

Association between cognitive impairment and oral anticancer agent use in older patients with metastatic renal cell carcinoma

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SUPPLEMENTAL MATERIALS

Supplemental Methods

Hispanic Classification

The Hispanic classification included the following North American Association of Central Cancer Registries (NAACCR) Hispanic Identification Algorithm (NHIA) designations: Mexican; Puerto Rican; Cuban; South or Central American, excluding Brazil; other specified Spanish/Hispanic origin, including Europe; Spanish/Hispanic/Latino, not otherwise specified (NOS); NHIA surname match only; and Dominican Republic. This group included Hispanic beneficiaries of any race.¹⁻⁷

Groups within the “Other” Race Category

The “other” race designation encompassed these groups: American Indian, Aleutian, Alaskan Native, or Eskimo (included all indigenous populations of the Western hemisphere); Chinese; Japanese; Filipino; Hawaiian; Korean; Vietnamese; Laotian; Hmong; Kampuchean, including Khmer and Cambodian; Thai; Asian Indian or Pakistani, NOS; Asian Indian; Pakistani; Micronesian, NOS; Chamorro; Guamanian, NOS; Polynesian, NOS; Tahitian; Samoan; Tongan; Melanesian, NOS; Fiji Islander; New Guinean; Other Asian, including Asian, NOS and Oriental, NOS; Pacific Islander, NOS; Other; and Unknown.

Adherence

In addition to the analyses described in the manuscript body, oral anticancer agent (OAA) adherence was analyzed as a binary variable, with ≥ 80 percent of days covered (PDC) in the 90 days following index drug fill defining adherence. It was analyzed using a log-binomial regression. This was repeated for oral antihypertensive drug adherence in a subset of users with hypertension.

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Supplemental Materials Abbreviations

AIDS, acquired immunodeficiency syndrome

CI, confidence interval

ESRD, end-stage renal disease

HR, hazard ratio

ICD-10-CM, International Classification of Diseases, Tenth Revision, Clinical Modification

ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification

IQR, interquartile range

MCI/D, mild cognitive impairment/dementia

mRCC, metastatic renal cell carcinoma

NA, not applicable

NAACCR, North American Association of Central Cancer Registries

NHIA, NAACCR Hispanic Identification Algorithm

NOS, not otherwise specified

OAA, oral anticancer agent

PDC, percent of days covered

Ref, reference group

SEER, Surveillance, Epidemiology and End Results cancer registry

Appendix A. Diagnosis codes used for identification of mild cognitive impairment and dementia

ICD-9-CM Codes	ICD-10-CM Codes
Dementia	
046.11, 046.19, 290.0, 290.10, 290.11, 290.12, 290.13, 290.20, 290.21, 290.3, 290.40, 290.41, 290.42, 290.43, 294.0, 294.10, 294.11, 294.2*, 294.20, 294.21, 294.8, 331.0, 331.11, 331.19, 331.2, 331.7, 331.82, 797	A81.00, A81.01, A81.09, F01.50, F01.51, F02.80, F02.81, F03.90, F03.91, F04.*, F05.*, F06.0, F06.1, F06.8, G13.2, G13.8, G30.*, G31.01, G31.09, G31.1, G31.2, G31.83, G91.4, G94.*, R41.81, R54.*
Mild cognitive impairment	
331.83	G31.84

