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### FACTORS FAVORING THE ERRONEOUS ULTRASOUND CLASSIFICATION OF THE DEGREE OF MYOMETRIAL INFILTRATION IN ENDOMETRIAL CARCINOMA

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**Introduction/Background\*** Determining the degree of myometrial infiltration allows establishing the best therapeutic approach for each patient as it is an important factor in predicting nodal metastases.

Few prospective studies comparing the diagnostic performance of transvaginal ultrasound (TVS) and magnetic resonance imaging (MRI) in the preoperative local staging of endometrial carcinoma have been reported. In fact, a recent meta-analysis has shown that both techniques have similar diagnostic accuracy. However, to the best of our knowledge, there has been no prospective comparison of the diagnostic performance of TVS and MRI in the same group of patients with low-grade endometrial cancer.

The aim of this study was to analyse which factors could influence the ultrasound assessment of the myometrial infiltration.

**Methodology** Observational prospective study performed at a single tertiary care centre from 2016 to 2020, comprising 156 consecutive patients diagnosed by endometrial sampling as having an endometrioid grade 1/grade2 endometrial cancer. TVS and MRI were performed prior to surgical staging for assessing MI, which was estimated using subjective examiner's impression and Karlsson's method for both TVS and MRI. During surgery, intraoperative assessment of MI was also performed. Definitive pathological study considered as reference standard.

Univariate logistic regression model has been used to study the association between potential confounding variables and the ultrasound assessment of myometrial infiltration.

**Result(s)\*** Variables such as age older than 65 years old, endometrial thickness determined by ultrasound greater than 15 mm, ultrasound pattern of moderate-abundant vascularization, definitive G3 histological grade and presence of lymphovascular invasion in definitive AP study are related to a higher risk of ultrasound misclassification. The first three variables tend to cause an overestimation of the MI degree, while the last two tend to cause its underestimation.

**Conclusion\*** When assessing myometrial infiltration by transvaginal ultrasound we should remind that there are some confounding variables which could make us misclassify myometrial infiltration.

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### IN RL95-2 AND KLE MODEL CELL LINES OF MODERATELY AND POORLY DIFFERENTIATED ENDOMETRIAL CARCINOMA, ESTROGENS CAN BE FORMED VIA THE SULFATASE PATHWAY

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**Introduction/Background\*** Endometrial cancer (EC) is the most common gynecological malignancy in the western world. EC

has traditionally been divided into type I, which is estrogen dependent, and type II, where associations with estrogens were only recently uncovered. Both types of EC arise after menopause when tumor tissue depends on formation of estrogens from inactive steroid precursors. In EC, active estrogens can be formed from circulating estrone sulfate (E1-S) via sulfatase pathway by the sulfatase (STS) and reductive 17 $\beta$ -hydroxysteroid dehydrogenase type 1 (HSD17B1) enzymes.

**Methodology** In our study, we aimed to investigate the role of estrogens in model cell lines of moderately (type I) and poorly (type II) differentiated EC: RL95-2 and KLE cells, respectively. We evaluated expression of genes involved in E1-S transport, estrogen biosynthesis and oxidative metabolism, and examined cellular uptake of E1-S, formation of estrogens from E1-S, and effects of estrogens on cell proliferation.

**Result(s)\*** Gene expression analysis revealed up-regulated expression of several E1-S uptake transporters: *SLCO1A2* (3434-fold), *SLCO1B3* (2302-fold), *SLCO1C1* (381-fold), *SLCO3A1* (19-fold), *SLC22A9* (5-fold), *SLC10A6* (5-fold), and functional studies showed increased E1-S uptake in KLE cells versus RL95-2 cells. Higher levels of STS were confirmed in RL95-2 cells, which also better metabolized E1-S to estrone (E1), compared to KLE cells. In KLE cells, disturbed balance in the expression of genes encoding reductive and oxidative HSD17B enzymes enhanced activation of E1 to estradiol (E2), compared to RL95-2 cells, and physiological E1 concentrations stimulated KLE cell proliferation. Additionally, gene expression analysis in KLE versus RL95-2 cells indicated increased *CYP1B1* expression (17-fold) as responsible for formation of carcinogenic 4-hydroxycatechols, and down-regulation of genes that encode phase II metabolic enzymes: *COMT* (6-fold), *NQO1* (13-fold), *NQO2* (7-fold), and *GSTP1* (2-fold). This suggested decreased detoxification of carcinogenic metabolites in KLE cells.

**Conclusion\*** Our results indicate that in cell lines of type I and type II EC, estrogens can be formed via the sulfatase pathway, and can promote proliferation of poorly differentiated EC. This supports the importance of estrogens in poorly differentiated (type II) EC. Further studies in tissue samples of type II EC are needed to confirm our findings.

