2022-RA-873-ESGO VALIDATION STUDY OF THE 'NOGGO-GIS ASSAY' BASED ON OVARIAN CANCER SAMPLES FROM THE FIRST-LINE PAOLA-1/ ENGOT-OV25 PHASE-III TRIAL

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Introduction/Background Several clinical trials have demonstrated that the maintenance with a PARP inhibitor with or without bevacizumab following platinum-based therapy improved PFS in advanced ovarian cancer patients. The benefit was significant greater in homologous recombination deficient (HRD) patients according to Myriad myChoice test. The PAOLA-1 olaparib+bevacizumab maintenance regimen was approved in USA/Europe/Japan for HRD and BRCA positive patients. Using sample from the PAOLA-1/ENGOT-ov25 we evaluated the novel 'NOGGO-GIS ASSAY' as part of the ENGOT HRD-European-Initiative.

Methodology A hybrid capture NGS assay based on the Agilent XTH2 chemistry and SNP backbone, was developed for the detection of somatic driver mutations in key cancer genes, BRCA1/2 mutations, HRR gene mutations and HRD in combination with a bioinformatic analysis pipeline based on publicly available tools. The assay was clinically validated using 468 ovarian cancer samples from the PAOLA-1/ENGOT-ov25 trial.

Results Here we report the first results of the 'NOGGO-GIS ASSAY' validation compared to the Myriad myChoice clinical trial. The assay is based on widely available hybrid capture chemistry, to cover 57 genes and approx. 20.000 SNP loci, automated for parallel processing of 48 samples per run and requires 50 ng of genomic DNA extracted from tissue section with at least 30% of tumor content with a low failure rate of around 5%. The performance characteristics of the NOGGO GIS Assay are comparable to the PAOLA-1/ENGOT-ov25 clinical trial assay. The NOGGO GIS Assay showed a similar impact of olaparib +bevacizumab on PFS with a comparable Hazard Ratio for HRD positive patients.

Conclusion The 'NOGGO-GIS ASSAY' based on widely available components was validated on clinical trial samples showing performance characteristics similar to the clinical trial assay. The low failure rate, low input material required, HRD and BRCA1/2 and mutation status in 57 clinically relevant genes makes this a highly attractive option for analysis of FFPE samples.

2022-RA-1023-ESGO EXPRESSION OF P16 AND KI67 IN CERVICAL HIGH GRADE SQUAMOUS INTRAEPITHELIAL LESION IN WOMEN UP TO 30 YEARS OLD

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Introduction/Background Immunohistochemistry is a technique that evaluates the association of biomarkers with morphological changes, offering a higher level of reproducibility, sensitivity, and specificity in the diagnosis of many neoplasms, with p16 associated with high-risk HPV and ki-67 with cell multiplication. The aim is to determine the expression of p16 and Ki67 in high-grade intraepithelial lesions in patients aged 30 years or younger and correlate clinical outcome.

Methodology Retrospective cross-sectional study, that analyzes women diagnosed with HSIL treated at the gynecology outpatient clinic of the University Hospital. Demographic and clinical data and follow-up were collected from the hospital records. Descriptive analyses were expressed by measures of central tendency and dispersion. To identify possible associations between qualitative variables, the chi-square test was used. Spearman correlation were conducted between the variables of interest.

Results The average age of the participants was 27 years, and the majority were healthy 49 (72.1%) and non-smokers 47 (69.1%). Only 21 (30.9%) of them had completed high school and 5 (7.4%) had higher education. Considering the anatomopathological characteristics, most participants had cervical intraepithelial neoplasia (CIN) III (77.9%) and, to a lesser extent, cervical intraepithelial neoplasia (CIN) II (22.1%). Practically all were positive for P16INK4a and Ki67 (97.1% and 98.5%, respectively), and 65 (95.6%) were discharged from the outpatient clinic, with only 1 (1.5%) relapsed during follow-up. The analyzes did not show correlations between any of the variables of interest (e. g. age, age less than or equal to 30 years, parity, smoking and immunosuppression), with the outcomes studied (positive P16INK4a and Ki67) (Spearman correlations, $p>0.05$ for all the analyses). Furthermore, P16INK4a and Ki67 were positively related (Spearman, $\rho=0.702$, $p\leq0.001$).

Conclusion It was not possible to prove that the use of biomarkers helps in the diagnosis and prognosis of precursor lesions in women aged up to 30 years.

2022-RA-1061-ESGO PAGET'S DISEASE OF THE NIPPLE

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Introduction Paget's disease of the nipple corresponds to the infiltration of the nipple-areolar complex by tumor cells. It is a rare condition that can be either isolated or associated, most often, with a homolateral breast cancer. Clinically, it presents as an eczematous rash with an erythematous, exudative or scaly, well-demarcated, slightly infiltrated area, which the patient often describes as a burn on the nipple and areola. The interest of imaging based on echomammography and breast MRI is therefore to look for an underlying cancer. The diagnosis of Paget's disease is made either by cytological scraping of the nipple or, at best, by nipple-areolar biopsy. Its management is conditioned by the presence or not of an underlying breast cancer.

