BRCA1/2 mutations). Interestingly, Chechen BRCA1 c.3629_3630delAG allele was not observed among patients of Ingush ethnicity, despite these nations are believed to have common Nakh (Vainakh) roots. In Ingush patients, there were two recurrent alleles in the BRCA2 gene (c.5351dupA: 5 out 13 BRCA1/2 mutations; L1686X: 3 out 13 mutations). BRCA2 Q3299X mutation was repeatedly observed across several ethnic groups. OC patients from Kabardino-Balkaria had unusually high frequency of germ-line ATM truncating alleles (3/49, 6%); all 3 ATM mutations were represented by distinct ATM pathogenic variants.

Conclusion Genetic analysis of non-selected ovarian cancer patients is highly efficient in revealing ethnicity-specific BRCA1/2 mutations. Contribution of BRCA1/2 pathogenic alleles in OC and BC morbidity is high across various ethnic groups. Founder BRCA1/2 alleles are characteristic for some but not all North Caucasus nations.

2022-RA-1360-ESGO CIRCULATORY HMGB-1 AS A PLAUSIBLE DIAGNOSTIC MARKER IN LIQUID BIOPSY OF CERVICAL CANCER

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Introduction/Background Cervical cancer (CaCx) is one of the common malignancies in women worldwide. Autophagy is a significant hallmark of cancer wherein high mobility group box 1 (HMGB-1) plays a crucial role. Aberrant expression of HMGB-1 is associated with tumor development, progression and poor prognosis. There are no reports available studying HMGB-1, autophagy related molecule in context to clinical significance in cancer cervix. Thus, we aim to investigate the association between HMGB-1 and its associated molecules (RAGE, p53 & p62) in CaCx. We have also evaluated the clinical significance of serum HMGB-1 in CaCx diagnosis.

Methodology 50 subjects including 20 CaCx patients, 20 healthy women and 10 controls having gynecological disorder other than malignancy were recruited. Circulatory levels of HMGB-1 were measured by ELISA. mRNA and protein levels of HMGB-1 and its associated molecules were quantitated using Q-PCR and western blotting respectively in tissues of study subjects. The data obtained were then validated *in vitro* by siRNA-based silencing of HMGB-1. Data was statistically analyzed and ROC curve was plotted.

Results Circulatory levels of HMGB-1 were significantly higher in patients as compared to controls. mRNA and protein expression of HMGB-1 were significantly higher in tumor tissues. The levels of RAGE, p53 and p62 were also significantly altered than their expression in controls at mRNA and protein levels. ROC curve analysis showed better sensitivity and specificity for HMGB-1 for non-invasive diagnosis of CaCx in liquid biopsy. Furthermore, siRNA-mediated targeting of HMGB-1 significantly altered expression of associated molecules, thus, validating the patients' data.

Conclusion HMGB-1 level could be a useful marker for evaluating disease and diagnosis in non-invasive liquid biopsy. Autophagy mediated HMGB-1/RAGE pathway might play a significant role in pathogenesis of CaCx. Validation in larger patient cohort might exploit HMGB-1 as a novel non-invasive diagnostic marker for CaCx in liquid biopsy in future.

2022-RA-1446-ESGO COMPREHENSIVE ASSESSMENT OF GENE MUTATIONS REVEALED OVERLAPPING DEPENDENCIES FOR PARPI AND CHEMOTHERAPY RESPONSE IN OVARIAN CANCER

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Introduction/Background PARP inhibitors (PARPi) have revolutionized the therapeutic landscape of epithelial ovarian cancer (EOC) prolonging the progression-free survival, especially in *BRCA1/2* mutations carriers or in patients with defects in homologous recombination (HR) repair. However, it remains uncertain which PARPi to apply and how to select responders using clinical and molecular characteristics, especially in forefront therapy when platinum sensitivity is still unknown.

Methodology We selected 33 promising genes that showed a prediction of enhanced PARPi sensitivity after a systematic literature review and the exploration of publicly available CRISPR-*Cas9* library screens and Genomics of Drug Sensitivity in Cancer data. We performed functional assessment in six constitutively *Cas9* expressing OC cell lines and subsequent examined our set of genes using a CRISPR-*Cas9* mutagenesis assay with various PARPi and carboplatin.

Results Our functional screen identified ten novel potential PARPi response biomarkers, with different impact on cell fitness and drug response.*ATM* was the only gene that produced an enhanced olaparib sensitivity in all the cell lines.Acquired olaparib sensitivity was also observed for *MUS81*, *NBN*, *RAD51B/C*, *RNASEH2A*, *PALB2*, *XRCC1*, and *XRCC3* in at least 3 cell lines.*CDK12* was identified as an essential gene in all the cell lines tested without altering the response to Olaparib.Since the best clinical biomarker of PARPi sensitivity remains the sensitivity to chemotherapy, we next compared dropout rates of top candidate genes under different PARPi (olaparib, niraparib, talazoparib) and carboplatin. Interestingly, we observed almost identical results, independently of tested gene and drug compound. This confirming the strong correlation of cancer cell response to DNA damaging drugs.

Conclusion Our data show various overlapping gene dependencies suggesting a general mechanism-of-action of PARPi and chemotherapy. Genetic screen of the identified set of genes correlated with PARPi sensitivity may allow a better stratification of patients with increase benefit to this treatment.

