Alliance for Clinical Trials in Oncology Z6051:
A Phase III Prospective Randomized Trial Comparing Laparoscopic-assisted Resection Versus Open Resection for Rectal Cancer

ClinicalTrials.gov Identifier: NCT00726622

I. Study Background

A. Design

A randomized phase III trial evaluating the safety and efficacy of laparoscopic resection for rectal cancer. Using a 1:1 randomization, patients go on to

- Arm A: Open rectal resection
- Arm B: Laparoscopic rectal resection

B. Objectives

- Primary
    - To test the hypothesis that laparoscopic-assisted resection for rectal cancer is not inferior to open rectal resection, based on a composite primary endpoint of oncologic factors which are indicative of a safe and feasible operation. If all oncologic parameters are satisfied, the resection is considered successful:
        - Circumferential margin > 1 mm
        - Negative distal margin
        - Completeness of TME (both complete and nearly complete TME)
- Secondary
    - Patient-related benefit of laparoscopic-assisted resection for rectal cancer vs. open rectal resection (blood loss, length of stay, pain medicine utilization)
    - Disease-free survival and local pelvic recurrence at two years
    - Quality of life, sexual function, bowel and stoma function

C. Stratification Factors

- Tumor location
    - High rectum
    - Middle rectum
    - Low rectum
- Registering surgeon (surgeon performing surgery)
- Planned procedure

- Low anterior resection
- Abdominal perineal resection

D. Study History

08/15/2008 Study was activated

08/15/2011 Amendment 4, updated the objectives for the study, pathology review requirement, credentialing for robotics and added and optional biospecimen collection section.

10/01/2013 Study permanently closed to accrual.

II. Publication

A. Primary Endpoint Analysis

Fleshman J, Branda M, Sargent DJ, et al. Effect of Laparoscopic-Assisted Resection vs Open Resection of Stage II or III Rectal Cancer on Pathologic Outcomes: The ACOSOG Z6051 Randomized Clinical Trial. *JAMA.* 2015;314(13):1346-1355. doi:10.1001/jama.2015.10529.

III. Data Files

A. Primary Data file: Analysis

Note: Due to continued data cleaning, minor data updates have been included in this dataset.

Variable Description	Variable Name	Codes	Notes
Study Identifier	STUDY	Z6051	
Subject	SUBJECT	Character values	De-identified patient ID
Patient Reference	PATREF		Patient Reference aligning with Navigator ID
Randomized	ARM	1 = Open Resection	

Variable Description	Variable Name	Codes	Notes
Treatment Arm		2 = Laparoscopic Resection	
Evaluable for primary analysis	EVAL_PA	0 = No 1 = Yes	462 were used in the primary analysis (EVAL_PA=1)
Baseline and Demographics data was excluded	EXCLUDED	0 = Data was included 1 = Excluded due to improper consent 2 = Excluded due to patient request and consent withdrawal	Data for 481 patients was reported (EXCLUDED=0)
Surgery per protocol as randomized	SURGPROT	Y = Yes N = No C = Laparoscopic was converted to open resection	3 patients had protocol surgery, but had improper consent and were excluded (These patients are denoted by SURGPROT=Y and EXCLUDED=1)
Reason patient did not have protocol surgery	SURGRSN	1 = withdrew consent 2 = improper consent 3 = metastasis 4 = patient chose surveillance over surgery 5 = refused open resection 6 = site withdrew patient due to noncompliance Missing = Patient underwent protocol surgery	For patients that did not undergo surgery
Modified intent to treat patient population	---	---	Select patients where EVAL_PA = 1 and SURGPROT = Y N = 435
Per protocol patient population	---	---	Select patients where EVAL_PA=1 (this includes patients that received protocol surgery as allocated and patients in the laparoscopic arm whose surgery were

Variable Description	Variable Name	Codes	Notes
			converted to open resection) N = 462
Stratification Factors ***As presented in the manuscript, data for 5 patients was not included. Reasons for these cases are provided in the variable EXCLUDED. The following variables are set to missing for these 5 cases.***			
Planned operative procedure	PLANPROC	1 = Low anterior resection 2 = Abdominal perineal resection	
Site of primary tumor	TUMLOC	1 = High rectum 2 = Middle rectum 3 = Low rectum	
Enrolled by Top 10 accruing surgeon	TOP10SURG	Y = Yes Missing = surgeon performing the surgery was not one of the top 10 accruing surgeons	Registering surgeon was a stratification factor. The dataset includes an indicator variable for the top 10 accruing surgeons.
Identifier for top 10 accruing surgeon	TOP10SURGID	Character value Missing = surgeon performing the surgery was not one of the top 10 accruing surgeons	
Demographic and Clinical Characteristics ***As presented in the manuscript, data for 5 patients was not included. Reasons for these cases are provided in the variable EXCLUDED. The following variables are set to missing for these 5 cases.***			
Gender	SEX	1 = Male 2 = Female	
Age at randomization	AGE	Continuous	
Race	RACE	1 = White 2 = Black or African American 3 = Other 9 = Unknown/Not Reported	Category "Other" includes: • Native Hawaiian or other Pacific Islander • Asian • American Indian or

