A Retrospective Review of Treatment Discontinuation and Survival in Patients With Advanced Renal Cell Carcinoma Treated With Sunitinib or Sorafenib
Zhimei Liu,1 Ji Zheng,1 Aylin Altan Riedel,2 Jonathan Johnson,2 James Burke2
1Novartis Pharmaceuticals Corporation, East Hanover, NJ, United States; 2i3 Innovus, an Ingenix Company, Eden Prairie, MN, United States

Background
• The prognosis for patients with metastatic renal cell carcinoma (mRCC) is poor. Patients have an overall median survival of less than a year, and less than 10% survive beyond 5 years prior to the introduction of recent targeted therapies1
• The multi-targeted tyrosine kinase inhibitors sunitinib and sorafenib have been approved for the treatment of mRCC in the United States. Both sunitinib and sorafenib inhibit vascular endothelial growth factor and platelet-derived growth factor receptors2,3
• Sunitinib and sorafenib have both been shown in clinical trials to increase progression-free survival in mRCC patients. However, neither drug has been shown to lead to long-term disease-free survival in significant numbers of patients4
• The median duration of treatment was 6 months in a large phase 3 trial of sunitinib and 5.8 months in a large phase 3 trial of sorafenib5,6
• A different perspective on drug effectiveness may be obtained in a real-world setting, as many clinical studies employ inclusion criteria based on disease prognosis and may not be reflective of patients in the general population

Objective
• Examine treatment patterns in a “real-world” population of advanced RCC patients receiving sunitinib and/or sorafenib therapy and evaluate survival rates following discontinuation of these therapies

Methods
Study Design
• A retrospective claims study of commercially insured and Medicare patients in the United States
• Data was obtained from an insurance claims database of a national health plan and included medical data, pharmacy data, enrollment information, and death data

Patient Population
• A diagnosis code for RCC (ICD-9-CM code of 189.0 in any position) sometime between January 1, 2003 and December 31, 2007
• Continuous health plan enrollment for 90 days before the index date (defined as the earliest date of RCC diagnosis)
• At least 18 years of age
• Use of sunitinib and/or sorafenib during the follow-up period (lasting until death or March 31, 2008)

Outcome Measures
• Discontinuation — Defined as discontinuation of index therapy (sunitinib or sorafenib) with no restart of medication prior to the end of the follow-up period
• For patients who used both sunitinib and sorafenib during the follow-up period, discontinuation from the last fill of either drug (whichever occurs latest) was identified
• Discontinuation date — Defined as the date of the last fill for sunitinib or sorafenib + 30 days supply from that claim
• Treatment duration — For patients who discontinued therapy, duration of treatment was measured as the number of months from initiation of index therapy to discontinuation of therapy
— For patients who did not discontinue therapy, duration of treatment was calculated as the number of months from initiation of index therapy to the minimum of the end of the follow-up period, the date at which death data was captured, or the death date
• Survival — Length of survival time was right-censored at the date at which death data was captured for patients who survived beyond that date
— Median survival times were estimated by the Kaplan-Meier method

