Objectives: The benefit of lymph node surgery (LNS) in early-stage endometrioid ovarian carcinoma (ENOC) is unknown. Only vague data on impact of endometrioid histotype is available. Prior studies examining the benefit of LNS in ENOC have been hampered by small numbers, and large-scale studies that consider modern classification are needed.

Methods: After launching a transatlantic initiative, a cohort of 785 ENOC was assembled from 22 centers across Canada and Europe. Histotype was confirmed by central expert pathology review and immunohistochemistry, followed by extensive chart review. Complete lymphadenectomy was defined as such when at least 10 pelvic and 10 paraaortic LN were removed.

Results: A total of 71 blood samples was collected from n=35 patients. HPV cfDNA was successfully detected in 25/35 (71%) patients. A significant correlation between tumor burden and HPV cfDNA detection was observed: while HPV cfDNA was detectable in most patients (20/22) with locally advanced or metastatic disease, detection was successful in only 5/13 patients with early-stage disease (p=0.001). HPV-types detected in plasma samples matched results from tumor tissue HPV testing. Sequential sampling showed a dynamic decrease of HPV cfDNA levels in line with treatment response in all patients.

Conclusions: In this proof-of-concept study HPV cfDNA levels were measured using a highly sensitive Next-Generation-Sequencing-based approach targeting a panel of 13 high-risk HPV-types. cfDNA sequencing was compared to HPV testing in corresponding paraffin embedded tumor sample. Sequential plasma samples were taken from four patients receiving primary chemoradiation.

Focused plenary: Translational science

Objectives: Human papillomavirus (HPV) related cervical cancer is the fourth most frequent cancer in women worldwide. Currently patient follow-up and therapy monitoring is solely based on clinical examination and cross-sectional imaging. The aim of this study was to investigate the potential use of HPV cell-free circulating DNA (cfDNA) in plasma samples of patients with cervical cancer.

Methods: In this proof-of-concept study HPV cfDNA levels were measured using a highly sensitive Next-Generation-Sequencing-based approach targeting a panel of 13 high-risk HPV-types. cfDNA sequencing was compared to HPV testing in corresponding paraffin embedded tumor sample. Sequential plasma samples were taken from four patients receiving primary chemoradiation.

Results: A total of 71 blood samples was collected from n=35 patients. HPV cfDNA was successfully detected in 25/35 (71%) patients. A significant correlation between tumor burden and HPV cfDNA detection was observed: while HPV cfDNA was detectable in most patients (20/22) with locally advanced or metastatic disease, detection was successful in only 5/13 patients with early-stage disease (p=0.001). HPV-types detected in plasma samples matched results from tumor tissue HPV testing. Sequential sampling showed a dynamic decrease of HPV cfDNA levels in line with treatment response in all patients.

Conclusions: In this proof-of-concept study we were able to detect HPV cfDNA in primary and recurrent cervical cancer. Our findings may hold potential to develop a powerful and easily accessible tool in cervical cancer management.
KRAS and PIK3CA gene mutation on fertility preserving treatment outcome in patients with endometrial cancer and endometrial atypical hyperplasia (EC/EAH).

Methods A total of 135 EC/EAH patients receiving fertility preserving treatment and molecular classification were retrospectively reviewed. The distribution of the four types of molecular classification was described. The impact of MMRd and NSMP, as well as PTEN, KRAS and PIK3CA gene mutation on treatment outcome was also analyzed.

Results Most of the patients were classified as non-specific molecular profile (NSMP) (117/135, 86.7%), while 14 patients (10.4%) were mismatch repair deficient (MMRd), 1 patient (0.7%) was POLE-mutated, and 3 patients (2.2%) were p53 abnormal. Patients with NSMP and MMRd achieved similar cumulative CR rates at 16 weeks, 32 weeks, and 48 weeks of treatment in either EC or EAH patients. Patients harboring pathogenic or likely pathogenic PTEN mutations (PTENmut-P/LP) achieved lower cumulative 32-week CR rate (22/47, 46.8% PTENmut-P/LP vs 50/74, 67.6% PTEN-others; P=.023; OR 0.422 (95%CI 0.199–0.896). Kaplan-Meier analysis presented similar results. Univariate analysis showed that insulin-resistance and PTENmut-P/LP were related to poor treatment outcomes. In multivariate analysis, insulin-resistance (HR 0.435; 95%CI 0.269–0.702; P=0.001) and PTENmut-P/LP (HR 0.533; 95%CI 0.324–0.885; P=0.015) remained independent negative predictors of fertility preserving outcomes.

