Patient Reported Toxicities from Molecularly Targeted Therapies in Renal Cell Carcinoma (RCC)

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Abstract

Background: Multiple new therapies are now approved for patients (pts) with advanced RCC. As these agents enter widespread use, their perceived toxicities may differ from those reported in the literature and limit treatment duration and clinical outcomes. Patient reporting of toxicities may more accurately identify side effects most relevant to pts.
Methods: In an effort to collect patient-reported side effects from RCC pts treated with novel therapies, an on-line survey was developed. RCC pts were recruited through the Kidney Cancer Association.
Results: 177 pts completed the survey and 146 (64%M/36%F) received medication for RCC. Most common geographical regions were Midwest (20.8%); Northeast (17.4%); South/Southeast (16.7%); West (11.8%); and outside the U.S. (9.7%). 68 pts (47.2%) were treated at teaching hospitals; 55 pts (38.2%) in private oncology offices; and 21 pts (14.6%) at community hospitals. First-line treatments included sunitinib (Su) (52.1%, n=73); sorafenib (So) (15.7%, n=22); high dose IL-2 (14.3%, n=20); clinical trial (12.9%, n=18); bevacizumab (Bev) (5%, n=7); interferon (4.3%, n=6) and temsirolimus (Tem) (3.6%, n=5). The most common side effects reported for Su were fatigue (92.9%, n=65), altered taste (90%, n=63) and diarrhea (83.8%, n=57); So: hand foot syndrome (95.2%, n=20) and fatigue (95%, n=19); Bev: fatigue (83.3%, n=5) and altered taste (83.3%, n=5); Tem: fatigue, altered taste and rash (100%, n=4). Pts reported that the most difficult side effects from Su were diarrhea and fatigue (25%, n=18); So: hand foot syndrome (72.7%, n=16); Bev: fatigue (42.9%, n=3); Tem: rash (60%, n=3). Side effects necessitated changing the schedule, dose, or stopping Rx in 82% (n=18) of So pts and in 40% (n=28) of Su pts. QOL was affected very much/extremely for 56.6% of pts (n=73).
Conclusions: These results suggest that the patient-reported impact of molecularly targeted agent side effects may be more significant than suggested by phase III clinical trials. These results also identify specific side effects towards which improved symptom management strategies and enhanced patient education can be directed. Better side effect management may increase treatment duration and improve clinical outcomes.

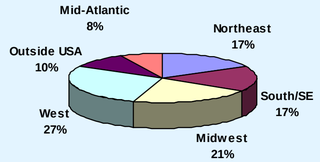
Introduction

- Quality of life and patient reported side effect information is not well characterized in the large Phase III and expanded access protocols of newly FDA approved kidney cancer agents.
- These studies typically involve investigator reported adverse events of patients treated at large academic medical centers rather than community practices.
- Prescribing patterns may vary based on geographical location or practice setting.
- Side effects often negatively impact quality of life which is of major importance to patients with metastatic disease.
- With recent FDA approval of targeted agents, clinicians may not be well prepared to manage side effects.

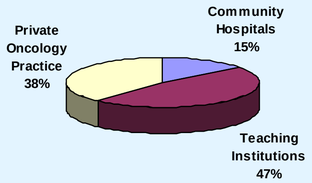
Results

Male	**60.9% (n=92)**
Female	**36.1% (n=52)**
Mean Age	**64 (35-80)**
Race	
Caucasian	**86.1% (n=124)**
Non-Caucasian	**13.9% (n-20)**

