months 6 and 12. The reason for discontinuation was the occurrence of AEs in all 3 patients. A detailed description of sunitinib treatment modalities during the observation period is listed in Table 3.

Among the 268 patients who had available data on sunitinib dose and frequency, 71 patients received the 50-mg-daily 4 weeks on/2 weeks off standard schedule, and 197 patients received other sunitinib doses and frequencies. At month 3, among the patients who received the 50-mg-daily 4 weeks on/2 weeks off standard schedule at study entry, 4 patients received sunitinib therapy with any alternative schedule, 18 patients discontinued sunitinib therapy, and 49 patients continued to receive standard therapy.

At month 6, among the patients who continued to receive standard therapy at month 3, 3 patients received sunitinib therapy with any alternative schedule, 18 patients discontinued sunitinib therapy, and 28 patients continued to receive standard therapy. At month 12, among the patients who remained on standard therapy at month 6, only 1 patient received a reduced dose of 37.5 mg daily 4 weeks on/2 weeks off standard schedule, 10 patients discontinued sunitinib therapy, and 17 patients remained on the 50-mg-daily 4 weeks on/2 weeks off standard schedule. A detailed description of sunitinib dosage schedules is shown in Figure 3.

DISCUSSION

OSSMAR is the first study in the Middle East involving several Arab countries and evaluating the use of real-time sunitinib in the treatment of mRCC. As a result, this study is of primary importance because it allows for a better assessment of the actual effectiveness and practical AEs of sunitinib in the population in our region.

However, our study has limitations, like most real-life studies. It was a retrospective study, and the sample was limited by size in a fairly diverse area and by a large number of patients who had been lost to follow-up over time.

The patients included in our study were younger compared with those included in the pivotal and real-life studies.[11,13,16,17] As in other real-life studies, we included patients with histology of nonclear-cell RCC, which was not the case in pivotal studies. Fewer patients underwent nephrectomy in the OSSMAR study (52%) compared with all pivotal trials, where the nephrectomy rate exceeded 85%.

TABLE 3. Descriptive Statistics for Sunitinib Treatment Modalities at Each Visit (N = 289)

Sunitinib Treatment	By Month 3	Months 3 to 6	Months 6 to 12
Sunitinib discontinuation*			
No. of patients	227	172	99
Yes	21 (9.3)	35 (20.3)	27 (27.3)
No	206 (90.7)	137 (79.7)	72 (72.7)
In case of sunitinib discontinuation			
New treatment			
No. of patients	5	11	9
Palliative care	0 (0.0)	1 (9.1)	0 (0.0)
Radiotherapy	1 (20.0)	1 (9.1)	2 (22.2)
Everolimus	2 (40.0)	3 (27.3)	3 (33.3)
Temsirolimus	1 (20.0)	0 (0.0)	1 (11.1)
Sorafenib	0 (0.0)	2 (18.2)	0 (0.0)
Nivolumab	1 (20.0)	1 (9.1)	1 (11.1)
Interferon	0 (0.0)	1 (9.1)	0 (0.0)
Axitinib	0 (0.0)	1 (9.1)	0 (0.0)
Pazopanib	0 (0.0)	2 (18.2)	2 (22.2)
Vinblastine	0 (0.0)	1 (9.1)	0 (0.0)
Gemcitabine plus carboplatin	0 (0.0)	0 (0.0)	1 (11.1)
Change in sunitinib dose			
No. of patients	208	93	6
No	180 (86.5)	79 (84.9)	0 (0.0)
Yes	28 (13.5)	14 (15.1)	6 (100.0)
In case of sunitinib dose change			
New dose (mg)			
No. of patients	28	14	6
25	10 (35.7)	4 (28.6)	2 (33.3)
37.5	17 (60.7)	8 (57.1)	3 (50.0)
50	0 (0.0)	2 (14.3)	1 (16.7)
Missing	1 (3.6)	0 (0.0)	0 (0.0)
Temporarily discontinuation*			
No. of patients	227	172	99
No	209 (92.1)	160 (93.0)	96 (97.0)
Yes	18 (7.9)	12 (7.0)	3 (3.0)
Reason for temporary discontinuation			
No. of patients	18	12	3
Adverse events	13 (72.2)	8 (66.7)	3 (100.0)
Disease progression	1 (5.6)	0 (0.0)	0 (0.0)
Poor tolerance	1 (5.6)	1 (8.3)	0 (0.0)
Insurance problem	1 (5.6)	1 (8.3)	0 (0.0)
Financial issues	2 (11.1)	2 (16.7)	0 (0.0)

NOTE. Data are No. (%) unless otherwise indicated.
*Calculated only for alive patients.

