Real-World Evidence of Nivolumab Monotherapy in Advanced Renal Cell Carcinoma from a Multicenter Retrospective Cohort Study by the Spanish Genitourinary Oncology Group

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Supplementary Material

Supplementary Tables:

- Supplementary Table 1
- Supplementary Table 2
- Supplementary Table 3
- Supplementary Table 4
- Supplementary Table 5
- Supplementary Table 6
- Supplementary Table 7
- Supplementary Table 8
- Supplementary Table 9
- Supplementary Table 10
- Supplementary Table 11
- Supplementary Table 12
- Supplementary Table 13
- Supplementary Table 14

Supplementary Table 1. Number of patients included per medical center.

Medical center	Patients, *n (%)*
CHUAC	11 (5)
CHUO	14 (6)
CHUS	49 (22)
CHUVI	12 (5)
HCUV	16 (7)
HGU	16 (7)
HULA	13 (6)
HUMV	21 (10)
HULP	26 (12)
HURS	12 (5)
ICO	5 (2)
IVO	19 (9)
HUV	8 (4)

Abbreviations: CHUAC, Complejo Hospitalario Universitario de A Coruña; CHUO, Complejo Hospitalario Universitario de Ourense; CHUS, Complejo Hospitalario Universitario de Santiago de Compostela; CHUVI, Complejo Hospitalario Universitario de Vigo; HCUV, Hospital Clínico Universitario de Valencia; HGU, Hospital Galdakao-Usansolo; HULA, Hospital Universitario Lucus Augusti; HUMV, Hospital Universitario Marqués de Valdecilla; HULP, Hospital Universitario La Paz; HURS, Hospital Universitario Reina Sofía; ICO, Catalan Institute of Oncology; IVO, Instituto Valenciano de Oncología; HUV, Hospital Universitario del Vinalopó.

Supplementary Table 2. Drugs received prior to nivolumab.

Characteristics	Patients
First line, *n (%)*	222
Pazopanib	89 (40)
Sunitinib	120 (54)
Other[a]	13 (6)
Second line, *n (%)*	79
Axitinib	18 (26)
Cabozantinib	23 (33)
Everolimus	13 (19)
Pazopanib	9 (13)
Sunitinib	7 (11)
Other[b]	9 (13)
Third line or beyond, *n (%)*	24
Axitinib	11
Cabozantinib	7
Everolimus	5
Sunitinib	4
Other[c]	8
Median nivolumab doses, *n (range)*	7 (1-125)
Discontinued treatment, *n (%)*	203 (91)
Reasons for discontinuation, *n (%)*	
Progression	156 (70)
Death	9 (4)
Adverse event	23 (10)
Other	24 (11)

[a]Axitinib (n=1), Everolimus (n=4), Sorafenib (n=2), Chemotherapy (n=4), Interleukin-2 (n=1), Tivozanib (n=1).
[b]Sorafenib (n=6), Savolitinib (n=2), Chemotherapy (n=1).
[c]Pazopanib (n=3), Sorafenib (n=3), Chemotherapy (n=1), Interferon alfa (n=1).

Supplementary Table 3. Univariable logistic regression analyses for response.

Characteristics	Univariable analysis	
	OR (95% CI)	P value
Sex (male *vs* female)	0.89 (0.45-1.81)	0.74
Age (<75 *vs* ≥75 years)	0.54 (0.19-1.29)	0.2
ECOG-PS (≥2 *vs* 0-1)	0.32 (0.05-1.15)	0.13
IMDC risk score (poor *vs* intermediate/good/missing)	0.47 (0.17-1.11)	0.11
Histology (ccRCC *vs* non-ccRCC/missing)	0.99 (0.44-2.49)	0.99
Prior nephrectomy (yes *vs* no)	0.80 (0.31-2.33)	0.65
Corticosteroid use (yes *vs* no/missing)	0.74 (0.16-2.41)	0.65
CNS metastases (yes *vs* no)	1.94 (0.49-6.71)	0.31
Number of prior therapies (>1 *vs* 1)	0.53 (0.25-1.03)	0.07
Number of metastatic sites (≥3 *vs* <3)	0.70 (0.37-1.32)	0.28

Abbreviations: ccRCC, clear cell renal cell carcinoma; CI, confidence interval; ECOG-PS, Eastern Cooperative Oncology Group Performance Status; IMDC, International Metastatic Renal Cell Carcinoma Database Consortium; OR, odds-ratio.

