Estimated cost of adverse event (AE) management for metastatic renal cell carcinoma (mRCC) patients treated with a VEGFR TKI

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Background

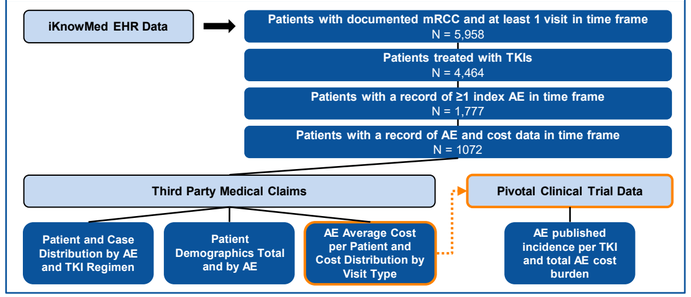
- Renal cell carcinoma (RCC) is the most common form of kidney cancer found in adults, with approximately 80,000 new cases annually in the United States[1]
- The majority of patients relapse after front line treatment requiring therapeutic innovation in later treatment lines[2]
- Over the past decade, the treatment paradigm for mRCC has shifted to the use of targeted therapies like vascular endothelial growth factor (VEGFR) tyrosine kinase inhibitors (TKIs) alone or more recently in combination with immunotherapy drugs (IO) and mammalian target of rapamycin (mTOR) inhibitors[3]
- VEGFR TKIs are known to have challenging tolerability profiles that have implications on patient compliance and treatment cost associated with management of adverse events (AEs)[4]
- Tivozanib (TIVO), a VEGFR TKI, was approved in March 2021 for the treatment of adult patients with relapsed or refractory advanced renal cell carcinoma (RCC) following two or more prior systemic therapies[5]
- There is limited information currently available on the cost burden of AEs associated with VEGFR TKIs approved for mRCC treatment
- This retrospective medical record and claims analysis was conducted in July 2022 for the purposes of quantifying the healthcare resource burden of managing VEGFR TKI class effect AEs associated with the use of these therapies in real-world mRCC patients, and to estimate the cost differences across different TKIs currently in use

Methods

Study Design

- Patients with documented mRCC who were at least 20 years of age and were treated with commercially available TKI therapies (sorafenib, sunitinib, pazopanib, axitinib, lenvatinib, cabozantinib) between January 2015 to March 2021 were identified using clinical and diagnostic information from the iKnowMed electronic medical record (EMR) database (an Ontada database)
- Records from eligible patients were matched to 3rd party insurance claims from a proprietary in-house Ontada database

Figure 1. Study Design



- AEs of interest were selected for analysis based on clinical relevance, commonality across the therapeutic class, and association with VEGFR TKI use alone or in combination with other RCC therapies
  - AEs of Interest Included: nausea, asthenia/fatigue, diarrhea, hypertension, mucositis/stomatitis, vomiting, rash, palmar-plantar erythrodysesthesia (PPE)/hand-foot syndrome (HFSR), proteinuria, renal failure, and hemorrhagic events
- The first occurrence of each VEGFR TKI class-effect AE (index AE) was identified through matching with the third-party claims dataset, and associated costs within a 90-day follow-up window were captured to determine average total cost associated with each index AE
  - Evidence suggests that the median duration of VEGFR TKI class effect AEs is consistently ≤90 days (range: 14-90 days), and thus a conservative 90-day window of cost attribution per index AE was captured
  - Average AE cost was assumed to be the same regardless of the specific TKI received
- VEGFR TKI class effect AE incidence data was derived from published grade ≥3 incidence rates in the latest line pivotal randomized, controlled RCC trial or as pooled incidence of pivotal studies denoted in the prescribing information for each VEGFR TKI regimen included
- Average per patient AE cost data was applied to incidence data to estimate regimen-specific AE total cost burden within a hypothetical 1M member plan providing coverage to the 19 expected eligible mRCC patients undergoing treatment in the 3L+ setting

Results

- A total of 1,072 mRCC patients treated with at least one VEGFR TKI and a record of at least one index AE of interest were successfully matched to cost data within the inclusion time frame, and contributed a total of 1,667 relevant AEs
- Over 70% of patients were between 60 and 79 years old, and across all AE types patients with an Eastern Cooperative Oncology Group Performance core (ECOG PS) of 1 were most represented
- All TKIs approved for mRCC during the observation period were represented, with 77% of patients taking a TKI alone, 15% taking a TKI + IO, and 7% taking a TKI + mTOR; captured AEs were proportionally distributed across regimen type, suggesting no significantly higher AE occurrences were attributable to specific regimen type
- Of all studied AEs, hypertension and asthenia/fatigue were most common, consistent with current literature[6]
- Outpatient visits contributed more to the total average cost for every AE type except hypertension, renal failure and hemorrhagic events
- Average cost per AE ranged from $76 (proteinuria) to $1,687 (mucositis/stomatitis)
- The highest total cost for AE management was attributed to lenvatinib and everolimus use at $13,303, followed closely by sunitinib at $13,092
- Tivozanib treatment was associated with the lowest total cost of AE management at $7,523, driven by the relatively lower incidence of certain high-cost AEs (e.g., diarrhea, PPE, nausea)