Methodology Five cases of STUMP treated in the department of gynecology-obstetrics I at the CHU Hassan II in Fez between 2018 and 2021 were analyzed retrospectively.

Results Of the 05 patients, we had isolated paget in 1 case, and i twas associated with breast carcinoma in 4 cases All patients had surgical treatment. Anatomopathological analysis of the surgical specimens revealed paget disease of the nipple in all cases.

Conclusion It's important to know the clinical presentation of Paget's disease of the nipple, as well as the interest of imaging and anathomopathological study in the diagnosis of these lesions. To finally define the principles of therapeutic management.

2022-RA-1142-ESGO CYTOLOGICAL FEATURES OF GYNECOLOGIC TRACT CARCINOMAS WITH NEUROENDOCRINE DIFFERENTIATION

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Introduction/Background Gynecologic neuroendocrine carcinomas are rare, aggressive malignancies. The most common site is the cervix followed by the endometrium, ovary, vagina and vulva. Histological subtype and site of origin are major prognostic factors. We sought to characterize the cytomorphological features of these malignancies and compare them with histologic features.

Methodology Institutional databases were queried for gynecologic neuroendocrine carcinomas diagnosed between 2000 and 2021. All available cytological and surgical specimens were reviewed by 3 pathologists to evaluate the cytological and histopathological characteristics.

Results There were 22 patients (aged 29–74 years, median 48 years). Primary sites included cervix (n=13, small cell carcinoma), ovary (n=6; 3 small cell carcinoma of hypercalcemic type and 3 small cell neuroendocrine carcinoma) and endometrium (n=3; 2 small cell carcinoma and 1 large cell carcinoma). Results are summarized in table 1.Most cases showed round-to-oval nuclei with irregular contours. Among cervical specimens, common features were high cellularity, high nuclear: cytoplasmic ratio and moderate pleomorphism. Nuclear molding, naked nuclei, coarse chromatin and the absence of nucleoli were more prominent in cytologic specimens; mitoses, apoptosis, necrosis and the presence of rare nucleoli were more prominent in surgical specimens.In ovarian carcinomas, high nuclear:cytoplasmic ratio, naked nuclei, small to intermediate nucleoli and finely or coarsely granular chromatin were more prominent in cytologic specimens. Nuclear molding, mitoses and necrosis were more prominent in surgical specimens.For endometrial tumors, common cytological features included high cellularity, small clusters to single cells, high nuclear:cytoplasmic ratio, moderate pleomorphism, finely or coarsely granular chromatin, mitoses, and apoptosis.

Conclusion Given the rarity of neuroendocrine carcinomas arising in the gynecologic tract, a high index of suspicion is important when encountering neuroendocrine-like morphologic features in cytologic specimens in patients with suspected gynecologic malignancy. Careful attention to the morphology and confirmatory immunochemistry and molecular testing is important for accurate diagnosis.

Abstract 2022-RA-1142-ESGO Table 1 Summary of predominant cytomorphologic and histologic findings

Neuroendocrine Carcinoma	Cervical		Ovarian		Endometrial	
Specimen	Cytologic	Surgical	Cytologic	Surgical	Cytologic	Surgical
Cellularity	High	High	High	High	High	N/A
Architecture	3D clusters to single cells	Trabecular to a nested	3D clusters to single cells	Nested or nested and sheets	Small clusters and single cells	N/A
N/C ratio	High	High	High	Moderate	High	N/A
Nuclear Shape	Round to oval	Round to oval	Round to oval	Round to oval	Round to oval	N/A
Nuclear Contour	Irregular	Irregular	Irregular	Smooth to slightly irregular	Irregular	N/A
Nuclear Molding	Prominent	Prominent to Focal	not prominent	not prominent	Prominent	N/A
Nuclear Pleomorphism	Moderate	Moderate	Significant	Mild	Moderate	N/A
Chromatin Quality	Coarse to salt and pepper	Salt and pepper only	Coarse to salt and pepper	Salt and pepper only	Coarse to salt and pepper	N/A
Naked Nuclei	Present	Absent	Present	Absent	Present	N/A
Nucleoli	Absent	Rare single and small	Single small to intermediate	Rare single and small	Absent	N/A
Mitotic Figures	Frequent	Frequent	Frequent	Frequent	Frequent	N/A
Apoptotic Bodies	Significant	Significant	Significant	Rare to Absent	Significant	N/A
Necrosis	Not readily identifiable	Not readily identifiable	Not readily identifiable	Readily identifiable	Absent	N/A