Appendix B. Diagnosis codes used for identification of patient comorbidities

ICD-9-CM Codes	ICD-10-CM Codes
Acquired immunodeficiency syndrome (AIDS)	
042.*, 043.*, 044.*	B20.*
Cerebrovascular disease	
362.34, 430.*, 431.*, 432.*, 433.*, 434.*, 435.*, 436.*, 437.*, 438.*	G45.0*, G45.1*, G45.2*, G45.4*, G45.8*, G45.9*, G46.*, H34.0*, I60.*, I61.*, I62.*, I63.*, I65.*, I66.*, I67.1*, I67.2*, I67.4*, I67.5*, I67.6*, I67.7*, I67.81, I67.82, I67.84, I67.89, I67.9*, I68.*, I69.*
Chronic pulmonary disease	
416.8*, 416.9*, 490.*, 491.*, 492.*, 493.*, 494.*, 495.*, 496.*, 500.*, 501.*, 502.*, 503.*, 504.*, 505.*, 506.4*, 508.1*, 508.8*	I27.2*, I27.81, I27.89, I27.9*, J40.*, J41.*, J42.*, J43.*, J44.*, J45.2*, J45.3*, J45.4*, J45.5*, J45.90, J45.99, J47.*, J60.*, J61.*, J62.*, J63.*, J64.*, J65.*, J66.*, J67.*, J68.4*, J70.1*, J70.2*, J70.3*, J70.4*, J70.8*
Congestive heart failure	
398.91, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, 425.4*, 425.5*, 425.7*, 425.8*, 425.9*, 428.*	I09.81, I11.0*, I13.0*, I13.2*, I42.0*, I42.5*, I42.6*, I42.7*, I42.8*, I42.9*, I43.*, I50.*
Diabetes (mild to moderate)	
250.0*, 250.1*, 250.2*, 250.3*, 250.8*, 250.9*	E10.1*, E10.618, E10.62, E10.63, E10.64, E10.65, E10.69, E10.8*, E10.9*, E11.0*, E11.1*, E11.618, E11.62, E11.63, E11.64, E11.65, E11.69, E11.8*, E119, E13.00, E13.01, E13.10, E13.11, E13.618, E13.62, E13.63, E13.64, E13.65, E13.69, E13.8*, E13.9*
Diabetes with complication	
250.4*, 250.5*, 250.6*, 250.7*	E10.2*, E10.3*, E10.4*, E10.5*, E10.610, E11.2*, E11.3*, E11.4*, E11.5*, E11.610, E13.2*, E13.3*, E13.4*, E13.5*, E13.610
End stage renal disease	
585.6 or ESRD eligibility flag	N18.6 or ESRD eligibility flag
Hemiplegia or paraplegia	
334.1*, 342.*, 343.*, 344.0*, 344.1*, 344.2*, 344.3*, 344.4*, 344.5*, 344.6*, 344.9*	G04.1*, G11.4*, G80.*, G81.*, G82.*, G83.0*, G83.1*, G83.2*, G83.3*, G83.4*, G83.9*
Hypertension	
401.*, 402.*, 403.*, 404.*, 405.*, 437.2*	I10.*, I11.*, I12.*, I13.*, I15.0*, I15.2*, I15.8*, I15.9*, I16.*, I67.4*

ICD-9-CM Codes	ICD-10-CM Codes
Mild liver disease	
070.22, 070.23, 070.32, 070.33, 070.44, 070.54, 070.6*, 070.9*, 570.*, 571.*, 573.3*, 573.4*, 573.8*, 573.9*, V42.7*	B17.9*, B18.0*, B18.1*, B18.2*, B19.0*, B19.9*, K70.0*, K70.1*, K70.2*, K70.3*, K70.40, K70.9*, K71.0*, K71.10, K71.2*, K71.3*, K71.4*, K71.5*, K71.6*, K71.7*, K71.8*, K71.9*, K72.00, K73.*, K74.0*, K74.1*, K74.2*, K74.3*, K74.4*, K74.5*, K74.6*, K75.2*, K75.3*, K75.4*, K75.8*, K75.9*, K76.0*, K76.1*, K76.2*, K76.3*, K76.4*, K76.5*, K76.89, K76.9*, K77.*, Z48.23, Z94.4*
Moderate or severe liver disease	
456.0*, 456.1*, 456.2*, 572.2*, 572.3*, 572.4*, 572.8*	I85.*, K70.41, K71.11, K72.01, K72.1*, K72.9*, K76.6*, K76.7*
Myocardial infarction	
410.*, 412.*	21.*, I22.*, I25.2*
Peptic ulcer disease	
531.*, 532.*, 533.*, 534.*	K25.*, K26.*, K27.*, K28.*
Peripheral vascular disease	
093.0*, 437.3*, 440.*, 441.*, 443.1*, 443.2*, 443.8*, 443.9*, 447.1*, 557.1*, 557.9*, V43.4*	A52.01, E08.51, E08.52, E09.51, E09.52, E10.51, E10.52, E11.51, E11.52, E13.51, E13.52, I67.0*, I67.1*, I70.*, I71.*, I73.1*, I73.8*, I73.9*, I77.7*, I79.*, K55.1*, K55.8*, K55.9*, Z95.82
Rheumatologic disease	
446.5*, 710.0*, 710.1*, 710.2*, 710.3*, 710.4*, 714.0*, 714.1*, 714.2*, 714.8*, 725.*	M05.*, M06.*, M31.5*, M31.6*, M32.*, M33.*, M34.*, M35.0*, M35.3*, M36.0*