Table 1. Adverse Event Average Total Cost, Distribution of Cost by Visit Type, and Case Distribution by Regimen

Adverse Event (AE)	Total Pts. (N)	Total AEs (N)	Percentage of AE Cases by TKI Regimen			Contribution of Visit Type to Total AE Cost			Average Per Patient AE Cost
			TKI Only (77%)	TKI + IO (16%)	TKI + mTOR (7%)	In-Patient (%)	Out-Patient (%)	Other* (%)	
Hypertension	558	624	79%	16%	5%	41%	34%	25%	$894
Asthenia /Fatigue	302	327	75%	18%	7%	27%	54%	19%	$416
Renal Failure	164	172	79%	12%	9%	81%	10%	9%	$512
Nausea	120	126	71%	18%	11%	11%	61%	27%	$1,131
Hemorrhagic Events	108	113	85%	10%	5%	59%	20%	21%	$601
Diarrhea	89	95	76%	14%	11%	2%	29%	69%	$1,371
Vomiting	84	86	73%	16%	10%	14%	43%	43%	$928
Rash	43	45	60%	36%	4%	2%	62%	36%	$1,370
Proteinuria	30	33	82%	9%	9%	0%	59%	41%	$76
PPE/HFSR	27	28	71%	18%	11%	0%	98%	2%	$1,316
Mucositis /Stomatitis	16	18	44%	39%	17%	1%	31%	68%	$1,687

*Other visit type contributing to costs include drug administration, emergency visit, pathology, and laboratory visits

Table 2. Estimated Costs of Managing AEs Associated with VEGFR TKI Treatments

Adverse Event (Grade 3 or 4)	tivozanib			cabozantinib			axitinib			lenvatinib + everolimus			sunitinib		
	Inc (%)	Inc (3L N)	Cost ($)	Inc (%)	Inc (3L N)	Cost ($)	Inc (%)	Inc (3L N)	Cost ($)	Inc (%)	Inc (3L N)	Cost ($)	Inc (%)	Inc (3L N)	Cost ($)
Hypertension	24	4.56	4,077	16	3.04	2,718	16	3.04	2,718	13	2.47	2,208	13	2.47	2,208
Asthenia /Fatigue	13	2.47	1,028	13	2.47	1,028	16	3.04	1,265	18	3.42	1,423	26	4.94	2,055
Renal Failure	2.5	0.48	246	2.5	0.48	246	2.5	0.48	246	10	1.9	973	2.5	0.48	246
Nausea	0	0	0	4	0.76	860	3	0.57	645	5	0.95	1,074	6	1.14	1,289
Hemorrhagic Events	2.5	0.48	288	2.5	0.48	288	2.5	0.48	288	6	1.14	685	2.5	0.48	288
Diarrhea	2	0.38	521	11	2.09	2,865	11	2.09	2,865	19	3.61	4,949	10	1.9	2,605
Vomiting	1	0.19	176	2	0.38	353	3	0.57	529	7	1.33	1,234	5	0.95	882
Rash	1	0.19	260	0.5	0.1	137	0.5	0.1	137	0	0	0	2	0.38	521
Proteinuria	2.5	0.48	36	2.5	0.48	36	2.5	0.48	36	8	1.52	116	2.5	0.48	36
PPE/HFSR	1	0.19	250	8	1.52	2,000	5	0.95	1,250	0	0	0	8	1.52	2,000
Mucositis /Stomatitis	2	0.38	641	2	0.38	641	1	0.19	321	2	0.38	641	3	0.57	962
Total	**$7,523**			**$11,172**			**$10,300**			**$13,303**			**$13,092**		

Inc: Incidence; 3L N: Number of 3L mRCC covered patients (19 x Inc %). AE costs totals are reflective of the sum of costs associated with incidence of AEs per 19 patients on 3L and 4L treatment. AE costs for 19 patients, the estimated number of 3L and 4L patients enrolled in a hypothetical plan of 1M members, was modeled using published AE incidence (from clinical trials, published in product package inserts using pooled data or study data specific to latest-line population, if available) and AE treatment costs (from Ontada claims data analysis). Midpoint incidence was used as calculation value for values reported as a non-specific range (e.g. [2.5%] used as calculation value for incidence of <5%) in proteinuria, renal failure, and hemorrhagic events categories. Asthenia and fatigue incidence values were aggregated together.

Conclusions

- This study demonstrated that healthcare costs incurred from management of VEGFR TKI class effect AEs differ based on the specific AE and type of intervention required, and ranged from $76 - $1687 per patient, per AE
- The estimated total cost burden of VEGFR TKI class effect AE management for a particular regimen varied by TKI tolerability profile and the published AE incidence rates
- The use of tivozanib in the 3L+ mRCC setting suggests potential cost offsets when compared to other TKI regimens

The estimated costs of managing VEGFR TKI class-effect AEs were lowest with tivozanib, and highest with lenvatinib + everolimus, indicating potentially differential healthcare resource burden by TKI regimen

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