P53 IMMUNOHISTOCHEMISTRY AS A SURROGATE FOR *TP53* MUTATIONAL ANALYSIS IN ENDOMETRIAL CANCER BIOPSIES

Naveena Singh[1], Anna Piskorz[2], Tjalling Bosse[3], Mercedes Jimenez-Linan[4], Arjun Jeyarajah[1], Ranjit Manchanda[1], C Blake Gilks[6], James Brenton[2], Martin Köbel[7]

[1]Barts Health NHS Trust, London, UK; [2]University of Cambridge, Cambrige, UK; [3]University of Leiden, Leiden, The Netherlands; [4]Addenbrooke's Hospital, Cambridge, UK; [5]Vancouver General Hospital, Vancouver, British Columbia, Canada; [6]University of Calgary, Calgary, Alberta, Canada

Background and Aims

p53 immunohistochemistry (IHC) has high specificity for *TP53* mutation in ovarian carcinoma. Four molecular subtypes of endometrial carcinoma (EC) have been identified; accuracy of p53 IHC as a surrogate for *TP53* mutation and thereby for serous-like EC is not established. We aimed to test whether p53 IHC predicts *TP53* mutation in EC biopsies, universally and/or as part of a molecular classification algorithm and to compare interpretation results of p53 IHC between laboratories.

Methods

200 EC biopsies were selected from 5 histopathology laboratories to include serous:non-serous high grade:G1-2 endometrioid EC in a 2:1:1 ratio. Local p53 IHC results were compared to central reference results. Central p53 IHC results were compared to tagged-amplicon NGS *TP53* sequencing results.

Results

There was 95% complete concordance between local and central p53 IHC results. On preliminary results, deleterious *TP53* mutations were detected in 104/170 cases (excluding cases with failed analysis (n=23) and those showing heterogeneous p53 IHC (n=7)). Correlation between *TP53* mutation and p53 IHC (Table 3) shows 91% accuracy (sensitivity 90.4%; specificity 91.2%). Correlation between *TP53* mutation and p53 IHC as part of an algorithm, ie after exclusion of mismatch repair defective and DNA polymerase epsilon exonuclease domain (POLE) mutant cases, shows 93% accuracy (sensitivity 96.6%; specificity 84.8%).

Conclusions

p53 IHC shows excellent inter-laboratory/inter-observer agreement in EC biopsy specimens. Our preliminary results suggest that p53 IHC is a robust biomarker of 'serous-like' EC in biopsy material, especially as part of an algorithm.