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A Retrospective Medical Record Review of First-Line Sunitinib Administration Schedules and Outcomes Among Patients With Metastatic Renal Cell Carcinoma in Latin America

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BACKGROUND

- Over the past decade, targeted therapies have yielded significant improvement in the clinical outcomes of patients with metastatic renal cell carcinoma (RCC). The current practice guidelines (depending on risk status) recommend combination therapies of tyrosine kinase inhibitors (e.g., axitinib, cabozantinib, lenvatinib) with checkpoint inhibitors (i.e., pembrolizumab, nivolumab) as preferred regimens[1,2]
  - At the time of study conduct, first-line treatment with sunitinib malate (sunitinib), bevacizumab plus interferon, or pazopanib were the recommended regimens[3]
- The standard administration schedule for sunitinib as first-line treatment for metastatic RCC is 50 mg per day for 4 weeks, followed by no treatment for 2 weeks (i.e., a 4/2 schedule)
- However, recent studies have suggested that a schedule modified to 2 weeks of sunitinib followed by 1 week of no treatment (i.e., a 2/1 schedule) improves tolerability and has comparable outcomes. A change to the schedule may result in fewer grade 3 or grade 4 toxicities and increased treatment duration[3-10]
- Real-world clinical outcomes among patients in Latin America who have switched sunitinib from the 4/2 schedule to the 2/1 schedule or initiated sunitinib on the 2/1 schedule remain unexplored

OBJECTIVE

- To assess clinical outcomes among patients diagnosed with metastatic RCC in Latin America who switched from the 4/2 schedule to the 2/1 schedule of first-line sunitinib

METHODS

Study Design

- This study was a retrospective, multicenter, observational medical record review of adult patients diagnosed with metastatic RCC who initiated first-line sunitinib on the 4/2 schedule and then switched to the 2/1 schedule or initiated on the 2/1 schedule between 1 January 2014 and 30 June 2018
  - The date the patient switched to or initiated first-line treatment on the 2/1 schedule was the index date
- **Figure 1** presents a graphical summary of the study design, and **Table 1** shows the patient selection criteria

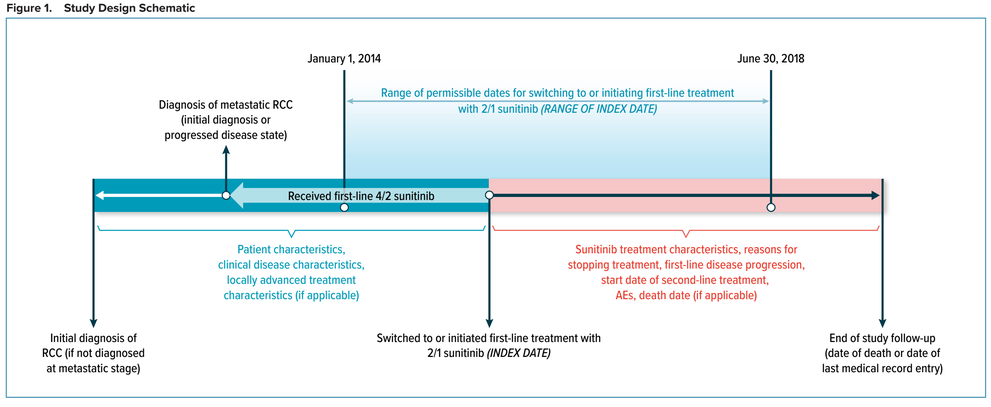
Study Measures and Data Analyses

- An electronic data collection form (DCF) was used to abstract data on patient demographics, clinical characteristics, first-line treatment patterns (e.g., time to switch from 4/2 to 2/1; treatment duration on 4/2 schedule, treatment duration on 2/1 schedule, and total treatment durations), first-line tumor response, first-line disease progression from the start of the 4/2 schedule and the start of the 2/1 schedule, adverse events (AEs), and vital status
- Data were descriptively summarized separately among patients who switched first-line sunitinib from the 4/2 schedule to the 2/1 schedule and among patients who initiated treatment on the 2/1 schedule
- Time-to-event outcomes (i.e., treatment duration, progression-free survival, overall survival) were described using the Kaplan-Meier method

Table 1. Patient Selection Criteria

Inclusion criteria	Exclusion criteria
Diagnosed with metastatic RCC with clear cell histology	Evidence of other active malignant neoplasms (except nonmelanoma skin cancer or carcinoma in situ) within 5 years before switching to the sunitinib 2/1 schedule or within 5 years of initiation of the 2/1 schedule
Initiated first-line treatment for metastatic RCC with sunitinib on the 4/2 schedule or on the 2/1 schedule (Brazil and Colombia only)	
Switched to the 2/1 schedule or initiated the 2/1 schedule during first-line treatment between 1 January 2014 and 30 June 2018	
Aged 18 years or older when switching to the 2/1 schedule or when initiating the 2/1 schedule	