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### EFFECTIVENESS AND SAFETY OF LENVATINIB AND PEMBROLIZUMAB (LENPEM) THERAPY FOR ENDOMETRIAL CANCER (EC): RESULTS FROM A RUSSIAN MULTICENTER DATABASE

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**Introduction/Background\*** The Study 111 established LenPem as a treatment option in patients with advanced endometrial cancer following prior systemic therapy. LenPem has a higher objective response rate (ORR) and progression-free survival (PFS) with a different toxicity profile. The aim of this study was to gather data regarding the efficacy and safety of LenPem when used in the real-world treatment of EC. This is the first study to examine LenPem using (?) in EC patients treated in Russia in real practice.

**Methodology** Retrospective chart review identified 34 patients administered LenPem for treatment of recurrent EC in Russia from March 2020 to March 2021. Demographic and clinical data were analyzed.

**Result(s)\*** Thirty-four patients (median age 66,9 years, range 57–83 years; 20,6% of patients with serous carcinoma, 82,4% ECOG ≤1, 64,7% pts with ≥2 relapses, 38,2% patients with ≥3 prior platinum-based chemotherapeutic regimens) received 1-14 cycles (median 3). In 23 patients who were examined for efficacy, the response rate (RR) was 26.2% and stabilization observed in 69.6% cases. Incidence of grade =>3 adverse events was similar to that in prior studies (overall 97%). The most common side effects in this study and study 111 were fatigue (64,7% and 51,1%, respectively), hypertension (47,1% and 61,7%, respectively), diarrhea (8,8% and 53,2% respectively) and stomatitis (8,8% and 35,1% respectively). Overall, 29,4% pts required dose reduction due to toxicity and in 11,8% cases required discontinuation due to disease progression.

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	Overall (n=23),%	Study 111 EC arm (n=94), %, Inv. Assessment
CR	4,3	7,4
PR	21,7	29,8
SD	69,6	46,8
PD	4,3	10,6

**Conclusion\*** Outcomes of advanced EC patients treated in Russia with LenPem following prior systemic therapy are comparable to those demonstrated in the Study 111. LEN appears to be effective and safe in real world practice in EC.

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### DEVELOPING NURSE LED PHONE CLINIC FOR ENDOMETRIAL CANCER FOLLOW-UP IN PRE COVID-19 ERA LEADING TO EFFICIENT FOLLOW UPS IN PANDEMIC TIMES

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**Introduction/Background\*** Systematic review says seventy percent of endometrial carcinoma recurrences are associated with symptoms. Is it safe to do nurse led phone clinic(NLPC) led by nurses and doctors.

**Methodology** Retrospective audit done on endometrial cancer patients in Northampton general hospital, treated from October 2013 and October 2018 and analysed the recurrence rate and presentation. Started NLPC in 2018. Wrote up a

guideline and letter format for the nurses. Patient satisfaction Questionnaire done

**Result(s)\*** Of 448 endometrial cancer patients in the above stated period, there were 57 recurrences. 8/57 patients were completely asymptomatic and was diagnosed in the first 2 years of follow up. However, 92% of the patients presented with symptoms at the time of presentation.

On these databases NLPC was conducted with a prescribed format and on early stage endometrial cancers and further patient satisfaction assessed which was 98%.

**Conclusion\*** Majority of the cancer recurrence presented with symptoms, hence Nurse Led Phone follow up Clinics (NLPC) for selected cases is justified. Implementing NLPC leads to cut down in number clinic appointments, thus saving resources and give quality care to the more complex cases.

At the beginning of Covid 19 , phone clinics were simplified as practice was already in place in the department.

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### IMPACT OF OBESITY ON SENTINEL LYMPH-NODE MAPPING IN PATIENTS WITH APPARENT EARLY-STAGE ENDOMETRIAL CANCER: A PROPENSITY-MATCHED MULTICENTER STUDY

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**Introduction/Background\*** Obese patients pose both surgical and anesthetic challenges, as their comorbidities contribute to adverse outcomes.

In this setting, minimally invasive approach and the introduction of the Sentinel Lymph-Node (SLN) algorithm in endometrial cancer (EC) treatment acquire a particular relevance, allowing to reduce both operative times and surgical difficulties.

However, conflicting data exists on the impact of Body Mass Index (BMI) on SLN detection.

The primary study endpoint was to investigate the impact of obesity on overall detection rate, bilateral mapping, and mapping failure rate. In addition, we evaluated possible differences in terms of surgical management and 'empty packet dissection' rate among the two study groups.

**Methodology** Multicenter, propensity-matched, retrospective study.

Data of patients with apparently early-stage EC were retrospectively retrieved. Study population was divided into women with BMI </> 30 (respectively Group-1 and Group-2). To lower the selection bias, a propensity matched analysis was performed. Matching was based on the most relevant variables impacting SLN detection, such as histotype (endometrioid vs non-endometrioid), age (</>65 years old), presence of lymphovascular space invasion.

**Result(s)\*** Eight-hundred forty-four women were enrolled in the study. After a 1:1 propensity matched analysis, a total of 764 patients were identified (Group-1 n=382, Group-2 n=382). A 1.156-fold increase in the risk of mapping failure for every 5 units of increase in BMI (OR 1.156, 95% CI 1.033-1.294, p=0.012) was found, with a consequently decrease in bilateral mapping and overall detection rate