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SWOG

PROSPECTIVE COMPARATIVE EFFECTIVENESS TRIAL FOR MALIGNANT BOWEL OBSTRUCTION

NCT #02270450

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SWOG, ALLIANCE, ECOG-ACRIN, NRG

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CA043/City of Hope Medical Center
CA078/Loma Linda University
FL065/Moffitt Cancer Center
IL043/Rush University Medical Center
KS004/University of Kansas
MA011/University of Massachusetts
MI014/University of Michigan
MN024/Essential Health Cancer Center
NC010/Duke University Medical Center
NJ022/ Hackensack University Medical Center
NM004/University of New Mexico Cancer Center
NY024/Columbia MU-NCORP
NY064/North Shore University Hospital
NY065/Long Island Jewish Medical Center
NY394/Southside Hospital
OK003/University of Oklahoma
PA075/University of Pennsylvania/Abramson Cancer Center
PA093/Temple University
RI005/Rhode Island Hospital
SC008/MUSC MU-NCORP
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TN030/University of Tennessee
TN086/Methodist Hospital, Germantown
TN089/West Clinic – Wolf River
TX012/Baylor University Medical Center
TX035/MD Anderson Cancer Center
TX041/Baylor College of Medicine/Dan L Duncan Comprehensive Cancer Center
TX059/University of Texas Health Science Center at San Antonio
TX182/University of Texas Health Science Center at San Antonio
UT003/University of Utah Medical Center
VA008/ Winchester Medical Center (Valley Health)
WI013/Froedtert and the Medical College of Wisconsin
11030/Princess Margaret Centre
55004/INEN (Instituto Nacional de Enfermedades Neoplásicas) - Peru
48007/INCan (Instituto Nacional de Cancerología) - Mexico
15002/INC (Instituto Nacional de Cancerología Bogotá) - Colombia

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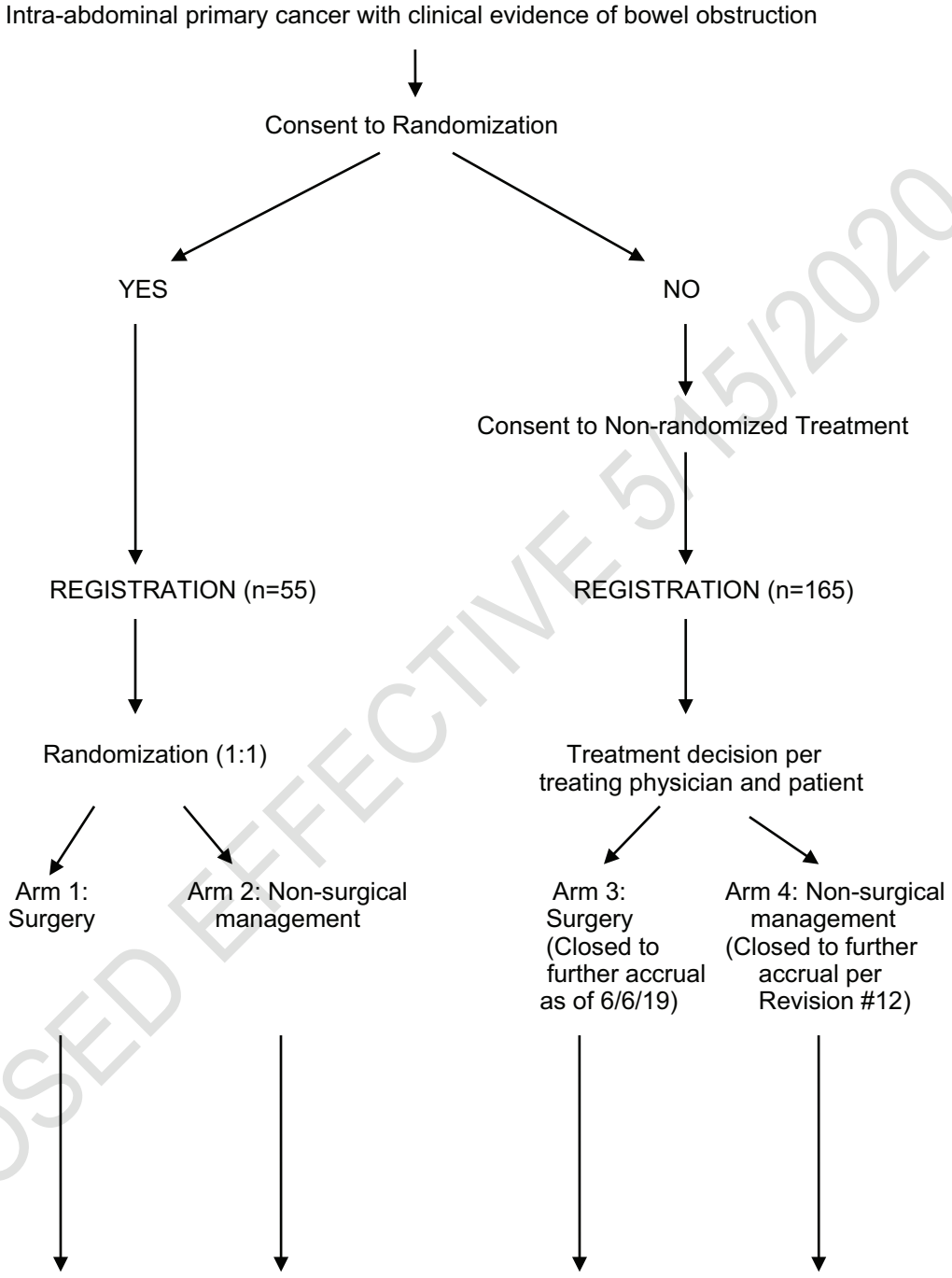
CANCER TRIALS SUPPORT UNIT (CTSU) ADDRESS AND CONTACT INFORMATION

CONTACT INFORMATION		
For regulatory requirements:	**For patient enrollments:**	**For study data submission:**
Regulatory documentation must be submitted to the CTSU via the Regulatory Submission Portal: Regulatory Submission Portal (Sign in at www.ctsu.org, and select the Regulatory Submission sub-tab under the Regulatory tab.) Institutions with patients waiting that are unable to use the Portal should alert the CTSU Regulatory Office immediately at 866-651-2878 to receive further information and support. Contact the CTSU Regulatory Help Desk at 866-651-2878 for regulatory assistance.	Please refer to the patient enrollment section of the protocol for instructions on using the Oncology Patient Enrollment Network (OPEN) which can be accessed at https://www.ctsu.org/OPEN_SYSTEM/ or https://OPEN.ctsu.org. Contact the CTSU Help Desk with any OPEN-related questions at ctsucontact@westat.com.	Data collection for this study will be done exclusively through Medidata Rave. Please see the data submission section of the protocol for further instructions. Other Tools and Reports: Institutions participating through the CTSU continue to have access to other tools and reports available on the SWOG Workbench. Access this by using your active CTEP-IAM userid and password at the following url: https://crawb.crab.org/TXWB/ctsulogon.aspx
The most current version of the **study protocol and all supporting documents** must be downloaded from the protocol-specific Web page of the CTSU Member Web site located at https://www.ctsu.org. Access to the CTSU members' website is managed through the Cancer Therapy and Evaluation Program - Identity and Access Management (CTEP-IAM) registration system and requires user log on with CTEP-IAM username and password. Permission to view and download this protocol and its supporting documents is restricted and is based on person and site roster assignment housed in the CTSU RSS.		
For patient eligibility or data submission questions contact the SWOG Data Operations Center by phone or email: 206/652-2267 cancercontrolquestion@crab.org **For treatment or toxicity related questions** contact the Study Chair by phone or email: (Dr. Robert S. Krouse at 215/662-2015).		
For non-clinical questions (i.e. unrelated to patient eligibility, treatment, or clinical data submission) contact the CTSU Help Desk by phone or e-mail: CTSU General Information Line – 1-888-823-5923, or ctsucontact@westat.com. All calls and correspondence will be triaged to the appropriate CTSU representative.		
The CTSU Website is located at https://www.ctsu.org.		

SCHEMA



All patients will be followed until death, 53 weeks after registration, or other reason for removal from protocol follow-up per Section 7.6, whichever occurs first.

