Reviewer’s report

Title: Temporal and geographic variation in the systemic treatment of advanced prostate cancer

Version: 0 Date: 24 Nov 2017

Reviewer: Erin Grady

Reviewer's report:

While this topic is very interesting, it is unclear from the submitted paper whether or not this given group of patients includes Medicare patients which would likely yield the greatest number of patients with castration resistant prostate cancer. Perhaps some of the patients studied have "Medigap" coverage through Optum, but from the information on the DataMart's website, I cannot find the answer to this question. It should be clarified within the document. I believe Medicare claims data are available for study and this could yield potentially different information (especially if patients don't have the resources to obtain Medigap coverage).

Another issue with the study that deserves discussion is the issue that insurance denials are not discussed. It is not clear from the article if they have access to every time an order was placed for the drug of interest when it was denied. Speaking from experience in Nuclear Medicine, it is often the case that new radiopharmaceuticals have a challenging course. Generally, Medicare is fairly reliable, however, 3rd party insurers tend to be quite difficult which could add another layer of complexity to this study. Even within Medicare, some geographical differences exist in the United States. It would be an interesting question to know where the most denials are for your drug of interest and if there is an associated issue with access to care, in spite of a reasonable indication.

Some misleading numbers may be present with regard to Enzalutamide, Abiraterone and Ra-223 as they were not FDA approved at the start of the study's look-back to 2010.

A revision is needed on page 4 of the pdf packet at the end of the first paragraph under Background (line 32). The FDA label for Ra-223 dichloride is for "symptomatic bone
metastases" which can be interpreted differently compared to "significant pain" (usually a key indicator palliative radionuclide options done with agents other than Ra-223). In order to give patients the survival benefit, some centers are giving this agent even in the presence of more minor pain/symptoms. Consider adjusting the phraseology here.

Otherwise, this is an interesting study, but I'm not sure the results are widely applicable since more CRPC patients are likely of Medicare age and the ones studied here (if Medicare) are likely to have greater resources to afford Medigap coverage.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.
Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.
Unable to assess

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.
Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
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