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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 unstable 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), unstable (MMRi) and p53 mutated (p53+) patients. Our result demonstrated that the IHC stratification statistically correlated with the most relevant anatomical 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

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