

nuclear translocation of AR and ER were seen in several models after long-term exposure, also without affecting proliferation.

**Conclusion** Data indicates that targeting AR and ER pathways in EC is model specific, suggesting context-dependent signaling. Lack of measured effect on proliferation combined with altered HR expression in some models might point to clonal selection in response to HR activation.

2022-RA-1499-ESGO

#### DIFFERENTIAL RESPONSE OF IN-VITRO MISMATCH REPAIR-DEFICIENT HYPERMETHYLATED ENDOMETRIOD ENDOMETRIAL CANCER MODELS TO DNA-HYPOMETHYLATING AGENTS

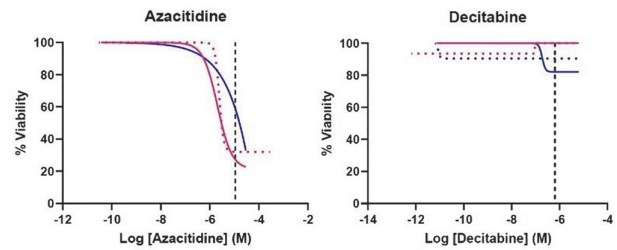
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**Introduction/Background** We sought to compare in-vitro mismatch-repair deficient endometrial cancer (EC) methylation and responses to DNA-hypomethylating agents using spheroid-based microcancer 3D tumor cell viability assay.

**Methodology** Study tumor was prospectively collected from a patient with stage 1B, grade 2 endometrioid EC. Characterization entailed whole exome, RNA, and MatePair analysis. Somatic mutations, structural variants and transcriptomic profiling were used to identify potential driver pathways for inhibition. Epigenomic profiling was completed with Assay for Transposase-Accessible Chromatin and DNA-methylation with Reduced Representation Bisulfate Sequencing. A comparative hyper-duplicated, p53-mutated EC underwent identical testing. 3D microcancers of these tumors were subjected to DNA-methyltransferase (DNMT) inhibition. Cell viability was determined by CellTiter-Glow Luminescent Assay. Data transformation and dose-response curves were generated by GraphPad Prism using four-parameter logistic regression. Inhibitory effect (IE) was defined as percent reduction ATP from baseline at maximum plasma concentration (Cmax).

**Results** Genomic sequencing revealed evidence of microsatellite instability with *POLE* variant of unknown significance. Global and promoter hypermethylation was observed in sample with fewer copy number variation. When contrasted with comparison tumor, we observed significant ( $p < 0.01$ ), albeit modest, global ( $\Delta\beta = 0.51$ ) and promoter ( $\Delta\beta = 0.52$ ) hypermethylation. Methylation of both *MLH1* and *PMS2* was observed. While both gene bodies were hypermethylated ( $\Delta\beta = 0.50$  and  $\Delta\beta = 0.15$  respectively), only *MLH1* was statistically different. Despite the lack of methylation of promoters for both genes, we noticed a gene expression fold reduction of 2.58 (*MLH1*) and 1.81 (*PMS2*). Inhibition of viability in both study and comparison was minimal by decitabine, shown by IE of 0 and 17.939, respectively. Conversely, IE of study tumor by azacitidine was more pronounced at 72.662, compared with 40.951 (figure 1).



**Abstract 2022-RA-1499-ESGO Figure 1** Normalized drug responses of study tumor (pink) and comparison tumor (blue) to azacitidine and decitabine. Dose-response curves of treatment were titrated for each agent across maximum inhibitory plasma concentration (black dotted line). Pink and blue dotted lines represent results of previous testing

**Conclusion** In MMR-D EC with *MLH1* hypermethylation, in-vitro tumor response to DNMT inhibition is superior for DNA/RNA incorporating azacitidine when compared to DNA-only incorporating decitabine.

2022-RA-1504-ESGO

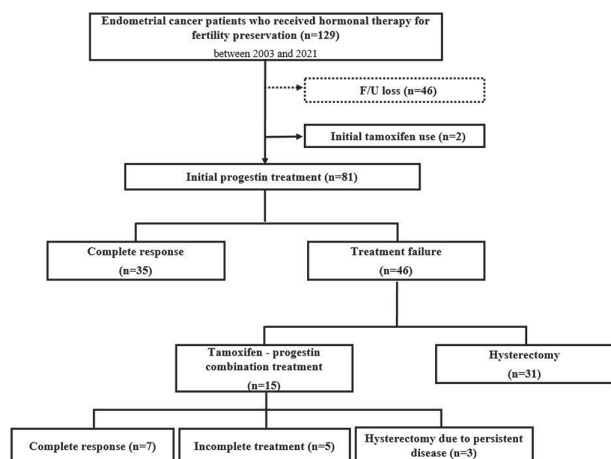
#### TAMOXIFEN-MEGESTROL ACETATE COMBINATION HORMONAL THERAPY IS AN EFFECTIVE FERTILITY-SPARING TREATMENT IN EARLY-STAGE ENDOMETRIAL CANCER PATIENTS WHO HAVE FAILED PROGESTIN ONLY HORMONAL THERAPY

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**Introduction/Background** Tamoxifen is a selective estrogen receptor modulator, which inhibits the binding of estradiol to estrogen receptors in endometrial cancer. It can also increase progesterone receptors, making tumors more responsive to progestin therapy. Hence, we investigated the effectiveness of tamoxifen-progestin combination (T-P) therapy as a fertility-sparing treatment option in early-stage endometrial cancer patients who have previously failed progestin only (P-only) therapy.