Supplementary Table 4. Univariable and multivariable logistic regression analyses for disease control.

Characteristics	Univariable analysis		Multivariable analysis	
	OR (95% CI)	P value	OR (95% CI)	P value
Sex (male *vs* female)	0.90 (0.49-1.62)	0.72	-	-
Age (<75 *vs* ≥75 years)	0.53 (0.26-1.07)	0.08	-	-
ECOG-PS (≥2 *vs* 0-1)	0.34 (0.12-0.88)	**0.03**	0.49 (0.16-1.42)	0.2
IMDC risk score (poor *vs* intermediate/good/missing)	0.38 (0.18-0.76)	**0.007**	0.56 (0.25-1.2)	0.14
Histology (ccRCC *vs* non-ccRCC/missing)	1.41 (0.68-2.98)	0.36	-	-
Prior nephrectomy (yes *vs* no)	1.97 (0.81-5.14)	0.14	-	-
Corticosteroid use (yes *vs* no/missing)	0.94 (0.34-2.66)	0.91	-	-
CNS metastases (yes *vs* no)	2.64 (0.74-12.31)	0.16	-	-
Number of prior therapies (>1 *vs* 1)	0.51 (0.28-0.88)	**0.02**	1.58 (0.86-2.82)	0.15
Number of metastatic sites (≥3 *vs* <3)	0.34 (0.20-0.59)	**0.0001**	0.40 (0.23-0.70)	**0.002**

Bold numbers indicate statistically significant values.

Abbreviations: ccRCC, clear cell renal cell carcinoma; CI, confidence interval; ECOG-PS, Eastern Cooperative Oncology Group Performance Status; IMDC, International Metastatic Renal Cell Carcinoma Database Consortium; OR, odds-ratio.

Supplementary Table 5. Distribution of histology by patient and disease characteristics.

Characteristics	ccRCC histology (n=188, 85%)	Non-ccRCC histology (n=33, 15%)	*P* value
Sex, *n (%)*			1
Male	137 (73)	24 (73)	
Female	51 (27)	9 (27)	
Age, *n (%)*			0.46
<75 years	153 (81)	29 (88)	
≥75 years	35 (19)	4 (12)	
ECOG-PS, *n (%)*			1
0-1	170 (90)	30 (91)	
≥2	18 (10)	3 (9)	
IMDC risk score, *n (%)*			1
Intermediate/good	148 (79)	27 (82)	
Poor	37 (20)	6 (18)	
Missing	3 (1)	0 (0)	
Prior nephrectomy, *n (%)*			0.53
Yes	171 (91)	29 (88)	
No	17 (9)	4 (12)	
Corticosteroid use, *n (%)*			0.26
Yes	16 (8)	0 (0)	
No	171 (91)	33 (100)	
Missing	1 (1)	0 (0)	
CNS metastases, *n* (%)			0.38
Yes	11 (6)	0 (0)	
No	177 (94)	33 (100)	
Number of prior therapies, *n* (%)			0.69
1	66 (35)	10 (30)	
>1	122 (65)	23 (70)	
Number of metastatic sites, *n (%)*			0.57
<3	102 (54)	20 (61)	
≥3	86 (46)	13 (39)	

Of the 222 cases, one was excluded from group comparison because histology was not specified (n = 221).
P values were computed excluding missing cases.
Abbreviations: ccRCC, clear cell renal cell carcinoma; CNS, central nervous system; ECOG-PS, Eastern Cooperative Oncology Group Performance Status; IMDC, International Metastatic Renal Cell Carcinoma Database Consortium.