1.0 OBJECTIVES

1.1 Primary Objective

a. To compare quality of life, as assessed by the number of days alive and outside of the hospital within the first 91 days (13 weeks) after registration, among patients with malignant bowel obstruction (MBO) who receive surgical intervention and similar patients treated non-surgically

1.2 Other Objectives

a. To explore whether there are differences in other health related quality of life (HRQOL) factors of particular interest in this population, including ability to eat, days with nasogastric tube, development of nausea, days of intravenous hydration, days eating solid foods and days drinking that are different for patients with MBO who receive surgical intervention as compared to non-surgical intervention.

b. To explore whether overall survival is different for patients with MBO who receive surgical intervention as compared to non-surgical intervention.

c. To estimate the effects of surgical versus non-surgical management on quality of life after adjustment for non-adherence to initially assigned/chosen treatment.

d. To explore whether there are clinical factors (e.g., ascites, albumin, carcinomatosis) that predict better quality of life outcomes for patients with malignant bowel obstruction who receive surgical intervention as compared to non-surgical intervention.

2.0 BACKGROUND

Patients with advanced cancer face challenges affecting quality of life (QOL). As the National Cancer Policy Board has identified, research addressing the needs of patients with incurable cancers is severely deficient and effectiveness has rarely been displayed by prospective trials. Malignant bowel obstruction (MBO) is a common problem for advanced cancer patients that involves considerable suffering. Common intra-abdominal primary cancers which lead to MBO are ovarian and colorectal cancers, although many other tumors are known to lead to this problem. There are two major treatment approaches for MBO: surgical management and medical management with specific classes of medications. It is the most frequent reason for surgical palliative care consults, although at least 25% do not go on to have a surgical procedure. *(1,2)* There is little evidence-based information to choose the optimal clinical care for most patients with an MBO, and the optimal treatment approach is unclear. This is especially true for patients with carcinomatosis, ascites, multiple obstructions, a recurrent obstruction, or palpable intra-abdominal disease. These patients remain a clinical conundrum for surgeons, medical oncologists, and palliative care specialists. Goals for these patients include being out of the hospital, the ability to eat, relief of nausea, pain control, and an increase in survival.

The few randomized clinical trials (RCT) for treatment of MBO that have been conducted were small and had limited ability to make clear statements related to therapy. *(3,4,5,6)* Also, these studies only examined medical approaches, which may not be the optimal treatment for many patients. Clinical trials have also been limited by heterogeneous populations, with diverse diagnoses, causes of MBO, sites of obstruction, and incomplete patient evaluations. In surgical studies outcome measures have been inconsistent and generally incomplete. *(7)* Attempts at comparisons for surgical versus non-surgical treatments have been prospective and suffered

from differences in arms based on performance status and surgical eligibility. *(8,9)* For patients who get anti-secretory medications in the preoperative setting for a small bowel obstruction, studies have shown that many of these patients can avoid surgery or do well after an operation. *(10,11)* This adds credence that one can safely manage an "operable" patient in a non-operative fashion, and potentially avoid surgery completely.

Patients randomized to non-surgical management or who, with their provider, choose not to have surgery will be given best medical care (BMC) medications at the discretion of the treating clinician. If a patient is showing clear signs of improvement (such as bowel function, eating or drinking), he or she will continue BMC and potentially be discharged from the hospital to their previous setting or possibly an interim care facility. If the patient does not improve, worsens or displays a desire to have an operation, the surgical team will re-evaluate at that time. A procedure may be offered, unless there are extenuating circumstances (the patient is no longer a surgical candidate related to poor clinical status or improvement such that the surgical team no longer feels there is a surgical indication). Percutaneous endoscopic gastrostomy (PEG) tubes will be considered as a BMC treatment due to the minimal invasiveness of these procedures and their utility to avoid a major operation. The intervention comparisons will be based on an intent to treat (ITT) approach using the randomized assignment in the RCT or the initial care plan in the non-randomized component. Changes in treatment approach are expected in both arms based on emerging issues and these will be documented so that sensitivity analyses may examine the extent to which these changes in treatment received alter the primary findings.

Rationale: This study has the potential to be practice-changing for clinicians treating patients with MBO. As MBO can effect up to 51% of ovarian cancer patients and 28% of colorectal cancer patients, this study would have a huge impact on the care of many cancer survivors. *(12)* Patients with MBO suffer from multiple symptoms, notably nausea and vomiting, uncomfortable abdominal distention, crampy abdominal pain, or the inability to eat or drink. This typically leads to hospitalization and being away from loved ones. This study is designed to assess whether patients' quality of life, as assessed primarily by days out of the hospital, will benefit from surgical intervention or whether in fact these operations provide little clinical benefit in this advanced cancer population. Further, we will evaluate the relationship between MBO and QOL with a specific emphasis on patient-initiated modifications in intake related to MBO.

While being at home is likely the most important outcome patients seek from their treatment of MBO, there are multiple secondary outcomes that are imperative to understand when comparing surgical versus non-surgical treatments. These include multiple symptoms that directly effect HRQOL, such as nausea, vomiting, feeling bloated, pain, and the ability to eat. The ability to eat and drink has a clear relationship to QOL. This is related not only to the enjoyment of food through taste and feeling sated, but also the socialization process. *(13)* It is extremely difficult to accurately assess food intake in the hospital, and current clinical approaches do not assess after discharge. Therefore, understanding what patients are able to eat and drink is of critical importance, as well as subjectively understanding the relationship between MBO and patient's intake.

The endpoints chosen were based on the extensive literature and clinical experience with MBO patients. The primary endpoint is "Days out of the hospital and alive". There is ample evidence that the primary goal for patients with end stage disease is to be at home/out of the hospital. *(14,15,16,17,18,19,20)* While it is imperative to collect other quality of life data, this is the optimal objective outcome for this population. Over 90% of hospice care is at home; therefore, days out of the hospital means days out of the acute care setting. While this is typically at home, it can also be at an inpatient hospice facility.

We propose a novel hybrid design, using a small randomized trial embedded in a larger non-randomized component. The joint analysis of these two components will rely on the RCT to provide an unbiased treatment effect estimate while using the information from the non-randomized component to add precision. This approach recognizes the strong need for a

randomized comparison in this setting to reduce bias while acknowledging the challenges of mounting a full-scale RCT in this patient population.

The RCT is the gold standard for clinical trials. Randomization provides comparable groups so that outcomes can be directly attributed to intervention. Physicians tend to be risk averse and thus are more likely to perform interventions on lower-risk patients. *(21)* Without randomization, the bias in treatment allocation may be subtle and unmeasurable, resulting in unreliable findings.

Despite these advantages, randomized trials have some disadvantages, including an often artificial population based on many defined eligibility criteria and selection associated with volunteering. When studying an issue for patients facing the end-of life, there are added difficulties in making a large RCT successful. A RCT may be deemed inappropriate by many in asking patients and families to agree to a random treatment plan in a life-threatening setting, especially options that are so dramatically different. This reasoning also affects the major concern noted by previous reviewers when a RCT was presented to cooperative groups: this trial may fail to meet accrual goals. This legitimate concern is two-fold: 1) patients may be unwilling to agree to be randomized to such diverse treatment options, and 2) surgeons are unlikely to consistently accrue their patients where they likely have great bias as to which treatment is better. In a similar study, despite the fact that a majority of urologic surgeons in North Thames stated that a randomized trial was needed to determine the impact of surgery on stress incontinence, none would agree to participate because of beliefs in the correctness of their own practice style. *(22)* Thus, although "collective equipoise" may exist, the absence of "individual equipoise" may substantially hamper the conduct of a full-scale RCT. *(23)* Thus while a large RCT seems untenable, the potential biases of a non-randomized component in this setting seem equally problematic as it would provide a result whose validity could not be assessed.

While the research team believes there is sufficient equipoise to randomize to such a trial, it is likely infeasible to accrue the entire population to a RCT at this time. Therefore, this study proposes to accrue a large number (n=180) and randomize a subset of these (n=50) accruing at selected institutions demonstrating substantial interest in and commitment to this question. This combined approach builds on the strengths of each design to give more reliable results. While the RCT component of this hybrid design could be considered a pilot trial, by embedding this trial in a larger non-randomized component, we believe we will have stronger inference than could be achieved by either alone.

Inclusion of Women and Minorities

This study was designed to include women and minorities, but was not designed to measure differences of intervention effects. The anticipated accrual in the ethnicity/race and sex categories is shown in the table below.

