

Overall and progression-free survival according to MSKCC score in first-line sunitinib treatment of metastatic renal cell carcinoma (mRCC)

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BACKGROUND

Data on the efficacy and safety of all targeted therapies for metastatic renal cell carcinoma (mRCC), including sunitinib, were collected in the Czech RENIS patient registry (<http://renis.registry.cz/>). RENIS provides a large, unique, longitudinal sample enabling an analysis of long-term effectiveness and prognostic data of patients treated with sunitinib stratified according to adverse/risk factors assessed using the Memorial Sloan Kettering Cancer Center (MSKCC) score.

The aim of this study was to analyze the long-term overall (OS) and progression-free survival (PFS) of sunitinib, when used as a first-line treatment, based on MSKCC risk group scores including MSKCC scores for two intermediate subgroups. Secondly, the best overall response rate was explored.

Table 1. Patient characteristics based on MSKCC risk groups and MSKCC score details

	MSKCC favorable	MSKCC intermediate	MSKCC poor	MSKCC intermediate		All patients
				1 AF	2 AFs	
Patient characteristics						
n	806	1450	134	969	481	2390
Gender (female, %)	27.9%	27.9%	27.6%	26.9%	29.9%	27.9%
Age at diagnosis (yr): median	57.9	61.5	62.6	60.8	62.8	60.3
Clear cell carcinoma (%)	95.8%	94.2%	94.0%	93.7%	95.2%	94.7%
Papillary carcinoma (%)	3.7%	5.0%	5.3%	5.5%	4.0%	4.6%
Other carcinomas (%) [†]	0.5%	0.8%	0.7%	0.8%	0.8%	0.7%
The stage at diagnosis (%)						
I	25.9%	9.6%	0.7%	12.1%	4.6%	14.6%
II	20.1%	9.9%	1.5%	12.3%	5.2%	12.9%
III	22.3%	17.3%	11.2%	18.2%	15.6%	18.7%
IV	13.6%	54.6%	83.6%	47.9%	68.0%	42.4%
Unknown	18.0%	8.6%	3.0%	9.6%	6.7%	11.5%
Primary tumor grade (%)						
G1	9.4%	6.8%	6.0%	7.1%	6.0%	7.6%
G2	42.4%	31.7%	33.6%	33.7%	27.4%	35.4%
G3-4	27.2%	44.6%	47.0%	41.0%	51.8%	38.8%
GX	21.0%	17.0%	13.4%	18.2%	14.8%	18.2%
Detailed MSKCC score						
n	806	1450	134	969	481	2390
ECOG 0-1 (%)	100%	92.9%	70.1%	94.9%	88.8%	94.0%
ECOG 2+ (%)	–	7.1%	29.9%	5.1%	11.2%	6.0%
Serum calcium ≤ 2.5 μmol/l (%)	100%	91.4%	53.0%	93.6%	86.9%	92.1%
Serum calcium > 2.5 μmol/l (%)	–	8.6%	47.0%	6.4%	13.1%	7.9%
Hemoglobin normal (%)	100%	61.2%	9.0%	77.1%	29.1%	71.3%
Hemoglobin <LLN (%)	–	38.8%	91.0%	22.9%	70.9%	28.7%
Time from diagnosis to tx initiation ≥ 1 year (%)	100%	30.6%	8.2%	39.6%	12.5%	52.8%
Time from diagnosis to tx initiation < 1 year (%)	–	69.4%	91.8%	60.4%	87.5%	47.2%
LDH normal (%)	100%	90.8%	41.8%	94.7%	82.7%	91.1%
LDH > 1.5-time ULN	–	9.2%	58.2%	5.3%	17.3%	8.9%

[†]Chromophobe carcinoma, Bellini duct carcinoma, oncocytoma tumor. *AF = adverse factor, MSKCC = Memorial Sloan Kettering Cancer Center (MSKCC) score, OS = overall survival, PFS = progression-free survival, n = number of included patients, yr = years, GI=well differentiated; G2: moderately differentiated; G-4 poorly differentiated/undifferentiated; GX: grade cannot be assessed or unknown; tx = treatment.