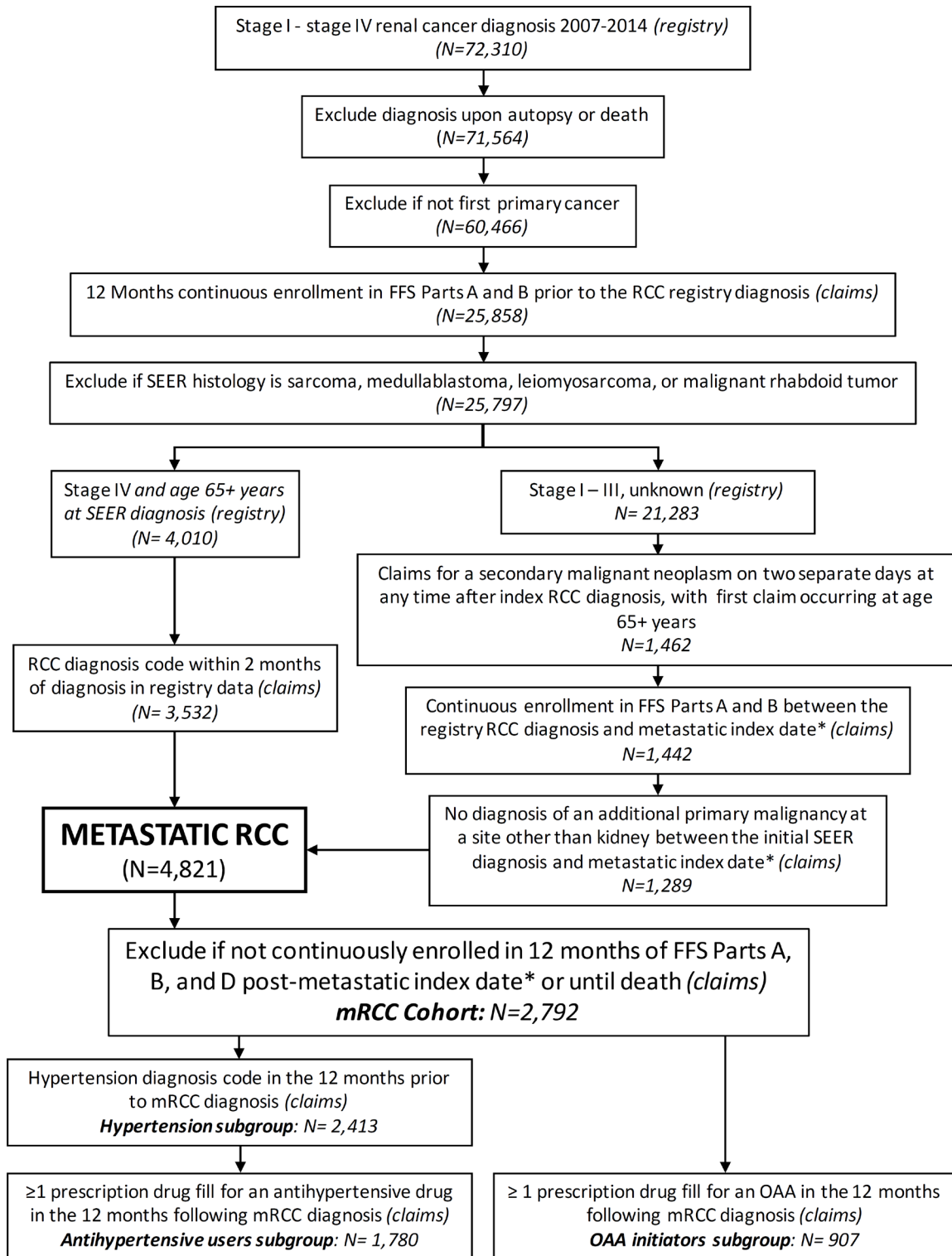
Appendix C. Included oral antihypertensive drugs

The table below lists the generic drug names of the oral antihypertensive drugs included in this study. Note that ophthalmic formulations were excluded.

Aldosterone receptor blockers
eplerenone spironolactone
Alpha-1 blockers
doxazosin prazosin terazosin
Angiotensin converting enzyme inhibitors
benazepril captopril enalapril fosinopril lisinopril moexipril perindopril quinapril ramipril trandolapril
Angiotensin II antagonists
candesartan eprosartan Irbesartan losartan olmesartan telmisartan valsartan
Beta-blockers
atenolol betaxolol bisoprolol metoprolol metoprolol extended release nadolol propranolol propranolol long-acting timolol
Beta-blockers with intrinsic sympathomimetic activity
acebutolol

penbutolol pindolol
Calcium-channel blockers: nondihydropyridines
diltiazem extended release verapamil immediate release verapamil long acting verapamil
Calcium-channel blockers: dihydropyridines
amlodipine felodipine isradipine nicardipine sustained release nifedipine long-acting nisoldipine
Central alpha-2 agonists and other centrally acting drugs
clonidine clonidine patch reserpine guanfacine
Combined alpha- and beta-blockers
carvedilol labetalol
Direct vasodilators
hydralazine minoxidil
Loop diuretics
bumetanide furosemide torsemide
Potassium-sparing diuretics
amiloride triamterene
Thiazide diuretics
chlorothiazide chlorthalidone hydrochlorothiazide polythiazide indapamide metolazone