Results

Patient Demographics

<table>
<thead>
<tr>
<th></th>
<th>Total (N = 451)</th>
<th>Sunitinib (N = 222)</th>
<th>Sorafenib (N = 229)</th>
<th>Sorafenib + Sunitinib (N = 102)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;35</td>
<td>4 0.9</td>
<td>2 0.9</td>
<td>2 0.9</td>
<td>0 0.0</td>
</tr>
<tr>
<td>35 – 39</td>
<td>12 2.7</td>
<td>9 4.1</td>
<td>3 1.3</td>
<td>0 0.0</td>
</tr>
<tr>
<td>40 – 44</td>
<td>21 4.7</td>
<td>18 8.1</td>
<td>3 1.3</td>
<td>0 0.0</td>
</tr>
<tr>
<td>45 – 49</td>
<td>26 5.8</td>
<td>22 9.9</td>
<td>4 1.8</td>
<td>0 0.0</td>
</tr>
<tr>
<td>50 – 54</td>
<td>61 13.5</td>
<td>38 17.1</td>
<td>22 9.7</td>
<td>11 0.0</td>
</tr>
<tr>
<td>55 – 59</td>
<td>61 13.5</td>
<td>41 18.6</td>
<td>19 8.3</td>
<td>13 0.6</td>
</tr>
<tr>
<td>60+</td>
<td>122 26.9</td>
<td>79 35.5</td>
<td>43 18.6</td>
<td>10 0.0</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>323 71.6</td>
<td>189 85.3</td>
<td>82 35.9</td>
<td>94 93.3</td>
</tr>
<tr>
<td>Female</td>
<td>128 28.4</td>
<td>33 14.7</td>
<td>147 64.1</td>
<td>8 6.7</td>
</tr>
<tr>
<td>Insurance type</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Commercial</td>
<td>380 84.3</td>
<td>219 98.6</td>
<td>161 69.3</td>
<td>59 57.8</td>
</tr>
<tr>
<td>Medicare</td>
<td>71 15.7</td>
<td>3</td>
<td>1.3</td>
<td>23 22.2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Average</th>
<th>SD</th>
<th>Median</th>
<th>Min</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>60.01 (10.83)</td>
<td>—</td>
<td>60.01</td>
<td>21.00</td>
<td>117.00</td>
</tr>
<tr>
<td>Survival</td>
<td>57.95 (9.42)</td>
<td>—</td>
<td>57.95</td>
<td>36.00</td>
<td>70.00</td>
</tr>
<tr>
<td>Length of Treatment (Months)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (N = 102)</td>
<td>Sunitinib (N = 57)</td>
<td>Sorafenib (N = 45)</td>
<td>Sorafenib + Sunitinib (N = 8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adverse Events</td>
<td>31.67</td>
<td>8.00</td>
<td>0.00</td>
<td>15.76</td>
<td>7.62</td>
</tr>
<tr>
<td>Interstitial edema</td>
<td>5.11</td>
<td>1.00</td>
<td>0.00</td>
<td>1.66</td>
<td>3.24</td>
</tr>
<tr>
<td>Hypertension</td>
<td>15.00</td>
<td>3.00</td>
<td>0.00</td>
<td>7.16</td>
<td>5.00</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
</tbody>
</table>

| Adverse Events | 22.48 | 4.64 | 21.15 | 9.05 | 9.87 | 8.42 |

| Adverse Events | | | | |
| --- | --- | --- | --- | |
| Interstitial edema | 5.11 | 1.00 | 0.00 | 1.66 | 3.24 | 3.24 |
| Hypertension | 15.00 | 3.00 | 0.00 | 7.16 | 5.00 | 5.00 |
| Hypothyroidism | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Hematologic | 22.48 | 4.64 | 21.15 | 9.05 | 9.87 | 8.42 |

Sunitinib: 60.01 (10.83) —
Sorafenib: 57.95 (9.42) —
Sorafenib + Sunitinib: 57.95 (9.42) —

Conclusions
• Of the 264 patients who discontinued therapy, median survival following therapy discontinuation was 5.4 months
• Median survival following discontinuation of therapy was 10.8 months for patients treated with sorafenib alone, 5.2 months for patients treated with sunitinib alone, and 4.7 months for patients receiving both treatments
• Of the 264 patients who discontinued therapy, median survival following therapy discontinuation was 5.4 months
• Median survival following discontinuation of therapy was 10.8 months for patients treated with sorafenib alone, 5.2 months for patients treated with sunitinib alone, and 4.7 months for patients receiving both treatments
• Future research should investigate whether other treatment options may improve prognosis following discontinuation of sunitinib/sorafenib therapy

Data Limitations
• Claims data do not provide reason(s) why a medication was discontinued
— It is difficult to determine the precise date of discontinuation because a pharmacy claim reflects when a medication was filled