METHODS

Data from mRCC patients treated using sunitinib as first-line treatment were collected in RENIS between 06/2007 and 01/2018 (export date 8th January 2018). In total, 2975 patients initiated targeted therapy with sunitinib. Of those: (i) 469 patients were excluded due to prior systemic therapy (chemotherapy, cytokines), (ii) 114 were excluded due to unavailability of the primary diagnosis date necessary for the calculation of the MSKCC score, and (iii) 2 patients did not have the MSKCC score assessed and were excluded.

OS and PFS were evaluated for subgroups defined by the MSKCC score as follows: (a) favorable risk (0 adverse factors (AF)), (b) intermediate-risk (pooled 1–2 AFs), and (c) poor risk (3+ AFs). The OS/PFS of the intermediate-risk group was further stratified into two subgroups: (i) 1 AF and (ii) 2 AFs. A detailed breakdown of MSKCC scores is shown in **Table 1**.

All OS/PFS data were analyzed using Kaplan-Meier estimates. Differences in OS/PFS between risk groups were assessed using median survival, 95% confidence intervals (CI), and the log-rank test. Subsequently, we assessed the best overall response rate and the OS/PFS for 1-, 3-, 5- and 10-year survival.

RESULTS

Between the years 2006 and 2017, 2390 patients initiated first-line treatment using sunitinib with 806, 1450, and 134 patients in the favorable, intermediate, and poor MSKCC risk groups, respectively. Within the intermediate subgroup, 969 patients had 1 AF, and 481 patients had 2 AFs. **Table 1** shows patient characteristics, including a detailed breakdown of MSKCC scores within the respective MSKCC risk groups.

Better MSKCC risk group had improved OS and PFS ($p < 0.001$). Regarding the MSKCC for the two intermediate sub-groups, 1 AF was associated with improved survival compared to patients with 2 AFs ($p < 0.001$) (**Figure 1 & 2** and **Table 2**):

- Median OS was 28.5 months (95% CI 26.3-30.5) in all patients.
- Median OS in MSKCC risk groups was 44.7 months (95% CI 40.9-50.5) (favorable), 24.1 months (95% CI 21.9-26.0) (intermediate) and 9.5 months (95% CI 7.2-14.1) (poor).
- Median OS in MSKCC intermediate subgroups was 28.2 months (95% CI 25.9-30.7) (1 AF) and 16.2 months (95% CI 14.5-20.2) (2 AFs).
- 5-year OS was 26.8% (95% CI 24.3%-29.2%) in all patients, while in MSKCC risk groups 5-year OS results were as follows: 35.6% (95% CI 31.2%-40.1%) (favorable), 23.4% (95% CI 20.4%-26.4%) (intermediate) (26.5% (95% CI 22.7%-30.3%) [1 AF], 16.5% (95% CI 11.8%-21.2%) [2 AFs]), and 3.2% (95% CI 0.0%-8.8%) (poor).
- Median PFS was 10.6 months (95% CI 9.9-11.5) in all patients.
- Median PFS in MSKCC risk groups was 17.0 months (95% CI 15.4-18.8) (favorable), 9.0 months (95% CI 8.3-9.5) (intermediate), and 4.5 months (95% CI 3.9-6.1) (poor).
- Median PFS in MSKCC intermediate subgroups was 10.1 months (95% CI 9.4-11.4) (1 AF) and 6.2 months (95% CI 5.5-7.5) (2 AFs)

Table 2 shows improvements in the best overall response rate for the more favorable MSKCC risk group and within the two intermediate subgroups (1 AF vs. 2 AFs):

- Objective response rate (complete response + partial response) was 26.5% in all patients.
- Objective response rate in MSKCC subgroups was 33.0% (favorable), 24.1% (intermediate) (26.7% [1 AF], 18.7% [2 AFs]), and 13.4% (poor).

