Adv Ther (2017) 34:2452–2465
DOI 10.1007/s12325-017-0628-2

ORIGINAL RESEARCH

Clinical and Economic Outcomes in Elderly Advanced Renal Cell Carcinoma Patients Starting Pazopanib or Sunitinib Treatment: A Retrospective Medicare Claims Analysis

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Received: August 30, 2017 / Published online: October 26, 2017

ABSTRACT

Introduction: Studies indicate similar survival and toxicity between pazopanib and sunitinib, but few have examined real-world outcomes among elderly patients with advanced renal cell carcinoma (RCC). The purpose of this retrospective claims analysis was to assess real-world overall survival (OS), healthcare resource utilization (HRU), and healthcare costs (both all-cause and associated with RCC diagnosis) among elderly advanced RCC patients starting pazopanib or sunitinib treatment.

Methods: Advanced RCC patients aged 65 years or older who started first-line treatment with pazopanib or sunitinib (index drug; the initiation date was the index date) were identified from the 100% Medicare database plus Part D linkage (January 1, 2006 to December 31, 2014). Patients were stratified by index drug and matched 1:1 with use of propensity scores based on baseline characteristics. OS was assessed from the index date to death and compared by Kaplan–Meier analyses and univariable Cox models; patients were censored at the end of eligibility/data. Monthly HRU and costs from an intent-to-treat perspective were compared by Wilcoxon signed-rank tests.

Results: Baseline characteristics were balanced after matching (both $N = 522$). Treatment with pazopanib was associated with significantly longer median OS compared with treatment with sunitinib (18.2 months vs 14.6 months, respectively; log-rank $p = 0.015$). Pazopanib was associated with significantly lower monthly all-cause costs compared with sunitinib ($8845 vs $10,416, respectively), as well as lower inpatient costs associated with RCC diagnosis ($1542 vs $2522), fewer monthly inpatient admissions (0.179 vs 0.262), and shorter length of inpatient stay (1.375 days vs 1.883 days; all $p \leq 0.004$).

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Electronic supplementary material The online version of this article (doi:10.1007/s12325-017-0628-2) contains supplementary material, which is available to authorized users.

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Conclusions: Among elderly Medicare patients with advanced RCC, first-line pazopanib tretament was associated with significantly longer OS, as well as lower healthcare costs and HRU, compared with first-line sunitinib treatment.

Keywords: Advanced renal cell carcinoma; Claims analysis; Elderly; Healthcare costs; Healthcare resource utilization; Medicare; Overall survival; Pazopanib; Sunitinib

INTRODUCTION

Renal cell carcinoma (RCC) is one of the ten most common cancers in the USA, with approximately 63,990 new cases expected to be diagnosed in 2017 [1, 2]. Older patients have an increased risk of RCC, which is typically diagnosed between the ages of 50 and 70 years [3]. Many RCC patients receive a de novo diagnosis of advanced RCC (aRCC) [locally advanced (25%) or metastatic (30%)] or progress to advanced disease stages [4]. Despite advances in therapy and early detection methods, the incidence of RCC and the RCC-related mortality rate have increased over time [5–8].

Among the vascular endothelial growth factor receptor tyrosine kinase inhibitors (TKIs) approved for first-line aRCC therapy, the angiogenesis inhibitors pazopanib (approved in 2009) and sunitinib (approved in 2006) are two common oral treatment options [9–11]. Although pazopanib and sunitinib were found to have similar overall survival (OS) in the noninferiority clinical trial COMPARZ, real-world evidence has been mixed, and outcomes may differ depending on the age of the patient [11–13]. For example, OS was found to be similar among patients receiving pazopanib or sunitinib in the International Metastatic Renal Cell Carcinoma Database Consortium (IMDC) [12], but a recent retrospective claims analysis of Surveillance, Epidemiology, and End Results (SEER)–Medicare data (median age 68 years) reported longer OS with first-line pazopanib treatment versus first-line sorafenib or sunitinib treatment [13]. Conversely, Canadian adults with metastatic RCC (mRCC) experienced longer OS with first-line sunitinib treatment versus first-line pazopanib treatment (31.7 months vs 20.6 months, $p = 0.028$) according to a prospective database study (2011–2015) published in 2017 [14]. In addition, pazopanib may be better tolerated in elderly patients and in those with multiple comorbidities, which may impact patients' healthcare resource utilization (HRU) and healthcare costs [15]. Pazopanib was preferred over sunitinib among patients with aRCC (70%) as well as physicians (61%) in the randomized crossover trial PISCES, which assessed patient preference for these drugs as well the drugs' toxicity and tolerability [16]. Furthermore, several studies have noted lower costs and more quality-of-life years among RCC patients who received first-line pazopanib treatment versus first-line sunitinib treatment [17–19], although it is unclear whether this also applies to older patients.

