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# CLINICAL IMPACT OF MUCINOUS AND POORLY DIFFERENTIATED TUMORS ON THE OUTCOME OF PATIENTS WITH STAGE II COLON CANCER: A TOSCA SUBGROUP ANALYSIS

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## Abstract

**Background:** ASCO and ESMO guidelines have identified inadequate sampling of lymph nodes, pT4 primary tumors, obstruction or perforation, lymphovascular and perineural invasion, and poorly differentiated tumors as negative prognostic factors supporting the clinicians in treating their patients with stage II colon cancer (CC). However, the influence of histological subtypes on the risk of death or disease recurrence remains controversial.

**Methods:** The phase III, multicenter, randomized TOSCA trial compared 3 versus 6 months of fluoropyrimidine-oxaliplatin adjuvant chemotherapy in 3,759 patients with high-risk stage II or stage III CC. Objective of this sub-study was to investigate whether the histological subtype [(mucinous adenocarcinoma (MUC) or non-mucinous adenocarcinoma (NMUC)] had an impact on the treatment duration in terms of relapse-free survival (RFS) and overall survival (OS) in the subgroup of patients with high-risk stage II, grade 3 CC.

**Results:** Out of 3,614 patients from 130 centres enrolled in the per-protocol population defined in the TOSCA trial, 474 patients were included in this analysis. No statistical differences were detected between 3 versus 6 months treatment duration group in both histological subgroups. The proportion of patients with right-sided cancer was higher in the subgroup of patients with MUC rather than in NMUC. After a median follow-up of 62 months, 60 progression/deaths and 38 deaths were observed. A significant interaction between treatment duration and histology was observed on both RFS (p=0.027) and OS (p=0.017). In the subgroup of patients with MUC, a worse RFS (adjusted hazard ratio [HR], 3.95; 95% confidence interval [CI], 1.03–15.17; p = 0.045) and OS (HR, 9.56; 95% CI, 1.14–79.98; p = 0.037) was detected for patients treated in the 3 months arm. No statistically significant differences were detected in the subgroup of patients with NMUC.

**Conclusions:** Both MUC and poorly differentiated subtypes have unfavourable clinical characteristics. Patients with MUC, grade 3, stage II CC require special attention and may need 6 months of oxaliplatin-based chemotherapy. Larger studies are required to clarify the potential negative effect of the histological subtype in improving the prognosis of these patients.