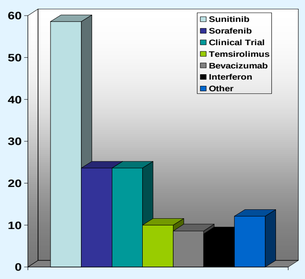
Demographics



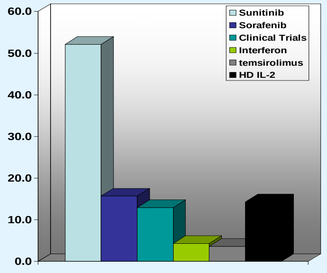
Geographical Distribution



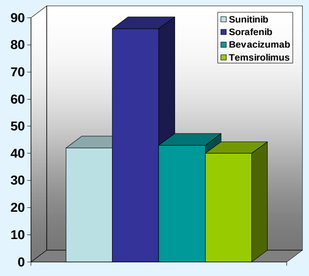
Practice Setting



First Treatment Offered



First Therapy Received



Side effects necessitating dose modification or discontinuation

Sunitinib	Fatigue	93%(n=65)
	Altered taste	90%(n=63)
	Diarrhea	84%(n=57)
Sorafenib	Hand foot Syndrome	95%(n=20)
	Fatigue	95%(n=19)
Bevacizumab	Fatigue	83%(n=5)
	Altered taste	83%(n=5)
Temsirolimus	Fatigue	100%(n=4)
	Altered taste	100%(n=4)
	Rash	100%(n=4)

Most Common Side Effects

Sunitinib	Diarrhea	25% (n=18)
	Fatigue	
Sorafenib	Hand foot syndrome	73% (n=16)
Bevacizumab	Fatigue	43% (n=3)
Temsirolimus	Rash	60% (n=3)

Most Difficult Side Effects

Medication	Any Grade	Grade 3-4
Sunitinib (n=375)[1]		
Fatigue	51%	7%
Diarrhea	53%	5%
Hand-Foot Syndrome	20%	5%
Rash	19%	2%
Sorafenib (n=451)[2]		
Fatigue	37% (n=165)	5% (n=22)
Diarrhea	43% (n=195)	2% (n=11)
Hand-Foot Syndrome	30% (n=134)	6% (n=25)
Rash	40% (n=180)	1% (n=4)
Temsirolimus (n=208)[3]		
Fatigue	51%	11%
Diarrhea	27%	1%
Hand-Foot Syndrome	-----	----
Rash	47%	4%

Reported AEs from Pivotal Phase III Trials

	Sunitinib	Sorafenib	Temsirolimus	Bevacizumab
Not at all	2.9% (n=2)	1.1% (n=0)	20.0% (n=1)	0.0% (n=0)
Slightly	15.7% (n=11)	9.1% (n=2)	0.0% (n=0)	14.3% (n=1)
Somewhat	22.9% (n=16)	31.8% (n=7)	60.0% (n=3)	71.4% (n=5)
Very much	42.9% (n=30)	36.4% (n=8)	0.0% (n=0)	14.3% (n=1)
Extremely	15.7% (n=11)	22.7% (n=5)	20.0% (n=1)	0.0% (n=0)

Impact of Side Effects on Quality of Life

Methods

An online survey was developed for metastatic kidney cancer patients exploring first line and current treatment; side effects and management; and quality of life. The survey was reviewed by several kidney experts for completeness and accuracy. RCC patients were recruited through the Kidney Cancer Association's e-newsletter and patient forum. Results were tabulated using descriptive statistics.

Discussion

- Results indicate that targeted agents have significant side effects which negatively impact quality of life.
- Better side effect management strategies are critical to maintaining the quality of life in balance with improved clinical outcomes.
- Improved side effect management may also improve duration of therapy and patient compliance and therefore potentially improve clinical outcomes.
- 40-60% of RCC patients receiving sunitinib, sorafenib and temsirolimus felt their side effects were worse than expected.

Future Implications

- Our survey identified several patient reported side effects which significantly altered quality of life and may be useful in directing interventional studies for management of specific side effects.
- Improved patient education with respect to expected side effects and management strategies are needed.

References

1. Motzer RJ, Hutson TE, Tomczak P, et al. Sunitinib versus interferon alfa in metastatic renal-cell carcinoma. N Engl J Med 2007;356:115-124.
2. Escudier B, Eisen T, Stadler WM, et al. Sorafenib in advanced clear-cell renal-cell carcinoma. N Engl J Med 2007;356:125-134.
3. Hudes, G, Carducci, M, Tomczak, P, et al. Temsirolimus, interferon alfa, or both for advanced renal-cell carcinoma. N Engl J Med 2007:356:2271-2281.