References

Study supported by Novartis Pharmaceuticals Corporation.
A Retrospective Review of Treatment Discontinuation and Survival in Patients With Advanced Renal Cell Carcinoma Treated With Sunitinib or Sorafenib

Zhimei Liu, Ji Zheng, Aylin Altan Riedel, Jonathan Johnson, James Burke

*Novartis Pharmaceuticals Corporation, East Hanover, NJ, United States; 13 Innoven, an Innogenex Company, Eden Prairie, MN, United States

Background
- The prognosis for patients with metastatic renal cell carcinoma (mRCC) is poor. Patients have an overall median survival of less than a year, and less than 10% survive beyond 5 years prior to the introduction of recent targeted therapies.
- The multitargeted tyrosine kinase inhibitors sunitinib and sorafenib have been approved for the treatment of mRCC in the United States. Both sunitinib and sorafenib inhibit vascular endothelial growth factor and platelet-derived growth factor receptors.
- Sunitinib and sorafenib have both been shown in clinical trials to increase progression-free survival in mRCC patients. However, neither drug has been shown to lead to long-term disease-free survival in significant numbers of patients.
- The median duration of treatment was 6 months in a large phase 3 trial of sunitinib and 5.8 months in a large phase 3 trial of sorafenib.
- A different perspective on drug effectiveness may be obtained in a real-world setting, as many clinical studies employ inclusion criteria based on disease prognosis and may not be reflective of patients in the general population.

Objective
- Examine treatment patterns in a “real-world” population of advanced RCC patients receiving sunitinib and/or sorafenib therapy and evaluate survival rates following discontinuation of these therapies.

Methods

Study Design
- A retrospective claims study of commercially insured and Medicare patients in the United States.

Data
- Was obtained from an insurance claims database of a large national health plan and included medical data, pharmacy data, enrollment information, and death data.

Patient Population

Outcome Measures
- Discontinuation
  - Defined as discontinuation of index therapy (sunitinib or sorafenib) with no restart of medication prior to the end of the follow-up period
  - For patients who used both sunitinib and sorafenib during the follow-up period, discontinuation from the last fill of either drug (whichever occurs latest) was identified
- Discontinuation date
  - Defined as the date of the last fill for sunitinib or sorafenib + days supply from that claim
- Treatment duration
  - For patients who discontinued therapy, duration of treatment was measured as the number of months from initiation of index therapy to discontinuation of therapy
  - For patients who did not discontinue therapy, duration of treatment was calculated as the number of months from initiation of index therapy to the minimum of the end of the follow-up period, the date at which death data was captured, or the death date
- Survival
  - Length of survival time was right-censored at the date at which death data was captured for patients who survived beyond that date
  - Median survival times were estimated by the Kaplan-Meier method

Results

Patient Cohorts
- 451 patients were identified for study inclusion.
- 222 patients were treated with sunitinib alone.
- 127 patients were treated with sorafenib alone.
- 102 patients were treated sequentially with both sunitinib and sorafenib.

Patient Demographics
- The average age (standard deviation) was 60 years (11.16) for the total group.
- Sunitinib: 61.54 (12.74)
- Sorafenib: 60.10 (10.83)
- Sunitinib + Sorafenib: 57.95 (9.42)

Renal Cell Carcinoma Therapies Used Prior to Sunitinib/Sorafenib Treatment Period
- Table: Claims data do not provide reason(s) why a medication was discontinued.

Conclusions
- Of the 264 patients who discontinued therapy, median survival following therapy discontinuation was 5.4 months.
- Median survival following discontinuation of therapy was 10.8 months for patients treated with sunitinib alone, 5.2 months for patients treated with sorafenib and 2.6 months for patients receiving both treatments.
- Patients using sunitinib and/or sorafenib had a high rate of drug discontinuation and poor prognosis following discontinuation of therapy.
- Future research should investigate whether other treatment options may improve prognosis following discontinuation of sunitinib/sorafenib therapy.

