LYMPHADENECTOMY IN ENDOMETRIOID OVARIAN CARCINOMA PATIENTS WITH EARLY STAGE DISEASE: RESULTS FROM THE LEOPARD TRIAL

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Objectives The benefit of lymph node surgery (LNS) in early-stage endometrioid ovarian carcinoma (EOC) is unknown. Only vague data on impact of endometrioid histotype is available. Prior studies examining the benefit of LNS in EOC 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 EOC 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 Chart review and histopathologic data was available from 596 patients of which in 509(85.4%) cases tumor spread was confined to the pelvis (pT1a-pT2b,M0). Grade distribution included 221/509(43.4%) G1, 212/509(41.7%) G2 and 74/509(14.5%) G3 tumors. While LNS has been omitted in 239/509(47.0%) cases, complete pelvic and paraaortic LNS was performed in 77/509(15.1%) patients. LNS was restricted to pelvic nodes in 88/509(17.3%), to paraaortic nodes in 16/509(3.1%) and to sampling procedures in 77/509(15.1%) cases. Positive nodes were found in 6/509(1.2%) patients with early-stage EOC, all low-grade tumors were found to be node negative.

Conclusions LEOPARD results indicate that lymph node involvement is rare in early-stage EOC, even in high grade tumors. However, the variation in lymph node surgical practice was profound. Our team initiative stands to provide a powerful statement on the value of LNS, possibly improving precision care for EOC patients.

CIRCULATING HPV CELL-FREE DNA IN CERVICAL CANCER

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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.

PTEN AND MOLECULAR CLASSIFICATION AS PROGNOSTIC FACTORS TO PREDICT FERTILITY PRESERVING TREATMENT OUTCOMES IN PATIENTS WITH ENDOMETRIAL CANCER AND ENDOMETRIAL ATYPICAL HYPERPLASIA

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Objectives This study aimed to investigate the impact of molecular classification and other oncogenes including PTEN,
ACTIONABLE GERMLINE MUTATIONS IDENTIFIED THROUGH TUMOR SEQUENCING: EVALUATION OF ESMO GUIDELINES IN GYNECOLOGIC MALIGNANCY

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Objective: 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 (Mandelker 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, SDH, 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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Objective: 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 assessed. 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 5.9 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%) vs 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.