Although more than half of patients receive a diagnosis of RCC after the age of 65 years [20], to our knowledge, no studies have specifically assessed real-world clinical and economic outcomes among elderly patients with aRCC. Such assessments could provide insight into the comparative benefits of vascular endothelial growth factor receptor TKIs and help inform treatment selection. Therefore, to address this gap in the literature, the present study assessed real-world OS, HRU, and healthcare costs among elderly patients with aRCC in the Medicare database who started first-line pazopanib or sunitinib treatment.

METHODS

Data Source

The data used in this study were retrieved from the 100% Medicare database plus Part D linkage (spanning January 1, 2006 to December 31, 2014) provided by the Centers for Medicare & Medicaid Services. This database contains de-identified information collected by Medicare to pay for medical services provided to beneficiaries, and complies with the patient confidentiality requirements of the Health Insurance Portability and Accountability Act. The data

included enrollment and claims history from Medicare Part A and Part B, and prescription and drug information from Medicare Part D. The New England Institutional Review Board granted this study an exemption from institutional review board review on November 6, 2015. This article does not contain any new studies with humans or animals performed by any of the authors.

Sample Selection

Eligible patients had at least two RCC diagnoses [International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes 189.0x and 189.1x] on different days and at least two diagnoses of secondary neoplasm (ICD-9-CM codes 196.xx–199.xx) on different days. The earliest diagnosis of secondary neoplasm was required to be on or after the earliest diagnosis of RCC. Patients were also required to have started first-line treatment with pazopanib or sunitinib (*index drug*) on or after the first diagnosis of secondary neoplasm and between October 19, 2009 (the approval date of pazopanib), and January 1, 2014, to ensure at least 1 year of potential follow-up. The date of index drug treatment initiation was defined as the *index date*. Additionally, patients were required to be at least 65 years old at the start of the *baseline period* (defined as the 1 year before the index date) and to have continuous Medicare eligibility at least 1 year before and 1 month after the index date. Patients enrolled in a clinical trial (ICD-9-CM code V70.7) were excluded. Eligible patients were stratified into two cohorts (pazopanib or sunitinib) on the basis of the index drug.

Baseline Characteristics

Patient demographic and clinical characteristics (age, sex, race, follow-up duration from the index date, and year of RCC diagnosis) were assessed on the index date. During the baseline period, metastatic sites (i.e., lung, lymph node, bone, and liver), comorbidities (i.e., cardiovascular disease, hypertension, chronic pulmonary disease, diabetes, renal failure, and liver disease), and the Charlson comorbidity index score were assessed [21, 22].

Per-patient per-month (PPPM) healthcare costs were assessed during the baseline period. Healthcare costs (inflated to 2015 US dollars with use of the Consumer Price Index medical component) from the payer's perspective were identified by the Medicare paid amount [23]. Cost categories included total all-cause healthcare costs, pharmacy costs, medical costs (inpatient, emergency department, and outpatient), as well as skilled nursing facility costs, home health agency costs, and the costs of other medical services (e.g., laboratory tests).

Propensity Score Matching

One-to-one propensity score matching between the pazopanib and sunitinib cohorts was used to account for observable differences at the baseline. Propensity scores were calculated by logistic regression analysis. Covariates included age, sex, race, RCC diagnosis year, metastatic sites, comorbidities, Charlson comorbidity index, and baseline all-cause inpatient costs, outpatient costs, emergency department costs, and pharmacy costs.

Outcomes

OS, HRU, and healthcare costs were assessed among the propensity-matched cohorts during the study period. OS was defined as the time from the index date to the date of death from any cause. All-cause HRU and healthcare costs were assessed on a PPPM basis during the study period, measured from treatment initiation to the end of follow-up (intent-to-treat perspective). In addition, HRU and healthcare costs were summarized among claims with an ICD-9-CM diagnosis code for RCC (i.e., HRU and healthcare costs associated with RCC diagnosis). Measures of all-cause HRU and HRU associated with RCC diagnosis included inpatient admissions, days, and readmissions (i.e., an inpatient admission within 30 days of a preceding inpatient discharge), emergency department visits, and outpatient visits. All-cause healthcare costs included total

healthcare costs, pharmacy costs, medical costs (inpatient, emergency department, and outpatient), as well as skilled nursing facility costs, home health agency costs, and the costs for other medical services (e.g., laboratory tests). Healthcare costs associated with RCC diagnosis included inpatient costs, emergency department costs, and outpatient costs.

Time on treatment (TOT) with the first targeted therapy was calculated as the time from the index date to the earliest of treatment discontinuation (a prescription gap of more than 90 days) or death from any cause [24]. Subsequent treatments started during the study period as second and third targeted therapies following first-line pazopanib or sunitinib treatment were also assessed among the matched targeted therapy cohorts.