2022-RA-1449-ESGO THE PROGNOSTIC VALUE OF SERUM CA125 AND HE4 IN ENDOMETRIAL CANCERS STRATIFIED BY MOLECULAR SUBGROUP

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Introduction/Background Endometrial cancer is the commonest gynaecological malignancy. Molecular classification informs

prognosis, however markers that further risk-stratify intermediate groups are needed. Serum cancer antigen-125 (CA125) and human epididymis-4 (HE4) show promise as prognostic markers. The aim of this study was to evaluate the association between serum CA125, HE4 and endometrial cancer survival outcomes when stratified by molecular subgroup.

Methodology Pre-treatment serum CA125 and HE4 levels were measured and endometrial tumours classified according to WHO molecular classification. The relationship between biomarkers and survival was evaluated using Kaplan-Meier analysis and multivariable cox regression.

Results Overall, 327 women were included, with POLE status available for 216. Tumours were POLE-mutant (5%), p53-abnormal (11%), MMR-deficient (30%) and NSMP (54%). Median follow up was 50 months (IQR 30–60), during which 42 (13%) recurred and 71 (21%) women died. CA125≥35U/mL was independently associated with overall mortality [aHR=2.42 (95%CI:1.45–4.06), p=0.001), cancer specific death [aHR=2.00 (95%CI:1.04–3.87), p=0.04] and recurrence [aHR=2.69 (95%CI:1.38–5.27), p=0.004]. When stratified by molecular subgroup, CA125≥35U/mL and HE4≥150pmol/L were prognostic of overall survival in MMR-deficient [CA125: aHR=4.92 (95%CI:1.74–13.89), p=0.003 and HE4: aHR=4.03 (95%CI:1.34–12.11), p=0.01] and NSMP subgroups [CA125: aHR=3.72 (95%CI:1.30–10.67), p=0.01)].

Conclusion CA125 and HE4 may risk-stratify those at intermediate risk of recurrence and death. Evaluation in a larger population is required.

2022-RA-1457-ESGO GYNECOLOGICAL CANCER DETECTION USING FOURIER-TRANSFORMED INFRA-RED SPECTROSCOPY IN URINE SAMPLES: POTENTIAL AND ACCURACY OF MACHINE LEARNING PROCESSING

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Introduction/Background Making an early diagnosis of cancer is the challenge that modern medicine has been setting for several decades. In gynecology, no effective screening has yet been found and approved for endometrial and ovarian cancer, and, despite cervical cytology testing, cervical cancer remains a leading cause of morbidity and mortality among gynecological cancers worldwide. The emerging technique of liquid biopsy has been proposed as a method for detecting cancer in early stage using biofluids and their properties as biomarkers.

Methodology In this study, we tested the application of an artificial intelligence (AI) algorithm on infra-red spectra taken from urine samples from 84 female patients with gynecological cancer (28 breast, 32 endometrial, 24 ovarian and 10 cervical) and 200 non-tumor patients who were used as controls. The spectra were normalized, and outlier values were detected and removed using a DBSCAN algorithm. To overcome the possible problem of an unbalanced dataset, we used a SMOTE algorithm enhancing the generalization of the predictive model. The AI-model was trained and tested in classifying healthy urine samples vs different cancer types.

Results The spectra were divided into training- and testing-datasets with a ratio of 80/20 randomly + 10-fold cross validation and various classifiers were put under test: decision trees, discriminant analysis, support vector machines, logistic regression and random forest, with the latter giving the best results. In the classification report Precision-, Recall-, and F1-scores varied from 0.93 to 1.00, 0.88 to 1.00 and 0.94 to 0.99 respectively

Conclusion These results confirm the reports from previous, smaller studies and show that AI-models could be useful in differentiating biofluid samples, such as urine, between patients and healthy controls. Further research is needed in order to confirm the validity of the method and to assess its potential on clinical applications.

2022-RA-1480-ESGO TRANSLACOL PROJECT: DIGITAL-PCR HUMAN PAPILLOMA VIRUS (HPV) DETECTION FOR RECURRENCE PREDICTION IN EARLY CERVICAL CANCER PATIENTS WITHOUT PELVIC LYMPH NODE INVASION

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Introduction/Background In early cervical cancer (ECC) patients with nodal metastasis (N+) present worse survival. However, 10–15% of patients without nodal metastasis (N0) present the same survival to N+ patients.As in cervical cancer, HPV DNA could be assimilated to tumoral DNA, we evaluate the presence of HPV DNA in pelvic Sentinel lymph nodes (SLN) by new ultrasensitive droplet-based digital polymerase chain reaction (ddPCR) as a biomarker of survival.

Methodology Inclusion criteria: EEC patients who underwent pelvic SLN detection N0 in pelvic lymph nodes. Associated pelvic lymph nodes samples were available for 60 patients with HPV16, HPV18 or HPV33 positive tumours. In SLN, after DNA extraction, HPV16 E6, HPV18 E7 and HPV33 E6 gene were respectively targeted and detected by ultrasensitive ddPCR optimized on two different platforms, the RainDrop Digital PCR System (RainDance Technologies, Bio-Rad, Hercules, CA) or the Biorad system.We compare two groups according to HPV DNA in SLN: positive or negative.

Results There was no difference between the negative HPV DNA SLN group and the positive HPV DNA SLN group in terms of patients and surgical-pathological characteristics, treatments and time of follow-up. Two patients in negative HPV DNA SLN group and 6 in positive HPV DNA SLN group presented recurrence and the mean time of recurrence was