Supplementary Table 6. Distribution of IMDC risk score by patient and disease characteristics.

Characteristics	IMDC risk score intermediate/good (n=176, 80%)	IMDC risk score poor (n=43, 20%)	*P* value
Sex, *n (%)*			0.57
Male	130 (74)	30 (70)	
Female	46 (26)	13 (30)	
Age, *n (%)*			0.66
<75 years	143 (81)	37 (86)	
≥75 years	33 (19)	6 (14)	
ECOG-PS, *n (%)*			**<0.0001**
0-1	168 (95)	30 (70)	
≥2	8 (5)	13 (30)	
Histology, *n (%)*			1
ccRCC	148 (84)	37 (86)	
Non-ccRCC	27 (15)	6 (14)	
Missing	1 (1)	0 (0)	
Prior nephrectomy, *n (%)*			1
Yes	158 (90)	39 (91)	
No	18 (10)	4 (9)	
Corticosteroid use, *n (%)*			0.62
Yes	12 (7)	4 (9)	
No	163 (92)	39 (91)	
Missing	1 (1)	0 (0)	
CNS metastases, *n* (%)			1
Yes	9 (5)	2 (5)	
No	167 (95)	41 (95)	
Number of prior therapies, *n* (%)			**0.03**
1	54 (31)	21 (49)	
>1	122 (69)	22 (51)	
Number of metastatic sites, *n (%)*			**0.02**
<3	103 (59)	16 (37)	
≥3	73 (41)	27 (63)	

Of the 222 cases, three were excluded from group comparison because IMDC risk score was not specified (n = 219).

Bold numbers indicate statistically significant values.

P values were computed excluding missing cases.

Abbreviations: ccRCC, clear cell renal cell carcinoma; CNS, central nervous system; ECOG-PS, Eastern Cooperative Oncology Group Performance Status; IMDC, International Metastatic Renal Cell Carcinoma Database Consortium.

Supplementary Table 7. Distribution of prior nephrectomy by patient and disease characteristics.

Characteristics	Prior nephrectomy (n = 200, 90%)	No prior nephrectomy (n= 22, 10%)	*P* value
Sex, *n (%)*			0.2
Male	143 (72)	19 (86)	
Female	57 (28)	3 (14)	
Age, *n (%)*			0.55
<75 years	166 (83)	17 (77)	
≥75 years	34 (17)	5 (23)	
ECOG-PS, *n (%)*			0.45
0-1	182 (91)	19 (86)	
≥2	18 (9)	3 (14)	
IMDC risk score, *n (%)*			1
Intermediate/good	158 (80)	18 (82)	
Poor	39 (19)	4 (18)	
Missing	3 (1)	0 (0)	
Histology, *n (%)*			0.08
Clear cell	171 (86)	17 (77)	
Non-clear cell	29 (14)	4 (18)	
Missing	0 (0)	1 (5)	
Corticosteroid use, *n (%)*			0.66
Yes	14 (7)	2 (9)	
No	185 (92)	20 (91)	
Missing	1 (1)	0 (0)	
CNS metastases, *n* (%)			1
Yes	10 (5)	1 (5)	
No	190 (95)	21 (95)	
Number of prior therapies, *n* (%)			0.1
1	128 (64)	18 (82)	
>1	72 (36)	4 (18)	
Number of metastatic sites, *n (%)*			0.82
<3	109 (55)	13 (59)	
≥3	91 (45)	9 (41)	

P values were computed excluding missing cases.

Abbreviations: ccRCC, clear cell renal cell carcinoma; CNS, central nervous system; ECOG-PS, Eastern Cooperative Oncology Group Performance Status; IMDC, International Metastatic Renal Cell Carcinoma Database Consortium.

