

The consensus Immunoscore adapted to biopsies in patients with locally advanced rectal cancer: Potential clinical significance for a “Watch and Wait” strategy

Background: We investigated whether an adaptation to rectal biopsies of the recently validated consensus Immunoscore, could predict the response to neoadjuvant treatment and delineate clinical responders that could benefit from a “Watch and Wait” (W&W) strategy with acceptable outcomes. **Methods:** Initial biopsies from 273 patients with locally advanced rectal cancer (LARC) treated by neoadjuvant chemoradiotherapy (nCRT) followed by Total Mesorectal Excision (TME), were immunostained for CD3+ and cytotoxic CD8+ T cells and quantified by digital pathology to determine the Immunoscore within pre-treatment Biopsy (IS_B). Expression level of 44 immune related genes post-neoadjuvant treatment was investigated by Nanostring technology (n = 64 patients). Results were correlated with response to neoadjuvant treatment, disease free survival (DFS) and time to recurrence (TTR). Prognostic performance of IS_B was finally assessed in 73 LARC treated by W&W strategy. **Results:** IS_B Low, Intermediate and High were respectively observed in 23.3, 50.4 and 26.3 % of the cohort. IS_B was positively and significantly correlated with the response to nCRT, as evaluated by Dworak classification (P = .0034), ypTNM (P = .0003), down-staging (P = .0014), and neoadjuvant rectal (NAR) score, (P < .0001). IS_B status was also positively associated with the degree of local immune activation post-neoadjuvant treatment. IS_B High patients were at low risk of relapse, with 5-year DFS rates of 81.1 % (CI, 71.3-92.1 %) as compared to 57.8 % (CI, 45.9-72.9 %) in IS_B low patients. In multivariate analysis, IS_B was the only significant parameter at presentation associated with DFS (High vs Low: P = .001). Among W&W patients, significant difference was observed for TTR according to IS_B status (High vs Low: P = .025). **Conclusions:** IS_B could provide a reliable estimate of the response to nCRT and risk of recurrence in LARC patients' treated by TME or W&W strategy.

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