Supplementary Figure S1. Algorithm for assignment of study cohorts.
 Abbreviations: FFS, fee-for-service; mRCC, metastatic renal cell carcinoma; RCC, renal cell carcinoma; SEER, Surveillance, Epidemiology, and End Results



* Metastatic index date: date of the first metastatic claim for Stages I – III or first diagnosis on a claim for Stage IV

Supplementary Figure S2. Cumulative incidence of patients with metastatic renal cell carcinoma (mRCC) and preexisting hypertension filling their first oral antihypertensive drug prescription in first year after mRCC diagnosis, stratified by mild cognitive impairment or dementia status. P = 0.002.

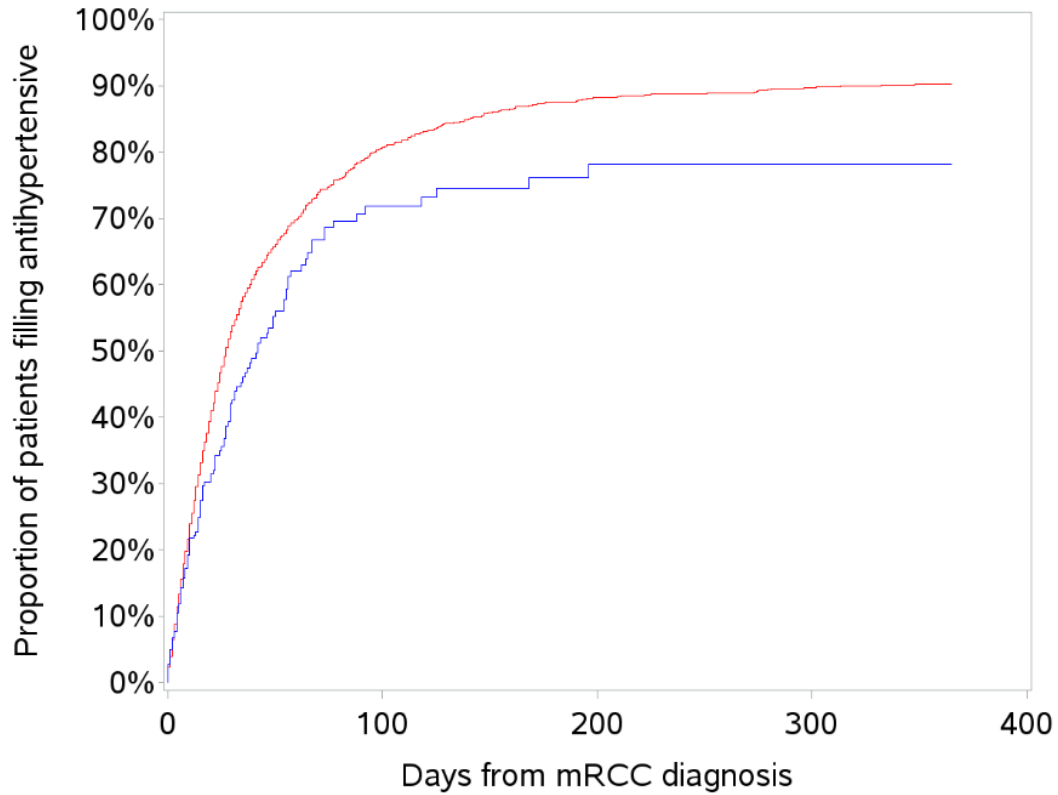


Figure Legend:

Red: Without preexisting mild cognitive impairment or dementia
Blue: With preexisting mild cognitive impairment or dementia

Supplementary Table S1. Likelihood of a patient initiating an oral anticancer agent (OAA) during the year following metastatic renal cell carcinoma (mRCC) diagnosis.