Supplementary Table 8. Distribution of number of metastatic sites by patient and disease characteristics.

Characteristics	<3 metastatic sites (n = 122, 55%)	≥3 metastatic sites (n = 100, 45%)	*P* value
Sex, *n (%)*			0.45
Male	92 (75)	70 (70)	
Female	30 (25)	30 (30)	
Age, *n (%)*			1
<75 years	101 (83)	82 (82)	
≥75 years	21 (17)	18 (18)	
ECOG-PS, *n (%)*			0.11
0-1	114 (93)	87 (87)	
≥2	8 (7)	13 (13)	
IMDC risk score, *n (%)*			**0.02**
Intermediate/good	103 (86)	73 (73)	
Poor	16 (12)	27 (27)	
Missing	3 (2)	0 (0)	
Histology, *n (%)*			0.57
Clear cell	102 (84)	86 (86)	
Non-clear cell	20 (16)	13 (13)	
Missing	0 (0)	1 (1)	
Corticosteroid use, *n (%)*			0.07
Yes	5 (4)	11 (11)	
No	117 (96)	88 (88)	
Missing	0 (0)	1 (1)	
CNS metastases, *n (%)*			**0.03**
Yes	2 (2)	9 (9)	
No	120 (98)	91 (91)	
Prior nephrectomy, *n* (%)			0.82
Yes	109 (89)	91 (91)	
No	13 (11)	9 (9)	
Number of prior therapies, *n* (%)			**0.007**
1	32 (26)	44 (44)	
>1	90 (74)	56 (56)	

Bold numbers indicate statistically significant values.

P values were computed excluding missing cases.

Abbreviations: ccRCC, clear cell renal cell carcinoma; CNS, central nervous system; ECOG-PS, Eastern Cooperative Oncology Group Performance Status; IMDC, International Metastatic Renal Cell Carcinoma Database Consortium

Supplementary Table 9. Distribution of central nervous system metastases by patient and disease characteristics.

Characteristics	CNS metastases (n = 11, 5%)	No CNS metastases (n = 211, 95%)	*P* value
Sex, *n (%)*			0.49
Male	7 (64)	155 (73)	
Female	4 (36)	56 (27)	
Age, *n (%)*			0.22
<75 years	11 (100)	172 (82)	
≥75 years	0 (0)	39 (18)	
ECOG-PS, *n (%)*			0.28
0-1	9 (82)	192 (91)	
≥2	2 (18)	19 (9)	
IMDC risk score, *n (%)*			1
Intermediate/good	9 (82)	167 (80)	
Poor	2 (18)	41 (19)	
Missing	0 (0)	3 (1)	
Histology, *n (%)*			0.37
Clear cell	11 (100)	177 (84)	
Non-clear cell	0 (0)	33 (15)	
Missing	0 (0)	1 (1)	
Corticosteroid use, *n (%)*			**< 0.0001**
Yes	5 (45)	10 (4)	
No	6 (55)	200 (95)	
Missing	0 (0)	1 (1)	
Prior nephrectomy, *n* (%)			1
Yes	10 (91)	190 (90)	
No	1 (9)	21 (10)	
Number of prior therapies, *n* (%)			0.75
1	3 (27)	73 (35)	
>1	8 (73)	138 (65)	
Number of metastatic sites, *n (%)*			**0.03**
<3	2 (18)	120 (57)	
≥3	9 (82)	91 (43)	

Bold numbers indicate statistically significant values.

P values were computed excluding missing cases.

Abbreviations: ccRCC, clear cell renal cell carcinoma; CNS, central nervous system; ECOG-PS, Eastern Cooperative Oncology Group Performance Status; IMDC, International Metastatic Renal Cell Carcinoma Database Consortium.