Racial Categories	DOMESTIC PLANNED ENROLLMENT REPORT				
	Ethnic Categories				
	Not Hispanic or Latino		Hispanic or Latino		Total
	Female	Male	Female	Male	
American Indian/Alaska Native	1	0	0	0	1
Asian	8	4	1	0	13
Native Hawaiian or Other Pacific Islander	0	0	0	0	0
Black or African American	24	7	2	1	34
White	76	30	33	13	152
More Than One Race	0	0	0	0	0

Total	109	41	36	14	200

Racial Categories	INTERNATIONAL (including Canadian participants) PLANNED ENROLLMENT REPORT				
	Ethnic Categories				
	Not Hispanic or Latino		Hispanic or Latino		Total
	Female	Male	Female	Male	
American Indian/Alaska Native	0	0	0	0	0
Asian	0	0	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0	0	0
Black or African American	0	0	1	0	1
White	0	0	11	8	19
More Than One Race	0	0	0	0	0
Total	0	0	12	8	20

3.0 DRUG INFORMATION

Drug information is not applicable to this study.

4.0 STAGING CRITERIA

Staging criteria are not applicable to this study.

5.0 ELIGIBILITY CRITERIA

NOTE: Patients must be eligible and evaluable for all eligibility criteria, regardless of study group (randomized vs non-randomized) and treatment (surgery vs non-surgical management)

Each of the criteria in the following section must be met in order for a patient to be considered eligible for registration. Use the spaces provided to confirm a patient's eligibility. For each criterion requiring test results and dates, please record this information on the Onstudy Form and submit via Medidata Rave® (see Section 14.0). Any potential eligibility issues should be addressed to the Data Operations Center in Seattle at 206/652-2267 prior to registration.

In calculating days of tests and measurements, the day a test or measurement is done is considered Day 0. Therefore, if a test is done on a Monday, the Monday 4 weeks later would be considered Day 28. This allows for efficient patient scheduling without exceeding the guidelines. **If Day 3 or 7 falls on a weekend or holiday, the limit may be extended to the next working day.**

5.1 Disease Related Criteria

a. Patient must have malignant bowel obstruction (MBO) as evidenced by all of the following *(24)*:

- Clinical evidence of a small bowel obstruction (via history, physical, and radiographic examination)
- Bowel obstruction below (distal to) ligament of Treitz
- Intra-abdominal primary cancer with incurable disease

b. Patients must have malignant bowel obstruction due to an intra-abdominal primary cancer, (i.e. GI, pancreas, ovarian, uterine, cervical, kidney, bladder, prostate, GIST [all sites], and sarcoma). Patients may still have primary tumor as long as it is not a primary large bowel obstruction from colorectal cancer.

c. Patient must be able to tolerate a major surgical procedure based on clinical evaluation, status of their cancer, and any other underlying medical problems.

d. A member of the patient's surgical team must indicate equipoise for the benefit of the surgical treatment for MBO. The surgeon must respond "Yes" to each of the following questions and sign the **S1316** Surgical Equipoise Documentation form for the patient to be eligible:

1. Is surgery for treatment of malignant bowel obstruction (MBO) being considered for this patient?

2. Do you have equipoise? If the treating team finds that an operation is required (e.g., for acute abdomen), or they would not offer the patient an operation (e.g., patient is too weak to tolerate surgery), then there is no equipoise.

e. Patients must not have signs of bowel perforation necessitating surgery or "acute" abdomen evidenced by peritonitis on physical exam within 2 days prior to registration.

5.2 Clinical/Laboratory Criteria

a. Patients must be registered to the study within 3 working days after being seen by surgical team for MBO or within 3 working days after completion of indicated treatment (e.g. TPN, anticoagulation reversal) to make them eligible for surgical intervention, whichever is later, and prior to any treatment (surgical or non-surgical) for MBO. Treatment is defined as any medication or invasive interventions beyond nasogastric decompression, hydration, pain medications or antiemetic medications. NOTE: Somatostatin analogues may be used prior to registration if that use is limited to not more than the two days just prior to registration.

b. Radiographic confirmation of MBO is required prior to registration. Scans may have been done before or after admission; scans done prior to admission must have been completed within 14 days prior to admission. CT scans are preferred.

c. Patients must have Zubrod Performance Status of 0-2 within 7 days prior to hospitalization (see Section 10.4).

d. Serum albumin must be planned to be collected after admission, but prior to treatment.

e. Patients must be able to complete the study questionnaires in English or Spanish.

f. Patients must be ≥ 18 years of age.

g. Prestudy history and physical must be obtained within 3 days prior to registration.

5.3 Regulatory Criteria

a. Patients or their legally authorized representative must be informed of the investigational nature of this study and must sign and give written informed consent in accordance with institutional and federal guidelines.

b. As a part of the OPEN registration process (see Section 13.4 for OPEN access instructions) the treating institution's identity is provided in order to ensure that the current (within 365 days) date of institutional review board approval for this study has been entered in the system.

c. Patients must consent and provide both their contact information and that of their representative for a monthly 24-hour dietary recall phone call to be conducted by the Arizona Diet, Behavior and Quality of Life Assessment Lab.

6.0 STRATIFICATION FACTORS

Randomization will be dynamically balanced according to primary tumor type (colorectal cancer vs. ovarian cancer vs. other cancer). *(25)*

7.0 TREATMENT PLAN

For treatment questions, please contact Dr. Krouse at 215-662-2015 or Dr. Deneve at 901/448-2919.

7.1 Eligible Participants

Eligible participants consenting to randomization will be randomized to receive surgery (Arm 1) or non-surgical management (Arm 2). Eligible patients consenting to non-randomized treatment will be assigned to Arm 3 if surgery is chosen and Arm 4 if non-surgical management is chosen. (Arm 4 has been closed to further accrual per Revision #12.)

Patients will consent to or decline randomization based on their response to the randomization question at the end of the Consent. Patients consenting to randomization will have treatment assignment determined at registration. Patients not consenting to randomization will be placed on the non-randomized component and must indicate their initial treatment choice (surgical or non-surgical management) at the end of the Consent. (Arm 4 has been closed to further accrual per Revision #12.)

7.2 Arms 1 and 3: Surgery

Patients on surgical management Arms 1 (randomized) and 3 (non-randomized) will undergo abdominal surgery as defined by the treating physician. Surgery is defined as an operative procedure. Information regarding patient treatment will be collected on the **S1316** Malignant Bowel Obstruction Treatment Form.

While randomization to Arm 1 will determine a patient's initial care, the treating physician will take changes in their clinical course or other circumstances into account in determining the ongoing care plan.

7.3 Arms 2 and 4: Non-surgical Management

Patients on non-surgical management Arms 2 (randomized) and 4 (non-randomized) will be offered non-surgical management as determined by the treating physician. Information

regarding patient treatment will be collected on the **S1316** Malignant Bowel Obstruction Treatment Form.

It is optional, but recommended, that patients receive a somatostatin analogue as an anti-secretory agent at an appropriate therapeutic dose. Somatostatin analogues include:

- Octreotide injection solution (50 mcg/mL; 100 mcg/mL; 200 mcg/mL; 500 mcg/mL; 1,000 mcg/mL)
- Sandostatin injection solution (50 mcg/mL; 100 mcg/mL; 200 mcg/mL; 500 mcg/mL; 1,000 mcg/mL)
- Sandostatin LAR Depot intramuscular powder for suspension (10 mg, 20 mg, 30 mg)
- Lanreotide subcutaneous solution (120 mg/0.5 mL; 90 mg/0.3 mL; 60 mg/0.2 mL)
- Pasireotide (Somatuline Depot) subcutaneous solution (120 mg/0.5 mL; 90 mg/0.3 mL; 60 mg/0.2 mL)

While randomization to Arm 2 will determine a patient's initial care, the treating physician will take changes in their clinical course or other circumstances into account in determining the ongoing care plan.

7.4 Dietary Recall

Dietary recalls are a self-reported diet measurement method that relies on the patient (or caregiver) to report all foods consumed in the prior 24-hour period. Standard USDA multi-pass methodology will be used to collect this self-reported information by telephone. The Dietary Recall will be collected by trained staff at the Arizona Diet, Behavior, and Quality of Life Assessment Lab. The patient or their representative will be contacted every 4 weeks by phone for up to one year after registration to conduct 24-hour dietary recalls. The patient will be queried on food and beverage consumed during the past 24-hours. The recalls will be qualified in terms of frequency of meals, primarily liquid, solids or mixed, use of feeding tubes/formulas as well as coding for commonly reported food avoidances. Patients will also be queried as to whether the 24-hour recall is typical of their intake in recent days, and if not how the intake differed (more liquid foods, less vegetables, avoidance of foods they are not tolerating) as well as when they recall making this change (by date of change). Each call will last on average about 15-20 minutes.