Cox proportional hazards regression was performed for patients with mRCC (N=2,792). Abbreviations: CI, confidence interval; HR, hazard ratio; MCI/D, mild cognitive impairment/dementia; NA, not applicable; Ref, reference group; SEER, Surveillance, Epidemiology and End Results cancer registry; ZIP, Zone Improvement Plan

<i>Patient Characteristic</i>	<i>Minimally-adjusted^{a, b} HR (95% CI)</i>	<i>Fully-adjusted^{a, c} HR (95% CI)</i>
Preexisting MCI/D	0.53 (0.37 - 0.74)	0.53 (0.38 - 0.76)
Age (continuous measure)	0.97 (0.96 - 0.98)	0.97 (0.96 - 0.98)
Race/ethnicity (ref = White Non-Hispanic)		
Black non-Hispanic		0.84 (0.61 - 1.16)
Hispanic		0.94 (0.74 - 1.19)
Other		1.13 (0.88 - 1.45)
Male sex		1.16 (1.00 - 1.34)
Married		1.13 (0.98 - 1.31)
Dual enrollment in Medicare and Medicaid		1.22 (1.03 - 1.45)
Lives in a metropolitan area		1.07 (0.89 - 1.29)
United States region (ref = West)		
Midwest		0.88 (0.70 - 1.11)
NA		1.01 (0.76 - 1.34)
Northeast		0.80 (0.66 - 0.98)
South		0.84 (0.68 - 1.05)
Residential ZIP code trait (ref = all lower quartiles)		
Highest quartile: Adults ≥25 years with less than a high school education		1.28 (1.06 - 1.55)
Highest quartile: Black race		0.91 (0.76 - 1.11)
Highest quartile: Impoverished households		0.92 (0.76 - 1.11)
Stage at initial SEER diagnosis (ref = IV)		
I		0.61 (0.47 - 0.78)
II		0.65 (0.44 - 0.96)
III		1.02 (0.83 - 1.25)
Unknown		1.04 (0.72 - 1.51)
Clear cell histology at initial RCC diagnosis		1.73 (1.40 - 2.14)
Prior nephrectomy		
Partial		0.86 (0.51 - 1.44)
Radical		0.95 (0.75 - 1.21)
Preexisting comorbidity		
Cerebrovascular disease		0.88 (0.74 - 1.05)

<i>Patient Characteristic</i>	<i>Minimally-adjusted^{a, b} HR (95% CI)</i>	<i>Fully-adjusted^{a, c} HR (95% CI)</i>
Congestive heart failure		1.05 (0.88 - 1.25)
Diabetes with complications		1.16 (0.96 - 1.39)
Hemiplegia or paraplegia		0.72 (0.43 - 1.22)
Hypertension		1.31 (1.06 - 1.62)
Mild liver disease		1.22 (1.02 - 1.46)
Myocardial infarction		0.98 (0.78 - 1.24)
Peptic ulcer disease		1.16 (0.79 - 1.7)
Peripheral vascular disease		0.90 (0.77 - 1.06)
Renal disease		0.91 (0.77 - 1.07)
Rheumatologic disease		0.98 (0.71 - 1.34)
Year of metastatic diagnosis		1.06 (1.03 - 1.09)

^a Statistically significant results are bolded.

^b The minimally-adjusted model included only age and MCI/D status .

^c Full adjustment included all listed patient characteristics.

Supplementary Table S2. Likelihood of a patient with metastatic renal cell carcinoma (mRCC) and preexisting hypertension receiving an oral antihypertensive drug during the year following mRCC diagnosis. Cox proportional hazards regression was performed for patients with mRCC and comorbid hypertension (N = 2,413). Abbreviations: CI, confidence interval; HR, hazard ratio; MCI/D, mild cognitive impairment/dementia; NA, not applicable; Ref, reference group; SEER, Surveillance, Epidemiology and End Results cancer registry; ZIP, Zone Improvement Plan

<i>Patient Characteristic</i>	<i>Minimally-adjusted^{a, b} HR (95% CI)</i>	<i>Fully-adjusted^{a, c} HR (95% CI)</i>
Preexisting MCI/D	0.78 (0.65 - 0.95)	0.77 (0.63 - 0.93)
Age (continuous measure)	0.99 (0.98 - 0.99)	0.97 (0.96 - 0.98)
Race/ethnicity (ref = White non-Hispanic)		
Black non-Hispanic		0.96 (0.78 - 1.18)
Hispanic		1.10 (0.92 - 1.32)
Other		0.88 (0.72 - 1.07)
Male sex		0.99 (0.90 - 1.10)
Married		1.07 (0.97 - 1.19)
Dual enrollment in Medicare and Medicaid		1.14 (1.01 - 1.29)
Lives in a metropolitan area		0.90 (0.79 - 1.03)
United States region (ref = West)		
Midwest		1.20 (1.02 - 1.41)
NA		1.17 (0.95 - 1.44)
Northeast		0.98 (0.85 - 1.13)
South		1.08 (0.92 - 1.26)
Residential ZIP code trait (ref = all lower quartiles)		
Highest quartile: Adults ≥ 25 years with less than a high school education		1.11 (0.97 - 1.28)
Highest quartile: Black race		1.02 (0.89 - 1.17)
Highest quartile: Impoverished households		0.91 (0.79 - 1.04)
Stage at initial SEER diagnosis (ref = IV)		
I		0.89 (0.76 - 1.05)
II		0.93 (0.72 - 1.19)
III		1.01 (0.86 - 1.18)
Unknown		1.04 (0.80 - 1.35)
Clear cell histology at initial RCC diagnosis		1.04 (0.91 - 1.18)
Prior nephrectomy		
Partial		1.15 (0.81 - 1.63)
Radical		1.00 (0.84 - 1.19)
Preexisting comorbidity		

