Should rectal cancer located 10-15 cm from the anal verge be defined as colon cancer

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Letters to the editor

Should rectal cancer located 10–15 cm from the anal verge be defined as colon cancer

Because colon and rectal tumours biologically differ, a clear separation of colon and rectal cancer for scientific research and treatment strategies is needed. However, the definition of the rectum is inconsistent across countries regarding location of the peritoneal reflection and distance from the anal verge. A recently published meta-analysis on individual patient data demonstrated that adjuvant chemotherapy after preoperative (chemo)radiotherapy and TME surgery did not improve overall survival, disease-free survival (DFS) and distant recurrence rates in patients with pathological stage II-III rectal cancer [1, 2]. In the meta-analysis, it was suggested that a subgroup of patients with rectal tumours 10–15 cm from the anal verge might benefit from adjuvant chemotherapy in terms of DFS and distant recurrences [2]. Consequently, it could be debated whether tumours located 10–15 cm from the anal verge should be defined as colon tumours rather than rectal tumours, since patients with stage III and high-risk stage II colon cancer do benefit from adjuvant chemotherapy [3]. Further investigation for patients with rectal tumours 10-15cm from the anal verge is essential, although a randomized trial is not feasible. Therefore, we report on the results of the PROCTOR/SCRIPT trial after a median follow-up of 5.5 years, with a focus on rectal tumours 10–15 cm from the anal verge. In this study, a multicenter randomized phase III trial, patients were randomly assigned to adjuvant chemotherapy or observation in patients with (y)pTNM stage II–III rectal cancer treated with preoperative (chemo)radiotherapy and TME surgery. Study design, patient characteristics, definitions of endpoints and exclusion criteria were described elsewhere [1]. In agreement with the previous reported results with a median follow-up of 5 years, no beneficial effect of adjuvant treatment was observed in the total study cohort ($N = 437$). However, a significant benefit in DFS (HR 0.59, 95% CI: 0.36-0.98, $P = 0.04$) was observed in patients randomized to adjuvant chemotherapy for (y)pTNM stage II–III rectal cancer located 10–15 cm of the anal verge treated with preoperative (chemo)radiotherapy and TME surgery (Figure 1). This beneficial effect has not been observed in patients with tumours located <5 cm and 5–9.9 cm from the anal verge (Figure 1). No significant interaction between distance from the anal verge and treatment group was detected. We acknowledge that the PROCTOR/SCRIPT trial was not powered to perform subgroup analysis. Based on the meta-analysis, supported by our updated data, we propose that tumours located 10–15 cm from the anal verge might be defined as