The patient and their representative's contact information will be collected at the baseline visit on the **S1316** Dietary Recall Contact Form and will be sent to the Arizona Diet, Behavior, and Quality of Life Assessment Lab via e-mail (scanned and sent as an attachment). Always follow your institutional HIPAA policies when emailing protected health information (PHI).

7.5 Study Schedule for All Patients

a. Baseline Visit

Patients must be registered to the study within 3 days after being seen by surgical team for MBO or within 3 days after completion of indicated treatment (e.g. TPN, anticoagulation reversal) to make them eligible for surgical intervention, whichever is later, and prior to any treatment (surgical or non-surgical) for MBO. After registration, the patient will receive treatment for MBO according to assigned study arm.

Patient follow-up for **S1316** is conducted entirely over the phone: no follow-up visits are required by the study. Therefore, it is strongly recommended that a Release of Information (ROI) document be signed by the patient after he or she is registered to the study. This will facilitate data collection for patient status and hospitalization data from other hospitals where the patient may be treated while on study follow-up.

Use the local ROI document, following the local institutional policy. Please use an ROI that covers the greatest length of time possible. An ROI that is valid for a year (the length of follow-up for **S1316**) is ideal. At a minimum, a ROI that is valid for at least 91 days (the time covered by the primary objective) should be used.

Equipoise: Prior to registration, a member of the patient's surgical team (S1316 site team member or attending physician) must indicate equipoise for the benefit of surgical treatment for MBO. The surgeon must respond "Yes" to the following two questions and sign the **S1316** Surgical Equipoise Documentation form for the patient to be eligible:

1. Is surgery for treatment of malignant bowel obstruction (MBO) being considered for this patient?

2. Do you have equipoise? If the treating team finds that an operation is required (e.g., for acute abdomen), or they would not offer the patient an operation (e.g., patient is too weak to tolerate surgery), then there is no equipoise.

The baseline visit will include data collection for the following forms:

1. **S1316** Surgical Equipoise Documentation form

2. **S1316** MDASI-GI (and **S1316** Cover Sheet for Patient-Completed Questionnaires)

3. **S1316** EQ-5D-5L (Weeks 2, 4, 8, and 12 only)

4. **S1316** Malignant Bowel Obstruction Treatment Form

5. **S1316** Malignant Bowel Obstruction Treatment Complications Form

b. Follow-up

Study site staff will contact patients via phone for assessments weekly for the first 13 weeks after registration and every 4 weeks thereafter, up to one year after registration. The **S1316** Follow-Up Form collects information on vital status and hospitalization. Site staff (CRA) will administer all forms as outlined below. All patient-completed study forms will be administered via telephone or in person, if patient is in the hospital and allows an in-person visit. Forms are submitted according to the schedule in Section 14.4. Follow-up assessments of patients are based from the date of registration. The time window for each assessment is +/- 2 days to allow for scheduling. If a follow-up call or visit is missed, the information that was missed will be included during the next completed call or visit.

Every effort should be made to collect the follow-up data in identical fashion across all study arms (surgical vs. non-surgical management, randomized vs. non-randomized)

c. Assessments through Week 13

The weekly phone calls (or in-person visits, if the patient is in the hospital) will include data collection for the following forms:

Patient interview:

1. **S1316** MDASI-GI
2. **S1316** EQ-5D-5L (Weeks 2, 4, 8, and 12 only)
3. **S1316** MBO Assessment

Site completed:

4. **S1316** Cover Sheet for Patient-Completed Questionnaires
5. **S1316** Hospitalization Days Record

d. Assessments if patient is re-admitted to hospital after initial discharge in the first 13 weeks

Assessments will include data collection of the following site completed forms:

1. **S1316** Malignant Bowel Obstruction Treatment Form
2. **S1316** Malignant Bowel Obstruction Treatment Complications Form
3. **S1316** Somatostatin Analogue Treatment Form

e. Assessments after Week 13

The phone calls every 4 weeks will include data collection of the following forms:

Patient interview:

1. **S1316** MDASI-GI
2. **S1316** MBO Follow-up Form

Site completed:

3. **S1316** Cover Sheet for Patient-Completed Questionnaires

7.6 Criteria for Removal from Protocol Follow-Up

a. Completion of 53 weeks on study.

b. If a medical condition arises which in the opinion of the treating investigator precludes patient's participation in this study, the patient will then be removed from study follow-up.

c. The patient may refuse all future follow-up data collection or contacts at any time for any reason. Follow-up through the treating investigator for hospitalizations and vital status will continue unless the patient specifically refuses to allow passive follow-up. (NOTE: The patient may refuse any follow-up data collection or contact at any time for any reason. If patient no longer wants to complete any

future study phone calls, if appropriate, the site should ask if the follow-up calls can be made solely to the patient's designated representative before removing a patient from follow-up.)

7.7 Discontinuation of Protocol Follow-up

All reasons for discontinuation of follow-up must be documented in the **S1316** Off Protocol Notice.

NOTE: Patients who discontinue follow-up will no longer be contacted for the scheduled telephone assessments (including contact via a designated representative), but known hospitalization data and vital status should still be reported.

7.8 Follow-Up Period

All patients will be followed until death, 53 weeks after registration, or other reason for removal from protocol follow-up per Section 7.6, whichever occurs first. Patients are to remain on study follow-up even if they elect to receive follow-up care at a different institution.

8.0 TOXICITIES TO BE MONITORED AND DOSE MODIFICATIONS

8.1 NCI Common Terminology Criteria for Adverse Events

Two different versions of the NCI Common Terminology Criteria for Adverse Events (CTCAE) will be used on this study.

a. Serious Adverse Event (SAE) reporting

The CTCAE (NCI Common Terminology Criteria for Adverse Events) Version 5.0 will be utilized **for SAE reporting only**. The CTCAE Version 5.0 can be downloaded from the CTEP home page (https://ctep.cancer.gov) All appropriate treatment areas should have access to a copy of the CTCAE Version 5.0.

b. Routine toxicity reporting

This study will utilize the CTCAE Version 4.0 for routine toxicity reporting. A copy of the CTCAE Version 4.0 can be downloaded from the CTEP home page (https://ctep.cancer.gov). All appropriate treatment areas should have access to a copy of the CTCAE Version 4.0.

9.0 STUDY CALENDAR

REQUIRED STUDIES	Hospital Admission/ Baseline	W 1	W 2	W 3	W 4	W 5	W 6	W 7	W 8	W 9	W 10	W 11	W 12	W 13	F/U every 4 Weeks through Wk 53
PHYSICAL															
History and Physical Exam π	X														
Weight and Performance Status	X														
Patient Assessment α		X	X	X	X	X	X	X	X	X	X	X	X	X	
LABORATORY															
Serum Albumin	X														
CBC †	X														
Electrolyte Panel (sodium, potassium, bicarbonate, chloride, BUN, creatinine) †	X														
SCANS															
CT or MRI for disease assessment	X														
X-ray/Abdominal Plain Film Ω	X														
PATIENT QUESTIONNAIRES & FOLLOW-UP															
S1316 Cover Sheet for Patient-Completed Questionnaires	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
S1316 MDASI-GI	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
S1316 EQ-D5	X		X		X				X				X		
S1316 MBO Assessment		X	X	X	X	X	X	X	X	X	X	X	X	X	
S1316 MBO Follow-Up															X
S1316 Hospitalization Days Record β														X	
S1316 Dietary Recall Contact Information Form	X														
Dietary Recall δ		X				X				X				X	X
TREATMENT															
Surgery (Arms 1 and 3)		X													
Non-surgical management (Arms 2 and 4)		X													

Footnotes:

α Weekly follow-up during Weeks 2-13 will take place by phone or in person if patient is in the hospital (see Section 7.5b).
β Assessment done weekly; data reported at Week 13.
† Recommended laboratory values to be collected on the **S1316** On Study Form if testing is performed.
δ To be administered monthly by phone by the Arizona Diet, Behavior and Quality of Life Assessment Lab (see Section 7.4).
π Including pathology report of primary intra-abdominal cancer (see Section 14.4b).
Ω If CT is obtained for MBO confirmation, then it may be used rather than x-ray.