In our study, as in the pivotal studies, the most common sites of metastases were the lung, followed by the lymph nodes, bones and liver.[11,13]

Efficacy was evaluated several times in our study. Median time to progression in the patient population was 5.7 months, and the percentage of patients who were alive by

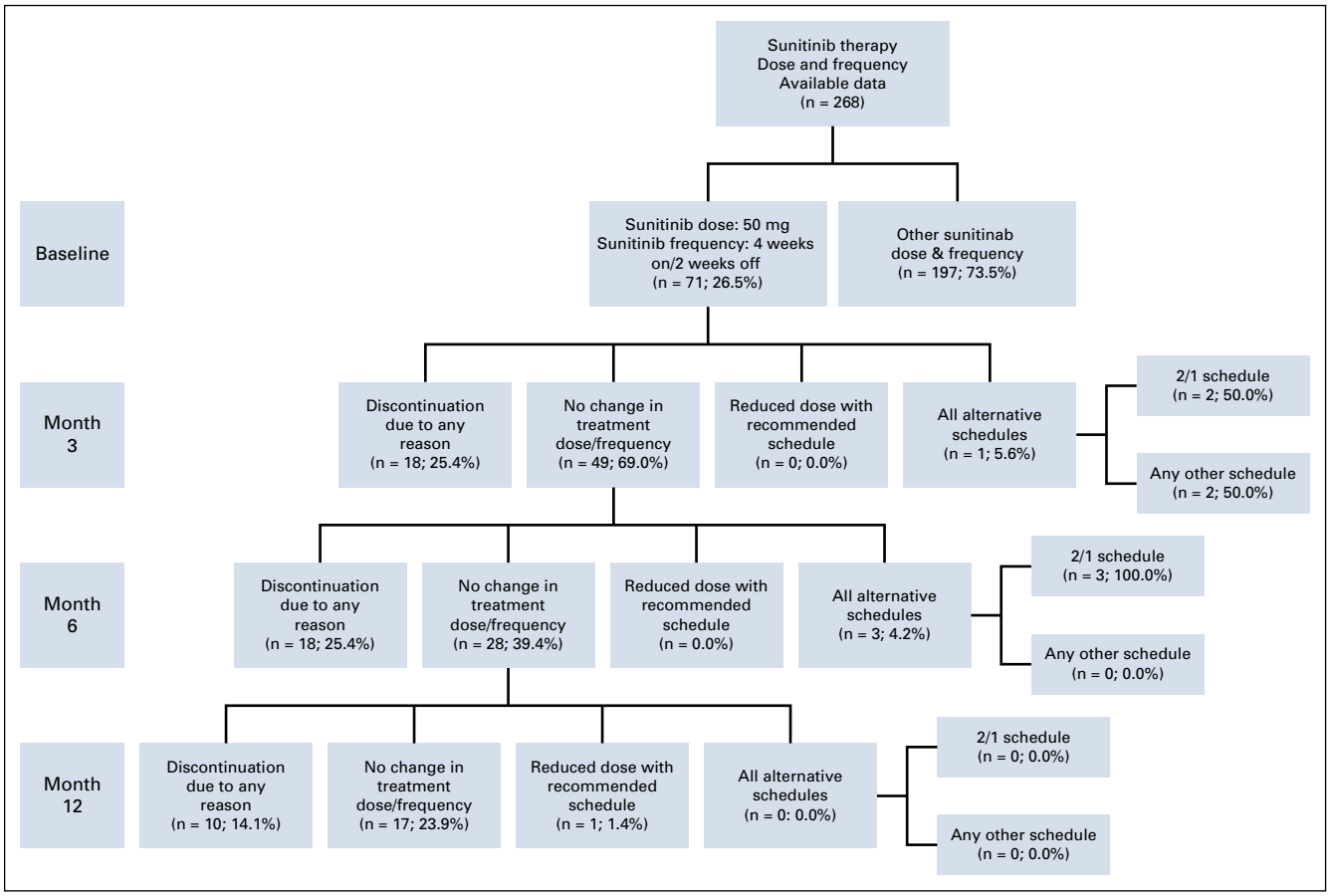

FIG 3. Sunitinib dosage schedules.

months 12 and 24 was 34.3% and 11.4%, respectively. These numbers are lower than those published in other trials.[11,12] This could be explained by the lower number of patients with nephrectomy in OSSMAR, the retrospective nature of this study, the large number of patients lost to follow-up, and the fact that this was a real-life study. However, the difference in median time to progression between risk groups (using both MSKCC criteria and expanded MSKCC criteria) was statistically significant.

In our study, a lower number of patients experienced both AEs of any grade and major AEs, compared with much higher numbers in the pivotal studies.[11,13] This is probably explained by the fact that monitoring is often less strict in real-life studies, whereas data collection and AE reports remain more stringent in trials. Overall, the AEs mainly concerned the digestive and hematologic systems in our study and in those already published.[11,13,16,17]

In summary, the results are suggestive or indicative of the general treatment outcome of patients with mRCC in the Middle East using sunitinib in routine clinical practice. The limitation of the study is that it was retrospective with a high number of patients lost to follow-up. Reported AEs were similar to those described in the literature, but at lower frequencies.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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