

## **Topoisomerase I but not thymidylate synthase is associated with improved outcome in patients with resected colorectal cancer treated with irinotecan containing adjuvant chemotherapy.**

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### **Source**

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### **Abstract**

#### **BACKGROUND:**

Thymidylate synthase (TS) and Topoisomerase I (Topo I) are significant biomarkers in colorectal cancer (CRC). We aimed to study the expression of TS and Topo I in patients with resected CRC who received adjuvant chemotherapy and correlated it with clinical outcome.

#### **METHODS:**

All patients diagnosed with CRC between 1989 and 2007 and treated with adjuvant chemotherapy within Hellenic Cooperative Oncology Group's (HeCOG) protocols, were identified. Archival paraffin-embedded tumor tissues were used for immunohistochemical detection of TS and Topo I. Immunohistochemistry was performed on tissue microarray slides using monoclonal antibodies against TS and Topo I. The results were correlated with survival (OS) and disease free survival (DFS).

#### **RESULTS:**

A cohort of 498 patients with a median age of 61 years and Dukes' stage B (49%) and C (51%) fulfilled the criteria of the study. All patients received adjuvant 5-FU-based chemotherapy, 38% irinotecan-containing. Positive TS and Topo I expression was found in 43% and 48% of cases, respectively. Five-year OS was 74% and DFS was 68%. In univariate analysis no association of TS and Topo I expression with OS and DFS was identified. In multivariate analysis however, Topo I expression was associated with a reduced risk of death (HR = 0.61, 95% CI 0.42-0.88,  $p = 0.009$ ). In the irinotecan-treated subgroup, those patients who expressed Topo I had a better OS (HR = 0.47, 95% CI 0.23-0.94,  $p = 0.033$ ).

#### **CONCLUSION:**

Patients with resected CRC expressing Topo I seem to benefit from irinotecan-containing adjuvant chemotherapy. However randomised prospective trials are needed to confirm these results.