CONCLUSIONS

Better MSKCC risk scores were associated with significantly longer OS and PFS, and the best overall response rates. To our knowledge, this is the largest published sunitinib-treated mRCC cohort described in the context of MSKCC risk groups.

Figure 1. Overall survival based on all MSKCC risk groups

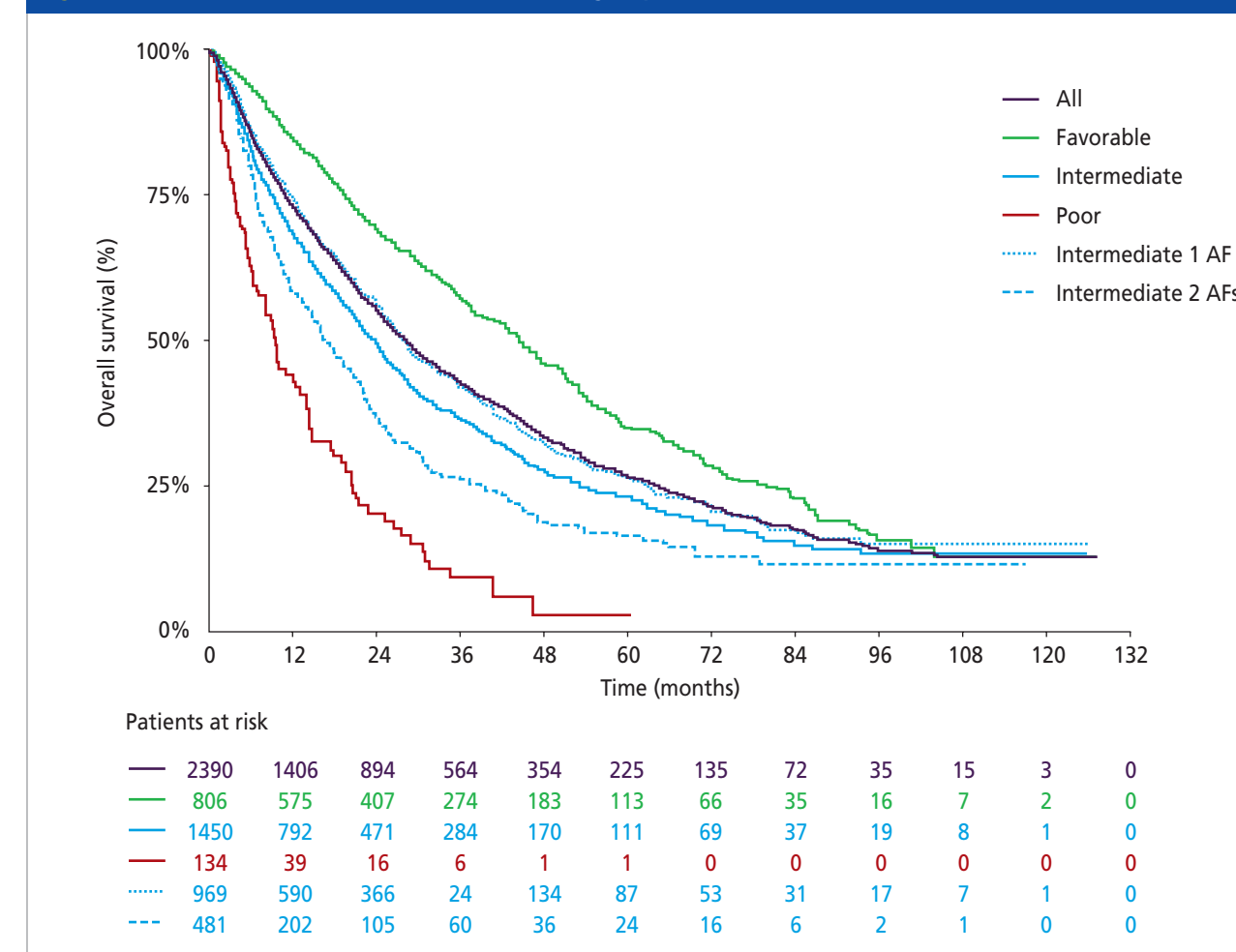


Figure 2. Progression-free survival based on all MSKCC risk groups

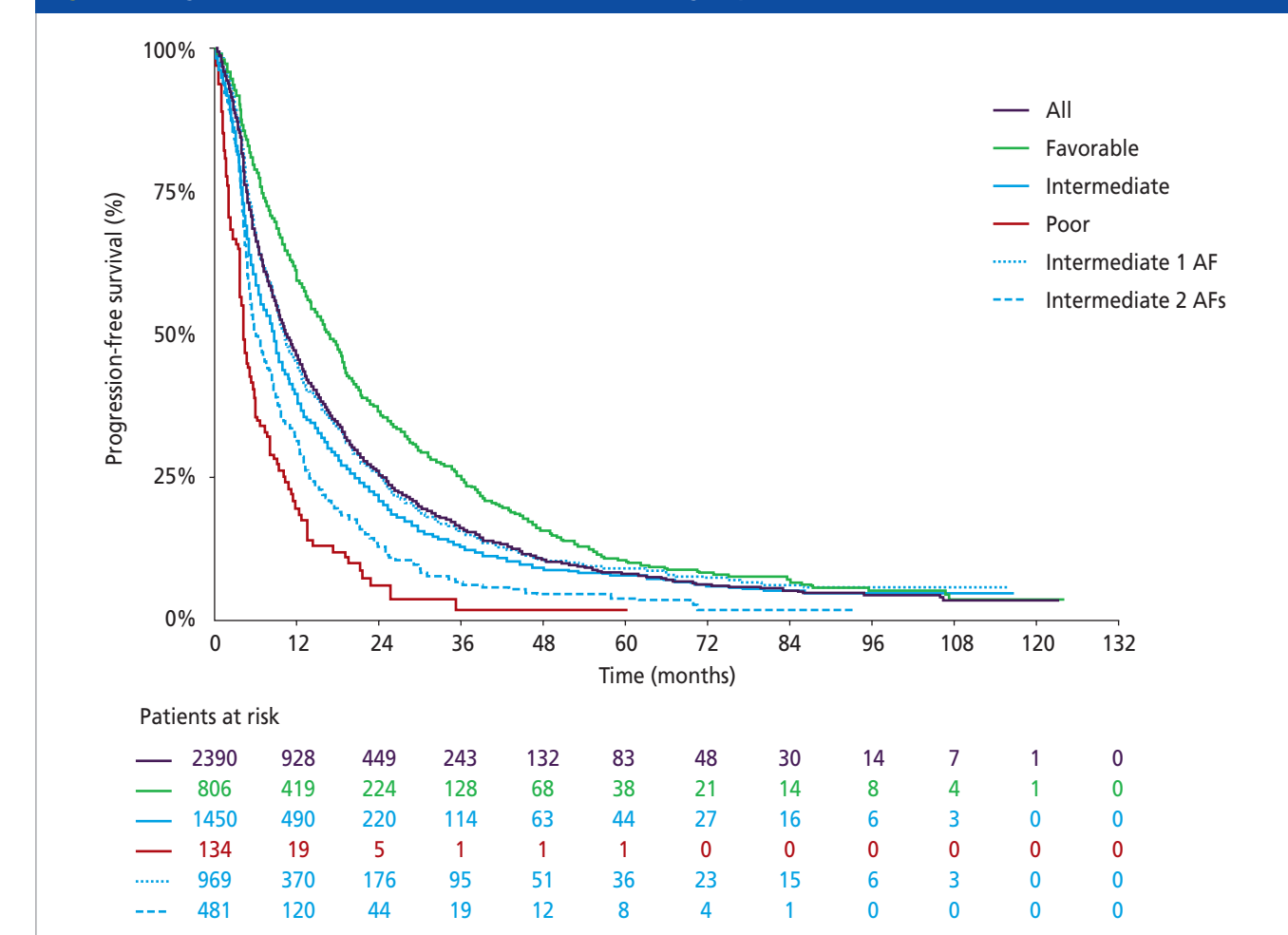


Table 2. Response rate, overall survival and progression-free survival results for sunitinib treatment based on MSKCC risk groups

