Significance of ERBB2 Overexpression in Therapeutic Resistance and Cancer-Specific Survival in Muscle-Invasive Bladder Cancer Patients Treated with Chemoradiation-Based Selective Bladder-Sparing Approach

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PURPOSE: To investigate the associations of ERBB 2 overexpression with chemoradiation therapy (CRT) resistance and cancer-specific survival (CSS) in muscle-invasive bladder cancer (MIBC) patients treated with the CRT-based bladder-sparing protocol.

METHODS AND MATERIALS: From 1997 to 2012, 201 patients with cT2-4aN0M0 bladder cancer were treated with CRT (40 Gy with concurrent cisplatin) following transurethral resection of bladder tumor (TURBT). Basically, patients with tumors that showed good CRT response and were amenable to segmental resection underwent partial cystectomy (PC) with pelvic lymph node dissection for bladder preservation; otherwise, radical cystectomy (RC) was recommended. Included in this study were 119 patients in whom TURBT specimens were available for immunohistochemical analysis of ERBB 2 expression. Following CRT, 30 and 65 patients underwent PC or RC, respectively; the remaining 24 patients did not undergo cystectomy. Tumors were defined as CRT-resistant when patients did not achieve complete response after CRT. Associations of ERBB 2 overexpression with CRT resistance and CSS were evaluated.

RESULTS: CRT resistance was observed clinically in 56% (67 of 119 patients) and pathologically (in cystectomy specimens) in 55% (52 of 95 patients). ERBB 2 overexpression was observed in 45 patients (38%). On multivariate analysis, ERBB 2 overexpression was an independent predictor for CRT resistance clinically (odds ratio, 3.6; P=.002) and pathologically (odds ratio, 2.9; P=.031). ERBB 2 overexpression was associated with shorter CSS (5-year CSS rates, 56% vs 87% for the ERBB 2 overexpression group vs the others; P=.001). ERBB 2 overexpression was also an independent risk factor for bladder cancer death at all time points of our bladder-sparing protocol (pre-CRT, post-CRT, and post-cystectomy).

CONCLUSIONS: ERBB 2 overexpression appears relevant to CRT resistance and unfavorable CSS in MIBC patients treated with the CRT-based bladder-sparing protocol. ERBB 2-targeting treatment may improve the outcomes of such patients.