Statistical Analyses

Baseline characteristics were compared between the unmatched pazopanib and sunitinib cohorts by Wilcoxon rank-sum tests for continuous variables and χ^2 tests for categorical variables. Baseline characteristics and outcomes were compared between the matched cohorts by Wilcoxon signed-rank tests for continuous variables and McNemar tests for categorical variables. Proportions and means with standard deviations were reported before and after propensity score matching; medians were also reported after matching.

OS was compared between the matched targeted therapy cohorts with use of Kaplan–Meier analyses with log-rank tests and univariable Cox proportional hazards models that reported the hazard ratio with the 95% confidence interval. Patients without an event were censored at the end of continuous eligibility or the study period (December 31, 2014), whichever occurred earlier.

HRU and healthcare costs during the study period, both all-cause and associated with RCC diagnosis, were compared between the matched cohorts by Wilcoxon signed-rank tests; differences in mean costs were computed. In all comparative analyses, $p < 0.05$ was used to determine significance.

TOT was assessed by Kaplan–Meier analysis. Subsequent treatments were assessed as the number and proportion of patients starting each type of targeted therapy among patients who started a second or third targeted therapy.

RESULTS

Baseline Characteristics

A total of 1711 patients older than 65 years met all criteria for inclusion (Fig. 1). Of these, 526 started first-line pazopanib treatment and 1185 started first-line sunitinib treatment.

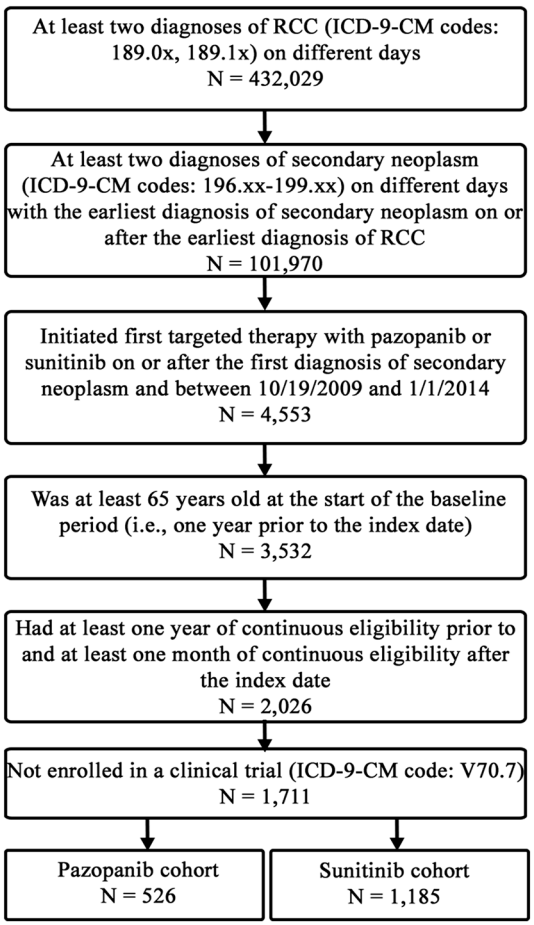

Fig. 1 Sample selection of adult patients with aRCC who received first targeted therapy with pazopanib or sunitinib. *aRCC* Advanced renal cell carcinoma, *ICD-9-CM* International Classification of Diseases, Ninth Revision, Clinical Modification, *N* Number

Patient baseline characteristics were largely similar between the cohorts before matching, with a few exceptions (Table 1). Both cohorts had a mean age of approximately 75 years (pazopanib cohort 74.8 ± 6.0 years, sunitinib cohort 74.7 ± 5.9 years) and were approximately 58% male (58.4% and 57.6%, respectively). Compared with the sunitinib cohort, larger proportions of patients in the pazopanib cohort were white (88.0% vs 83.8%, respectively; $p = 0.024$), received a diagnosis of RCC during 2010–2014 (61.4% vs 53.8%; $p = 0.003$), and had lung metastases (56.7% vs 50.3%; $p = 0.015$). At the baseline, patients in the pazopanib cohort also had higher monthly outpatient costs ($404 ± $414 vs $344 ± $395; $p < 0.001$) but lower monthly all-cause pharmacy costs ($143 ± $261 vs $161 ± $324; $p = 0.004$) compared with patients in the sunitinib cohort. Propensity score matching of the pazopanib and sunitinib cohorts yielded 522 matched pairs with balanced baseline characteristics (Table 1).

Overall Survival

Among elderly patients with aRCC, first-line pazopanib treatment was associated with significantly longer OS compared with first-line sunitinib treatment (hazard ratio 0.83, 95% confidence interval 0.72–0.97; $p = 0.016$). Median OS was 18.2 months among the pazopanib cohort and 14.6 months among the sunitinib cohort (log-rank $p = 0.015$; Fig. 2). Among patients in the pazopanib cohort, 317 experienced an event and 205 were censored. Among patients in the sunitinib cohort, 378 experienced an event and 144 were censored.