Figure 1. Study Design Schematic



RESULTS

- The final sample consisted of 57 patients with metastatic RCC from 4 countries in Latin America **(Table 2)**
  - Of this total, 42 initiated first-line sunitinib on the 4/2 schedule and switched to the 2/1 schedule, and 15 patients initiated and remained on sunitinib on the 2/1 schedule. Details on demographic and clinical characteristics are summarized in **Table 2**
- Among the 42 patients who switched to the 2/1 schedule, the median duration of sunitinib treatment on the 4/2 schedule was 3.9 months, and the median duration of sunitinib treatment on the 2/1 schedule was 6.3 months **(Table 3)**
  - The most common reason for switching to the 2/1 schedule was AEs (31 patients [73.8%]), followed by performance status (10 patients [23.8%]) **(Figure 2)**
- Among 15 patients who initiated first-line sunitinib treatment on the 2/1 schedule, the median duration of sunitinib treatment on the 2/1 schedule was 9.2 months **(Table 3)**
- Among patients who experienced diarrhea on the 4/2 schedule, 35.5% had improved (decreased) diarrhea severity or no diarrhea on the 2/1 schedule **(Table 4)**
- Among patients who experienced mucositis on the 4/2 schedule, 66.7% had improved (decreased) mucositis severity or no mucositis on the 2/1 schedule **(Table 4)**
- Complete response was achieved by 0% on the 4/2 schedule and 14.0% on the 2/1 schedule (including patients who switched and initiated on 2/1 schedule); partial response was achieved by 38.1% on the 4/2 schedule and 33.3% on the 2/1 schedule; stable disease was achieved by 28.6% on the 4/2 schedule and 33.3% on the 2/1 schedule **(Figure 3)**
- Across all patients (N = 57), patients who switched to or initiated first-line sunitinib treatment on the 2/1 schedule), 31 (54.4%) experienced disease progression.
  - The median progression-free survival from the start of the 2/1 schedule was 16.1 months (95% confidence interval, 11.4 months to not estimable).
- Median overall survival from the start of the 2/1 schedule was 45.1 months (95% confidence interval, 27.5 months to not estimable)

Table 2. Demographics and Clinical Characteristics of Patients With Metastatic RCC Who Received First-Line Sunitinib

Characteristics	4/2 → 2/1		2/1	
Total patients (N, %)	**42**	**100.0%**	**15**	**100.0%**
Age at start of 2/1 sunitinib (index date)				
Mean (SD)	61.9 (8.6)		59.5 (10.3)	
Median	63.0		60.0	
Sex (n, %)				
Female	23	54.8%	3	20.0%
Male	19	45.2%	12	80.0%
Race (n, %)				
Hispanic/Latino/Latina	24	57.1%	2	13.3%
White/Caucasian	12	28.6%	7	46.7%
Black/African	1	2.4%	3	20.0%
Other	1	2.4%	0	0.0%
Unknown	4	9.5%	3	20.0%
Insurance type during metastatic RCC treatment (n, %)				
Public health plan	11	26.2%	7	46.7%
Private health plan	31	73.8%	6	40.0%
Other: PAMI	1	2.4%	0	0.0%
Unknown	0	0.0%	2	13.3%
Country[a]				
Argentina	32	76.2%	0	0.0%
Brazil	5	11.9%	7	46.7%
Colombia	3	7.1%	8	53.3%
Ecuador	2	4.8%	0	0.0%
Stage at initial diagnosis (n, %)				
I	1	2.4%	0	0.0%
II	6	14.3%	1	6.7%
III	6	14.3%	1	6.7%
IV	17	40.5%	10	66.7%
Unknown	12	28.6%	3	20.0%
Common sites of metastases at metastatic diagnosis (n, %)				
Lung/pleura	25	59.5%	8	53.3%
Lymph nodes	13	31.0%	3	20.0%
Bone	10	23.8%	2	13.3%
Liver	8	19.0%	1	6.7%
Adrenal gland	5	11.9%	2	13.3%
Risk group at the time of the schedule switch (index date)[b]				
Reported MSKCC (n, %)	42	100.0%	15	100.0%
Low-risk	23	54.8%	7	46.7%
Intermediate-risk	14	33.3%	6	40.0%
Poor-risk	5	11.9%	2	13.3%
Reported IMDC/Heng criteria (n, %)	15	35.7%	0	0.0%
Favorable-risk	3	7.1%	0	0.0%
Intermediate-risk	11	26.2%	0	0.0%
Poor-risk	1	2.4%	0	0.0%

IMDC = International mRCC Database Consortium; MSKCC = Memorial Sloan Kettering Cancer Center; SD = standard deviation.

