Efficacy and safety data from patients with advanced renal cell cancer treated with tivozanib hydrochloride after progression on sorafenib

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Abstract

Introduction

Two randomized, open-label, multi-center trials (NCT01307108 and NCT01307011) have shown tivozanib to be safe and active as second-line therapy for patients with advanced renal cell cancer.1-3 Tivozanib is a potent, selective inhibitor of vascular endothelial growth factor receptor (VEGFR)-1, -2, and -3 with a long half-life of 4.5–5.1 days allowing once-daily administration with a consistent dosing regimen.4,5

Objectives

The primary objectives of the study were:

- To allow long-term access to either tivozanib or sorafenib for patients who participated in TIVO-1 and experienced clinical benefit and acceptable tolerability within their randomly assigned treatment arm.
- To allow access to tivozanib for patients who participated in TIVO-1 and failed sorafenib treatment progression disease per RECIST 1.0 on protocol.
- The secondary objectives of the study were to assess response rate, PFS, OS, and tolerability for all participating patients.

Methods

Study Design

This was an open-label, multi-center extension study (NCT01307108) of Tivozanib (TIVO-1 Phase III) that randomized patients to sorafenib (Sorafenib) or tivozanib (Tivozanib). Patients were randomized in a 1:1 ratio to sorafenib or tivozanib.

Participants

Patients were randomized to sorafenib or tivozanib and were eligible to continue treatment in the extension study if they had received tivozanib in the extension study and were able to continue treatment due to clinical benefit or acceptable tolerability. Patients continued treatment with the same drug they had received in TIVO-1.

Table 1: Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Tivozanib After Sorafenib (n=156)</th>
<th>Sorafenib After Sorafenib (n=156)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Race, n (%)</td>
<td>Central/Eastern Europe</td>
<td>138 (88)</td>
</tr>
<tr>
<td></td>
<td>Rest of world</td>
<td>18 (12)</td>
</tr>
<tr>
<td></td>
<td>Australia/New Zealand</td>
<td>8 (5)</td>
</tr>
<tr>
<td></td>
<td>Asian</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Gender, n (%)</td>
<td>Male</td>
<td>117 (75)</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>45 (30)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>&lt;65</td>
<td>115 (74)</td>
</tr>
<tr>
<td></td>
<td>≥65</td>
<td>41 (26)</td>
</tr>
</tbody>
</table>
| Age group, n (%) | AEs ongoing at the time of crossover were classified as medical history and only reported as an on-study AEs if they occurred in the 90 days prior to, or on-study during, the on-study follow-up period.

Results

Patients were generally well-matched with no significant differences in the baseline characteristics between the two treatment groups. There were no new safety signals observed in the extension study compared to TIVO-1. The most common adverse events (AEs) were hypertension and fatigue, which were consistent with the low rates of dose reduction and interruption observed in TIVO-1 patients who received tivozanib as a first-line targeted therapy (12% and 18%, respectively)4

Discussion and Conclusions

In this interim report, tivozanib has demonstrated antitumor activity after radiographic progression on sorafenib.

- Tivozanib CR: 13% (95% CI: 8.5–19) %
- Tumor shrinkage >74% of patients
- PFS: 6.6 months (95% CI: 5.3–12)
- The antitumor activity of tivozanib may be contributing to the OS of patients randomized to sorafenib in TIVO-1 (see Motzer et al. Poster #350)
- Rates of dose reduction and dose interruption due to AEs for tivozanib as second-line therapy documented in this study were low (10% and 12%, respectively)
- These were consistent with the low rates of dose reduction and interruption observed in TIVO-1 patients who received tivozanib, as a first-line targeted therapy (12% and 18%, respectively)4
- The AEs profile of vasoactive therapies for sorafenib was similar to that of tivozanib as first-line targeted therapy in TIVO-1, with the exception of hypertension.
- Hypertension on extensions of sorafenib was approximately half as common as observed in TIVO-1.
- All grades in this study were 26% and 44% in TIVO-1.
- Grade 3/4 in this study were 12% vs 26% in TIVO-1.
- The liver safety of reported hypertension on the extension study may be related to effective management of this class of antihypertensives on prior sorafenib.

- Study is currently in progress and patient follow-up is ongoing.

References

1. Nakahara K, Taguchi S, Morizawa T et al., 2011, high partial response of vascular endothelial growth factor receptor tyrosine kinases, has bioactivity and inhibits the function of VEGF receptors.
3. Mok SC, Ngan CY, Sim KH et al., Tivozanib hydrochloride versus sorafenib as first-line targeted therapy for patients with advanced renal cancer; Results from a Phase II, randomized, open-label, multi-center trial. - J Clin Oncol 2012 Dec 20:20(36):4432-4439

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