HRU and Healthcare Costs

During the study period, first-line pazopanib treatment was associated with significantly fewer PPPM inpatient admissions (0.179 vs 0.262, mean difference 0.082; $p < 0.001$) and inpatient days (1.375 vs 1.883, mean difference 0.508; $p = 0.004$) compared with first-line sunitinib treatment (Table 2). The trend was similar for HRU associated with an RCC diagnosis. The pazopanib cohort had significantly fewer mean monthly inpatient admissions associated with an RCC diagnosis (0.174 vs 0.246, mean difference 0.072; $p = 0.004$) and inpatient days (1.073 vs 1.578, mean difference 0.505; $p = 0.006$) compared with the sunitinib cohort.

Additionally, the pazopanib cohort incurred significantly lower monthly total all-cause healthcare costs ($8845 vs $10,416, mean difference $1571; $p = 0.002$), total all-cause medical costs ($5460 vs $6904, mean difference $1444; $p = 0.002$), and all-cause inpatient costs ($2914 vs $4035, mean difference $1120; $p = 0.003$) compared with the sunitinib cohort (Table 2). Again, a similar trend was observed for costs associated with an RCC diagnosis: the pazopanib cohort had significantly lower monthly inpatient costs associated with an RCC diagnosis ($1542 vs $2522, mean difference $980; $p = 0.002$) compared with the sunitinib cohort.

Treatment Patterns

First targeted therapy with pazopanib was associated with a median TOT of 4.8 months; first targeted therapy with sunitinib was associated with a median TOT of 4.1 months [24]. A similar proportion of patients started a second targeted therapy in the pazopanib and sunitinib cohorts (45.8% vs 42.9%); 17.8% of both cohorts started a third targeted therapy (see Fig. S1). Among the pazopanib cohort, the three most common second-line targeted therapies were everolimus (37.7%), axitinib (18.4%), and sunitinib (18.4%); the three most common third-line therapies were axitinib (35.5%), everolimus (21.5%), and sunitinib (14.0%). Among the sunitinib cohort, the three most common second-line targeted therapies were everolimus (34.8%), temsirolimus (26.3%), and pazopanib (17.9%); the three most common third-line therapies were everolimus (25.8%), axitinib (19.4%), and pazopanib (18.3%).

DISCUSSION

This real-world claims analysis found that among elderly patients with aRCC enrolled in

Table 1 Baseline characteristics among the first targeted therapy cohorts, before and after propensity score matching

	Before matching			After matching		
	Pazopanib (*N* = 526)	**Sunitinib (*N* = 1185)**	***p***	**Pazopanib (*N* = 522)**	**Sunitinib (*N* = 522)**	***p***
Demographics at index date						
Age (years)[a,b]	74.8 ± 6.0	74.7 ± 5.9	0.733	74.8 ± 6.0 (74.0)	75.2 ± 6.3 (74.5)	0.354
Male[a]	307 (58.4%)	682 (57.6%)	0.754	305 (58.4%)	303 (58.0%)	0.900
Race[a]						
White	463 (88.0%)	993 (83.8%)	0.024[c]	459 (87.9%)	460 (88.1%)	0.917
Black	29 (5.5%)	85 (7.2%)	0.204	29 (5.6%)	25 (4.8%)	0.572
Other or unknown	34 (6.5%)	107 (9.0%)	0.075	34 (6.5%)	37 (7.1%)	0.705
Follow-up duration after the index date (months)[b]	15.7 ± 10.7	17.2 ± 13.7	0.570	15.7 ± 10.7 (14.7)	15.7 ± 12.5 (13.8)	0.919
Year of RCC diagnosis[a]						
2006–2009	203 (38.6%)	548 (46.2%)	0.003[c]	202 (38.7%)	200 (38.3%)	0.888
2010–2014	323 (61.4%)	637 (53.8%)	0.003[c]	320 (61.3%)	322 (61.7%)	0.888
Metastatic sites[a]						
Lung	298 (56.7%)	596 (50.3%)	0.015[c]	294 (56.3%)	280 (53.6%)	0.358
Lymph node	102 (19.4%)	187 (15.8%)	0.066	100 (19.2%)	102 (19.5%)	0.876
Bone	168 (31.9%)	405 (34.2%)	0.365	167 (32.0%)	171 (32.8%)	0.792
Liver	75 (14.3%)	175 (14.8%)	0.783	75 (14.4%)	76 (14.6%)	0.931
CCI [a, b]	9.2 ± 2.4	9.2 ± 2.4	0.811	9.2 ± 2.4 (9.0)	9.2 ± 2.4 (9.0)	0.956
Comorbidities[a]						
Cardiovascular disease	343 (65.2%)	737 (62.2%)	0.233	341 (65.3%)	338 (64.8%)	0.842
Hypertension	474 (90.1%)	1072 (90.5%)	0.821	470 (90.0%)	471 (90.2%)	0.916
Chronic pulmonary disease	181 (34.4%)	438 (37.0%)	0.311	181 (34.7%)	177 (33.9%)	0.791
Diabetes	227 (43.2%)	569 (48.0%)	0.063	227 (43.5%)	223 (42.7%)	0.797
Renal failure	248 (47.1%)	547 (46.2%)	0.705	246 (47.1%)	264 (50.6%)	0.279
Liver disease	27 (5.1%)	78 (6.6%)	0.249	27 (5.2%)	19 (3.6%)	0.228