<i>Patient Characteristic</i>	<i>Minimally-adjusted^{a, b} HR (95% CI)</i>	<i>Fully-adjusted^{a, c} HR (95% CI)</i>
Cerebrovascular disease		0.85 (0.68 - 1.06)
Congestive heart failure		1.00 (0.89 - 1.12)
Diabetes with complications		0.53 (0.38 - 0.76)
Hemiplegia or paraplegia		1.02 (0.87 - 1.19)
Hypertension		1.07 (0.96 - 1.19)
Mild liver disease		1.07 (0.96 - 1.20)
Myocardial infarction		1.02 (0.87 - 1.19)
Peptic ulcer disease		0.93 (0.82 - 1.07)
Peripheral vascular disease		1.19 (1.06 - 1.35)
Renal disease		1.00 (0.88 - 1.14)
Rheumatologic disease		0.99 (0.76 - 1.29)
Year of metastatic diagnosis		1.01 (0.99 - 1.03)

^a Statistically significant results are bolded.

^b The minimally-adjusted model included only age and MCI/D status .

^c The fully-adjusted model was adjusted for all listed patient characteristics.

Supplementary Table S3. Likelihood of a patient with metastatic renal cell carcinoma (mRCC) and preexisting hypertension initiating an oral anticancer agent (OAA) during the year following mRCC diagnosis. Cox proportional hazards regression for time to OAA initiation, among patients with mRCC and a preexisting hypertension diagnosis (N=2,413). Abbreviations: CI, confidence interval; HR, hazard ratio; MCI/D, mild cognitive impairment/dementia; NA, not applicable; Ref, reference group; SEER, Surveillance, Epidemiology and End Results cancer registry; ZIP, Zone Improvement Plan

<i>Patient Characteristic</i>	<i>Minimally-adjusted^{a, b} HR (95% CI)</i>	<i>Fully-adjusted^{a, c} HR (95% CI)</i>
Preexisting MCI/D	0.57 (0.40 - 0.82)	0.58 (0.40 - 0.84)
Age (continuous measure)	0.97 (0.96 - 0.98)	0.97 (0.96 - 0.98)
Race/ethnicity (ref = White non-Hispanic)		
Black Non-Hispanic		0.82 (0.59 - 1.14)
Hispanic		0.88 (0.68 - 1.13)
Other		1.13 (0.87 - 1.47)
Male sex		1.19 (1.02 - 1.39)
Married		1.15 (0.98 - 1.35)
Dual enrollment in Medicare and Medicaid		1.30 (1.09 - 1.57)
Lives in a metropolitan area		1.03 (0.85 - 1.25)
United States region (ref = West)		
Midwest		0.79 (0.61 - 1.01)
NA		1.04 (0.77 - 1.40)
Northeast		0.83 (0.67 - 1.02)
South		0.81 (0.64 - 1.02)
Residential ZIP code characteristic (ref = all lower quartiles)		
Highest quartile: Adults ≥25 years with less than a high school education		1.30 (1.06 - 1.59)
Highest quartile: Black race		0.97 (0.80 - 1.19)
Highest quartile: Impoverished households		0.88 (0.72 - 1.09)
Stage at initial SEER diagnosis (ref = IV)		
I		0.58 (0.45 - 0.76)
II		0.67 (0.45 - 1.00)
III		1.07 (0.86 - 1.32)
Unknown		1.06 (0.73 - 1.54)
Clear cell histology at initial RCC diagnosis		1.70 (1.36 - 2.12)
Prior nephrectomy		
Partial		0.90 (0.53 - 1.53)
Radical		0.97 (0.76 - 1.23)

<i>Patient Characteristic</i>	<i>Minimally-adjusted^{a, b} HR (95% CI)</i>	<i>Fully-adjusted^{a, c} HR (95% CI)</i>
Preexisting comorbidity		
Cerebrovascular disease		0.94 (0.67 - 1.31)
Congestive heart failure		0.89 (0.75 - 1.06)
Diabetes with complications		0.76 (0.45 - 1.28)
Hemiplegia or paraplegia		1.06 (1.03 - 1.09)
Hypertension		0.88 (0.75 - 1.05)
Mild liver disease		0.87 (0.73 - 1.03)
Myocardial infarction		0.97 (0.76 - 1.23)
Peptic ulcer disease		1.28 (1.06 - 1.54)
Peripheral vascular disease		1.06 (0.89 - 1.27)
Renal disease		1.18 (0.98 - 1.42)
Rheumatologic disease		1.15 (0.78 - 1.70)
Year of metastatic diagnosis		0.90 (0.53 - 1.53)

^a Statistically significant results are bolded.

