RESULTS: The analysis was based on 210,000 women, who contributed 470,000 women years of exposure. The observed prevalence of prognostic factors at baseline showed typical features of US and European COC users. However, the mean age in the E2/E2Val cohort was higher compared to the E1/E1 cohort (31 years ±7.89 vs 31 years ±7.76, respectively). A time-to-event analysis of the VTE data was carried out based on the extended Cox model. Validity of the model was demonstrated by the standardized differences summarized over strata as weighted average yielded upon PS subclassification, which were consistently <0.25 and mostly <0.1. A comparison between cohorts showed a decreased risk of venous thromboembolism in users of COCs containing E2/E2Val vs users of COCs containing EE ≤30 μg; adjusted hazard ratio: 0.49 (95% CI 0.28-0.84). A risk reduction in the E2/E2Val cohort was also observed with regards to arterial thromboembolic events; adjusted hazard ratio: 0.26 (95% CI, 0.08-0.83).

CONCLUSIONS: Data presents a solid safety assessment of combined hormonal preparations in over 200,000 pre-menopausal women and shows a decreased cardiovascular risk of E2/E2Val when compared to low-dose EE. This provides reassurance for current users of E2/E2Val-containing COCs and opens new perspectives for the development of safe and effective endometriosis treatments, such as the recently developed product containing E2/NETA, in combination with relugolix.

SUPPORT: This analysis was supported by a grant from Myovant Sciences. Dataset is owned by ZEG Berlin GmbH.

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INCREASED CELLULAR SENESCENCE IN DEEP INFILTRATING ENDOMETRIOSIS. Helena Malvezzi, MSc,1 Camila Hernandez, PhD,1 Bruna C. de Azevedo, PhD,1 Carla A. Piccinato, PhD,1 Juliana Meola, PhD,2 Sérgio Podgace, M.D. PhD,3 1Albert Einstein Hospital, São Paulo, Brazil; 2Universidade de São Paulo, Ribeirão Preto, Brazil.

OBJECTIVE: Endometriosis is characterized by increased inflammatory process and to be apoptosis resistant. Senescence cells are apoptosis resistant and present the senescence associated secretory phenotype (SASP). Cellular senescence is an irreversible suspension of cell proliferation process, responsible for controlling tissue growth. In endometriosis, senescence cells would be regulating cell cycle block which would favor disease maintenance and progression.

DESIGN: A cross-sectional study with biopsies of deep infiltrating endometriotic lesions and ectopic endometrium from women with (n=27) and control endometrium from women without endometriosis (n=19) in both cycle phase (secretory and proliferative).

MATERIALS AND METHODS: Biopsy tissues were prepared for senescence markers (p16 and Lamin b1) detection using immunohistochemistry technique followed by histometry to calculate antibody positive areas in the tissue. For tissue IL-17A detection, multiplex assay was used. Wilcoxon test was used for pared samples and gamma generalized linear models to evaluate groups relationship. Alfa lower than 0.05 was considered significant.

RESULTS: Deep infiltrating lesion from secretory and proliferative phase had 4.4 (p<0.001) and 2.82 (p<0.001) times more p16 expression than secretory and proliferative endometrium. Also, proliferative endometrium had 3.05 (p<0.002) times more p16 expression than secretory endometrium. Although no difference between cycle phases was detected, lesions had less lamin b1 expression compared to eutopic endometrium (p=0.016). Higher concentration of IL-17A was found in the proliferative phase of the lesions (p=0.014) compared to proliferative endometrium and in the secretory phase of the endometrium (p=0.014) compared to control endometrium. IL-17A increases p16 expression in 1.04 times (p=0.029).

CONCLUSIONS: Deep infiltrating lesions presents more senescence markers than eutopic endometrium, as the increase in p16 expression and the depletion in lamin b1 expression. The p16 protein plays a critical role in regulating cell senescence, being a potent inhibitor of cell proliferation and lamin b1 is associated with maintaining the structure of the nuclear membrane during cell cycle processes. Our results suggest that IL-17A increases p16 expression and as there were more IL-17A and p16 in lesions compared to eutopic endometrium, we believe that IL-17A could be favoring p16 expression in deep infiltrating lesions and thus maintaining an inflammatory and senescent environment. This environment, in addition to providing a basal state of inflammation, may be causing more cells to enter senescence, favoring disease maintenance.

REFERENCES: À

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