an NGS panel, identifying challenges in case classification and possible solutions.

**Methodology** We performed the FoundationOne CDx NGS panel on 60 EC and assigned molecular subtype: POLE mutated (POLEmut), mismatch repair deficient (MMRd), pi3 abnormal (pi3abn) or no specific molecular subtype (NSMP).

**Result(s)** In 55 patients the molecular classification was successful. A pathogenic POLE mutation was detected in 9 cases (POLEmut). 20 were MMRd (12 MSI-high, 8 MSI-indeterminate based on the NGS panel MSI classifier) and a known or presumed mismatch repair (MMR) gene mutation was found in 7 of these. Of the remaining 26 cases, 17 carried a TP53 mutation (p53abn) and the remaining 9 were considered to be NSMP. The tumor mutation burden (TMB) was significantly different (p<0.001) in the molecular subtypes (A) and high TMB (>55 mut/MB) was 100% specific for POLEmut EC (p<0.001). High TMB was specific for known pathogenic POLE mutations and was not elevated in cases with solely non-pathogenic POLE mutations (B).

In non-POLEmut cases, TMB was higher in MSI-high and MSI-indeterminate than microsatellite stable (MSS) cases (C), and a TMB of >7 mut/MB was 100% specific for MMRd EC. There was one MSS EC with a TMB of 18 mut/MB but it showed loss of MLH1 and PMS2 proteins on immunostaining and was classified as MMRd.

**Conclusion** An NGS panel can be used in the molecular classification of EC when there is sufficient tumor cellularity. TMB can be used as an adjunct in molecular subtype diagnosis for tumors that are difficult to classify. Additionally, TMB can potentially serve as a diagnostic adjunct in cases with POLE mutation of unknown significance.
Introduction/Background Transvaginal ultrasound scanning (TVUS) to measure the endometrial thickness (ET) has historically been recommended as a first-line investigation of patients with postmenopausal bleeding. The aim of the study was to determine the diagnostic performance of endometrial thickness measured by transvaginal sonography in diagnosing endometrial cancer with postmenopausal bleeding. The following data were extracted from the patient records: age at sampling, age at menopause, parity, body mass index (BMI), American Society of Anesthesiologists physical status rating (ASA), history of hypertension and diabetes, endometrial thickness and the histology from the endometrial sampling. The endometrial thickness measurement was acquired in the mid sagittal plane at the thickest part. All patients underwent D&C, with optional previous hysteroscopic evaluation (at the discretion of the attending) under general anesthesia.

Result(s) A total of 158 patient records that met the criteria were identified. The prevalence of endometrial cancer was 15.2%. Endometrial thickness was a statistically significant independent predictor of the presence of endometrial cancer and atypical endometrial hyperplasia (OR 1.19 95% CI 1.09-1.29 for each 1mm increase in thickness, p<0.001). The ROC curve analysis in our study had an AUC of 0.83 (p<0.001) and identified a cut-off level for endometrial thickness of 8mm which was associated to a sensitivity of 88.9%, specificity of 65.6%, PPV of 34.8% and NPV of 96.6% for the detection of endometrial cancer. Using a cut-off for endometrial thickness of ≤3mm achieved 100% sensitivity.

Conclusion None of the analyzed cut-off points for endometrial thickness achieved optimal diagnostic accuracy, as all cut-off values associated to sensitivity rates above 95% had false positive rates of over 60%. Nevertheless, an endometrial thickness cut-off of 3mm, due to the associated high sensitivity, can safely be used to identify women with postmenopausal bleeding who are highly unlikely to harbor endometrial cancer and that can forego initial endometrial sampling.