

Peer Review File

Article Information: <https://dx.doi.org/10.21037/tau-22-690>

Reviewer A

The authors provide a well written and thorough clinical review of 5-ARIs.

We would recommend the following points be reviewed

1. The authors mention hirsutism in their introduction and conclusion but do not mention the utility of 5-ARIs in this disease process in the paper. We would ask the authors to either remove the hirsutism or add an additional section discussing 5-ARI's role in this pathology

Reply 1: We thank the reviewer for their expertise and insight. We agree with the comments made and have made the following adjustments to our submission.

Changes in the text: We have included a brief description and indication of 5-alpha reductase inhibitor uses in the management of Hirsutism.

Refer to Track changes labelled: Reviewer A – point 1 – heading 'Other Non-Urological Indications for 5-ARIs, second paragraph

2. The authors do a nice job summarizing the use of 5-ARIs for BPH, they also mention the reduction of prostate volume by 27% however they do not mention the time course it takes for this reduction, while most urologists understand that 5-ARIs generally take months to take effect adding this may be of benefit to practitioners who are unaware of the prolonged timeline

Reply 2: We thank the reviewer for their expertise and insight into this topic. We agree with the comment and again have made appropriate adjustments and inclusion in the submission.

Changes in the text: Under the topic of BPH, we have included in the discussion the current evidence regarding the time taken for effect and discernable reduction in both prostate volume and symptoms.

Refer to Track changes labelled: Reviewer A- point 2 – Heading 'Benign Prostate Hyperplasia', third paragraph

3. The authors do discuss the studies highlighting 5-ARIs prior to TURP and the effects of hemostasis, there is no mention of the affects of 5-ARIs on angiogenesis. Commonly 5-ARIs can be utilized in men with BPH with recurrent episodes of gross hematuria, we would ask the authors to discuss the effects of BPH on angiogenesis and its potential role in recurrent hematuria related to BPH

Reply 3: We again thank the reviewer for their expertise and insight. We agree with the comments made and have made inclusions in our paper.

Changes in the text: Under the heading of BPH, we have included current evidence and

guidelines regarding the use of 5-alpha reductase inhibitors and their use in hematuria associated with BPH.

Refer to Track changes labelled: Reviewer A- point 3- Heading 'Benign Prostate Hyperplasia', Sixth paragraph

4. With regard to prostate cancer the authors did a nice job of reviewing 5-ARIs and their effect on prostate cancer. There is no mention of PSA and screening however in this section and again while known to most highlighting the role of 5-ARIs and PSA would be important. How long would it take the PSA to cut in half on 5-ARI therapy, etc.

Reply 4: We thank the reviewer for their expertise and insight. We agree with the comment and have made appropriate inclusions into our submission.

Changes in the text: Under the prostate cancer subheading, we have included a paragraph outlining the mechanism and quantitative effect 5ARIs have on PSA, along with the time taken to effect.

Refer to Track changes labelled: Reviewer A – point 4 - Heading 'Prostate Cancer', Fifth paragraph

Reviewer B

This is good review for 5ARI.

Also, authors commented the relationship with COVID-19.

Reply 1: We thank the reviewer for their time taken to review our paper. We believed no changes were required based upon the reviewer's comments.

Reviewer C

This is a well written review targeting the role of 5-ARI's in different diseases. I recommend re-wording the conclusion regarding SARS-Cov2. The data is very weak, similar to the early data on prostate cancer carcinogenesis. The conclusion should be very critical.

Reply 1: We thank the reviewer for their expertise and insight into this topic. We agree with the comments and have amended our conclusion

Changes in the text: We have made it clear in our conclusion that the current evidence regarding SARS-CoV-2 is very weak and as such no definitive effect can be discerned. Further research is required.

Refer to Track changes labelled: Reviewer C – point 1

This is a nice review giving a well written overview on 5-ARI's. However, there are not many new topics discussed.

Reply 2: We thank the reviewer for their comments and expertise on this topic. We agree in part with this comment.

There are several exciting prospects and developments that clinicians should be abreast of with regard to 5ARIs. We felt the recent debunking of the Prostate Cancer Prevention Trials data suggesting 5-ARIs users were observed as having a high-grade malignancy was noteworthy. Further, 5-ARIs potential link in preventing SARS-CoV-2 is both relevant and topical.

Changes in the text: No changes were made to our submission based upon this review.