10.0 CRITERIA FOR EVALUATION AND ENDPOINT ANALYSIS

10.1 Primary Endpoint

The primary endpoint for this study is number of days alive and outside the hospital within the first 91 days after enrollment, as recorded on the **S1316** Hospitalization Days Record. The time window for each weekly assessment is +/- 2 days to allow for practical CRA/patient considerations including (but not limited to) scheduling of telephone calls and possible missed telephone calls.

10.2 MDASI-GI

The MDASI-GI is a well-validated instrument with each item, based on a 0-10 scale, designed as an independent domain related to specific HRQOL issues for patients with gastrointestinal cancers. While the MDASI is not intended to produce a total score, one can calculate a total symptom index. It is a valid, reliable, and concise tool to measure the severity of symptoms for patients with GI cancer. This will give the ability to compare outcomes for many of the most important patient reported outcomes for MBO patients, such as nausea, vomiting, feeling bloated, and pain. A movement of two points on each 0-10 point scale is considered as clinically meaningful and cutoff scores for indication of clinical deficits have been defined by the tool authors.

10.3 EQ-5D-5L

The EQ-5D-5L is designed for the collection of health state values using a visual analogue scale with the end points labeled best imaginable health state at the top and worst imaginable health state at the bottom having numeric values of 100 and 0 respectively. The EQ-5D-5L has been widely used in clinical trials in quality-adjusted survival efforts. *(26,27,28,29)* We will combine the MDASI-GI index score with EQ-5D-5L total score to produce a quality-adjusted life years (QALY)- adjusted outcome measure. *(30)*

10.4 Performance Status

Patients will be graded according to the Zubrod Performance Status Scale.

POINT	DESCRIPTION
0	Fully active, able to carry on all pre-disease performance without restriction.
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work.
2	Ambulatory and capable of self-care but unable to carry out any work activities; up and about more than 50% of waking hours.
3	Capable of limited self-care, confined to bed or chair more than 50% of waking hours.
4	Completely disabled; cannot carry on any self-care; totally confined to bed or chair.

11.0 STATISTICAL CONSIDERATIONS

11.1 Design overview

This study is a hybrid design, incorporating both a randomized and a non-randomized component. Eligibility is defined identically in both components with the exception that patients in the randomized component will consent to randomization to either surgical management or non-surgical management (best supportive non-surgical palliative care) of their MBO in a 1:1 ratio. Randomization will determine their initial care, although the treating physician will take changes in their clinical course or other circumstances into account in determining their ongoing care plan. Patients who are medically eligible for the randomized trial but who do not consent to randomization will be offered registration into the non-randomized component. Their initial care plan (surgical versus non-surgical), as determined by the patient and his/her treating physician at the time of registration will be documented and considered their initial care plan for the analyses. If the treating team finds that an operation is required (e.g., for acute abdomen), or they would not offer the patient an operation (e.g., patient is too weak to tolerate surgery), then there is no equipoise and patient will not be accrued to the study.

The advantages of this hybrid design are that it uses the strengths of both the RCT to give an unbiased estimate of treatment differences while allowing us to accrue a larger and likely broader range of MBO patients who are eligible for surgery but unwilling to be randomized. By allowing more patients to participate while maintaining greater control of their care, we hope to improve power and potentially expand the inference to a more clinically relevant population who are treated according to usual practice patterns. These results may have higher external validity than a stand-alone through their inclusion of broader and more generalizable patient and physician populations. *(31,32)*

11.2 Primary Endpoint

The primary endpoint for this study is number of days alive and outside the hospital within the first 91 days after enrollment. Patients will be assessed for number of days admitted to the hospital every 7 days for 91 days.

11.3 Primary analyses

All eligible patients will be included in the analysis using the general modeling strategy pioneered by Prentice et al. for pooling data from a randomized trial and parallel non-randomized component. *(33,34,35,36,37)* For randomized patients, the analysis will be based on their assigned treatment according to the intent to treat (ITT) principle. For the non-randomized component, a pseudo-ITT approach will be used where patients will be included in the treatment group identified at enrollment as their initially chosen care plan (surgical versus non-surgical), as documented at registration. The primary analysis will pool data from both components using a multivariate linear regression model (after possible rescaling, if necessary to improve the distribution assumptions), including a parameter for study component. Factors considered likely to confound the association of treatment and outcome in the non-randomized component will be carefully modeled in the regression. Potential residual bias in the treatment group comparison from the non-randomized component will be assessed by estimating the interaction term between treatment group and study component (randomized vs. non-randomized). If, after adjustment for covariates, there is no evidence of substantial bias, the main treatment effect parameter in the reduced model (without the interaction term) will serve as the

basis for inference. If there is evidence of significant bias in the non-randomized component relative to the randomized component, the estimates from both the randomized and non-randomized components will be reported but the primary analysis will be based on the randomized component alone.

If the approach of Prentice et al., proves unwieldy because the number of covariates required to adjust for imbalance in the non-randomized component is too large for the sample size available, we will pursue the use of propensity scores. *(38,39,40,41,42,43)* In this approach, a logistic regression model would be developed in non-randomized component data to estimate the probability of selecting surgery using the baseline covariate data, both from patients and providers. The propensity score for each patient is then simply the estimated probability; this score can be used in the regression model instead of adjusting for individual confounders.

Missing data is a problem best handled by reducing it as much as possible. We have defined the primary endpoint in a way that should avoid most problems for this measure. By counting "good days" as days alive and not in the hospital, and having the CRAs maintain frequent (weekly) telephone contact with patients and their families, we expect that missingness on the primary outcome variable will be minimized. We anticipate that patients re-admitted to the hospital will generally return to the same institution as where they were enrolled, but if not, the weekly site calls will collect hospitalization and other relevant data. For other elements, we will attempt to limit the extent of missing data by assuring that only those data necessary for the study are collected, by developing database reports and triggers to monitor the completeness of data and alert CRAs to missing values, and by providing feedback to sites with higher than desirable frequencies of missing data.

11.4 Secondary analyses

A strategy similar to that used for the primary endpoint will be employed for secondary endpoints. For other HR-QOL type endpoints (e.g., ability to eat, days of nasogastric tube, intravenous hydration, solid food, etc.) we will examine the distribution properties of these variables and determine whether a normal approximation is adequate, or whether a transformation would be required or another generalized linear model would be preferable. For failure time endpoints, such as overall survival, the analyses will be based on a Cox regression model where we will have the option of stratifying on study component and selected other key covariates rather than modeling them in the regression. QALY-adjusted analyses will incorporate the EQ-5D-5L, as described in Cheville et.al. *(44)*

Specific to dietary outcomes we will describe total self-reported energy intake, macronutrient intake in patients with MBO and relation to time since MBO and if this differs for those undergoing surgery versus no surgery. Similarly we will evaluate the same associations with the dietary exposure of interest being frequency of meals and alternately composition of meals (liquids, solids, mixed, feeding formulas [oral or enteral]).

Adherence adjusted analyses: Although the primary analysis will be based on the intent to treat (ITT) principle, if a substantial fraction (> 30%) do not receive the initially assigned/chosen treatment, we will conduct a sensitivity analysis that takes into account the patient's received treatment through inverse probability weighting.

In exploratory analyses we will examine the extent to which we can identify subgroups of patients for whom differences in treatment effects may differ from the overall result, i.e.,

are there subgroups of individuals for whom surgery is particularly beneficial or particularly contra-indicated? To address this question, the final model for the primary analyses in the pooled data will be expanded using interaction terms between selected baseline factors and treatment assignment.

Sample sizes permitting, those of particular interest will be analyzed based on the following hypotheses:

1. Patients with ascites who undergo a surgical procedure will have poorer outcomes than those who are treated by non-surgical management.

2. Patients who have albumin < 3.0 who undergo a surgical procedure will have poorer outcomes than those who are treated by non-surgical management.

3. Patients with carcinomatosis evident in more than one quadrant of the abdomen who undergo a surgical procedure will have poorer outcomes than those who are treated by non-surgical management.

Additional analyses will be conducted in the non-randomized component to examine predictors of treatment, and the diversity of treatment within each arm (e.g., type of surgical procedure and medications used), patterns of care over time, including the frequency with which a patient initially selecting one treatment approach is crossed over to the other strategy, etc.

