00120 Spectrum of TP53 Mutations and p53 Immunohistochemical Staining Characteristic on POLE Mutated Grade 3 Endometrioid Endometrial Carcinomas, a Single Institution Study.

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Aims: Grade 3 endometrioid endometrial carcinomas (Gr3 EECs) with POLE mutations are associated with good prognosis. In contrast, uterine serous carcinomas (USCs) are associated with poor prognosis, characterized by TP53 mutations and p53 protein immunohistochemical (IHC) positive staining. EEC mutational profiling into subgroups is used for therapeutic management in some countries. We aimed to study the TP53 mutational spectrum and p53 IHC staining characteristics of somatic POLE mutated Gr3 EECs.

Methodology: Twelve clinically well annotated KKH patients with follow up data, diagnosed with Gr3 EEC between 2009 and 2013 and harbouring POLE mutations were identified from a previously published dataset. Somatic TP53 mutations with at least 10% allele frequency were analyzed to identify mutation types and common functional hotspots (R175, G245, R248, R249, R273, and R282). Only mutations present in the Catalogue of Somatic Mutations (COSMIC) database and classified as pathogenic were included. Formalin fixed paraffin embedded (FFPE) tissue sections from ten cases were available for study and were stained with p53 IHC (D07 RTU; Ventana) according to the manufacturer's instructions. Using the PORTEC4a clinical trial criteria, tumours with p53 strong and diffuse staining > 90% of tumour or localized over a well demarcated tumour area (>1cm) were considered positive.

Result: All 12 patients with somatic POLE mutated Gr3 EEC demonstrated 100% recurrence free survival (median follow-up 52.5) at time of censure. Three cases harboured missense pathogenic somatic TP53mutations. No splice, nonsense, frameshift mutations or common functional hotspot mutations were identified. p53 IHC was available in two of the TP53 mutated cases. Both were p53 IHC negative. One showed focal localized p53 IHC positivity (<10%) and one showed no staining.

Conclusion: Somatic TP53 mutations can occur in POLE mutated Gr3 EECs. Over reliance on mutational profiling without full appreciation of p53 IHC results and morphology can result in misdiagnosis of prognostically poor USCs.