Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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European Association of Urology

Letter to the Editor

Re: Herjan J.T. Coelingh Bennink, Jean-Michel Foidart, Frans M.J. Debruyne. Treatment of Serious COVID-19 with Testosterone Suppression and High-dose Estrogen Therapy. Eur Urol 2021;80:523–5

Coelingh Bennink et al [1] have proposed clinical treatment of COVID-19 with androgen deprivation therapy using high-dose estrogen (ADET) in combination with the gonadotropin-releasing hormone antagonists degarelix and transdermal estradiol for both male and female patients. The proposal is based on the hypothesis that the therapy will have an antiandrogen effect in suppressing ACE2 and TMPRSS2, key proteins involved in SARS-CoV-2 viral cell entry, while increasing estrogen levels to reduce inflammation and cytokine production, immune complications that are linked to COVID-19.

The study needs to consider several factors before starting clinical trials, including age and sex restrictions, potent hormonal side-effects, and the efficacy of degarelix.

First, we suggest setting the age criterion for patients to >60 yr, as this approach was previously used for prostate cancer patients with a mean age of 74 yr (range 59–85 yr) [2]. Because both androgen deprivation therapy (ADT) and ADET have not been tested in female patients and women have 10- to 20-fold lower testosterone levels in comparison to men [1], we suggest more valid evidence and reasons to justify the use of the proposed therapy for female patients to prevent a decrease in quality of life.

According to Rhee et al [3], ADT has a wide range of serious adverse effects. It is associated with higher risk of hypercholesterolemia, myocardial infarction, diabetes, and renal impairment. As ADET might also cause obesity, gynecomastia, sexual dysfunction, and depression [3], the mental health and quality of life of male patients needs to be taken into consideration as well. Similarly, use of high-dose estrogen in severe COVID-19 cases is also controversial, as several studies indicate that it has prothrombotic and procoagulation effects, with possible links to ventricular arrhythmias and sudden cardiac arrest [4]. As Coelingh Bennink et al suggest using combination therapy, such treatment may pose a serious risk to the health of hospitalized COVID-19 patients who are already in a critical condition.

A randomized clinical trial by Sayyid at al [5] involving 39 patients with prostate cancer demonstrated that degarelix had little effect on testosterone and luteinizing hormone levels, in contrast to luteinizing hormone–releasing hormone (LHRH) agonists, which are traditionally used for ADT. According to the results, the mean testosterone level for the degarelix versus LHRH agonist groups was 11.59 versus 13.03 nmol/L at baseline, and 1.57 versus 1.40 nmol/l in week 4. The study also revealed no significant difference for weeks 8 and 12. Thus, the use of degarelix is also questionable.

We appreciate the proposal by Coelingh Bennink and colleagues [1] to use hormonal treatment as a novel therapy for hospitalized COVID-19 patients. However, we have concerns regarding the condition of patients in this trial, the rationale for evaluating the risks of ADET side-effects, and the contradiction in using degarelix as one of the therapy agents. We recommend considering these issues for a better study design and approach, such as specific COVID-19–targeted nonhormonal therapy.

Conflicts of interest: The authors have nothing to disclose.

Acknowledgments: We thank Nazarbayev University for providing the opportunity to carry out this research. Yingqiu Xie has received research funding from the Nazarbayev University Faculty-Development Competitive Research Grants Program (ID 16797152 and ID 16796808).

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DOI of original article: https://doi.org/10.1016/j.eururo.2021.08.003.

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August 11, 2021