p53 immunohistochemistry on 39.4% with a sensitivity of 98.5% to detect p53abn (99.6% negative predictive value). Cytologic features including tumor giant cells, smudged chromatin, cherry-red/macronucleoli, and atypical mitoses accurately predicted p53abn. In 7/292, p53abn upgraded ESGO risk groups (2 to intermediate-risk, 5 to high-risk). EEC12/stage IA patients had an excellent cause-specific 5-year survival of 98.5%.

Conclusions Pathologists can select cases for p53 testing with high sensitivity and low risk of false negativity. Molecular characterization of endometrial carcinomas has great potential to refine ESGO risk classification for a small subset but offers little value for approximately half of endometrial carcinomas, namely, EEC12/stage IA.

EPV104/#228 EMERGING IMMUNOTHERAPY PARADIGMS IN ADVANCED ENDOMETRIAL CANCER: THE EFFECT OF ONLINE EDUCATION ON CLINICIAN KNOWLEDGE AND CONFIDENCE

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Objectives This study determined whether online continuing medical education (CME) could improve the knowledge of oncologists (oncs) and obstetricians/gynaecologists (obs/gyns) regarding the rationale and evidence for immunotherapy paradigms in advanced endometrial cancer.

Methods A 30-minute online video lecture was launched for physicians outside the USA August 2020 with data collected to November 2020. Educational effect assessed with repeated-pairs pre-/post-activity- individual participants serving as own control. 3 multiple-choice, knowledge questions and 1 self-efficacy, 5-point Likert scale confidence question were analyzed. Chi-squared test assessed pre- to post-activity change (5% significance level, P <.05). Magnitude of change in total number of correct responses overall, and for each question, determined with Cramer's V (<.06=Modest, 0.06–0.15=Noticeable, 0.16–0.26=Considerable, >.26=Extensive).

Results 142 obs/gyns and 60 oncs completed pre- and post-activity questions. Positive educational effect was observed for obs/gyns (noticeable effect, V=.092, P<.01; average% of correct responses increasing from 33 to 42%) and oncs (noticeable effect, V=.150, P=.0043; average% of correct responses increasing from 47 to 62%). Increases in correct responses post-activity seen for questions on response to 2nd line chemotherapy (% relative improvement, obs/gyn: 23%, oncs 22%), rationale for immunotherapy (obs/gyns: 24%, oncs: 72%), data for the dostarlimab GARNET trial (obs/gyns: 36%, oncs: 21%). Confidence in knowledge of the evidence for immunotherapy strategies increased post-activity (total average confidence shift: 27% obs/gyns and 40% oncs). Overall, 22% of learners' responses were improved and 39% of learners' responses were reinforced.

Conclusions This online CME activity resulted in a positive educational impact for both clinical specialties. However, education gaps remained evident post-activity.

EPV105/#237 COMBINATION TARGETED TREATMENT WITH MEK AND PAN-ERBB INHIBITORS ENHANCES ANTITUMOR ACTIVITY IN ERBB AMPLIFIED EX-VIVO SEROUS ENDOMETRIAL CANCER CELLS

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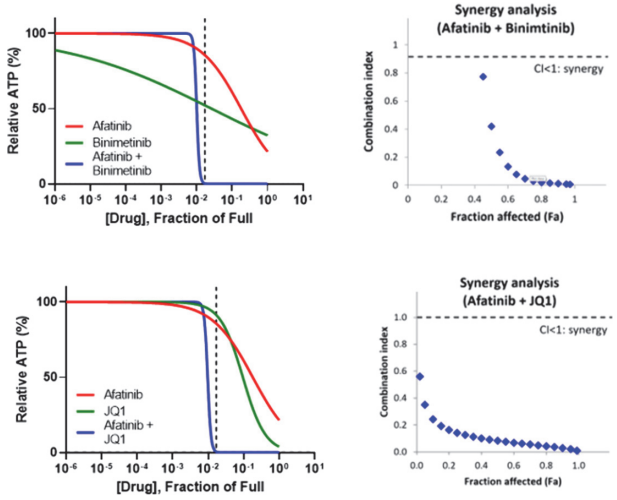
Objectives ERBB pathway alterations present therapeutic targets in high grade endometrial cancer (EC), but efficacy can be limited by persistent co-activation of other ERBB binding partners. The efficacy of dual-inhibition MEK+pan-ERBB or BET+pan-ERBB in an ERBB2/ERBB3 amplified EC was investigated via 3D microcancer ex-vivo cell assay.