	MSKCC favorable	MSKCC intermediate	MSKCC poor	MSKCC intermediate		All patients
				1 AF	2 AFs	
Best overall response						
n	806	1450	134	969	481	2390
Objective response rate (%) [†]	33.0%	24.1%	13.4%	26.7%	18.7%	26.5%
Complete response (%)	7.4%	4.6%	0.7%	5.8%	2.1%	5.3%
Partial response (%)	25.6%	19.5%	12.7%	20.9%	16.6%	21.2%
Stable disease (%)	35.1%	32.9%	18.7%	33.7%	31.2%	32.8%
Progressive disease (%)	15.9%	24.0%	39.6%	22.7%	26.6%	22.1%
Unable to determine or not reported (%)	16.0%	19.0%	28.4%	16.8%	23.5%	18.5%
Overall survival						
n	806	1450	134	969	481	2390
Median survival (95% CI)	44.7 months (40.9-50.5)	24.1 months (21.9-26.0)	9.5 months (7.2-14.1)	28.2 months (25.9-30.7)	16.2 months (14.5-20.2)	28.5 months (26.3-30.5)
	Log-rank p-value < 0.001			Log-rank p-value < 0.001		–
1-year survival (95% CI)	85.0% (82.4-87.6)	69.1% (66.6-71.7)	44.3% (35.0-53.7)	74.3% (71.4-77.2)	58.0% (53.1-62.9)	73.3% (71.4-75.2)
3-year survival (95% CI)	57.3% (53.4-61.3)	37.1% (34.1-40.1)	9.6% (3.1-16.2)	42.0% (38.3-45.7)	26.3% (21.4-31.2)	42.9% (40.5-45.2)
5-year survival (95% CI)	35.6% (31.2-40.1)	23.4% (20.4-26.4)	3.2% (0.0-8.8)	26.5% (22.7-30.3)	16.5% (11.8-21.2)	26.8% (24.3-29.2)
10-year survival (95% CI)	13.5% (8.1-18.9)	13.8% (10.5-17.0)	–	15.1% (11.0-19.1)	–	12.7% (9.8-15.7)
Progression-free survival						
n	806	1450	134	969	481	2390
Median survival (95% CI)	17.0 months (15.4-18.8)	9.0 months (8.3-9.5)	4.5 months (3.9-6.1)	10.1 months (9.4-11.4)	6.2 months (5.5-7.5)	10.6 months (9.9-11.5)
	Log-rank p-value < 0.001			Log-rank p-value < 0.001		–
1-year survival (95% CI)	61.8% (58.3-65.3)	40.7% (38.0-43.4)	20.8% (13.1-28.5)	45.1% (41.8-48.4)	31.6% (27.1-36.1)	46.9% (44.7-49.0)
3-year survival (95% CI)	25.1% (21.7-28.5)	13.0% (11.0-15.1)	1.8% (0.0-5.1)	15.9% (13.2-18.6)	7.0% (4.2-9.7)	16.6% (14.9-18.4)
5-year survival (95% CI)	10.4% (7.7-13.2)	8.0% (6.2-9.8)	1.8% (0.0-5.1)	9.7% (7.3-12.0)	4.5% (2.1-6.9)	8.4% (7.0-9.9)
10-year survival (95% CI)	3.7% (1.2-6.2)	–	–	–	–	3.7% (2.1-5.3)

[†]Complete response + partial response together. *AF = adverse factor. CI = confidence interval, MSKCC = Memorial Sloan Kettering Cancer Center (MSKCC) score, OS = overall survival, PFS = progression-free survival, n = number of included patients.

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