CLINICAL RELEVANCE OF CIRCULATING ESR1 MUTATIONS 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.

METHODS
This single-center retrospective study was performed at the Henri Becquerel Center (Rouen) and looked for 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 cancer and 54.5% had received chemotherapy in whom progressed. 68.1% of the patients had low-grade endometrial cancer, with no cases of symptomatic progression 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.

EGSO GUIDELINES ON THE MANAGEMENT OF ENDOMETRIAL CANCER: STRENGTHS AND CONTROVERSIES IN FRANCE AND FRENCH-SPEAKING SWITZERLAND. RESULTS OF A DELPHI SURVEY

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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, radio logically 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.

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Methodology

A Delphi survey was carried out among a panel of French and French-speaking Swiss experts. The questionnaire included 58 questions divided into 8 categories: characterization of experts, histomolecular characteristics, radiological data, management of low-risk, intermediate-risk, intermediate-high-risk, high-risk and metastatic cancers. The experts were asked to reply on a 9-point scale, both on the validity and the clarity of each suggestion. After the answers were analyzed, a second round was sent to the same experts for selected suggestions. To be accepted, each proposal had to obtain a median greater than or equal to 7/9.

Results

The study was conducted between December 2021 and March 2022. 58 (57.4%) of 101 experts responded in the first round and 41 proposals were found. 5 questions were voted redundant and 19 discordant. These questions were reworded and partially split and at the end of the 2nd round, out of the 20 proposals 16 were validated and 4 rejected. In total, the study presents an analysis of 61 questions.

Conclusion

These consensual recommendations are expected to standardize the management of endometrial cancer in France and French-speaking Switzerland and to optimize clinical practices.

Introduction/Background

The significance of lymphadenectomy in uterine cancer has not yet been completely established. However, excessive lymphadenectomy significantly reduces the postoperative quality of life. Hence, noninvasive and highly accurate lymph node metastasis (LNM) diagnostic methods are strongly needed as alternatives to dissection. Therefore, we attempted a novel approach for the LNM diagnosis, in which the probability of metastasis is calculated using preoperative clinical variables and biomarker measurements.

Methodology

Preoperative clinical variables included serum tumor marker values and magnetic resonance imaging findings etc. Each variable’s discrimination power was evaluated by univariate analysis and validated combination of variables that contributed most to the LNM discrimination. The most promising mRNA biomarkers that correlate with expression difference between ‘positive’ and ‘negative’ groups were identified by CAGE (Cap Analysis Gene Expression), a genome-wide analysis.

Results

Ten clinical variables that contributed most to the LNM discrimination were extracted. Two promising biomarkers, SEMA3D and Novel isoform of TACC2, and two companion markers were identified. For all uterine cancers,