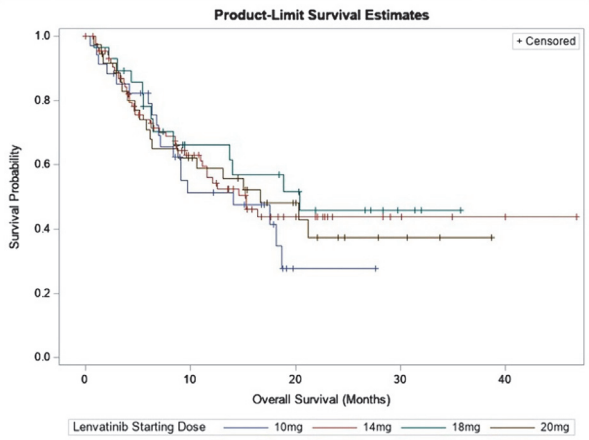

Abstract PR023/#503 Figure 2

9.7% carcinosarcoma, 10.1% mixed, and 2.8% clear cell. 82.9% were MMRp and 4.6% were MMRd. Median dose intensity of lenvatinib was 14 mg. Lenvatinib starting dose was 20 mg in 17.1%, 18 mg in 12.9%, 14 mg in 41%, 10 mg in 15.7%. Rates of any grade >=3 AE related to lenvatinib were 20 mg (13.5%), 18 mg (17.9%), 14 mg (7.9%), 10 mg (17.6%) (p=0.31). Pembrolizumab dosing was 200 mg Q3W in 85.6% and 400 mg Q6W in 6.5%. ORR (p=0.38), PFS (p=0.97) & OS (p=0.31) were similar in White vs. Black patients. ORR in relation to Lenvatinib starting dose 20 mg, 18 mg, 14 mg, 10 mg was 27%, 35.7%, 39.3%, 44.1% (p=0.08). In relation to Lenvatinib starting dose, 12-month PFS rates were 40%, 35%, 35%, 47% respectively (p=0.92), 12-month OS were 59%, 66%, 56%, 51% respectively (p=0.79), and median duration of therapy was 5.1, 4.1, 4.8, 4.6 months respectively (p=0.52).

Conclusion/Implications In a real-world analysis, the predominant starting dose is 14 mg lenvatinib and 200 mg pembrolizumab. Grade >=3 AE's, 12-month PFS/OS, ORR & duration of therapy related to lenvatinib starting dose were not statistically different.

PR024/#394 MOLECULAR PROFILING OF P53 MUTANT ENDOMETRIAL CANCER REVEALS DISTINCT SUBGROUPS WITH OPPORTUNITIES FOR PERSONALIZED THERAPEUTIC APPROACHES

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Introduction Endometrial cancer (EC) can be classified into four molecular subgroups: POLE mutant, MSI/dMMR, non-specific profiles and P53 mutant (P53mut). P53mut EC comprise ~20% of cases and have the worst prognosis. There is an urgent medical need to better understand P53mut EC in order to propose effective new therapeutic strategies.

Methods We conducted a retrospective analysis of P53abn EC patients from PORTEC3 (NCT00411138) with available DNA for a large-scale panel sequencing (Discovery Cohort). Results were confirmed on an independent cohort of EC patients (Gustave Roussy, France and National University Cancer Institute, Singapore) identified by their molecular profile using FoundationOneCDX or FoundationOne Liquid CDX panel (Validation Cohort). Molecular findings were correlated with clinicopathologic features from medical record review.

Results 39 P53abn cases were included in the discovery cohort. Molecular profiling was able to distinguish 4 mutually exclusive subgroups: CCNE1 amplified (15%), ERBB2 amplified (21%), PTEN alteration (21%) and a non-specific group. In the Validation Cohort, 71 P53mut EC patients were included. Median age was 66 years, 40% were serous, 30% endometrioid and 20% carcinosarcoma. 38% presented with primary metastatic diseases. We detected the same four molecular subgroups defined by CCNE1amp (13%), ERBB2amp (16%), and PTEN mutation or loss (34%). Only two patients (3%) harbored co-alterations. We did not observe any overall survival difference between these subgroups.

Conclusion/Implications Among P53mut EC, we detected 3 nearly mutually-exclusive molecular subgroups: CCNE1 amplified, ERBB2 amplified and PTEN loss, accounting together for 60% of cases. Whether these subgroups might benefit from personalized therapeutic strategies is currently being explored.

PR025/#182 PROTEOGENOMICS DELINEATE PATHOGENESIS, MOLECULAR CHARACTERISTICS, AND PREDICTORS OF PROGESTIN RESPONSE IN EARLY-ONSET ENDOMETRIOID ENDOMETRIAL CANCER

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Introduction Endometrial carcinoma (EC) remains a public health concern with a growing incidence particularly in younger women. Women with early-onset endometrioid EC (EEEC) who wish to maintain fertility are a worldwide concern, and biomarkers for predicting which patients will respond to progestin-based fertility-sparing therapy are a major unmet clinical need.

Methods To comprehensively characterize the proteogenomic characteristics of the early-onset endometroid endometrial carcinoma (EEEC), we conducted a multi-omics study (genomics, and proteomics) with FFPE tissues from paired tumor and normal tissues of 222 endometrioid ECs (including 81 EEECs younger than 40 who mainly received fertility-sparing treatment) and 14 atypical endometrial hyperplasia (AEH) patients from Tongji and Fudan Hospital (TJFD cohort) in China.

Results EEEC was featured by exclusive germline muataions,a higher BMI and downstream dysregualted lipid metabolism