

Evaluation of DNA repair biomarkers in high-risk endometrial cancer: a TransPORTEC pilot study

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Aims:

To describe the expression of DNA repair biomarkers in high-risk endometrial cancer (EC) and evaluate their prognostic value.

Methods:

TransPORTEC is an international consortium dedicated to translational research within the PORTEC-3 trial. To evaluate the expression of biomarkers to be tested in PORTEC-3, an independent pilot TMA was constructed using FFPE tumor samples of high-risk EC representative of patients enrolled in PORTEC-3. Expression of DNA-pk, 53BP, PARP and FANCD2 was scored by immunohistochemistry using an H-score (0-300). Markers were analysed with a Cox model to predict overall survival (OS) and distant relapse free survival (DRFS).

Results:

Samples from 120 patients with high risk EC were collected including G3 endometrioid (47%), G3 serous (15%), clear cell (11%) and G1/2 endometrioid (27%) tumors. Treatment details were available on 95 patients and included radiotherapy (86%) and/or chemotherapy (16%). Median H-scores were 53BP=148 (SD: 72), DNAPk=15 (SD:53), PARP=175 (SD:79) and FANCD2=12 (SD:36). OS for the 13% of patients lacking expression of all 4 markers (H-score=0) was 57 months versus 28.2 for patients expressing all 4 markers ($p=0.1$). There was a trend for improved DRFS with low DNAPk (10-year DRFS=48% vs 37%, $p=0.07$) and with low PARP (10-year DRFS=50% vs 30%, $p=0.08$) expression.

Conclusions:

While numbers are small, there is a trend for low DNAPk and PARP expression to predict good outcome. Whether DNA repair profile predicts benefit from adjuvant chemotherapy will be investigated in TransPORTEC. Evaluation of a more complete panel of DNA repair markers is ongoing and will be presented.