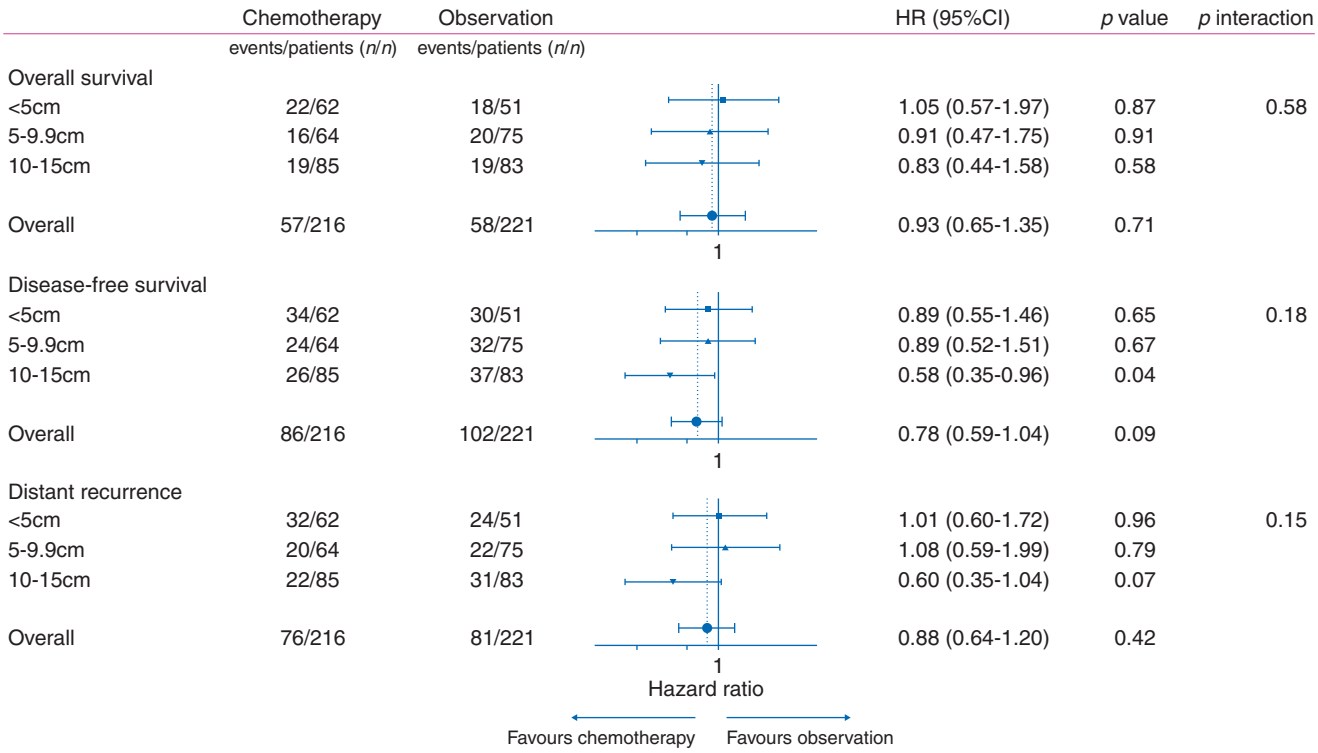

Figure 1. Overall survival, disease-free survival and distant recurrence for all patients and by patient subgroups.

colon tumours instead of rectum tumours considering the suggested beneficial effect on DFS of adjuvant chemotherapy.

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The authors have declared no conflicts of interest.

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Different efficacy of ramucirumab in patients with metastatic gastric and gastroesophageal junction cancer according to ECOG performance status

Yoon et al. [1] reported the first randomized, phase II trial of ramucirumab, an anti-vascular endothelial growth factor receptor-2 monoclonal antibody, as front-line therapy in patients with advanced adenocarcinoma of the esophagus or gastric/gastroesophageal junction. Unfortunately, the addition of ramucirumab to front-line mFOLFOX6 did not improve progression-free survival (PFS) in these patients. We noted from the subgroup analysis of PFS in Figure 3A Yoon et al. [1] that, although not statistically significant, ramucirumab shows improved efficacy in patients with Eastern Cooperative Oncology Group (ECOG) performance status (PS)=1 compared with ECOG PS 0 (hazard ratio 0.88 and 1, respectively). Based on these findings, we extended this subgroup analysis to all ramucirumab data available from literature. The studies were identified according to the following inclusion criteria: (i) ramucirumab-based experimental arm; (ii) the presence of a control arm for comparison (placebo or not); (iii) the presence of data on PFS according to ECOG PS. The following exclusion criteria were used: (i) insufficient data available to estimate the outcomes; (ii) animal studies; (iii) <10 participants in each arm and (iv) non-randomized studies. The summary estimates were generated using a fixed-effect model (Mantel–Haenszel method) [2] or a random-effect model (DerSimonian–Laird method) [3] depending on the absence or presence of heterogeneity (I^2). Three studies were included in the analysis (Table 1).

Table 1. Characteristics of the analysed trials and data on progression-free survival according ECOG performance status

Study	Phase	Primary endpoint	Number of patients experimental arm	Number of patients control arm	Line	Experimental drug	Control arm	Jaded score
Yoon et al. [1]	II	PFS	84	84	I	Ramucirumab+mFOLFOX6	Placebo+mFOLFOX6	3
RAINBOW [5]	III	OS	330	335	II	Ramucirumab+paclitaxel	Placebo+paclitaxel	5
REGARD [6]	III	OS	238	117	II	Ramucirumab	Placebo	5

Study	ECOG 0		Hazard ratio	ECOG ≥1		Hazard ratio
	Number of patients Experimental arm	Number of patients Control arm		Number of patients Experimental arm	Number of patients Control arm	
Yoon et al. [1]	40	43	0.52	43	41	0.83
RAINBOW [5]	117	144	0.778	213	191	0.771
REGARD [6]	67	31	1.075	171	86	0.682

PFS, progression-free survival; OS, overall survival.