MISMATCH REPAIR DEFICIENCY IS NOT APPLICABLE AS BIOMARKER IN CERVICAL CANCER, YET MSH-2 HAS STRONG PROGNOSTIC VALUE

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Introduction/Background Although early detected cervical cancer is associated with good survival, prognosis for late-stage disease is poor and treatment options are sparse. Mismatch-repair (MMR) deficiency has surfaced as a predictor of immune checkpoint inhibitor responses in several cancer types, but its value in cervical cancer remains unclear. This study aimed to define the incidence of MMR deficiency and establish its prognostic significance as well as the value of separate MMR proteins in cervical cancer.

Methodology Expression of the MMR proteins MLH-1, PMS-2, MSH-2, MSH-6 was investigated by immunohistochemical staining (IHC) in a prospectively collected, population-based cervical cancer cohort of 508 patients with corresponding clinicopathological and follow-up data. Staining was scored as either negative or positive and was further defined by the staining index (SI), consisting of area and intensity of staining varying from 1–9. MMR deficiency was defined as negative expression in one or more of the proteins. Also, gene set enrichment analyses were performed and differentially expressed or mutated genes were identified, across the RNA and whole-exome sequencing cohorts (n=72 and n=75, respectively), consisting of data obtained from fresh tissue.

Results Eight tumours (1.5%) were MMR deficient, four of which were of neuroendocrine histology. MMR status did not independently correlate with survival when adjusted for histologic type (HR 1.93, p=0.222). Low MSH-2 (SI ≤4, n=48) associated with poor survival (HR: 1.94 p=0.02), also when corrected for tumour stage, type and patient age (HR 2.06, p=0.013). Furthermore, the MSH-2 low tumours associated with high tumour mutational burden (p=0.003) and a high frequency of (frameshift) mutations in the double-strand break repair gene RAD50 (p<0.001).

Conclusion MMR deficiency is rare in cervical cancer and exhibits no independent relationship to survival in the current study. Low MSH-2 level is an independent prognostic marker for poor survival in cervical cancer.

THE IMPORTANCE OF PATHOLOGICAL ULTRASTAGING FOR SENTINEL LYMPH NODE BIOPSY IN CERVICAL CANCER, THE FINAL OUTCOME OF THE SENTIX STUDY (CEEGOG-CX01; ENGOT-CX2; NCT02494063)

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Introduction/Background One of the advantages of sentinel lymph node (SLN) biopsy is the removal of only a small number of lymph nodes with the highest risk of involvement. Pathological SLN ultrastaging allows detection of metastases not identified during standard histological examination. Sentix is an international prospective cohort study on SLN biopsy in cervical cancer with closed recruitment, which allowed to evaluate the importance of SLN ultrastaging and its intensity (examined levels) for the detection of N1.

Methodology Eligible stages: T1a1/L1 (≤4 cm for fertility sparing), no suspicious lymph nodes on imaging, bilateral SLN detection. SLNs were intraoperatively examined by one section (standard assessment corresponding to the examination of non-SLN), and consequently processed by an intensive protocol for ultrastaging (paraffin blocks sectioned completely in 150–200 µm intervals; two sections from each level, stained with H&E and immunohistochemically). SLNs were submitted for central quality control.

Results Final cohort of 647 patients was analysed. Standard SLN examination revealed macrometastases (MAC), micrometastasis (M), and isolated tumour cells (ITC) in 36, 10, and