Reviewer's report

Title: Phase II clinical trial of sorafenib plus interferon-alpha treatment for patients with metastatic renal cell carcinoma in Japan

Version: 2  Date: 1 April 2015

Reviewer: Vsevolod MATVEEV

Reviewer's report:

The manuscript of Masatoshi et al. is an original multicenter prospective study assessing the efficacy of combination of Sorafenib 400 mg b.d. + low doses of INF-alpha (3 dosages of 3 million U per week for 2 weeks) as a first line treatment of metastatic RCC. While both agents had demonstrated modest response rate in several randomized studies, the potential benefit of combining of two drugs is studied insufficiently as well as toxicity profile of this combination.

Although, authors have demonstrated improved PFS and OS for the whole cohort of 42 patients, the distribution of patients according to MSKCC risk group is not clear. Absence of patients with poor and intermediate MSKCC prognosis may partly explain the improved clinical outcome and question the advantage of combination.

Combination of sorafenib and INF-alpha was associated with common for both drugs adverse events. Despite the fact that the study did not show any significant difference in adverse events when compared with patients in phase II study of sorafenib alone in Japan, 45% of patients in the current study had to discontinue treatment due to side effects, which is significantly higher than in studies where Sorafenib was used as a single agent. The rate of discontinuation of Sorafenib due to toxicity in TARGET trial was only 10% (1).

Recent randomized phase II trial failed to show any advantage of combining the two drugs in terms of survival (2) in mRCC patients, although the doses of INF-alpha were different from the regimen used by authors. Until the benefit of combination of sorafenib with INF-alpha is not proved in phase III randomized trials it should not be recommended as a treatment option for untreated mRCC patients outside clinical trials.


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

Quality of written English: Acceptable
Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:
'I declare that I have no competing interests' below