11.5 Sample size

Our goal is to randomize at least 50 eligible patients, in equal proportions, to surgical or non-surgical care and register 130 eligible patients to the non-randomized component. Available data from 144 patients for whom number of good days could be determined show the mean number of good days of 33 with standard deviation of 25. With a total of 180 eligible patients with equal numbers in each treatment group, we would have 90% power to detect a 14-day difference in the mean number of good days using a two-sided, 0.05-level t-test. We have increased the overall target sample size to 200 to allow for potential losses to follow-up and incomplete data, for potential inefficiencies associated with imbalance in the number treated in each group in the non-randomized component and for the need to adjust for differences in baseline characteristics. For an analysis restricted to the trial alone with 50 patients randomized, the power would be .51. While this is a low power for a trial, we know that fear of randomization represents the dominant reason patients give for refusing to participate in clinical trials so to help assure adequate accrual, the sample size of the randomized component is small. *(45)*

Updated sample size: In October 2017, the DSMC recommended that “after the cohort accrual goal is reached, the randomization portion of the trial may continue for a probationary six-month period. The DSMC would then carefully evaluate the feasibility of randomizing patients to this trial and evaluate the ability achieve the objectives of the trial.” This recommendation followed the observation that accrual to the randomized arms has been considerably slower than expected. Accrual to the two treatment arms in the non-randomized cohort was also found to be unbalanced, favoring the non-surgical arm by more than 2:1. In accordance with the monitoring plan, the sample size targets are hereby adjusted to reflect the DSMC’s recommendations. Accrual to the non-randomized arms will continue until 166 patients have been registered in the non-randomized arms, with specific efforts to increase enrollment in the surgical choice arm. After the non-randomized arms are closed, the study will continue to accrue patients to

the randomized component during the subsequent six months. At that time, the DSMC will evaluate the feasibility of continuing to full accrual is reached (200 patients total).
June 2019 update: With the closure of the non-randomized component (with 165 of the targeted 166 patients) and the recent success in accruing patients to the randomized component (with 34 now randomized), the study has demonstrated the feasibility of meeting the original randomization goal. The study investigators have requested and the NCI has approved an increase in total accrual to 220, which would allow the randomized component to reach the initial target of 50 eligible patients randomized, consistent with the design as originally conceived.

11.6 Estimate of Accrual Rate

The anticipated accrual rate is based on the number of potential study patients available at the participating institutions. Conservatively, there will be at least 350 potential patients per year at the participating institutions with the presenting diagnosis of MBO based on the study definition. Due to multiple factors, expected accrual each year will be significantly less than 350 patients. Reasons include ineligibility, patient refusal, or inability to recruit the patient in the prescribed 3 working days post-surgical consultation criteria. SWOG has no prior experience in recruiting these patients to draw from so we have set a target of 6 patients/month, which would allow for complete enrollment in 3 years, including IRB approval and study ramp-up time.

11.7 Trial Monitoring

A Data and Safety Monitoring Committee will oversee the conduct of the study. The Committee consists of four members from outside of SWOG, 3 SWOG members, 3 nonvoting representatives from the National Cancer Institute (NCI), and the Group Statistician (non-voting). The members of this Committee will receive confidential reports every 6 months from the SWOG Statistical Center, and will meet at the Group's bi-annual meetings as necessary.

Trial monitoring will focus on accrual, with particular attention to the rate of accrual to the randomized component as well as the distribution of the selected treatment in the non-randomized component and comparison of baseline characteristics between the randomized control trial and non-randomized components. If after 12 months of active recruitment at the key participating centers, accrual to the randomized component is less than 12, we will consider a redesign to complete accrual as a non-randomized study only. If there is evidence of the ability to recruit a larger number of patients to the randomized comparison, we will consider limiting the non-randomized component enrollment. Similarly, if during the course of the trial we learn that a large fraction of patients are not adhering to their assigned treatment, we will consider discontinuing the randomized control trial portion. For the non-randomized portion, if a large fraction (75%) of patients are not adhering to their initially chosen treatment, we will consider closing accrual to the over-subscribed arm, either temporarily or permanently. These decisions will be made blinded to all information on endpoint comparisons. If after 12 months of active recruitment at the key centers, accrual to the overall study is less than 30, we will consider stopping based on infeasibility of recruitment.

No formal interim analyses for efficacy or safety are planned for several reasons. Both of these treatment options are commonly used in clinical practice. These patients are in very advanced stages of disease and deaths are expected. The randomized component, on its own, is underpowered and, in total, represents the minimum information one might expect to have at an interim analysis of a full-scale trial. If accrual to the randomized portion is substantially greater than anticipated, so that the expected number randomized

exceeds 100, we will institute a single interim analysis when the data are complete for 50 randomized patients.

12.0 DISCIPLINE REVIEW

Discipline review is not necessary for this study.

13.0 REGISTRATION GUIDELINES

13.1 Registration Timing

Patients must be registered to the study within 3 working days after surgical consult for MBO or within 3 days after completion of indicated treatment (e.g. TPN, anticoagulation reversal) to make them eligible for surgical intervention, whichever is later, and prior to any treatment for MBO (no more than two working days prior to planned start of treatment).

13.2 Investigator/Site Registration

Prior to the recruitment of a patient for this study, investigators must be registered members of a Cooperative Group. Each investigator must have an NCI investigator number and must maintain an "active" investigator registration status through the annual submission of a complete investigator registration packet to CTEP.

a. CTEP Registration Procedures

Food and Drug Administration (FDA) regulations and National Cancer Institute (NCI) policy require all individuals contributing to NCI-sponsored clinical trials to register and to renew their registration annually. To register, all individuals must obtain a Cancer Therapy Evaluation Program (CTEP) Identity and Access Management (IAM) account (https://ctepcore.nci.nih.gov/iam). In addition, persons with a registration type of Investigator (IVR), Non-Physician Investigator (NPIVR), or Associate Plus (AP) (i.e., clinical site staff requiring write access to OPEN, RAVE, or TRIAD or acting as a primary site contact) must complete their annual registration using CTEP's web-based Registration and Credential Repository (RCR) (https://ctepcore.nci.nih.gov/rcr). Documentation requirements per registration type are outlined in the table below.

Documentation Required	IVR	NPIVR	AP	A
FDA Form 1572	✔	✔		
Financial Disclosure Form	✔	✔	✔	
NCI Biosketch (education, training, employment, license, and certification)	✔	✔	✔	
HSP/GCP training	✔	✔	✔	
Agent Shipment Form (if applicable)	✔			
CV (optional)	✔	✔	✔	

An active CTEP-IAM user account and appropriate RCR registration is required to access all CTEP and CTSU (Cancer Trials Support Unit) websites and applications. In addition, IVRs and NPIVRs must list all clinical practice sites and IRBs covering their practice sites on the FDA Form 1572 in RCR to allow the following:

- Added to a site roster

- Assigned the treating, credit, consenting, or drug shipment (IVR only) tasks in OPEN
- Act as the site-protocol PI on the IRB approval

Additional information can be found on the CTEP website at <https://ctep.cancer.gov/investigatorResources/default.htm>. For questions, please contact the RCR ***Help Desk*** by email at < RCRHelpDesk@nih.gov>.

b. CTSU Registration Procedures

This study is supported by the NCI Cancer Trials Support Unit (CTSU).

1. **IRB Approval:**

Each investigator or group of investigators at a clinical site must obtain IRB approval for this protocol and submit IRB approval and supporting documentation to the CTSU Regulatory Office before they can be approved to enroll patients. Assignment of site registration status in the CTSU Regulatory Support System (RSS) uses extensive data to make a determination of whether a site has fulfilled all regulatory criteria including but not limited to: the following:

- An active Federal Wide Assurance (FWA) number
- An active roster affiliation with the Lead Network or a participating organization
- A valid IRB approval
- Compliance with all protocol specific requirements.

In addition, the site-protocol Principal Investigator (PI) must meet the following criteria:

- Active registration status
- The IRB number of the site IRB of record listed on their Form FDA 1572
- An active status on a participating roster at the registering site.

Sites participating on the NCI CIRB initiative that are approved by the CIRB for this study are not required to submit IRB approval documentation to the CTSU Regulatory Office. For sites using the CIRB, IRB approval information is received from the CIRB and applied to the RSS in an automated process. Signatory Institutions must submit a Study Specific Worksheet for Local Context (SSW) to the CIRB via IRB Manager to indicate their intent to open the study locally. The CIRB's approval of the SSW is then communicated to the CTSU Regulatory Office. In order for the SSW approval to be processed, the Signatory Institution must inform the CTSU which CIRB-approved institutions aligned with the Signatory Institution are participating in the study.