Table 1 continued

	Before matching			After matching		
	Pazopanib (*N* = 526)	**Sunitinib (*N* = 1185)**	***p***	**Pazopanib (*N* = 522)**	**Sunitinib (*N* = 522)**	***p***
Monthly per-patient healthcare costs to the payer (2015 US dollars)[b]						
Total all-cause healthcare costs	3005 ± 3133	2952 ± 3074	0.797	2998 ± 3142 (2030)	3114 ± 2792 (2216)	0.244
Total all-cause medical costs	2862 ± 3081	2791 ± 3035	0.968	2855 ± 3090 (1902)	2960 ± 2747 (2028)	0.243
Inpatient costs[a]	1629 ± 2498	1601 ± 2355	0.394	1633 ± 2506 (831)	1700 ± 2194 (1145)	0.290
Emergency department costs[a]	37 ± 76	43 ± 103	0.631	37 ± 76 (0)	39 ± 80 (0)	0.927
Outpatient costs[a]	404 ± 414	344 ± 395	<0.001[c]	393 ± 369 (295)	388 ± 448 (269)	0.146
Skilled nursing facility costs	117 ± 497	146 ± 604	0.258	118 ± 499 (0)	138 ± 557 (0)	0.577
Home health agency costs	106 ± 264	100 ± 265	0.581	106 ± 265 (0)	103 ± 256 (0)	0.884
Other medical service costs	569 ± 723	557 ± 784	0.459	568 ± 723 (331)	593 ± 798 (319)	0.700
Total all-cause pharmacy costs[a]	143 ± 261	161 ± 324	0.004[c]	143 ± 262 (91)	154 ± 311 (112)	0.108

Baseline characteristics were assessed during the 1 year before initiation of the first targeted therapy with pazopanib or sunitinib.

CCI Charlson comorbidity index, *RCC* renal cell carcinoma

[a] Covariate used in the propensity score matching

[b] The mean and standard deviation are given, with the median in parentheses.

[c] $p < 0.05$ for pairwise comparison of the pazopanib cohort with the sunitinib cohort; before propensity score matching, Wilcoxon rank-sum tests were used for continuous variables and χ^2 tests were used for categorical variables; after matching, Wilcoxon signed-rank tests were used for continuous variables and McNemar tests were used for categorical variables

Medicare, first-line pazopanib treatment was associated with significantly longer OS compared with first-line sunitinib treatment (18.2 months vs 14.6 months, respectively). In addition, patients who received pazopanib had fewer monthly inpatient visits and days (both all-cause and associated with an RCC diagnosis), lower all-cause healthcare, medical, and inpatient costs, and lower inpatient costs associated with an RCC diagnosis compared with patients receiving sunitinib.

Prior comparisons of OS among patients with aRCC receiving pazopanib versus sunitinib have differed in study design, patient population, and results. For example, both the COMPARZ study, a phase III clinical trial involving patients with mRCC receiving first-line pazopanib or sunitinib treatment, and a real-world study using data from the IMDC found no significant differences in OS [11, 12]. However, the median ages of the patient populations in the COMPARZ trial were 61–62 years, and in the IMDC study the median ages were 62–65 years [11, 12]. In contrast, a retrospective claims analysis of patients with a median age of 68 years using SEER–Medicare data reported that first-line pazopanib treatment was associated with significantly longer

