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HER2-low expression and cell proliferation in urinary bladder carcinomas

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Background: Human Epidermal Growth Factor Receptor 2 (HER2) is involved in pathways that regulate normal cells growth and differentiation. The overexpression of HER2 protein leads to an uncontrolled cell growth and proliferation, contributing to aggressive forms of cancer. In late years, the cells with lower level of HER2 protein expression (HER2-low) were reclassified as distinct therapeutic target for anti-HER2 antibody-drug conjugate (ADC) in breast cancer.

The objective of this study was to assess if HER2-low expression is related to indicators of cell proliferation like EGFR expression and nuclear DNA content, in urinary bladder carcinomas.

Methods: Urinary bladder carcinomas obtained from 20 patients were analyzed by immunohistochemistry for HER2 and EGFR expression and by in situ hybridization for HER2 gene amplification. DNA content of tumor cells was investigated by flow cytometry for cell cycle phases and DNA ploidy level.

Results: HER2-low was present in 25% of urinary bladder carcinomas. Positive EGFR expression was detected in 3/7 HER2 negative cases, 3/5 HER2-low cases and in 4/8 HER2 positive cases. Two of the three tumors HER2-low and EGFR positive were aneuploid and with lymph node metastasis. The S-phase fraction and G2/M phase were higher in HER2-low tumors than in HER2 negative tumors. No difference was observed regarding the incidence of lymph node metastasis in HER2-low group and HER2 negative group.

Conclusions: The HER2-low urinary bladder carcinomas seem to have a higher rate of proliferation than HER2 negative tumors. These HER2-low cases may be new candidates for anti-HER2 ADC therapy for bladder cancer.