Methods Tumor was prospectively collected from a patient with stage IIIc1 serous EC. Whole exome, mRNA, and Mate-Pair genomic characterization was performed. Tumor cells were grown in 3D culture and subjected to titrating drug treatments. Cell viability was determined by the CellTiter-Glo Luminescent Assay. Data transformation and dose-response curves were generated using GraphPad PRISM using the variable slope model. CalcuSyn software with the Chou-Talalay method analyzed drug interactions and synergy. Afatinib, binimetanib, and JQ1 were used to inhibit pan-ERBB, MEK1/2, BET, respectively. For translational relevance, inhibitory effect was defined as percent reduction in ATP from baseline at the



Abstract EPV105/#237 Figure 1 Microcancer ex vivo exposure to MEK+pan-ERBB inhibitors. Dose response curves of single and combination treatments (left) were 10-fold titrated across 8 log doses for each agent. The highest concentration (i.e. fraction of ful (FoF)=1) of afatnib, binimetinib and afatinib+JQ1 was 3 uM, 10 uM, and 50 uM, respectively. The physiologically achieavable concentration of afatinib is insicated (dotted lines). A comnination index (CI, right) was used to assess synergy with afatinib+binimtinib and afatinib+JQ1 as shown by Fa-CI plots.

physiologically achievable concentration (maximum plasma concentration (Cmax) value).

Results Sequencing revealed amplifications of ERBB2 (17q12), RAF1, c-myc, and ERBB3 (12q13.2) low-level gain. Inhibition of viability was moderate by single agents: Afatinib, binimetanib, JQ1, as shown by inhibitory effect values of 14.4%,47.8%, 8.8%, respectively at physiologically achievable concentrations (Cmax) of afatinib. Combinations demonstrated increasing inhibitory effect values: 99.7% for Afatinib+ binimetanib, and 99.5% for Afatinib+JQ1. Synergy was evidenced for both combinations by a combination index <1 (figure 1).

Conclusions Combined inhibition of pan-ERBB with inhibition of MEK or BET proteins synergistically suppress viability in patient-derived serous EC harboring ERBB amplifications.

EPV106/#249 ENDOMETRIAL CANCER IMMUNOHISTOCHEMICAL RISK STRATIFICATION IN A LARGE UTERINE-CONFINED CANCER SERIES

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Objectives The aim of this study is to assess the clinical reproducibility and the oncological validity of the Endometrial cancer (EC) risk stratification based on the molecular information given by the immunohistochemistry (IHC).

Methods Retrospective IHC analyses were conducted in a large series of 778 pre-operative uterine-confined ECs, studying the presence/absence of MLH1, MSH2, MSH6, to define the mismatch repair (MMR) stable or instable phenotype; the presence of p53 mutations and other molecular features. The molecular profile was correlated with histological, clinical and prognostic EC patients' data.

Results Based on the IHC, we defined 3 EC populations: MMR stable (MMRs), instable (MMRi) and p53 mutated (p53+) patients. Our result demonstrated that the IHC stratification statistically correlated with the most relevant anatomo-clinical features: FIGO stage (p<0.001), grading (12,5% G3 in MMRs vs 22.9% in MMRi vs 95.3% in p53+, p<0.001), histotype (Type II 6.2% in MMRs vs 5.3% in MMRi vs 87.5% in p53+, p<0.001), presence of LVSI (positive in 16.3% in MMRs vs 23.8% in MMRi vs 38.7% in p53+, p<0.001), myometrial invasion and tumor dimension (p=0.003 and p<0.001 respectively). Again, the 3 IHC populations statistically reflected the EC risk class ESGO-ESMO-ESP classification 2020 (p<0.001). These results were confirmed also in Kaplan-Meier curves in terms of over-all survival (OS) and disease-free survival (DFS) (p<0.001) (figure 1).

Conclusions In this large series, we demonstrated that the pragmatic and systematic use of IHC may have an important role to properly stratify, in terms of histological features and clinical outcome, the uterine-confined EC patients.

EPV107/#258 ENGOT-EN11/GOG-3053/KEYNOTE-B21: PHASE 3 STUDY OF PEMBROLIZUMAB OR PLACEBO IN COMBINATION WITH ADJUVANT CHEMOTHERAPY WITH/WITHOUT RADIOTHERAPY IN PATIENTS WITH NEWLY DIAGNOSED HIGH-RISK ENDOMETRIAL CANCER

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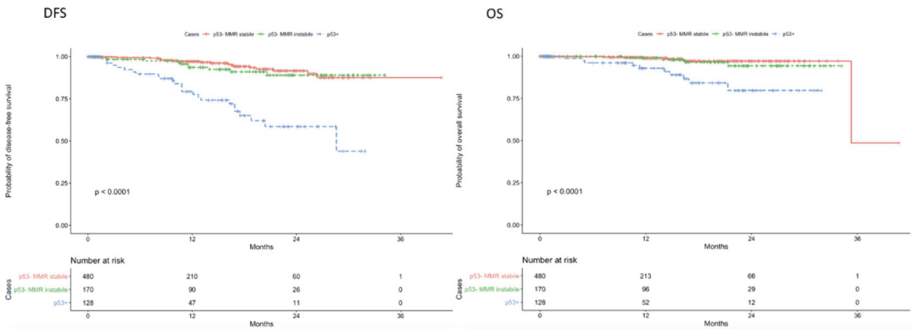
Objectives Pembrolizumab, an anti–PD-1 antibody, has demonstrated activity as monotherapy and in combination with lenvatinib in patients with previously treated mismatch repair (MMR) deficient and MMR proficient endometrial cancer (EC). ENGOT-en11/GOG-3053/KEYNOTE-B21 (NCT04634877) is a phase 3, randomized, double-blind study of pembrolizumab or



Abstract EPV106/#249 Figure 1