Supplementary Table 10. Treatment response by histology.

	ccRCC (n = 188, 85%)	Non-ccRCC (n = 33, 15%)	*P* value
Response, *n (%)*	45 (24)	7 (21)	0.83
Complete response	15	0	
Partial response	30	7	
No response, *n (%)*	143 (76)	26 (79)	
Stable disease	55	7	
Progression disease	76	17	
Not evaluable	12	2	
Disease control, *n (%)*	100 (53)	14 (42)	0.26
Complete response	15	0	
Partial response	30	7	
Stable disease	55	7	
No disease control, *n (%)*	88 (47)	19 (58)	
Progressive disease	76	17	
Not evaluable	12	2	

Of the 222 cases, one was excluded from group comparison because histology was not specified (n = 221).
Abbreviations: ccRCC, clear cell renal cell carcinoma.

Supplementary Table 11. Treatment response by IMDC risk score.

	IMDC risk score intermediate/good (n = 176, 80%)	**IMDC risk score poor (n = 43, 20%)**	***P* value**
Response, *n (%)*	45 (26)	6 (14)	0.16
Complete response	13	0	
Partial response	32	6	
No response, *n (%)*	131 (74)	37 (86)	
Stable disease	54	8	
Progression disease	68	24	
Not evaluable	9	5	
Disease control, *n (%)*	99 (56)	14 (33)	**0.006**
Complete response	13	0	
Partial response	32	6	
Stable disease	54	8	
No disease control, *n (%)*	77 (44)	29 (67)	
Progressive disease	68	24	
Not evaluable	9	5	

Of the 222 cases, three were excluded from group comparison because IMDC risk score was not specified (n = 219).

Bold numbers indicate statistically significant values.

Abbreviations: IMDC, International Metastatic Renal Cell Carcinoma Database Consortium.

Supplementary Table 12. Treatment response by prior nephrectomy.

	Prior nephrectomy (n = 200, 90%)	No prior nephrectomy (n = 22, 10%)	*P* value
Response, *n (%)*	47 (23)	6 (27)	0.79
Complete response	15	0	
Partial response	32	6	
No response, *n (%)*	153 (77)	16 (73)	
Stable disease	60	2	
Progression disease	83	10	
Not evaluable	10	4	
Disease control, *n (%)*	107 (54)	8 (36)	0.18
Complete response	15	0	
Partial response	32	6	
Stable disease	60	2	
No disease control, *n (%)*	93 (46)	14 (64)	
Progressive disease	83	10	
Not evaluable	10	4	

Supplementary Table 13. Treatment response by central nervous system metastases.

	CNS metastases (n = 11, 5%)	No CNS metastases (n = 211, 95%)	*P* value
Response, *n (%)*	4 (36)	49 (23)	0.3
Complete response	2	13	
Partial response	2	36	
No response, *n (%)*	7 (64)	162 (77)	
Stable disease	4	58	
Progression disease	3	90	
Not evaluable	0	14	
Disease control, *n (%)*	8 (73)	107 (51)	0.22
Complete response	2	13	
Partial response	2	36	
Stable disease	4	58	
No disease control, *n (%)*	3 (27)	104 (49)	
Progressive disease	3	90	
Not evaluable	0	14	

Abbreviations: CNS, central nervous system.

Supplementary Table 14. Distribution of treatment response by number of metastatic sites.

	<3 metastatic sites (n = 122, 55%)	**≥3 metastatic sites (n = 100, 45%)**	***P* value**
Response, *n (%)*	32 (26)	21 (21)	0.43
Complete response	12	3	
Partial response	20	18	
No response, *n (%)*	90 (74)	79 (79)	
Stable disease	45	17	
Progression disease	40	53	
Not evaluable	5	9	
Disease control, *n (%)*	77 (63)	38 (38)	**0.0003**
Complete response	12	3	
Partial response	20	18	
Stable disease	45	17	
No disease control, *n (%)*	45 (37)	62 (62)	
Progressive disease	40	53	
Not evaluable	5	9	

Bold numbers indicate statistically significant values.