Accepted Manuscript

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PII: S0002-9378(17)32366-9

DOI: 10.1016/j.ajog.2017.11.583

Reference: YMOB 11952

To appear in: *American Journal of Obstetrics and Gynecology*

Received Date: 27 September 2017

Accepted Date: 17 November 2017

Please cite this article as: Tomao F, Panici PB, Tomao S, Progesterone therapy in endometrial cancer, *American Journal of Obstetrics and Gynecology* (2017), doi: 10.1016/j.ajog.2017.11.583.

Letter to the Editor

Progesterone therapy in endometrial cancer

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The authors report no conflict of interest

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We read with interest the paper “All-cause mortality in young women with endometrial cancer receiving progesterone therapy” by Maria P. Ruiz et al (1). The authors reported that the use of primary progesterone therapy increased significantly from 2004 to 2014 and that utilization was less frequent in older women, white women, and women with unfavorable grading and substaging. Moreover, the authors note, “*its use was associated with decreased survival, particularly in women with stage IB tumors“*.

The results of this large study deserve some critical considerations. Given the demographic and clinical characteristics of the population, it appears that relatively few women were treated with primary progesterone therapy compared to primary hysterectomy. This trend is likely to generate contradictory bias. While oral progesterone therapy has remained largely unmodified over the past 10 years, surgery has undoubtedly improved greatly in terms of oncological outcomes and safety, thanks to better surgeons, expertise and improved technology (laparoscopy, robot assisted surgery). Moreover, the use of progesterone-releasing intrauterine devices has largely increased in the last 10 years in early endometrial cancer. Unfortunately, we don't know how many women were treated with oral or intrauterine progesterone, nor do we know the type and timing of surgical approach in women who underwent primary hysterectomy. We don't know the criteria used to select candidates for surgery, immediately or after primary progesterone therapy. We don't know how many women receiving primary progesterone therapy were also treated with resective hysteroscopy and how many received hysterectomy after primary progesterone therapy. Likewise we have no information about pharmaceutical selections (dosing, progestional agents, treatment interruptions and changes). According to recent data, the absence of such information undermines reliability of study results. (2, 3). This is not a small thing since some studies suggest

that the levonorgestrel intrauterine device could be superior to oral progestogens in the control of endometrial cancer and complex atypical hyperplasia (4). And we have to consider that use of progesterone delivering intrauterine device was rapidly increasing in the last years for neoplastic disorders in young patients. But above all, the study does not associate unfavorable survival data, in women treated with primary progesterone therapy, with the possible presence of risk factors for cardiovascular, thromboembolic and metabolic events. This greatly limits the validity of the authors' conclusions, especially considering the small sample sizes.

According to the above comments, it seems hard to state that primary progesterone therapy is less safe and less effective than primary hysterectomy in women with early endometrial cancer.

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