Molecular profiling of high-risk endometrial cancer; a *Trans*PORTEC pilot study

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Abstract

Aims: To investigate if molecular profiling improves risk assessment based on clinicopathologic characteristics in high-risk endometrial cancer.

Methods: *Trans*PORTEC is an international consortium dedicated to translational research related to the PORTEC-3 study. FFPE tumor samples were collected from four participating groups for this pilot series; tissue microarray was constructed and DNA isolated. Protein expression of p53 and MLH1 (as surrogate marker for sporadic-MSI) was analyzed using immunohistochemistry. Somatic hotspot analyses were performed using a panel of 14 genes known to be frequently mutated in gynecologic cancers.
Rates of distant metastasis (DM), relapse-free and overall survival (RFS, OS) were calculated with Kaplan-Meier method and log-rank test.

Results: Samples of 120 high-risk patients were included, 13 (11%) clear cell, 18 (15%) serous and 89 (74%) endometrioid (37 FIGO stage I grade 3, 18 stage II, 27 stage III and 6 stage IV). For endometrioid, serous and clear cell cancers 5-year RFS rates were 61.0%, 38.8%, and 12.4% (p=0.002) and OS 62.7%, 47.8%, and 11.4% (p<0.001). Molecular profiling within the endometrioid cancers resulted in prognostically different subgroups. Both in the *POLE*-mutant (N=13) and microsatellite-instable (N=12) patients no DM occurred, compared to p53 mutant (N=

N=19, 5-year DM 35.5%) and remaining patients (N= 45, 42.9%; p=0.02), and 5-year RFS of 91.7% and 74.1% for *POLE*-mutant and MSI vs. 55.7% (p53 mutant) and 47.6% (others), p=0.07.

Conclusion: Non-endometrioid endometrial cancers is associated with aggressive clinical course. Within high risk endometrioid cancers molecular analysis can be used to refine risk stratification and tailor adjuvant therapy.