Variable Description	Variable Name	Codes	Notes
			Alaska Native
Body mass index	BMI	Continuous	
Tumor distance from anal verge (cm)	TUMDIST	Continuous Missing values represent data unavailable	
Tumor size, largest dimension (cm)	TUMSIZE	Continuous Missing values represent data unavailable	
ECOG Performance Score	ECOGPS	0 = Asymptomatic and fully active. 1 = Symptomatic; fully ambulatory; restricted in physical strenuous activity. 2 = Symptomatic; ambulatory; capable of all self-care; more than 50% of waking hours are spent out of bed. Missing = patient not evaluated.	1 patient was not assessed by the enrolling physician, but the patient met criteria for eligibility even though the site could not specify score.
Baseline Clinical Stage	BSTAGECAT	Stage I Stage IIA Stage IIIA Stage IIIB Stage IIIC Stage IV	
Prior Therapy	PRTHERAPY	1 = Chemotherapy + radiation 2 = Chemotherapy 3 = Radiation alone 9 = Unknown (Site had documentation that the patient received neoadjuvant therapy, but was unable to document the type of therapy received)	
Prior Chemotherapy: fluorouracil	CHEMO5FU	Y Missing = patient did not receive 5-FU therapy	Indicator variable
Prior Chemotherapy: oxaliplatin	CHEMO_OXALI	Y Missing = patient did not receive oxaliplatin therapy	Indicator variable

Variable Description	Variable Name	Codes	Notes
Year of study registration	REGYR	2008 to 2013 Missing = patient withdrew consent; data not collected.	
Ineligible	INEL	Y = Ineligible N = Met all eligibility criteria Missing = eligibility review was not performed (this case is a patient that withdrew consent prior to pre-surgery visit)	
Reason for ineligibility	INELRSN	Character field Missing for patients who met all eligibility criteria	
Surgery ***(presented for evaluable patients only. If a patient is not evaluable, the following variables are set to missing.)***			
Surgical Approach	SURGAPP	1 = Low Anterior Resection (LAR) 2 = Low Anterior Resection (LAR) + Coloanal Anastomosis 3 = Abdominal Perineal Resection (APR) 4 = Low Hartmann 5 = Total Proctocolectomy	
Surgical approach for laparoscopic arm	LAPSURGAPP	1 = Laparoscopic 2 = Laparoscopic-assisted 3 = Hand-assisted 4 = Robotic-assisted	Provided only for patients who underwent laparoscopic resection
Ostomy created at time of resection	OSTOMY	1 = Yes, colostomy 2 = Yes, ileostomy 3 = No	
Sphincter preservation planned prior to surgery	SPHINCPRES	1= Yes 2 = No	
Margins examined by frozen section	MARGEXAM	1 = Yes 2 = No	
Rectum intact	RECTACT	1 = Yes 2 = No	

Variable Description	Variable Name	Codes	Notes
Minutes from open to close (operative time)	SURGTIME	Continuous	
Estimated total blood loss (mL)	BLOODLOSS	Continuous Missing values represent data unavailable	
Final incision length (cm)	INCISLEN	Continuous Missing values represent data unavailable	
Length of hospital stay (days)	HOSPITALD	Discrete values Missing values represent data unavailable	
Days in ICU	ICUD	Discrete values Missing values represent data unavailable	
Days requiring parenteral narcotics	NARCD	Discrete values Missing values represent data unavailable	
Days receiving oral analgesics	ANALGD	Discrete values Missing values represent data unavailable	
Days to first bowel movement post-op	FBOWELD	Discrete values Missing values represent data unavailable	
Days to first flatus post-op	FFLATD	Discrete values Missing values represent data unavailable	
Total length of resected sample (cm)	RESLENGTH	Continuous	
Distance to nearest radial margin (mm)	RADIAL_MM	Continuous Missing values represent data 'Not Applicable' (no residual tumor and no scar visible) or "Unable to Assess"	
Distance to distal margin (cm)	DISTAL_CM	Continuous Missing values represent data 'Not Applicable' (no residual tumor and no scar visible) or "Unable to Assess"	
Number of lymph nodes examined	LYMPHN	Discrete values	

Variable Description	Variable Name	Codes	Notes
Number of positive lymph nodes	LYMPHNP	Discrete values	
Pathologic Tumor Stage	PSTAGECAT	Stage 0 Stage I Stage IIA Stage IIB Stage IIIA Stage IIIB Stage IIIC Stage IV Missing= Patient not evaluated for Pathologic Tumor Stage	Post-surgery
Tumor size (residual tumor in cm)	TUMORSZ	Continuous Missing = no residual tumor in sample; for 3 additional patients data is not available	Applicable only to patients with residual tumor in sample.
Histologic grade	HGRADE	1 = Well differentiated 2 = Moderately differentiated 3 = Poorly differentiated 4 = Undifferentiated Missing = no residual tumor in sample; data for two patients with residual tumor was not available	Applicable only to patients with residual tumor in sample.
Attempted surgery was completed	SURGCOMP	1 = Yes 2 = No	
Anastomosis	ANASTO	1 = Yes 2 = No	Provided only for patients who underwent laparoscopic resection
Laparoscopic resection converted to Open resection	LAPSURGOPEN	1 = Yes Missing = Patient did not convert from laparoscopic to open resection.	Indicator variable Provided only for patients who underwent laparoscopic resection and

