# Stage II colorectal cancer: lack of prognostic model

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To the Editor: Colorectal cancer (CRC) is one of the most common malignant tumors worldwide (Gatta et al. 1998 [1], Repetto et al. 2003 [2]) with the disease incidence rising along with an advanced age (Wymenga et al. 2001 [3], Franceschi et al. 2001 [4]). The overall mortality from CRC is 60%, which represents the second leading cause of cancer death in western societies. In Finland, the incidence of CRC is 25/100.000, and 20/100.000 among males and females, respectively. Annually, 1.150 new cases are detected among males and 1.200 among women, representing 9.2% and 10% of all cancer cases, respectively (Finnish Cancer Registry, 2005). On the other hand, according to Benghazi Cancer Registry, 2003 [5] the colorectal cancer in eastern part of Libya is the most second frequent cancer after lung cancer in males and breast cancer in females. The average crude incidence rate is 6.4 (male) and 5.2 (female) cases per 100,000 inhabitants, representing 10.1% of male patients and 9.3% of female patients of all cancer cases.

Unfortunately, there has not been a major improvement in patient survival despite the advances made in our understanding of disease and in chemotherapy practice (Walker and Quirke, 2001[6]). Surgical cure of CRC is determined by stage of the tumor and its biological behaviour. Early CRCs can be cured with surgery alone. The decision to use adjuvant therapy to patients after curative surgical resection for stage II CRC (node-negative patients) is often difficult (Venook et al, 2004 [7]) and its routine use is not recommended (Graziano and Cascinu, 2003 [8]). In future, however, these decisions may be made more rationally as we learn how to incorporate the use of molecular markers and predictors in these patients. Recent guidelines advocate considering factors such as tumor differentiation, tumor perforation, number of lymph nodes examined, and T stage when assessing the likely benefit: risk ratio. Microsatellite instability and allelic imbalance seem to be strong predictors of good and poor prognosis, respectively, and in the near future, therapeutic decision-making models are likely to be further refined by the inclusion of such molecular markers [9]. The well-known and important prognostic factors in patients with CRC are histological tumor stage (Dukes-classification) including the depth of invasion and lymph node infiltration (Phillips et al 1984 [10], Wiggers et al, 1988 [11], Rapponen et al, 1996 [12]). Molecular markers may help deciding adjuvant therapy for a subgroup of these patients. Because the 5-year survival in stage II patients is approximately 70% with surgery alone (Wang et al, 2003 [13]), adjuvant therapy is not widely recommended and still no agreement exists on the use of chemotherapy for these patients (Di Fabio et al, 2004 [14]). However, it is well established that a sub-group of patients with stage II CRC are at high risk of recurrence and should be considered for adjuvant chemotherapy (Willett et al, 1999 [15]). Some studies have suggested a definite survival benefit from chemotherapy in this sub-group of node-negative patients (Venook et al, 2004). To date, most of the randomized trials have demonstrated a relative reduction in tumor recurrence but have not shown any significant impact on survival in stage II disease, however. It seems likely that this failure to demonstrate a survival benefit from adjuvant chemotherapy in stage II disease is due to the fact that these trials do not have enough statistical power due to small patient series. Nevertheless, the absolute survival advantage is only about 2% and clinicians need to weigh this against the costs and toxicities of the treatment when managing these patients (Haydon A, 2003 [16]). In brief, the main long-term goal of building up a prognostic model (index) in stage II CRC is to accurately: 1) Predict patients who are at high risk for developing recurrent disease, 2) Identify the patients among stage II cases who should benefit from adjuvant chemotherapy, and finally 3) Predict the overall disease outcome.

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