CAN BIOMARKERS PREDICT PATHOLOGIC COMPLETE RESPONSE AFTER PREOPERATIVE CHEMORADIOTHERAPY FOR RECTAL CANCER?

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AIMS

Approximately 20% of all patients with locally advanced rectal cancer (LARC) experience pathologically complete responses (pCR) following neoadjuvant chemoradiotherapy (nCRT) and standard surgery. Molecular biomarkers could have the potential to select patients than can benefit from CRT. The aims of this preliminary study were to evaluate the expression of two biomarkers, p53 and SOX2 and to correlate this expression with the pathologic response. The p53 tumor suppressor gene is the most frequently mutated tumor-associated gene in malignant human tumors, including colorectal cancer. Sex determining region Y-box 2 (SOX2) is a major regulator of self-renewal and pluripotency of embryonic stem, and is involved in tumor proliferation and differentiation. Our study attempted to outline the prognostic role of expression of these two biomarkers in pathologic specimens from patients with LARC before they underwent nCRT and radical surgery.

METHODS

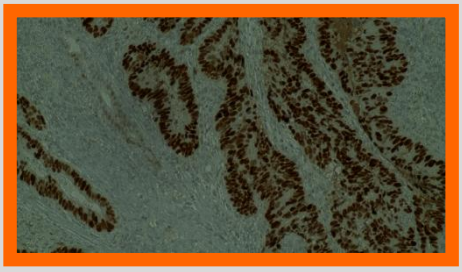
We retrospectively analyzed patients with LARC treated with intensity-modulated radiotherapy (IMRT) and concurrent Capecitabine was administered. Treatment response was evaluated in terms of disease down-staging and TRG scored according American Joint Commission on Cancer (AJCC). P53 and SOX2 expression was assessed by immunohistochemistry on paraffin embedded (FFPE) tumor samples collected before nCRT. Sections were incubated with p53 (DO7, Roche Ventana) and SOX2 (SP76, Roche Ventana) antibodies and staining was carried out on BenchMark XT Automated IHC/ISH slide staining system (Roche Ventana).

RESULTS

Between January 2017 and February 2018 45 patients with operable stage IIII rectal adenocarcinoma were treated. A dose of 50 Gy was prescribed with standard concomitant capecitabine. Surgery was scheduled 8-10 weeks after the completion of CRT. Histological score ranged from 0 (no staining), to + (<50%) and ++ (>50%). Of these, p53 and SOX2 were evaluated in 7 patients. P53 was overexpressed in TRG0 (28.6%), TRG2 (14.3%), TRG3 (14.3%). No association of SOX2 expressions with TRG was uncovered.

	Sox2	P53	TRG
1	0	++	0
2	0	++	2
3	+	++	0
4	0	0	2
5	0	0	3
6	0	++	3
7	0	0	0

P53 ++



Sox2 +

CONCLUSIONS

Our preliminary data indicate that SOX2 has no potential prognostic significance as observed, for example, in esophagogastric junction adenocarcinoma. p53 expression could be associated with clinical response to CRT but additional studies are needed. In future clinical trials of nCRT for rectal cancer, these biomarker should be prospectively evaluated to determine their utility as predictors of outcome.

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