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

[1]E Perrone*, [2]F De Felice, [3]I Capasso, [4]D Arciuolo, [1]E Distefano, [1]D Lorusso, [4]GF Zannoni, [1]G Scambia, [1]F Fanfani. *[1]Fondazione Policlinico Universitario A. Gemelli, IRCCS, Uoc Ginecologia Oncologica, Dipartimento Per La Salute Della Donna E Del Bambino E Della Salute Pubblica, Rome, Italy; [2]Policlinico Umberto I, 'Sapienza' University of Rome, Department of Radiotherapy, Rome, Italy; [3]Policlinico universitario Agostino Gemelli, Uoc Ginecologia Oncologica, Roma, Italy; [4]Fondazione Policlinico Universitario A. Gemelli, IRCCS, Gyneco-pathology and Breast Pathology Unit, Dipartimento Per La Salute Della Donna E Del Bambino E Della Salute Pubblica, Rome, Italy*

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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

[1]T Van Gorp*, [2]M Mirza, [3]A Lortholary, [4]I Vergote, [5]D Cibula, [6]A Walther, [7]A Savarese, [8]M-P Barretina-Ginesta, [9]F Ortaç, [10]C Papadimitriou, [11]L Bodnar, [12]C-H Lai, [13]K Hasegawa, [14]X Xie, [15]EL Barber, [16]RL Coleman, [17]S Keefe, [17]R Orlowski, [18]B Slomovitz. *[1]UZ Leuven, Gynaecological Oncology, Leuven, Belgium; [2]NSGO-CTU and Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark; [3]Centre Catherine de Sienne, Hôpital Privé Du Confluent, Nantes, France; [4]BGOG and University Hospitals Leuven, Leuven Cancer Institute, Leuven, Belgium; [5]Department of Obstetrics and Gynecology, General Faculty Hospital In Prague, First Faculty of Medicine, Charles University, Prague, Czech Republic; [6]Bristol Cancer Institute, University Hospitals Bristol, Bristol, UK; [7]Department of Medical Oncology, Istituto Nazionale Tumori Regina Elena, Rome, Italy; [8]Catalan Institute of Oncology and Girona Biomedical Research Institute, Medical School University of Girona, Girona, Spain; [9]Department of Obstetrics and Gynecology, Ankara University School of Medicine, Ankara, Turkey; [10]Aretaieio University Hospital, National and Kapodistrian University of Athens, Athens, Greece; [11]Department of Oncology and Immunooncology, Warmian-masurian Cancer Center of The Ministry of The Interior and Administration's Hospital, Olsztyn, Poland; [12]TGOG and Department of Gynecology and Obstetrics, Chang Gung Memorial Hospital, Linkou Branch, Taoyuan, Taiwan; [13]Department of Gynecologic Oncology, Saitama Medical University, Hidaka, Saitama Prefecture, Japan; [14]Women's Hospital, School of Medicine, Zhejiang University, Hangzhou, China; [15]Department of Gynecologic Oncology, Northwestern University Feinberg School of Medicine, Chicago, USA; [16]Department of Gynecologic Oncology, Us Oncology Research, The Woodlands, USA; [17]Oncology, Merck and Co., Inc., Kenilworth, USA; [18]Department of Gynecologic Oncology, Broward Health, Fort Lauderdale, USA*

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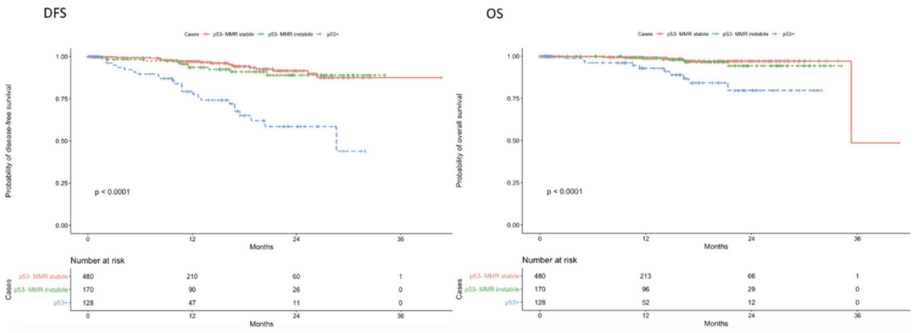
Objectives Pembrolizumab, an anti–PD-1 antibody, has demonstrated activity as monotherapy and in combination with lenvatinib in patients with previously treated mismatch repair (MMR) deficient and MMR proficient endometrial cancer (EC). ENGOT-en11/GOG-3053/KEYNOTE-B21 (NCT04634877) is a phase 3, randomized,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



Abstract EPV106/#249 Figure 1

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