Reviewer's report

Title: A Systematic Review and Meta-Analysis of Bone Metabolism in Prostate Adenocarcinoma

Version: 1 Date: 23 February 2010

Reviewer: James Lau

Reviewer's report:

The authors present a systemic review and meta-analysis of bone metabolism in prostate adenocarcinoma. They perform a computerized search by using Medline, Cancerlit and Embase databases. Thirty-one articles are included in their analyses. They report that PCa patients under ADT have a high risk of osteoporosis (RR, 1.3; p < 0.00001) and a higher risk of fractures (RR, 1.10; p < 0.00001) as compared to patients not having ADT. The total bone mineral density (BMD) was lower in men with ADT (p = 0.031) and the duration of ADT negatively correlates with BMD of the lumbar spine and total hip (Spearman’s rho = -.490 and -.0773; p = 0.028 and 0.001) and with total hip t score (Spearman’s rho = -.900; p = 0.037). The authors conclude that the use of ADT in patients with PCa reduces BMD increasing the risk of fractures in these patients.

The relationship of ADT and osteoporosis and fragility fracture is well established by previous studies. The findings here do not provide any additional clinical information about androgen deprivation therapy in prostate cancer. In addition, the manuscript is poorly written and very hard to read.

Major Compulsory Revisions.

1. It is hard to know what exactly the study question the authors attempt to address. For example, the authors state “the objective of the study is to clarify the relationship of prostate cancer and/or androgen deprivation therapy with osteoporosis” in the abstract section. Later, they state “the objective of this review is to determine the incidence of bone loss and osteoporosis in patients with PCa who are or are not treated with hormone therapy” in the introductory section. The authors need to clearly state the objectives with a clinically relevant and focused study questions.

2. The authors have provided incorrect or misleading information about the use bisphosphonates in the Discussion section.
   a. The authors state patients with bone metastases should receive bisphosphonates from the time of diagnosis. However, the reference they quote does not reflect what they claim. In addition, bisphosphonate, namely zolendronic acid, is indicated in men with hormone refractory prostate cancer and bone metastases.
   b. The authors state bisphosphonates are recommended for bone loss prevention in patients with prostate cancer who are receiving hormone therapy. It
is an incorrect/misleading statement. Limited evidence exists about bone loss and fracture prevention during ADT. Bisphosphonate is indicated only if men who are osteopenic/osteoporotic or when the absolute fracture risk warrants drug therapy.

3. The authors should list the studies that are included in the analyses of risk of osteoporosis and fracture.

Minor Essential Revisions
1. The following figures are mislabeled: Figure 3A is labeled as Fig 3, Figure 3B as 4, Figure 5A as 6, and Figure 5B is 7.
2. Osteoporosis definition is based on women not men. (Page 3 Paragraph 3)
3. It is not clear if the authors include any non-English language publications.
4. Any attempt made at collecting unpublished data?
5. During data abstraction, are the reviewers blinded to the authors and institution of the studies undergoing review.
7. In the Publication bias section, the authors mention Figure 2A. Do they mean Figure 3A or Figure 2 because there is no figure labeled as 2A. In the same section, they state “the Begg funnel plot that is related to figure 3”. Do they mean figure 3A and/or 3B?
8. The authors should discuss why “the lack of adjustment for the presence of metastasis….must be considered as a limitation of our study” (Page 11 second last paragraph).
9. The first paragraph on page 13, it is not clear what the point the authors want to make.

Level of interest: An article of limited interest

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

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests.