Supplementary appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Becattini C., Pace U., Pirozzi F., et al. Rivaroxaban for extended antithrombotic prophylaxis after laparoscopic surgery for colorectal cancer. N Engl J Med.

CONTENTS

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Table S1 Demographic and Clinical Characteristics of randomized and not randomized patients

Characteristic	**Randomized (N =582)**	**Not randomized* (N = 59)**
Age — yrs. Mean (SD)	65.2 (11.2)	66.7 (10.2)
Male sex — no. (%)	308 (52.9%)	36 (61.0%)
Comorbidities — no. (%)		
Systemic arterial hypertension	179 (30.8%)	9 (15.3%)
Diabetes	62 (10.7%)	3 (5.1%)
Ischemic heart disease and/or chronic heart failure	23 (4.0%)	3 (5.1%)
COPD	16 (2.7%)	2 (3.4%)
Previous cancer	12 (2.1%)	0 (--)
Liver disease	8 (1.4%)	1 (1.7%)
Neo-adiuvant therapy — no. (%)	96 (16.5%)	12 (20.3%)
Type of surgery — no. (%)		
Right emi-colectomy	180 (30.9%)	11 (18.6%)
Left emi-colectomy	146 (25.1%)	9 (15.3%)
Rectal anterior resection	171 (29.4%)	15 (25.4%)
Rectal anterior resection plus Miles	19 (3.3%)	1 (1.7%)
Other **	66 (11.3%)	5 (8.5%)
Duration of surgery, hours. Mean (SD)	3.1 (1.3)	3.9 (1.5)

* These patients were fully compliant with inclusion/exclusion criteria and provided informed consent before surgery but were not randomized

**description of intervention was not reported in 18 patients that did not underwent randomization

Table S2 Demographic and Clinical Characteristics of patients included and excluded from the modified Intention-to-treat analysis

Characteristic	**Included (N =569)**	**Excluded (N = 72)**
Age — yrs. Mean (SD)	65.2 (11.2)	66.9 (10.0)
Male sex — no. (%)	304 (53.4%)	40 (55.6%)
Comorbidities — no. (%)		
Systemic arterial hypertension	176 (30.9%)	12 (16.7%)
Diabetes	60 (10.5%)	5 (6.9%)
Ischemic heart disease and/or chronic heart failure	23 (4.0%)	3 (4.2%)
COPD	16 (2.8%)	2 (2.8%)
Previous cancer	11 (1.9%)	1 (1.4%)
Liver disease	8 (1.4%)	1 (1.4%)
Neo-adiuvant therapy — no. (%)	94 (16.5%)	14 (19.4%)
Type of surgery — no. (%)		
Right emi-colectomy	174 (30.6%)	17 (23.6%)
Left emi-colectomy	145 (25.5%)	10 (13.9%)
Rectal anterior resection	167 (29.3%)	19 (26.4%)
Rectal anterior resection plus Miles	18 (3.2%)	2 (2.8%)
Other *	65 (11.4%)	6 (8.3%)
Duration of surgery, hours. Mean (SD)	3.1 (1.3)	3.8 (1.4)

*Description of intervention was not reported in 18 patients that did not underwent randomization

Table S3 Reason for study treatment discontinuation by treatment group

	Rivaroxaban (N =287)	**Placebo (N = 282)**
Premature discontinuation* — no. (%)	12 (4.2%)	13 (4.6%)
Primary study outcome event — no. (%)	0	4 (1.4%)
Major bleeding — no. (%)	2 (0.7%)	0
Re-intervention — no. (%)	5 (1.7%)	1 (0.3%)
Adverse event — no. (%) Cutaneous Acute renal failure COVID 19 Other	2 (0.7%) 1 - - 1	2 (0.7%) - 1 1 -
Declined consent ** — no. (%)	3 (1.7%)	5 (1.8%)
Physician decision — no. (%)	2 (0.7%)	1 (0.3%)

*two patients had major bleeding and underwent re-intervention

** consent decline occurred after randomization

Table S4. Clinical Outcomes in the per protocol population in patients randomized to rivaroxaban or placebo*

Outcome	Rivaroxaban (N =287)	Placebo (N =282)	Risk difference* (95% CI)	P value		Hazard Ratio (95% CI)	Log Rank P Value
Primary efficacy outcome°							
Symptomatic objectively confirmed VTE, asymptomatic ultrasonography-confirmed DVT or VTE-related death at 28±2 days from laparoscopic surgery for colorectal cancer — no. (%)	3 (1.1%)	11 (4.0%)	-0.030 (-0.057 to -0.003)	0.028		0.27 (0.07-0.96)	0.030
Symptomatic VTE — no. (%)	1 (0.3%)	4 (1.4%)	--			--	
Asymptomatic ultrasonography-detected VTE	2 (0.7%)	7 (2.5%)	--				
Proximal DVT — no. (%)	0	4 (1.4%)	--			--	
PE or VTE-related deaths — no. (%)	0	0	--			--	
Secondary outcomes							
Symptomatic objectively confirmed VTE, asymptomatic ultrasonography-confirmed DVT, major bleeding or death at 28±2 days from surgery – no. (%)	5 (1.8%)	11 (4.0%)	-0.023 (-0.051 to 0.006)	0.119		0.45 (0.15-1.29)	0.124
Symptomatic objectively confirmed VTE, asymptomatic ultrasonography-confirmed DVT, major bleeding or death at 90 days from surgery – no. (%)	6 (2.1)	12 (4.3%)	-0.023 (-0.053 to 0.007)	0.140		0.49 (0.18-1.30)	0.143

VTE= venous thromboembolism, DVT= deep vein thrombosis

* according to the Mantel-Haenszel method

Figure S1 Time from randomization to secondary study outcome event at 90±2 days in patients randomized to receive rivaroxaban (dashed line) or placebo (continuous line) included in the modified intention to treat population