^b The minimally-adjusted model included only age and MCI/D status .

^c Fully adjustment model included all listed patient characteristics.

Supplementary Table S4. Likelihood of a patient with metastatic renal cell carcinoma (mRCC) and preexisting mild cognitive impairment or dementia (MCI/D) adhering to an oral anticancer agent (OAA). Log-binomial regression evaluated the association between prevalent MCI/D and binary OAA adherence (percent days covered $\geq 80\%$) during the first 90 days following initiation (N=907 initiating OAA). Abbreviations: CI, confidence interval; NA, not applicable; Ref, reference group; RR, risk ratio; SEER, Surveillance, Epidemiology and End Results cancer registry; ZIP, Zone Improvement Plan

<i>Patient Characteristic</i>	<i>Unadjusted RR (95% CI)</i>	<i>Adjusted^a RR (95% CI)</i>
Preexisting MCI/D	0.77 (0.50 - 1.19)	0.84 (0.55 - 1.28)
Age, in years (ref = 65-70)		
71-75		0.92 (0.79 - 1.07)
76-80		0.73 (0.60 - 0.89)
≥ 80		0.75 (0.60 - 0.94)
Race/ethnicity (ref = White Non-Hispanic)		
Black non-Hispanic		0.83 (0.58 - 1.19)
Hispanic		1.18 (0.96 - 1.46)
Other		1.16 (0.92 - 1.45)
Male sex		1.19 (1.03 - 1.38)
Married		0.88 (0.76 - 1.02)
Dual enrollment in Medicare and Medicaid		0.96 (0.81 - 1.14)
Lives in a metropolitan area		0.97 (0.80 - 1.17)
United States region (ref = West)		
Midwest		0.90 (0.72 - 1.12)
NA		0.96 (0.71 - 1.29)
Northeast		0.81 (0.65 - 1.01)
South		1.07 (0.85 - 1.34)
Residential ZIP code characteristic (ref = all lower quartiles)		
Highest quartile: adults ≥ 25 years with less than a high school education		1.06 (0.88 - 1.28)
Highest quartile: Black race		1.11 (0.91 - 1.36)
Highest quartile: Impoverished households		0.73 (0.60 - 0.89)
OAA at initiation (ref = sunitinib)		
Axitinib		0.85 (0.50 - 1.44)
Everolimus		1.07 (0.80 - 1.43)
Pazopanib		0.80 (0.68 - 0.95)
Sorafenib		0.71 (0.52 - 0.97)
Stage at initial SEER diagnosis (ref = IV)		
I		1.18 (0.94 - 1.48)

<i>Patient Characteristic</i>	<i>Unadjusted RR (95% CI)</i>	<i>Adjusted^a RR (95% CI)</i>
II		1.06 (0.74 - 1.52)
III		0.98 (0.80 - 1.20)
Unknown		1.22 (0.87 - 1.73)
Clear cell histology at initial RCC diagnosis		0.86 (0.70 - 1.05)
Prior nephrectomy		
Partial		1.06 (0.70 - 1.62)
Radical		1.12 (0.90 - 1.39)
Preexisting comorbidity		
Cerebrovascular disease		1.00 (0.84 - 1.20)
Congestive heart failure		0.88 (0.73 - 1.06)
Diabetes with complications		1.03 (0.86 - 1.23)
Hemiplegia or paraplegia		0.84 (0.44 - 1.64)
Hypertension		1.06 (0.85 - 1.32)
Mild liver disease		0.98 (0.82 - 1.18)
Myocardial infarction		0.82 (0.64 - 1.06)
Peptic ulcer disease		0.78 (0.48 - 1.25)
Peripheral vascular disease		1.09 (0.94 - 1.27)
Renal disease		1.09 (0.93 - 1.28)
Rheumatologic disease		0.90 (0.62 - 1.30)
Year of metastatic diagnosis		1.00 (0.97 - 1.03)

^a The model was adjusted for all listed patient characteristics. Statistically significant results are bolded.

