Reviewer's report

Title: Changing Paradigms in Management of metastatic Castration Resistant Prostate Cancer (mCRPC)

Version: 1

Date: 6 April 2014

Reviewer: Makito Miyake

Reviewer's report:

<Summary>
Development of treatment strategy for metastatic castration resistant prostate cancer (mCRPC) is one of the biggest clinical issues in the urologic oncology field. It is thought that hormone suppression therapy in the past two or three decades was not adequate. In the review manuscript, the authors overview mCRPC widely from the mechanism of development of mCRPC, history of treatment of mCRPC to a detailed update of novel treatment. This is well-written and clear for the leaders to understand, so that it would contribute to better understanding of mCRPC for urologic oncologists. The authors need to address the following comments and give decent answers for them before it is accepted by the journal.

<Comments>

Major Compulsory Revisions : 3

1) Page 9, line 8: The authors mention about Enzalutamide, a novel 2nd generation anti-androgen drug. Unfortunately, the section lacks the description about the difference in drug mechanism between 1st generation anti-androgen drugs (Bicalutamide and Flutamide) and 2nd generation one. There must be a significant difference in an aspect of molecular biology because Enzalutamide is effective greatly to the patients who are refractory to 1st generation anti-androgen drugs. It might be better to add description about that on the basis of previous papers and/or author’s speculation. Making a figure may be helpful.

2) Through the text, the authors mention mainly about the benefit in overall survival and progression-free survival and toxicity of new drugs. What about palliation of symptoms such as alleviation of bone disease-associated pain or reduction of opiate dosage. This may be another important issue for clinical management of mCRPC.

3) Table 1: The manuscript has two tables. They lack information about citation. Citation numbers have to be added to table 1 and table 2.

Minor Essential Revisions : 3

4) Page 5, line 4: The sentence ‘High does….’ seems to be grammatically incorrect. It should be corrected.
5) Through the text, there are words ‘phase x’ several times. Arabic numbers and roman numbers are used inconsistently. They should be consistent.

6) Page 7, line 18: ‘This study let to’ should be ‘This study led to’.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

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

**Declaration of competing interests:**

'I declare that I have no competing interests'