Variable Description	Variable Name	Codes	Notes
			converted to Open resection
Reason Lap. Resection was converted to Open Resection	LAPCONVRSN	1 = Locally advanced disease discovered at surgery 2 = Adhesions 3= Complication/adverse event 4 = Unable to complete rectal dissection safely 5 = Unable to complete anastomosis safely Missing = Patient did not convert from laparoscopic to open resection.	Provided only for patients who underwent laparoscopic resection
Surgical Success Outcomes ***(presented for evaluable patients only. If a patient is not evaluable, the following variables are set to missing.)***			
Completeness of TME resection	RESECOMP	1 = Complete 2 = Nearly Complete 3 = Incomplete Missing = Patient not evaluated	Parameter 3 for primary endpoint For a description of each value, please refer to section 10.1 of the protocol and the Final Pathology Form in the CRF packet.
Circumferential radial margin	CIRCUMMAR	1 = Positive 2 = Negative Missing values represent data 'Not Applicable' (no residual tumor and no scar visible)	
Circumferential radial margin > 1mm or distance = NA	CIRCUMGT1	≤ 1 mm > 1 mm	Parameter 1 for primary endpoint. Patients with N/A grouped in > 1 mm
Distal margin	DISTAL	1 = Positive 2 = Negative	Parameter 2 for primary endpoint.
Successful Resection	SUCCESSRES	1 = Successful resection 2 = Resection not successful	**Successful resection** (as defined in protocol section 10.1) meets

Variable Description	Variable Name	Codes	Notes
			the following 3 criteria: Circumferential margin >1, Negative distal margin, and Complete or Nearly Complete TME resection
Intraoperative and Postoperative Complications ***(presented for evaluable patients only. If a patient is not evaluable, the following variables are set to missing.)***			
Complications (intraoperative and postoperative)	IOCPOC	1 = Yes 0 = no complications reported	Indicator variable
Intraoperative Complications *(Indicator variables):*			
	IOC_RECTUM	1 = Yes 0 = did not experience this complication	Rectum
	IOC_COLON	1 = Yes 0 = did not experience this complication	Colon
	IOC_SBOWEL	1 = Yes 0 = did not experience this complication	Small bowel NOS
	IOC_URETER	1 = Yes 0 = did not experience this complication	Ureter
	IOC_BLADDER	1 = Yes 0 = did not experience this complication	Bladder
	IOC_SPLEEN	1 = Yes 0 = did not experience this complication	Spleen
	IOC_HEMOR	1 = Yes 0 = did not experience this complication	Hemorrhage/bleeding associated with surgery

Variable Description	Variable Name	Codes	Notes
	IOC_OTHER	1 = Yes 0 = did not experience this complication	Other intraoperative complications
	IOC_OTHERSP	Character field Missing = did not experience "other" complications	Comment for intraoperative complications= Other
Maximum grade of postoperative complications	POC_MAXGR	Discrete values, ranging from 0 to 5 0 = patient did not report post-operative complication Missing = data not available	Select POC_MAXGR values: 3, 4, 5 for severe postoperative complication
Anastomotic leak during postoperative period:	LEAKPOD	Y Missing = patient did not experience anastomotic leak during the postoperative period	Indicator variable
	LEAKTERM	Character field Missing = patient did not experience anastomotic leak during the postoperative period	Specifies the type of anastomotic leak experienced
30-day mortality ***(presented for evaluable patients only. If a patient is not evaluable, the following variables are set to missing.)*** *(NOTE: as presented in the manuscript, the 30-day mortality variables include a grade 5 AE that occurred 44 days after surgery)*			
	MORT30	Y = Yes Missing = patient was alive 30 days after surgery	Indicator variable
	MORT30COM	Character field Missing = patient was alive 30 days after surgery	Grade 5 AE description
	TTOGRD5	Discrete values Missing = patient was alive 30 days after surgery	Days to grade 5 AE
Rehospitalization (within 30 days from surgery)	REHOSP30	1 = Yes 2 = No	Indicator variable
Re-operation ***(presented for evaluable patients only. If a patient is not evaluable, the following variables are set to missing.)***			
Re-operation was necessary	REOP	1 = Yes Missing = Re-operation was not necessary	Indicator variable
Days from resection to re-operation	REOPD	Discrete values Missing = patient did not have re-operation	

Variable Description	Variable Name	Codes	Notes
Reason re-operation was necessary	REOPRSN	Character field Missing = patient did not have re-operation	