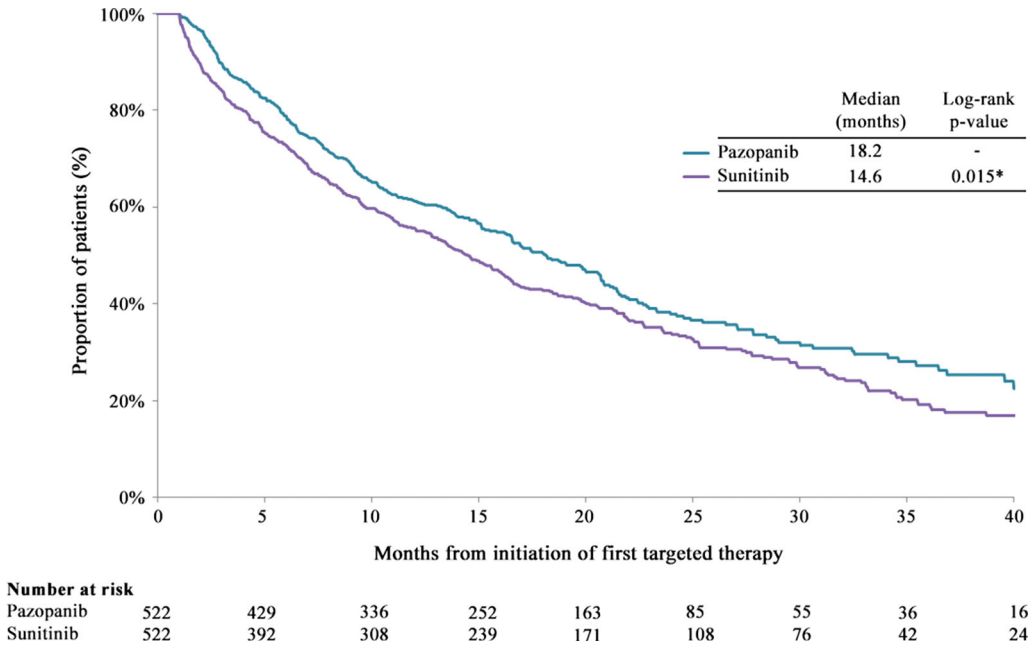

Fig. 2 Kaplan–Meier curve of overall survival by first targeted therapy among propensity-score-matched elderly patients with advanced renal cell carcinoma (aRCC)

OS compared with first-line sorafenib or sunitinib treatment [13]. Although the sample size for pazopanib was small ($N = 89$) in the study using SEER–Medicare data, this finding suggests that older age may impact the relative efficacy of pazopanib versus sunitinib in a real-world setting.

Older patients with RCC differ from younger patients in terms of frailty, organ reserve, and ability to tolerate treatment toxicity [25]. An analysis of elderly patients in six clinical trials of sunitinib reported similar OS among younger versus older patients with mRCC, but higher rates of several treatment-emergent adverse events among older patients; a similar analysis of pazopanib-treated patients has not been conducted [26]. However, in a randomized crossover trial (PISCES) comparing the effects of toxicity and tolerability of pazopanib and sunitinib on preferences of patients with aRCC, 70% of patients and 61% of clinicians preferred pazopanib [16]. Additionally, older patients with RCC typically have a higher comorbidity burden, and pazopanib is generally better tolerated by patients with high burden of comorbidities [15, 27, 28]. Therefore, it is possible that older patients with RCC experienced longer OS with pazopanib in the current analysis because of its superior tolerability, differentiated safety profile, or better quality of life versus sunitinib [11, 16, 29]. This is not to suggest that pazopanib would not be suitable for younger, healthier patients with aRCC; indeed, a 2017 review of the literature by Porta et al.[30] suggests that young and fit patients also stand to experience substantial benefits from pazopanib.

In addition, the intermittent interruption of TKI therapy with sunitinib (i.e., 4 weeks of therapy followed by 2 weeks without therapy) may have adverse effects on outcomes, and several studies have reported that alternative sunitinib schedules to maintain dosing density over 6-week cycles are associated with improved outcomes and tolerability [31, 32]. A potential mechanism behind the worse outcomes with intermittent sunitinib therapy may be compensatory angiogenesis and tumor proliferation during sunitinib "off-time," as has been suggested in a phase II trial of sunitinib in mRCC [31, 33]. Sunitinib dose reductions are common during the first cycle among elderly patients with mRCC, and may reduce

Table 2 Comparison of healthcare resource utilization and healthcare costs by first targeted therapy among the post-propensity-score-matched cohorts

