

MRC ST03 trial

Cunningham D, Stenning S, Smyth E et al. Peri-operative chemotherapy with or without bevacizumab in operable oesophagogastric adenocarcinoma (UK Medical Research Council ST03): primary analysis results of a multicentre, open-label, randomised phase 2–3 trial. *Lancet Oncol* 2017; 18: 357–70
[https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045\(17\)30043-8/fulltext](https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(17)30043-8/fulltext)

ST03 recruited 1063 patients from 87 UK hospitals.

P: Resectable oesophago-gastric adenocarcinoma (inclusion criteria were widened from gastric/type III tumours to include type I and II and lower oesophageal tumours)

I: Bevacizumab plus chemotherapy (6 cycles of epirubicin, cisplatin and capecitabine: 3 pre- and 3 post-surgery)

C: Chemotherapy (epirubicin, cisplatin and capecitabine: 3 pre- and 3 post-surgery)

O: Overall survival at 5 years (primary outcome), disease free survival, tumour regression grade

Results:

- Overall survival (3 years) was 50.3% in the chemotherapy alone group and 48.1% in the chemo/bevacizumab group.
- Wound healing complications were more prevalent in the bevacizumab group and in patients undergoing oesophagectomy, anastomotic leak rates were higher in the bevacizumab group (24% vs 10%). Recruitment of patients with lower oesophageal/junctional tumours was therefore stopped before the end of the trial.

Internal validity	Selection bias	Low: telephone randomisation service
	Detection bias	Low: overall survival is an objective outcome
	Performance bias	Unclear: surgeons and other caregivers were not blinded but this probably did not make a difference
	Attrition bias	Unclear:
	Selective outcome reporting	Low
External validity	P	Relatively broad: all histological types of 'resectable' gastro-oesophageal cancer
	I	Intervention (chemotherapy) relatively tightly standardised. Type of surgery at surgeons' discretion.
	C	
	O	Relatively patient-centred (survival) although no quality of life outcomes
	O	45 centres across Europe

Other criticisms: Inclusion of both gastric and oesophageal tumours and a generous targeted difference of 10% absolute difference in survival. Overall only about 40% of patients in each group actually completed the 6 cycles of chemotherapy.

How has this influenced practice? Bevacizumab has not been recommended for use in conjunction with existing chemotherapy regimens.