[a] Due to ethics and contracting challenges presented due to COVID-19, data abstraction was not conducted in Mexico and Costa Rica

[b] Overall, 36.8% of the patients' risk groups were reported directly by the physician. 63.2% were calculated during analysis based on reported components of the MSKCC prognostic criteria

Figure 2. Reasons for Switching to the 2/1 Schedule and Discontinuing the 2/1 Schedule

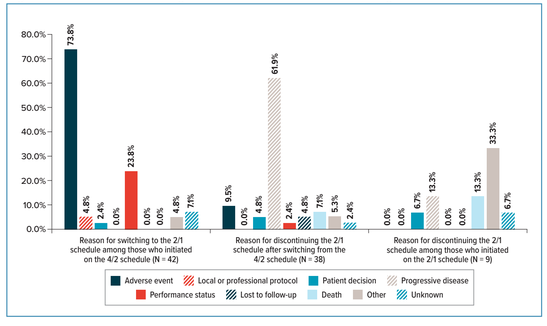


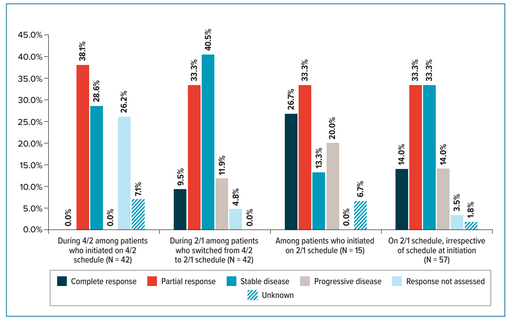
Table 3. Treatment Characteristics of First-Line Sunitinib

Characteristics	4/2 → 2/1				2/1	
	During 4/2		During 2/1		During 2/1	
Total patients (N, %)	**42**	**100.0%**	**42**	**100.0%**	**15**	**100.0%**
Duration of sunitinib on the respective schedule (months)						
Mean (SD)	4.6 (3.7)		7.5 (5.5)		13.6 (11.2)	
Median	3.9		6.3		9.2	
Discontinued sunitinib on the 2/1 schedule during observed follow-up (n, %)			38	90.5%	9	60.0%
Total number of cycles						
Mean (SD)	3.6 (2.7)		13.7 (14.4)		25.4 (22.0)	
Median	3		9.8		15.5	
Initial dose (mg) (n, %)	42	100.0%	42	100.0%	15	100.0%
Mean (SD)	50.0 (0.0)		48.2 (5.9)		50.0 (0.0)	
Median	50		50		50	
Number of patients with at least one dose change (n, %)	4	9.5%	3	7.1%	2	13.3%
Number of dose changes per patient						
Mean (SD)	1.0 (0.0)		1.3 (0.6)		1.0 (0.0)	
Median	1.0		1.0		1.0	

Table 4. Change in Diarrhea and Mucositis Severity After Switching From 4/2 to 2/1 Schedule

Characteristics	During 4/2 (4/2 → 2/1)	
Total patients (N, %)	**42**	**100.0%**
Diarrhea		
Observed during 4/2 schedule	31	73.8%
Improved in severity or not observed during 2/1 schedule	11	35.5%
Severity remained same during 2/1 schedule	18	58.1%
Severity worsened during 2/1 schedule	2	6.5%
Observed only during 2/1 schedule	4	9.5%
Mucositis		
Observed during 4/2 schedule	24	57.1%
Improved in severity or not observed during 2/1 schedule	16	66.7%
Severity remained same during 2/1 schedule	8	33.3%
Severity worsened during 2/1 schedule	0	0.0%
Observed only during 2/1 schedule	9	21.4%

Figure 3. Best Response on 4/2 and 2/1 Schedules of Sunitinib



LIMITATIONS

- All data captured in the DCF were limited to information available in the patients' medical records from the treatment centers
- Data were entered directly by the treatment centers to ensure that no inaccuracies in reporting occurred. To improve internal data consistency, several data checks were placed in the electronic DCF
  - However, responses were not checked separately against the patients' medical records by an additional reviewer
- The sample size of this study was relatively small; this may affect the generalizability of the results
  - However, to our knowledge, this is the only study that assessed real-world clinical outcomes among patients who switched from the 4/2 schedule to the 2/1 schedule of first-line sunitinib among patients with metastatic RCC in Latin America

CONCLUSIONS

- Patients who initiated first-line sunitinib treatment on the 4/2 schedule switched to 2/1 schedule primarily due to AEs, and less than 10% stopped sunitinib on the 2/1 schedule due to AEs. Moreover, no patients who initiated sunitinib treatment on the 2/1 schedule discontinued because of AEs
- An improvement in the severity of diarrhea and/or mucositis was observed after switching from the 4/2 schedule to the 2/1 schedule
- The 2/1 schedule has been shown in previous studies to have a better safety profile, which may result in better overall tolerability for sunitinib, potentially longer treatment duration, and better clinical outcomes

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