#371 TRIAGING OF HPV PCR-BASED CERVICAL CANCER SCREENING RESULTS BY INNOVATIVE BIOMARKER MRNA-BASED ASSAYS FOR REDUCTION OF OVER-REFERRAL AND OVERTREATMENT

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Introduction/Background WHO guidelines recommend HPV-PCR testing for primary screening. Due to low specificity (~20%) for detecting true dysplasia triage is necessary to avoid over-diagnosis and overtreatment. Because of its higher specificity (~60–80%), mRNA-based testing of cellular transformation-specific biomarkers is highly accurate in detecting clinically relevant pre-cancer. We report results of an innovative mRNA assay (QuantiGene-Molecular-Profiling-Histology, QG-MPH) on samples from real-world HIC and LMICs screening/triage routine and its potential to detect pre-cancer compared to standard of care.

Methodology QG-MPH (ThermoFisher) and targeted sequencing (ciRNAseq, Predica) were used for multiplexed mRNA quantification of 18 HR-HPV-oncogenes and cellular-biomarkers in cervical smear samples. Accuracy to identify CIN2+, CIN3+ and invasive cancer was calculated on condition-specific risk scores (ROC analysis: AUC >80% for CIN2/3 and > 92% for invasive cancer). Study smear samples from screening and triage populations in HIC (n=550, n=719) and LMIC (n= 893, n=110), respectively, were reanalyzed and results compared to standard of care assays. Study results were descriptively evaluated in the given context.

Results The QG-MPH assay discriminated <CIN2/CIN2+ lesions with higher accuracy than cytology or PCR. QG-MPH assay outperformed cytology (sens. >80% vs 50%; spec. 83% vs 80%) and PCR-based or co-testing strategies (sens. 83% vs 80%; spec. >80 vs 25–70%), respectively. Results are comprehensive diagnoses from the first screening smear within 48h. It reports i) 18 HR-HPV genotypes individually, ii) identifies and discriminates <CIN2 vs CIN2+ vs CIN3+ vs invasive cancer and iii) is prognostic for lesion development. Its high accuracy supports decision making on treatment strategies. Low complexity workup, robust transportable instruments and assay cost comparable to PCR-based tests allows use in LMIC.

Conclusion Molecular biomarker-based mRNA testing has the potential to solve current diagnostic problems of cervical cancer screening. Higher assay accuracy can reduce over-referral and restrict treatment to progressive lesions when indicated by biomarker expression reducing overtreatment of regressive dysplasia.

Disclosures QG-MPH patented by Charite-Universitaetsmedizin Berlin.

ciRNAseq patented by WL.

#408 SCORING SYSTEM FOR PREDICTING 3 AND 5-YEAR RECURRENCE IN EARLY-STAGE ADENOCARCINOMA OF CERVIX AFTER RADICAL HYSTERECTOMY

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Introduction/Background The purpose of this study is to develope a scoring system for predicting recurrence in early-stage adenocarcinoma of cervix after radical hysterectomy.

Methodology The medical records of 322 patients with stage IA2-IIB cervical cancer with adenocarcinoma who underwent radical hysterectomy were retrospectively reviewed.

Results There were 44 (13.7%) recurrences during the 57.6 months of median follow up period. The clinico-pathologic characteristics were analyzed with the univariate Cox proportional hazard method. Bootstrap resampling was performed 1,000 times for factors which showed statistical significance in this analysis. Histologic type, lymph node metastasis

(LNM), parametrial invasion, and lympho-vascular space invasion showed bootstrap higher than 500 and these factors were included in multivariate analysis and incorporated to build a scoring system. This model showed better accuracy in terms of concordance (C) index in predicting recurrence than FIGO stage, adjusted FIGO stage, LNM, and risk group (0.817 vs

0.541, 0.778, 0.738, and 0.778; respectively). The calibration plot for recurrence also showed good calibration.

Conclusion We have developed a robust scoring system that can provide accurate prediction of the recurrence in patients with adenocarcinoma of cervix.

Disclosures none

#413 INTEGRATED GENOMIC AND TRANSCRIPTOMIC ANALYSIS REVEAL THE ACTIVATION OF PI3K SIGNALING PATHWAY IN NON-HPV-ASSOCIATED CERVICAL CANCER

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Introduction/Background Cervical cancers are one of the most threatening female reproductive system tumors worldwide. Of whom, Non-HPV-associated cervical cancers (NHPV-CCs) are rare and poorly understood, yet associated with poorer outcomes compared to HPV-associated cervical cancers. To shed light on the molecular tumorigenesis of NHPV-CCs, we performed an integrated genomic and transcriptomic analysis to identify the characteristics of NHPV-CCs.

Methodology Twenty-five out of 1010 cervical cancer patients were identified to be HPV-negative by PCR, RT-PCR, and RNA-seq in our cancer center in 5 years. Genomic alterations and transcriptomic differences were profiled by whole exome sequencing (WES) and RNA-seq in all 25 patients. The TCGA-CESC cohort was analyzed for validation. The efficacy of PI3Kα inhibitor BYL719 in NHPV-CCs was detected in cell lines and patient-derived xenografts (PDX).

Results NHPV-CCs were characterized by poor prognosis and high tumor mutation burden compared to HPV-associated cervical cancers, as PIK3CA listing the top genomic alteration (36%). The PI3K/AKT signaling and FGFR signaling were significantly enriched in NHPV-CCs in both cohorts. The PI3Kα