2. **Downloading Site Registration Documents:**

Site registration forms may be downloaded from the **S1316** protocol page located on the CTSU members' website.

- Go to https://www.ctsu.org and log in to the members' area using your CTEP-IAM username and password
- Click on the Protocols tab in the upper left of your screen
- Either enter the protocol # in the search field at the top of the protocol tree, or
- Click on the By Lead Organization folder to expand

- Click on the SWOG link to expand, then select trial protocol **S1316** Click on LPO Documents, select the Site Registration documents link, and download and complete the forms provided.

3. **Requirements For S1316 Site Registration:**

IRB approval (For sites not participating via the NCI CIRB; local IRB documentation, an IRB-signed CTSU IRB Certification Form, Protocol of Human Subjects Assurance Identification/IRB Certification/Declaration of Exemption Form, or combination is accepted)

13.3 OPEN Registration Requirements

Patient enrollment will be facilitated using the Oncology Patient Enrollment Network (OPEN). OPEN is a web-based registration system available on a 24/7 basis. To access OPEN, the site user must have an active CTEP-IAM account (check at < https://ctepcore.nci.nih.gov/iam >) and a 'Registrar' role on either the LPO or participating organization roster. Registrars must hold a minimum of an AP registration type.

All site staff will use OPEN to enroll patients to this study. It is integrated with the CTSU Enterprise System for regulatory and roster data and, upon enrollment, initializes the patient in the Rave database. OPEN can be accessed at https://open.ctsu.org or from the OPEN tab on the CTSU members' side of the website at https://www.ctsu.org . To assign an IVR or NPIVR as the treating, crediting, consenting, drug shipment (IVR only), or investigator receiving a transfer in OPEN, the IVR or NPIVR must list on their Form FDA 1572 in RCR the IRB number used on the site's IRB approval.

OPEN will also ask additional questions that are not present on the SWOG Registration Worksheet. The individual registering the patient must be prepared to provide answers to the following questions:

a. Institution CTEP ID

b. Protocol Number

c. Registration Step

d. Treating Investigator

e. Credit Investigator

f. Patient Initials

g. Patient's Date of Birth

h. Patient SSN (SSN is desired, but optional. Do not enter invalid numbers.)

i. Country of Residence

j. ZIP Code

k. Gender (select one):
- Female Gender
- Male Gender

l. Ethnicity (select one):
- Hispanic or Latino
- Not Hispanic or Latino
- Unknown

m. Method of Payment (select one):
- Private Insurance
- Medicare
- Medicare and Private Insurance
- Medicaid
- Medicaid and Medicare
- Military or Veterans Sponsored NOS
- Military Sponsored (Including Champus & Tricare)
- Veterans Sponsored
- Self Pay (No Insurance)
- No Means of Payment (No Insurance)
- Other
- Unknown

n. Race (select all that apply):
- American Indian or Alaska Native
- Asian
- Black or African American
- Native Hawaiian or other Pacific Islander
- White
- Unknown

13.4 Registration Procedures

a. All site staff (SWOG and CTSU Sites) will use OPEN to enroll patients to this study. OPEN is a web-based application that is integrated with the CTSU Enterprise System for regulatory and roster data and, at the time of patient registration, initializes the patient in the Rave database. OPEN can be accessed at https://open.ctsu.org or from the OPEN tab on the CTSU members' side of the website at https://www.ctsu.org, or from the OPEN Patient Registration link on the SWOG CRA Workbench.

b. Prior to accessing OPEN site staff should verify the following:

- All eligibility criteria have been met within the protocol stated timeframes and the affirmation of eligibility on the Registration Worksheet has been signed by the registering investigator or another investigator designate. Site staff should refer to Section 5.0 to verify eligibility.
- All patients have signed an appropriate consent form and HIPAA authorization form (if applicable).
- The study site is listed as "approved" in the CTSU RSS.

c. Access requirements for OPEN:

- Site staff will need to be registered with CTEP and have a valid and active CTEP-IAM account. This is the same account (user ID and password) used for the CTSU members' web site. Additional information about obtaining a CTEP-IAM account can be found at http://ctep.cancer.gov/branches/pmb/associate_registration.htm. Questions should be directed to the CTEP Associate Registration Help Desk by e-mail at ctepreghelp@ctep.nci.nih.gov.
- To perform registrations, the site user must have been assigned the 'Registrar' role on the SWOG or CTSU roster.

1. If you are a SWOG member, to perform registrations on SWOG protocols you must have an equivalent 'Registrar' role on the SWOG roster. Role assignments are handled through SWOG.

2. If you are not a SWOG member, to perform registrations on SWOG protocols you must have the role of Registrar on the CTSU roster. Site and/or Data Administrators can manage CTSU roster roles via the new Site Roles maintenance feature under RSS on the CTSU members' web site. This will allow them to assign staff the "Registrar" role.

Note: The OPEN system will provide the site with a printable confirmation of registration and treatment information. Please print this confirmation for your records.

d. Further instructional information is provided on the OPEN tab of the CTSU members' side of the CTSU website at https://www.ctsu.org or at https://open.ctsu.org. For any additional questions contact the CTSU Help Desk at 1-888-823-5923 or ctsucontact@westat.com.

13.5 After Hours Registration

Patients participating in the non-randomized portion of the study may be registered under SWOG Policy #12. This policy specifies that registrations to the non-randomized portion of a study (1) after regular business hours (e.g., on holidays or weekends), or (2) while the site is unable to access the online registration program, may be completed by calling the Data Operations Center rather than using OPEN. To implement SWOG Policy #12 correctly, the institution must call the Data Operations Center leaving a voice mail message on the day treatment is to begin.

The **S1316** Registration of Non-Randomized Patients during Holidays and Weekends form must be completed prior to making the phone call and is available on the protocol abstract page of the SWOG Website (www.swog.org nd CTSU protocol page (www.ctsu.org).

For the initial registration, call 206/652-2267 with the following information:

a. Caller's full name and phone number

b. Study Number: **S1316**

c. Treating investigator

d. Treating institution

e. Patient Initials

f. Date of Registration
- Name/contact number of **S1316** CRA/RN authorized to register patients in OPEN at registering institution

13.6 Exceptions to SWOG registration policies will not be permitted.

a. Patients must meet all eligibility requirements.

b. Institutions must be identified as approved for registration.

c. Registrations may not be cancelled.

d. Late registrations (after initiation of treatment) will not be accepted.

14.0 DATA SUBMISSION SCHEDULE

14.1 Data Submission Requirement

Data must be submitted according to the protocol requirements for **ALL** patients registered, whether or not assigned treatment is administered, including patients deemed to be ineligible. Patients for whom documentation is inadequate to determine eligibility will generally be deemed ineligible.

14.2 Master Forms

Master forms can be found on the protocol abstract page on the SWOG website (www.swog.org) and (with the exception of the sample consent form and the Registration Worksheet) must be submitted on-line via the Web; see Section 14.3a for details.

14.3 Data Submission Procedures

a. Data collection for this study will be done exclusively through the Medidata Rave® clinical data management system. Access to the trial in Rave is granted through the iMedidata application to all persons with the appropriate roles assigned in Regulatory Support System (RSS). To access Rave via iMedidata, you must have an active CTEP-IAM account (check at https://ctepcore.nci.nih.gov/iam) and the appropriate Rave role (Rave CRA, Read-Only, CRA Lab Admin, SLA, or Site Investigator) on either the LPO or participating organization roster at the enrolling site. To hold the Rave CRA role or CRA Lab Admin role, the user must hold a minimum of an AP registration type. To hold the Rave Site Investigator role, the individual must be registered as an NPIVR or IVR. Associates can hold read-only roles in Rave. If the study has a DTL, individuals requiring write access to Rave must also be assigned the appropriate Rave tasks on the DTL.

Upon initial site registration approval for the study in RSS, all persons with Rave roles assigned on the appropriate roster will be sent a study invitation e-mail from iMedidata. To accept the invitation, site users must log into the Select Login (https://login.imedidata.com/selectlogin) using their CTEP-IAM user name and password, and click on the “accept” link in the upper right-corner of the iMedidata page. Please note, site users will not be able to access the study in Rave until all required Medidata and study specific trainings are completed. Trainings will be in the form of electronic learnings (eLearnings), and can be accessed by clicking on the link in the upper right pane of the iMedidata screen.