	Pazopanib ($N = 522$)		Sunitinib ($N = 522$)		Mean difference ($A - B$)	p
	Mean (A) ± SD	Median	Mean (B) ± SD	Median		
Monthly per-patient resource use						
All-cause use						
Inpatient admissions	0.179 ± 0.256	0.097	0.262 ± 0.379	0.123	−0.082	<0.001[a]
Inpatient days	1.375 ± 2.369	0.507	1.883 ± 3.325	0.724	−0.508	0.004[a]
Inpatient readmissions	0.046 ± 0.155	0.000	0.068 ± 0.217	0.000	−0.022	0.114
Emergency department visits	0.092 ± 0.169	0.032	0.104 ± 0.173	0.034	−0.012	0.429
Outpatient visits	1.275 ± 1.112	1.041	1.337 ± 1.272	0.993	−0.062	0.544
Associated with an RCC diagnosis						
Inpatient admissions	0.174 ± 0.263	0.084	0.246 ± 0.387	0.103	−0.072	0.004[a]
Inpatient days	1.073 ± 2.030	0.339	1.578 ± 3.162	0.487	−0.505	0.006[a]
Inpatient readmissions	0.050 ± 0.164	0.000	0.068 ± 0.235	0.000	−0.019	0.490
Emergency department visits	0.041 ± 0.097	0.000	0.044 ± 0.109	0.000	−0.002	0.778
Outpatient visits	0.862 ± 0.885	0.655	0.841 ± 0.858	0.575	0.021	0.580
Monthly per-patient healthcare costs to the payer (2015 US dollars)						
All-cause costs						
Total all-cause healthcare costs	8845 ± 6855	7484	10,416 ± 9245	8156	−1571	0.002[a]
Total all-cause medical costs	5460 ± 6627	3459	6904 ± 8741	4447	−1444	0.002[a]
Inpatient	2914 ± 5888	1077	4035 ± 8098	1464	−1120	0.003[a]
Emergency department	79 ± 166	12	97 ± 215	15	−18	0.183
Outpatient	523 ± 619	316	513 ± 720	292	10	0.525
Skilled nursing facility	318 ± 1049	0	445 ± 1346	0	−128	0.061
Home health agency	244 ± 425	0	305 ± 585	0	−61	0.166
Other medical services	1381 ± 1583	860	1509 ± 1608	966	−128	0.191
Total all-cause pharmacy costs	3385 ± 2580	3003	3512 ± 2503	3172	−127	0.395
Associated with an RCC diagnosis						
Inpatient costs	1542 ± 3671	280	2522 ± 6856	550	−980	0.002[a]

Table 2 continued

	Pazopanib ($N = 522$)		Sunitinib ($N = 522$)		Mean difference ($A - B$)	p
	Mean (A) ± SD	Median	Mean (B) ± SD	Median		
Emergency department costs	29 ± 87	0	33 ± 124	0	−4	0.487
Outpatient costs	346 ± 511	168	321 ± 575	141	25	0.130

Healthcare resource utilization and healthcare costs were measured from treatment initiation to the end of follow-up (intent to treat).

RCC renal cell carcinoma, *SD* standard deviation

[a] $p < 0.05$ for pairwise comparison of the pazopanib cohort with the sunitinib cohort using Wilcoxon signed-rank tests.

real-world treatment efficacy [34]. Unnecessary sunitinib dose reductions and treatment interruptions, which may occur during the first or subsequent cycles, have been correlated with a poorer prognosis and increased incidence of adverse events among patients with aRCC in the real world [32]. Thus, alternative dosing schedules that reduce the time the patient is not receiving therapy but maintain therapeutic blood plasma levels, such as every-other-day or low continual dosing [35], might warrant further investigation among elderly aRCC patients receiving sunitinib.

Furthermore, the current study's finding of significantly longer OS among patients in the pazopanib cohort may be partially explained by subsequent treatments. A higher proportion of pazopanib-treated versus sunitinib-treated patients used axitinib in the second line, and this difference could impact patient outcomes. Studies indicate that patients who start axitinib treatment in the second line have superior OS compared with patients who start second-line temsirolimus treatment [36, 37]. In the current study, a higher proportion of patients who received first-line pazopanib treatment received second-line axitinib treatment (18.4%) compared with patients who received first-line sunitinib treatment (12.1%). Conversely, a lower proportion of the pazopanib cohort started second-line temsirolimus treatment (15.9%) compared with the sunitinib cohort (26.3%). This finding suggests there may be a difference in treatment options offered to patients between physicians prescribing first-line pazopanib treatment versus first-line sunitinib treatment, although the current study was conducted at the patient level and thus cannot assess physician treatment preferences. Further studies of physician expertise and behavior in caring for elderly patients with aRCC, and how these characteristics affect patient outcomes, are needed.

In the present analysis, differences in total healthcare costs were largely driven by lower medical costs among patients treated with pazopanib. Within medical costs, reduced inpatient admissions and inpatient costs among the pazopanib cohort were the driving component. Pazopanib has been reported to be more cost-effective than sunitinib among both clinical and real-world patients with aRCC, although these studies have not focused specifically on elderly patients. Racsa et al. [19] examined commercial and Medicare claims of patients with aRCC of any age who started pazopanib or sunitinib treatment, and found higher medication and healthcare costs among sunitinib-treated patients. A 2015 claims analysis using data from the Truven MarketScan database came to similar conclusions regarding lower HRU and healthcare costs among patients with aRCC starting first-line pazopanib treatment versus first-line sunitinib treatment [18]. A 2015 cost-effectiveness analysis compared pazopanib and sunitinib for first-line mRCC treatment in the USA using data from pivotal trials [11, 16], and found that pazopanib was associated with more quality-adjusted life years at lower cost compared with sunitinib [17]. However, a 2016 study using claims of commercially insured patients in the Truven

MarketScan database reported that after substitution of a 42-day sunitinib supply (vs 28 or 32 days), there were no significant differences in costs compared with pazopanib [38]. Also of note, pazopanib has been found to be a more cost-effective treatment (irrespective of age) than sunitinib for aRCC in non-US health systems [39].