Data Limitations
- Claims data do not provide reason(s) why a medication was discontinued.
- It is difficult to determine the precise date of discontinuation because a pharmacy claim reflects when a medication was filled.

References

Presented at the Joint 15th Congress of the European Cancer Organization (ECCO) and 44th Congress of the European Society for Medical Oncology (ESMO), September 24–30, 2009, Berlin, Germany.
A Retrospective Review of Treatment Discontinuation and Survival
in Patients With Advanced Renal Cell Carcinoma
Treated With Sunitinib or Sorafenib
Zhimei Liu,1 Ji Zheng,1 Aylin Altan Riedel,1 Jonathan Johnson,2 James Burke2
1Novartis Pharmaceuticals Corporation, East Hanover, NJ, United States; 2i3 Innovus, an Ingenix Company, Eden Prairie, MN, United States

Background
• The prognosis for patients with metastatic renal cell carcinoma (mRCC) is poor. Patients have an overall median survival of less than a year, and less than 10% survive beyond 5 years prior to the introduction of recent targeted therapies1,2
• The multitargeted tyrosine kinase inhibitors sunitinib and sorafenib have been approved for the treatment of mRCC in the United States. Both sunitinib and sorafenib inhibit vascular endothelial growth factor and platelet-derived growth factor receptors3,4
• Sunitinib and sorafenib have both been shown in clinical trials to increase progression-free survival in mRCC patients. However, neither drug has been shown to lead to long-term disease-free survival in significant numbers of patients5,6
• The median duration of treatment was 6 months in a large phase 3 trial of sunitinib and 5.8 months in a large phase 3 trial of sorafenib5,6
• A different perspective on drug effectiveness may be obtained in a real-world setting, as many clinical studies employ inclusion criteria based on disease prognosis and may not be reflective of patients in the general population

Objective
• Examine treatment patterns in a “real-world” population of advanced RCC patients receiving sunitinib and/or sorafenib therapy and evaluate survival rates following discontinuation of these therapies

Methods
Study Design
• A retrospective claims study of commercially insured and Medicare patients in the United States
• Data was obtained from an insurance claims database of a large national health plan and Medicare patients in the United States

Patient Population
• A diagnosis code for RCC (ICD-9-CM code of 189.0 in any position) sometime between January 1, 2003 and December 31, 2007
• Continuous health plan enrollment for 90 days before the index date (defined as the earliest date of RCC diagnosis)
• At least 18 years of age
• Use of sunitinib and/or sorafenib during the follow-up period (lasting until death or March 31, 2008)

Outcome Measures
• Discontinuation — Defined as discontinuation of index therapy (sunitinib or sorafenib) with no restart of medication prior to the end of the follow-up period
• For patients who used both sunitinib and sorafenib during the follow-up period, discontinuation from the last fill of either drug (whichever occurs latest) was identified
• Discontinuation date — Defined as the date of the last fill for sunitinib or sorafenib + days supply from that claim
• Treatment duration — For patients who discontinued therapy, duration of treatment was measured as the number of months from initiation of index therapy to discontinuation of therapy
• For patients who did not discontinue therapy, duration of treatment was calculated as the number of months from initiation of index therapy to the minimum of the end of the follow-up period, the date at which death data was captured, or the death date
• Survival — Length of survival time was right-censored at the date at which death data was captured for patients who survived beyond that date
• Median survival times were estimated by the Kaplan-Meier method

Data Limitations
• Claims data do not provide reason(s) why a medication was discontinued
• It is difficult to determine the precise date of discontinuation because a pharmacy claim reflects when a medication was filled

Conclusions
• Of the 264 patients who discontinued therapy, median survival following therapy discontinuation was 5.4 months
• Median survival following discontinuation of therapy was 10.8 months for patients treated with sorafenib, 5.2 months for patients treated with sunitinib alone, and 4.7 months for patients receiving both treatments
• Future research should investigate whether other treatment options may improve prognosis following discontinuation of sunitinib/sorafenib therapy

References