**Methodology** We identified 129 patients with 2008 International Federation of Gynecology and Obstetrics stage IA-IB endometrioid endometrial cancer who received one or more hormonal treatment (HT) for preserving fertility between 2003 and 2021. P-only therapy included megestrol acetate (80–400 mg/day), medroxyprogesterone acetate (500 mg/day), and/or levonorgestrel-releasing intrauterine device. T-P therapy consisted of tamoxifen 20 mg/day for 3 weeks followed by megestrol acetate 160–400 mg/day for 3 weeks. We collected patients' baseline characteristics, HT regimens, cycles, doses, response to HT, and referral for hysterectomy. Patients who failed to follow-up at least 6 months before completion of HT and patients with grade 3 disease were excluded.



Abstract 2022-RA-1504-ESGO Figure 1

**Results** In total, 83 patients were included in this analysis. Two patients who received T-P as primary HT reached complete response (CR). Among patient who received P-only therapy (n=81), 35 (43.2%) achieved CR, while 46 (56.8%) did not. Of those with persistent disease, 31 (67.4%) underwent hysterectomy and others (n=15) were recommended T-P therapy. Except for five patients who did not complete medication, 10 patients completed T-P therapy at least 6 cycles with median observation period of 41.4 months. Among them, seven (70%) showed CR, and only three (30%) underwent hysterectomy for persistent disease.

**Conclusion** T-P therapy should be considered as one of the treatment options for early-stage endometrial cancer patients who have previously failed P-only therapy. More studies are needed to predict the response to HT by investigating the molecular classification of endometrial cancer.

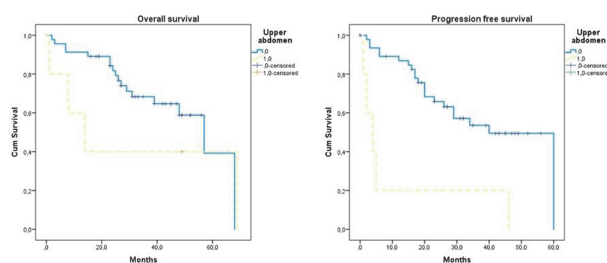
#### 2022-RA-1506-ESGO FACTORS AFFECTING SURVIVAL RATES OF PATIENTS WITH UTERINE CLEAR CELL CARCINOMA

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**Introduction/Background** Uterine clear cell carcinoma represents a rare and aggressive gynecologic malignancy that is primarily treated with surgery. Chemotherapy and radiotherapy have been used as adjuvant therapy to postpone survival, however, even in this setting the actual mortality rates remain high. In the present study we evaluated factors that affect survival rates of patients, including patient and tumor characteristics as well as administered therapy.

**Methodology** The study was based in a retrospective cohort of patients treated in a tertiary university hospital in Greece. Cox regression analysis was used to evaluate the impact of age, body mass index, tumor size, stage of the disease at primary treatment, presence of upper abdominal metastases on survival rates of patients.



Abstract 2022-RA-1506-ESGO Figure 1

**Results** Overall, 53 patients were included in the present study with a median follow-up of 48 months. The median progression free survival was 36.47 months (29.78, 43.16) and the median overall survival was 47.35 months (39.89, 54.82). Advanced stage disease significantly decreased the rates of patient survival (29.80 vs 40.18 months for progression free survival and 43.30 vs 53.17 months for overall survival). Patients with metastases to the upper abdomen had the most decreased survival rates (11.6 months vs 39.59 months for progression free survival and 32.2 months vs 48.26 months for overall survival). The use of chemotherapy did not decrease recurrence rates (HR 1.33, 95% CI 0.38, 4.71). Similar results were observed for external beam radiotherapy (HR 0.645, 95% CI 0.19, 2.21) and brachytherapy (HR 0.86, 95% CI 0.27, 2.76).

**Conclusion** Clear cell carcinoma is an extremely aggressive malignancy with survival rates of patients presenting at advanced stage being extremely short. Adjuvant therapy does not seem to benefit survival rates of patients with early stage disease.

#### 2022-RA-1508-ESGO UNIVERSAL MMR TESTING IN ENDOMETRIAL CARCINOMA: RESULTS AND CLINICOPATHOLOGIC CORRELATIONS FROM AN INDIAN CENTRE

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**Introduction/Background** Tumour testing for DNA mismatch repair (MMR) is recommended for all endometrial cancers (EC) and is incorporated into the new molecular classification. This study aimed to find the prevalence of MMR deficiency (dMMR), Lynch Syndrome (LS), and to evaluate the differences in prognostically important clinicopathologic features between MMR proficient (pMMR) and dMMR among Indian EC patients.

**Methodology** Clinical and pathologic information of women treated for EC between 2019–2020 were obtained from electronic medical records. Fisher exact test was used for comparison of categorical variables. Survival analysis was done using Kaplan-Meier method and Cox Proportional Hazards model.

**Results** Over 2 years 108 EC tumour testing was done and 24% (26 pts) were dMMR by immunohistochemistry.