Reviewer’s report

Title: Efficacy of Sorafenib on Metastatic Renal Cell Carcinoma in Asian Patients: Results from a Multicenter Study

Version: 1 Date: 10 February 2009

Reviewer: Jennifer JJ Knox

Reviewer’s report:

This study aimed to confirm the efficacy and explore the toxicity or sorafenib treatment for metastatic RCC in an ethnic Chinese patient population. The 98 patients followed prospectively on this study do provide valuable information about this drug therapy that is not available from the western-based TARGET phase III trial or other data. It is of value to practitioners treating Asian populations and contributes to the overall data set for this drug in this disease. The authors do not over-state their conclusions. This data-set does suggest, but does not prove that sorafenib is well tolerated and at least as efficacious in this population as shown in the TARGET trial.

There are major inherent biases in a single arm treatment ‘policy’ protocol where consecutive patients are registered. In addition some patients received combination sorafenib and interferon which is an experimental regimen. The authors do acknowledge many potential caveats of this design in their discussion.

Major revisions:

1) Stable disease is defined as > 4 wks in the abstract and > 4 months in discussion. Please use 1 definition and one really should choose > 4 months as 4 wks is not a clinically meaningful period of stable disease. Use this > 4 months in the disease control rate estimations.

2) Table 1: Patient characteristics contains some data relevant to early RCC. Add in recognised prognostic features of metastatic RCC. This will allow this population to be more easily compared to other publications. Please include...
   - MSKCC risk (poor, intermed or high) or a similar prognostication criteria
   - base-line sites of metastatic disease....suggest lung, liver, bone, lymph node
   - number of sites of mets..1,2,3 or more or unknown
   - histology...predom clear cell, non-clear cell, unknown

Minor revisions:

3) PFS is very close to median at time of this analysis. Can this not be updated now (Feb 2009) to give a more meaningful estimate than ‘not yet reached’?

4) the PFS and OS estimates appear better than TARGET outcomes (PFS >1 year vs 5.5 months on TARGET). Is this explained by patient selection as per baseline prognostic features (see # 2) or is this perhaps inherent to this ethnic
Chinese patient population. Is it influenced by weekly follow-up which likely exceeds western standards. Please comment.

5) Hand-foot syndrome appears more prevalent on your study than reported on TARGET. This was also seen on the hepatoma Asian-Pacific sorafenib trial compared with European SHARP trial. Please comment. Is there PK data or preliminary SNP data. Or is this perhaps a 'real world' estimate of true rates of hand-foot syndrome. Worthy of a comment in the discussion.

6) please comment if, in the authors opinion this data set should influence practice patterns in treating Metastatic RCC in China

Good luck

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I have received research funding for investigator-initiated studies from Bayer Inc and Pfizer Inc.