Supplementary Table S5. Likelihood of a patient with metastatic renal cell carcinoma (mRCC) and preexisting mild cognitive impairment or dementia (MCI/D) and hypertension adhering to an oral antihypertensive drug. Log-binomial regression assessed association between prevalent MCI/D and binary oral antihypertensive drug adherence (percent days covered $\geq 80\%$) in the 90 days after the first antihypertensive drug claim following mRCC diagnosis, among patients with mRCC who filled an antihypertensive prescription (N=1,780). Abbreviations: CI, confidence interval; NA, not applicable; Ref, reference group; RR, risk ratio; SEER, Surveillance, Epidemiology and End Results cancer registry; ZIP, Zone Improvement Plan

<i>Patient Characteristic</i>	<i>Unadjusted RR (95% CI)</i>	<i>Adjusted^a RR (95% CI)</i>
Preexisting MCI/D	0.66 (0.55 - 0.80)	0.71 (0.59 - 0.86)
Age, in years (ref = 65-70)		
71-75		1.03 (0.95 - 1.10)
76-80		1.00 (0.92 - 1.08)
≥ 80		0.87 (0.79 - 0.96)
Race/ethnicity (ref = White non-Hispanic)		
Black non-Hispanic		0.99 (0.87 - 1.14)
Hispanic		0.95 (0.85 - 1.06)
Other		0.94 (0.82 - 1.08)
Male sex		0.99 (0.93 - 1.05)
Married		1.04 (0.98 - 1.11)
Dual enrollment in Medicare and Medicaid		0.94 (0.86-1.02)
Lives in a metropolitan area		1.12 (1.03 - 1.22)
United States region (ref = West)		
Midwest		1.02 (0.92 - 1.12)
NA		0.94 (0.82 - 1.08)
Northeast		0.99 (0.91 - 1.07)
South		1.02 (0.93 - 1.12)
Residential ZIP code characteristic (ref = all lower quartiles)		
Highest quartile: adults ≥ 25 years with less than a high school education		1.02 (0.94-1.11)
Highest quartile: Black race		0.99 (0.91-1.07)
Highest quartile: Impoverished households		1.02 (0.94-1.11)
Stage at initial SEER diagnosis (ref = IV)		
I		1.27 (1.17 - 1.37)
II		1.27 (1.13 - 1.42)
III		1.17 (1.08 - 1.26)
Unknown		1.19 (1.02 - 1.38)
Clear cell histology at initial RCC diagnosis		1.11 (1.02 - 1.22)

<i>Patient Characteristic</i>	<i>Unadjusted RR (95% CI)</i>	<i>Adjusted^a RR (95% CI)</i>
Prior Nephrectomy		
Partial		1.03 (0.87 - 1.22)
Radical		1.08 (1.00 - 1.17)
Preexisting comorbidity		
Cerebrovascular disease		1.03 (0.89 - 1.19)
Congestive heart failure		0.96 (0.89 - 1.03)
Diabetes with complications		0.91 (0.70 - 1.19)
Hemiplegia or paraplegia		1.00 (0.99 - 1.02)
Hypertension		1.03 (0.96 - 1.10)
Mild liver disease		0.99 (0.93 - 1.06)
Myocardial infarction		0.90 (0.81 - 1.00)
Peptic ulcer disease		0.99 (0.91 - 1.07)
Peripheral vascular disease		0.99 (0.92 - 1.06)
Renal disease		1.09 (1.02 - 1.18)
Rheumatologic disease		0.92 (0.76 - 1.11)
Year of metastatic diagnosis		1.03 (0.87 - 1.22)

^a The model was adjusted for all listed patient characteristics. Statistically significant results are bolded.

Supplementary Table S6. Adherence to medication regimens by patients with metastatic renal cell carcinoma (mRCC). Among all oral anticancer agent (OAA) initiators in the mRCC cohort (N=907) and all antihypertensive users in the mRCC with prevalent hypertension cohort (N=1,780), 90-day OAA or antihypertensive adherence measured as percent of days covered (PDC), stratified by mild cognitive impairment or dementia (MCI/D) status. Abbreviation: IQR, interquartile range

	Sans prevalent MCI/D	Prevalent MCI/D	P-value
OAA Adherence			
N	872	35	
PDC median (IQR)	79.1% (46.1 - 97.8)	63.7% (32.9 - 92.3)	0.071
Initiators with PDC \geq 80%	49.6%	38.2%	0.193
Antihypertensive Adherence			
N	1659	121	
PDC median (IQR)	100% (70.3 - 100)	74.7% (32.9 - 100)	<0.001
Users with PDC \geq 80%	72.4%	47.9%	<0.001