2022-RA-783-ESGO CLINICAL RELEVANCE OF CIRCULATING *ESR1* MUTATIONS DURING ENDOCRINE THERAPY FOR ADVANCED HORMONE-DEPENDENT ENDOMETRIAL CARCINOMA

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Introduction/Background Endocrine therapy is frequently administered in patients with hormone dependent (HR+) metastatic endometrial cancer. *ESR1* mutations have emerged as a key mechanism of anti-aromatase (AA) resistance in HR+ metastatic breast cancer and can be monitored using circulating tumor DNA (ctDNA). The aim of this study was to explore the incidence of circulating *ESR1* mutations in patients treated by AA or megestrol acetate (M) for advanced endometrial carcinoma.

Methodology This single-center retrospective study was performed at the Henri Becquerel Center (Rouen) and looked for circulating *ESR1* gene mutations by droplet digital PCR (E380Q, L536R, Y537S, Y537N, Y537C, D538G, S463P) in patients with advanced HR+ endometrial carcinoma treated between 2008 and 2020 for at least 30 days by AA or M. Timepoints were before exposure and at progression/during endocrine therapy.

Results 22 patients were included: 13 were treated with AA, 12 of whom progressed; 9 patients were treated with M, 8 of whom progressed. 68.1% of the patients had low-grade endometrial carcinoma and 54.5% had received chemotherapy in the metastatic setting. The median duration of treatment was 106 days (min 47 – max 358) with AA and 132 days (min 91-max 272) with M. Under AA, there was no *ESR1* mutation at baseline, and one Y537C mutation at progression with a variant allele frequency (VAF) of 0.14%. Under M, one patient had a Y537C (VAF 0.2%) at baseline that disappeared during treatment. Another patient had a Y537S mutation emergence at progression after 91 days of treatment (VAF 1.83%). There was no significant difference between the circulating DNA concentration before and after hormone therapy ($p = 0.16$).

Conclusion *ESR1* mutations do not seem to be involved in the mechanisms of resistance to AA or M in HR+ endometrial cancer. The clinical relevance of their detection is not demonstrated.

2022-RA-784-ESGO MEDICALLY UNFIT WOMEN WITH EARLY-STAGE ENDOMETRIAL CANCER TREATED WITH THE LEVONORGESTREL INTRAUTERINE SYSTEM

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Introduction/Background To assess the clinical efficacy of the levonorgestrel intrauterine system (LNG-IUS) in the treatment of early-stage endometrial cancer in elderly morbidly obese women, whose multiple co-morbidities made the standard surgical treatment too risky to undertake.

Methodology A retrospective review was conducted and case series reports were prepared of all women diagnosed with endometrial cancer, from April 2011 to December 2016 at the Queen's Hospital, London, to identify women unfit for surgery and treated with the LNG-IUS.

Results Out of 438 women with endometrial cancer, Eight women with early-stage endometrial cancer were deemed unfit for surgery and underwent treatment with the LNG-IUS. All had grade 1 endometrioid endometrial adenocarcinoma, radiologically staged as 1a. Four women died of their co-morbidities, not related to endometrial cancer. One of them had 68 months of progression-free survival before death due to co-morbidities. One patient required a hysterectomy after 32 months of treatment with LNG-IUS and oral progestogens due to heavy vaginal bleeding. Three women have continued the LNG-IUS treatment with no evidence of progressive disease symptoms till date at a mean follow-up of 35.7 months.

Conclusion For women with multiple co-morbidities, the LNG-IUS offers an effective and safe treatment for early-stage, low-grade endometrial cancer, with no cases of symptomatic progression reported in our case series. In the frail and elderly, where the quality of life is of paramount importance, surgical treatment may not offer additional long-term survival benefits.

2022-RA-787-ESGO ESGO GUIDELINES ON THE MANAGEMENT OF ENDOMETRIAL CANCER. WEAKNESSES AND CONTROVERSIES IN FRANCE AND FRENCH-SPEAKING SWITZERLAND. RESULTS OF A DELPHI SURVEY

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Introduction/Background To assess the opinion of a panel of experts and obtain consensus on several issues from the ESGO recommendations on the management of endometrial cancer.