Conclusions PTEN mutation is identified as poor prognostic factor in patients receiving fertility preserving treatment, with a lower CR rate and longer treatment duration. MMRd patients achieved similar outcomes with NSMP. Molecular profiles might guide fertility preserving treatment in prognosis and treatment decisions.

Abstract O034/#772 Table 1 Outcomes in all and gynaecologic cancer patients

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Positive Tumor NGS, N (%)</th>
<th>Received Germline GT, N (%)</th>
<th>Positive Germline GT, N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>2396</td>
<td>454 (12.6)</td>
<td>162 (33.5)</td>
</tr>
<tr>
<td>Gynecologic</td>
<td>357</td>
<td>79 (22.1)</td>
<td>50 (70.9)</td>
</tr>
<tr>
<td>Ovarian</td>
<td>177</td>
<td>45 (25.4)</td>
<td>41 (91.3)</td>
</tr>
<tr>
<td>Uterine</td>
<td>149</td>
<td>33 (21.5)</td>
<td>15 (46.9)</td>
</tr>
<tr>
<td>Cervical/Vaginal</td>
<td>31</td>
<td>2 (6.5)</td>
<td>0</td>
</tr>
</tbody>
</table>

Abbreviations: NGS, next generation sequencing; GT, genetic testing

Objectives Focusing on gynecologic cancer, we aimed to describe the frequency of positive tumor NGS results that met ESMO 2019 recommendations for germline genetic testing (GT), receipt of germline GT and positive GT results in a large cancer cohort.

Methods Patients with tumor NGS within a large, urban healthcare system were retrospectively identified (Sept 2019–Feb 2022). ESMO guidelines were used to identify eligible patients with potentially actionable germline mutations on NGS (Mandekker et al. 2019). Chi-square analysis compared rates in gynecologic and all cancer patients.

Results In 3796 patients undergoing tumor NGS, 357 (9.4%) had gynecologic cancers: ovarian, 177 (49.6%); endometrial, 149 (41.7%); cervical/vulvar/vaginal, 31 (8.7%). There were 454/3796 (12.0%) total cancer patients and 79/357 (22.1%) gynecologic cancer patients with at least one positive tumor result meeting ESMO guidelines for germline GT (table 1). Of eligible patients, more gynecologic cancer patients received germline GT than total cancer patients (70.9% vs 35.7%, p<0.05). Among 56 gynecologic cancer patients receiving germline GT, 40 (71.4%) had positive results: BRCA1, 12; BRCA2, 11; MUTYH, 5; BRIP1, 5; RAD51C, 2; and one each CHEK2, SDHA, MLH1, MSH2, MSH6, NF1, PMS2.

Conclusions Germline GT rates in gynecologic cancer may be higher than in all cancer patients due to guidelines recommending all ovarian cancer patients get GT and all endometrial cancer patients be screened for Lynch syndrome. Nonetheless, education and reflex protocols to further improve germline GT rates are warranted as almost 30% of gynecologic cancer patients with eligible tumor results based on ESMO criteria still did not receive GT.

EXPLORING THE ROLE OF MOLECULAR ABERRATIONS IN PREDICTING RESPONSE TO EVEROLIMUS IN THE TREATMENT OF ENDOMETRIAL CANCER

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Abstracts

Objectives Everolimus-based treatment (ET) has proven efficacy in recurrent endometrial cancer (EC). The association of mutations found in biopsy specimens and response to ET is unclear.

Methods We performed a retrospective review of pts with EC treated with everolimus from 3/2016 to 12/2021. Next generation sequencing data were collected for KRAS, PIK3CA, CTNNB1, TP53, and PTEN mutations. The objective response rate (ORR) and clinical benefit rate (CBR at 6 months) were analyzed. Chi-squared or Fisher’s exact tests were used to analyze CBR differences between groups. Kaplan Meier methods were used to estimate survival (PFS and OS), modelled via Cox proportional hazards.

Results 89 patients were included. Average age at diagnosis was 59.9 years. The majority (62.9%) had endometrioid histology and 87.6% received everolimus and AI ± metformin. ORR was 40.0% (95% CI: 29.2 – 51.6%). CBR was 67.5% (95% CI: 56.1 – 77.6%). Median PFS was 5.98 months (95% CI: 4.57 – 8.28). TP53 wildtype had ORR 52.4% (95%CI: 36.4–68.0%) vs 22.7% (95%CI: 7.8–45.4%) in TP53 mutants. TP53wt had CBR 85.7% (95%CI: 71.5–94.6%) v 40.9% (95%CI: 20.7–63.6%) in TP53 mutants. Median PFS in TP53wt was 11.43 months v 2.76 months in TP53 mutants.