Use of molecular markers improves prognostic stratification in high risk endometrial cancer: a TransPORTEC collaborative study

Nickkho-Amiry M[1], Kaufmann A[2], Bosse T[3], Leary A[4], McKay H[5], Powell M[6], Mileshkin L[7], Creutzberg CL[3], Kitchener HC[1], Crosbie EJ[1], Edmondson RJ[1]

1 University of Manchester, UK
2 University of Newcastle upon Tyne, UK
3 Leiden University Medical Centre, NL
4 Institute Gustave Roussy, FR
5 University of Toronto, CA
6 Barts Hospital, UK
7 Peter McCallum Cancer Center, Melbourne, AUS

Introduction

The adjuvant treatment of high risk endometrial cancer remains controversial but defining subgroups of patients with good prognosis, who are unlikely to benefit from the addition of chemotherapy, is important but is difficult with standard morphological assessment.

Methods

We generated a panel of 120 cases of high risk endometrial cancer (FIGO stage 1B, Grade III, serous, clear cell). Tissue blocks were reviewed prior to TMAs being created. Sections were stained with commercially available antibodies to ER,PR, p53, mdm2 and p21. Cases were scored blinded and p53 and hormonal signatures, based on the expression of these 5 markers, were generated for each case. These were correlated with survival data.

Results

Tumours with serous and clear cell morphology had a worse prognosis than GIII endometrioid tumours ($p < 0.005$)

Tumours with an abnormal p53 signature were associated with a worse prognosis (hazard ratio 4.1). When the hormonal signature was added to the model there was no effect of p53 mutation in hormone receptor positive tumours but in hormone receptor negative tumours there was a highly significant effect of p53 with p53 wild type, hormone receptor negative tumours having a particularly favourable prognosis (hazard ratio 3.1).

Conclusions

These data suggest that the addition of simple molecular markers to routine diagnosis will define subgroups of patients with high risk disease who might have a favourable prognosis and who may be able to avoid the addition of chemotherapy to their adjuvant treatment. This hypothesis will be tested in the translational programme associated with the PORTEC3 study.