548 PROGNOSTIC BIOMARKERS FOR ATYPICAL ENDOMETRIAL HYPERPLASIA: A MINI REVIEW

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Introduction/Background* Atypical hyperplasia (AH) or endometrioid intraepithelial hyperplasia (EIN) refer to a pre-cancerous proliferation of the endometrial glands resulting in an increased ratio of glands to stroma (>3:1). We aimed to identify Immunohistochemistry (IHC) biomarkers to distinguish AH/EIN lesions associated with synchronous endometroid cancer (EC) or imminent progression to EC.

Methodology We performed a structured review of the published evidence on MEDLINE from inception to March 6, 2021 and selected the 5 most common "themes" (IHC biomarkers) as defined by the number of available studies and/or specimens included. We synthesised the evidence to provide a consensus on their prognostic value (synchronous cancer or imminent progression).

Result(s)* We identified 52 studies from 18 countries. The 5 most discussed biomarkers ("themes") were: Phosphatase and TENsin homolog (PTEN), stromal expression of p16 protein, nuclear localisation of b-catenin, Paired box gene 2 (PAX2), B-cell Lymphoma 2 expression (bcl-2). PTEN loss in AH was associated with increased risk of Endometrial Cancer (EC). Increased stromal p16 was observed in most EC specimens as well as AH compared to benign; EC had the highest expression. Nuclear β-catenin expression seems to increase from benign to pre-malignant AH but not from pre-malignant to EC. A progressive decrease of PAX2 expression was noted in transition from AH to EC.

Conclusion* Identification of the most common IHC biomarkers whose expression alter during the transition from benign to AH and subsequently EC can flag those cases that immediate definitive management with hysterectomy is needed. This is important when fertility plan is an argument against hysterectomy. Introduction of artificial intelligence algorithms provides the advantage of integrating multiple diagnostic markers in a single prognostic model.

760 INFLAMMATORY IMMUNE MICROENVIRONMENT IN CERVICAL HIGH-GRADE SQUAMOUS INTRAEPITHELIAL LESIONS PREDICTS RESPONSE TO TOPICAL IMIQUIMOD IMMUNOTHERAPY

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Introduction/Background* The treatment of cervical high-grade squamous intraepithelial lesion (cHSIL) by topical imiquimod (Aldara®) is investigated as an alternative for surgical large loop excision of the transformation zone (LLETZ), because of the latter's risk of causing cervical insufficiency and subsequent premature birth in following pregnancies. Imiquimod is effective in ~60% of cHSIL patients, at present we are not able to select women likely to succesfully respond. Therefore, studies on predictive biomarkers are needed to enable personalised therapy and to prevent unnecessary potential side effects. Here, we performed an in-depth analysis of the role of the pre-existing immune microenvironment in cHSIL in response to topical imiquimod.

Methodology Histologically confirmed cHSIL of 35 patients biopsied before and 10 weeks after treatment with topical imiquimod were analyzed by two multispectral seven-color immunofluorescence panels to investigate the T cell (CD3, CD8, FOXP3, PD1, TBET, TIM3, DAPI) and Myeloid cell (CD68, CD163, CD11c, CD14, CD33, PDL1, DAPI) composition in relation to treatment response. All 70 samples were scanned with the Vectra multispectral imaging system. Cells were automatically identified using a deep learning multispectral image analysis approach (inForm software).

Result(s)* Our data show that the immune microenvironment of complete responders (CR) prior to imiquimod therapy is characterized by a coordinated infiltration with T helper cells (activated PD1+/type 1 Tbet+) and pro-inflammatory M1 macrophages (CD68+CD163-) and dendritic cells (CD11c+). The lesions of non-responders (NR) lacked such a pro-inflammatory response and displayed an impaired influx of these pro-inflammatory lymphoid and myeloid cells. In contrast, the NR showed an increased infiltration by immunosuppressive regulatory T cells (CD3+FOXP3+). After 10 weeks of topical imiquimod application, the influx of pro-inflammatory CD4+ and CD8+ T cells was further increased in the CR but not in the NR patients, and the infiltration by macrophages was decreased.

Conclusion* Response of cHSIL to topical imiquimod is associated with the presence of a pre-existing pro-inflammatory process, resulting in the coordinated influx of several types of immune cells, which is then further amplified. Our findings indicate major potential of the immune microenvironment as predictive biomarker for the selection of cHSIL patients responding to topical imiquimod immunotherapy.

793 PATIENT-DERIVED ORGANOIDS REFLECT INTRA-TUMOURAL HETEROGENEITY IN HIGH GRADE SEROUS OVARIAN CANCER

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Introduction/Background* High Grade Serous Ovarian Cancer (HGSOC) frequently presents at an advanced stage with widespread disseminated disease. The majority of patients will ultimately relapse and develop platinum resistance. HGSOC is characterised by a high degree of genomic instability and heterogeneity which is not accounted for in current 2D cell line and murine models. 3D ex-vivo models such as patient-derived organoids (PDOs) are better able to recreate tumour