

## Peer Review File

Article Information: <https://dx.doi.org/10.21037/tau-24-12>

### Reviewer A

#### 1) General comments

In this manuscript (letter to the editor), the authors mention the possibility and promise of fezolinetant for the treatment of hot flashes among men with ADT. This is likely to be well written, and this paper may provide many clinicians with the expectations that fezolinetant may be also a new first-in-class treatment for hot flashes in men.

#### 2) Specific comments for revisions

Currently, no experimental and clinical studies to investigate an efficacy of fezolinetant on hot flashes caused by ADT have been available. On the other hand, are there any experimental data to demonstrate that hot flashes caused by ADT in men could be potentially involved in neurokinin B receptor or KNDy neurons? If available, please describe them concisely.

Thanks Reviewer A for your valuable comments

**Comment 1:** are there any experimental data to demonstrate that hot flashes caused by ADT in men could be potentially involved in neurokinin B receptor or KNDy neurons? If available, please describe them concisely.

**Reply 1:** the following statement and corresponding references have been added to the manuscript

**Changes in text:** “Although the relationship between neurokinin, oestrogen and thermoregulation has yet to be studied in human males, experiments in hypogonadal men demonstrate oestradiol (as opposed to testosterone) deficiency as the primary regulator of VMS in men.<sup>11</sup> Furthermore, mouse models have demonstrated KNDy neurons mediating systemic vasodilatation in both male and female mice.<sup>12</sup>” (page 2, line 18-22)

### Reviewer B

The article addresses an important subject regarding the side effect of hormonal suppression used in the treatment of advanced prostate cancer across various stages of the disease. Currently, there is a recommendation for intensified hormonal blockade in various contexts, and it would be worthwhile for future research to involve symptomatic treatment of vasomotor symptoms in this population with intensified hormonal blockade. There are still few studies in men, but the article is compelling for addressing and raising awareness about the very common side effect in men with hormonal blockade.

**Reply:** Our gratitude to Reviewer B for these encouraging comments.