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LETTER TO THE EDITOR

Predictive accuracy of hormone receptors in conservatively treated endometrial hyperplasia and early endometrioid carcinoma

Sir,

We thank Dr. Van Weelden and colleagues for their interest and their thorough analysis regarding our study.[1,2] We are pleased to discuss in this letter the concerns they raised.

First, although we appreciated their analysis about possible confounding factors, we believe that combining the data for premenopausal and postmenopausal women cannot significantly affect our results, as menopausal status has been shown not to affect the response of endometrial hyperplasia to conservative treatment.[3]

Second, magnetic resonance imaging is not the only tool recommended by the 2016 ESMO-ESGO-ESTRO Consensus Conference to exclude myometrial invasion and adnexal involvement. In fact, even ultrasound is considered as an alternative, if performed by an expert physician.[4] Hence, we believe that overt myometrial invasion and/or adnexal involvement were unlikely to be missed, regardless of the imaging technique adopted.

Third, regarding the exclusion of women from the analyses, it was not limited to women receiving oral progestins, but also regarded women treated with levonorgestrel-releasing intrauterine devices (LNG-IUD). We excluded these women because of the high risk of bias in the primary studies, as discussed in the relevant section of our manuscript. We believe that the inclusion of these women would have created a bias in the results.

Fourth, we agree with Van Weelden et al regarding the need for univocal and objective thresholds of estrogen receptor (ER) and progesterone receptor (PR) expression. This issue regards all immunohistochemical markers.[5] A subgroup analysis of different thresholds was not feasible, because of the unavailability of primary data. However, we excluded from the analysis all the studies that considered thresholds >10%, in order to reduce the risk of bias.

Lastly, we would remark that the main findings of our meta-analysis were incompletely mentioned by Dr. Van Weelden et al[1]. In fact, we did not propose the use of PR as a predictive marker in women treated with LNG-IUD. Instead, we reported that the predictive accuracy of ER and PR was insufficient to be determining in clinical practice.

In conclusion, ER and PR showed an association with the response of endometrial hyperplasia and early endometrioid carcinoma to progestin therapy (in particular LNG-IUD), but they could not be reliable as stand-alone predictive markers because of insufficient predictive accuracy. We agree with Van Weelden et al about the need for further predictive biomarkers, and we hope that our results may serve as a basis for future studies in this field.

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