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Tumor budding, an important prognostic factor in stage III colon cancer patients treated with oxaliplatin-based chemotherapy

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Background

Histological growth characteristics at the invasive front may reflect tumor aggressiveness. Specifically, tumor budding (TB), defined as single cancer cells or cluster comprising less than five cells and representing the dynamic process of epithelial-mesenchymal transition, is listed among prognostic markers in colon cancer (CC). However, its use for a better disease stratification needs to be further explored. Its prognostic role was thus evaluated in a phase III trial investigating 3 *vs* 6 months of oxaliplatin-based adjuvant treatment in stage III CC patients.

Methods

TB was evaluated on scanned hematoxylin and eosin-stained slides and scored by central review according to the criteria adopted by the 2016 International Tumor Budding consensus Conference (ITBCC2016) (number of buds per 0.785 mm2 in the hotspot), as Bd1 (0-4: low), Bd2 (5-9: intermediate), and Bd3 (≥10: high). Prediction of disease-free survival (DFS) and overall survival (OS) was analyzed by log-rank test. Clinico-pathologic features including vascular and perineural invasion, as well as tumor deposit, were associated with Bd category.

Results

Samples of 1048 CC patients were analyzed. Bd1, Bd2 and Bd3 were observed in 39%, 28% and 33%, respectively. Bd2 and Bd3 were associated with vascular and perineural invasions ($p<0.005$). No association was observed with tumor deposits or T/N risk groups. Bd category was significantly associated with DFS (1 vs 2-3: $p=0.0008$) and OS (1 vs 2-3: $p=0.0015$) with 3-year DFS rates of 79.5% vs 67.2% and 5-year OS rates were 89.2% vs 80.8% for Bd1 and Bd2-3, respectively. This prognostic role was confirmed in multivariable analysis adjusted on age, gender, risk group (low: T1-3/N1, high: T4 and/or N2), tumor grade, obstruction/perforation and treatment duration (3 vs 6months) for DFS (HR: 1.421; 95% CI:1.128-1.791, $p=0.0029$) and OS (HR: 1.627; 95% CI:1.203-2.200, $p=0.0016$).

Conclusions

In this large series from a randomized phase III trial, TB is an independent prognostic factor for OS and DFS in stage III CC patients treated with oxaliplatin-based standard adjuvant therapy. TB, adopted in the UICC TNM classification, should now be mandatory in every pathology report concerning patients resected from a stage III CC.

Legal entity responsible for the study

The authors.

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Disclosure

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