Although claims data comprise a large and valid real-world data sample, this study is subject to the limitations inherent in retrospective observational studies using claims data. Administrative claims data contain only diagnostic and procedure codes recorded for reimbursement purposes. In addition, retrospective databases may be subject to coding errors or data omissions, and patients may not have used the recorded medication as prescribed after a prescription has been filled. Thus, treatment initiation dates are approximate. Clinical measures of disease severity, including the results of laboratory tests and risk assessments, are not available in claims data and could not be included in the propensity score matching. The propensity score matching controlled for characteristics at the baseline. Factors that changed after the index date (e.g., new metastases, comorbidities, or treatments) that may have impacted clinical outcomes were not included in the match. Finally, the current study included only patients aged 65 years or older with aRCC who were covered by Medicare. The results may not generalize to other populations, such as Medicaid enrollees, the uninsured, or commercially insured patients with aRCC. This broad perspective does not provide insight into the reasons for treatment choice, including the preference to avoid particular adverse events.

CONCLUSIONS

In conclusion, this real-world claims analysis found that among elderly Medicare patients with aRCC, first-line pazopanib treatment was associated with significantly longer OS and lower healthcare costs and HRU (both all-cause and associated with an RCC diagnosis) compared with first-line sunitinib treatment.

ACKNOWLEDGEMENTS

Sponsorship for this study and article processing charges were funded by Novartis Pharmaceuticals Corporation. All authors had full access to all of the data in this study and take complete responsibility for the integrity of the data and accuracy of the data analysis. Medical writing assistance was provided by Shelley Batts, an employee of Analysis Group Inc. Support for this assistance was funded by Novartis Pharmaceuticals Corporation. All named authors meet the International Committee of Medical Journal Editors criteria for authorship for the manuscript, take responsibility for the integrity of the work as a whole, and have given final approval for the version to be published. A synopsis of the economic outcomes was presented at the American Society of Clinical Oncology Genitourinary Cancers Symposium 2017 (Orlando, FL, USA), February 16–18, 2017. A synopsis of the clinical outcomes was presented at the annual International Society for Pharmacoeconomics and Outcomes Research meeting (Boston, MA, USA), May 20–24, 2017. The results regarding the time patients received treatment with the first targeted therapy are also included in a manuscript submitted to the *Journal of Managed Care Pharmacy*; we cited the relevant conference abstract when discussing those results.

Disclosures. Sameer R. Ghate is an employee of Novartis and owns stock/stock options. Jose Ricardo Perez was an employee of Novartis during the conduct of the study and owns stock/stock options. Elyse Swallow is an employee of Analysis Group Inc., which has received consultancy fees from Novartis. Miranda Peeples is an employee of Analysis Group Inc., which has received consultancy fees from Novartis. Miriam L. Zichlin is an employee of Analysis Group Inc., which has received consultancy fees from Novartis. Mark K. Meiselbach is an employee of Analysis Group Inc., which has received consultancy fees from Novartis. Nanxin Li was an employee of Analysis Group Inc. during the conduct of the study. Neeraj Agarwal has been a consultant or advisor for Novartis, Pfizer, Exelixis, Cerulean Pharma,

Medivation, Eisai, and Argos Therapeutics. Nicholas J. Vogelzang has been a consultant for Novartis, Amgen, Celgene, Medivation, Eisai, Exelixis, and Roche, has spoken at Novartis, Astellas, Johnson & Johnson, Pfizer, Dendreon, Bayer/Algeta, GlaxoSmithKline, and Veridex/Janssen, and has received research support from Novartis, Bayer, Exelixis, Progenics, Bavarian Nordic, and Viamet. Sumanta K. Pal has been a consultant for Novartis, Pfizer, Aveo, Dendreon, and Myriad, and has spoken at Novartis, Pfizer, and Medivation.

Compliance with Ethics Guidelines. The New England Institutional Review Board granted this study an exemption from institutional review board review on November 6, 2015. This article does not contain any new studies with humans or animals performed by any of the authors. The Medicare claims data were de-identified and complied in accordance with the requirements of the Health Insurance Portability and Accountability Act.

Data Availability. The datasets used for the current study are subject to a data use agreement between the Centers for Medicare & Medicaid Services and Analysis Group Inc. and are not publicly available. Information about the data used in this study, including detailed descriptions and the process for obtaining them, is available at https://www.resdac.org/.

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