Users that have not previously activated their iMedidata/Rave account at the time of initial site registration approval for the study in RSS will also receive a separate invitation from iMedidata to activate their account. Account activation instructions are located on the CTSU website, Rave tab under the Rave resource materials (Medidata Account Activation and Study Invitation Acceptance). Additional information on iMedidata/Rave is available on the CTSU members’ website under the Rave tab at www.ctsu.org/RAVE/ or by contacting the CTSU Help Desk at 1-888-823-5923 or by e-mail at ctsucontact@westat.com.

b. Rave® may also be accessed via the SWOG CRA Workbench. Go to the SWOG web site (http://swog.org) and logon to the Members Area using the SWOG Roster ID Number and password. After logging on, click on *Workbenches*, then *CRA Workbench* to access the home page for the CRA Workbench and follow the link to Rave® provided in the left-hand navigation panel.

To access the CRA Workbench the following must be done (in order):

1. Registering individual is entered into the SWOG Roster and issued a SWOG Roster ID Number,
2. Registering individual is associated as an investigator or CRA/RN at the institution where the patient is being treated or followed,
3. Sites local Web User Administrator has added registering individual as a web user and has given you the appropriate system permissions to view data for that institution.

For assistance with points 1 and 2 call the Operations Office at 210/614-8808. For point 3, contact your local Web User Administrator (refer to the "Who is my Web User Administrator?" function on the swog.org Members logon page).

For difficulties with the CRA Workbench, please e-mail technicalquestion@crab.org.

c. Institutions participating through the Cancer Trials Support Unit (CTSU) please refer to the CTSU Participation Table on Page 3.

14.4 Data Submission Overview and Timepoints

a. WITHIN 24 HOURS OF REGISTRATION:

S1316 Dietary Recall Contact Information Form (see Model Consent Form)

b. WITHIN 7 DAYS OF REGISTRATION:

Submit the following:

S1316 Onstudy Form

S1316 Cover Sheet for Patient-Completed Questionnaires

Baseline **S1316** MDASI-GI

Baseline **S1316** EQ-5D-5L

Pathology Report of primary intra-abdominal cancer

Radiology reports from all scans (including CT scans) performed to assess MBO at baseline.

c. WITHIN 14 DAYS AFTER INITIAL HOSPITAL DISCHARGE FOR TREATMENT OF MBO:

Submit the following:

S1316 Malignant Bowel Obstruction Treatment Form

S1316 Malignant Bowel Obstruction Treatment Complications Form

S1316 Somatostatin Analogue Treatment Form

d. WITHIN 7 DAYS OF EACH WEEKLY ASSESMENT THROUGH WEEK 13:

Submit the following:

S1316 Cover Sheet for Patient-Completed Questionnaires

S1316 MDASI-GI

S1316 EQ-5D-5L (Weeks 2, 4, 8, and 12 only)

S1316 MBO Assessment

e. WITHIN 14 DAYS AFTER WEEK 13:

Submit the following:

S1316 Hospitalization Days Record

NOTE: The data for this form should be extrapolated from the discharge summaries.

f. WITHIN 14 DAYS AFTER EACH HOSPITAL DISCHARGE FOR HOSPITALIZATION FOR ANY REASON THROUGH WEEK 13:

Submit the following:

S1316 Malignant Bowel Obstruction Treatment Form

S1316 Malignant Bowel Obstruction Treatment Complications Form

S1316 Somatostatin Analogue Treatment Form

Source documentation for hospital admission and discharge dates (discharge summary or death summary) and operative reports, if applicable.

g. WITHIN 14 DAYS OF EACH ASSESSMENT EVERY 4 WEEKS AFTER WEEK 13:

Submit the following:

S1316 Cover Sheet for Patient-Completed Questionnaires

S1316 MDASI-GI

S1316 MBO Follow Up Form

h. WITHIN 3 DAYS OF REMOVAL FROM PROTOCOL FOLLOW-UP:

Submit the **S1316** Off Protocol Notice and final **S1316 Follow-Up Form**

i. WITHIN 4 WEEKS OF KNOWLEDGE OF DEATH:

Submit the Notice of Death, **S1316** Off Protocol Notice, and final **S1316 Follow-Up Form** (if the patient was still on protocol follow-up)

15.0 SPECIAL INSTRUCTIONS

15.1 Patient Questionnaires: Instructions for Administration

a. It is important to note that the time frame for providing ratings for the S1316 MDASI-GI should be rated with respect to the past 7 days. The schedule for the assessments is:

1. **S1316** MDASI-GI – Baseline, each week from Week 1-13, and every 4 weeks until Week 53.

2. **S1316** EQ-5D-5L – Baseline, Weeks 2, 4, 8, and 12.

b. Administration of Questionnaires

1. The first time the patient completes the questionnaires: Please read to the patient the instructions attached to each patient questionnaire. Explain the specific administration times for this protocol. Patients should be directed to report all symptoms and limitations whether or not they are related to the cancer, MBO, or its treatment.

2. It is permissible to assist patients with completing the questionnaires being careful not to influence the patient's response. Note on the **S1316** Cover Sheet for Patient-Completed Questionnaires what assistance was required and indicate reason (e.g., elderly, too sick, etc.). Discourage family members from: 1) being present while the patient completes the questionnaire and/or 2) influencing patient responses to the questions.

3. It is very important to review the questionnaires after the patient has completed them to be sure all of the questions have been answered and that only one answer is marked. a) If the patient has marked more than one answer per question, ask the patient which answer reflects how she is feeling. b) If the patient has skipped a question, tell the patient that a question was not answered and ask if she would like to answer the question. Always give the patient the option to refuse. Indicate on the form by the question that the patient did not want to answer this question.

4. If a patient refuses or cannot complete the questionnaire for some reason, then this must be documented on the **S1316** Cover Sheet for Patient Completed Questionnaires and submitted to the Data Operations Center in Seattle (see Section 14.3).

5. If a patient misses an assessment, a telephone interview must be scheduled and completed within two days of the originally scheduled time.

c. Additional quality control procedures:

1. When a patient is registered on **S1316**, a calendar should be made with dates of upcoming patient-completed questionnaires noted. A copy of this calendar can be given to the patient with the notation that the questionnaires should be completed. You may wish to photocopy the Study Calendar, Section 9.0, and include the patient's name and specific dates. A copy of this should be kept in the patient file.

2. If a patient refuses or cannot complete the patient questionnaires at one time point, he or she should be asked to do so at the next scheduled assessment time. Submit the **S1316** Cover Sheet for Patient-Completed Questionnaires documenting the reason why the questionnaires were not done.

3. Anyone involved in the collection of quality of life data in SWOG trials should review the training program available on the SWOG website accessible from three locations. On the SWOG Home Page (prior to member login), in the **QUICKLINKS** section on the bottom right corner of the page, there is a link to the Patient Reported Outcomes Training. The other two locations that the training is available are after SWOG member login on the CRA Workbench. The Training section and the New CRAs! section both contain access to the Patient Reported Outcomes (PROs) training module. The training program is a narrated set of slides designed to standardize the way quality of life data is collected from patients. Questions regarding the quality of life assessments can be addressed to the SWOG Data Operations Office (206/652-2267).

d. **S1316** Cover Sheet for Patient-Completed Questionnaires

For each time point, the nurse or CRA completes the **S1316** Cover Sheet for Patient-Completed Questionnaires. The Cover Sheet is submitted with the set of patient-completed forms at each scheduled assessment. The Cover Sheet is very important for tracking how and when the patient forms were completed. When a patient-completed form is not administered at a scheduled time point, it is important to know why the assessment did not occur; the form includes potential reasons for a patient not completing a form. See Section 14.0 for data submission guidelines.

16.0 ETHICAL AND REGULATORY CONSIDERATIONS

The following must be observed to comply with Food and Drug Administration regulations for the conduct and monitoring of clinical investigations; they also represent sound research practice:

Informed Consent

The principles of informed consent are described by Federal Regulatory Guidelines (Federal Register Vol. 46, No. 17, January 27, 1981, part 50) and the Office for Protection from Research Risks Reports: Protection of Human Subjects (Code of Federal Regulations 45 CFR 46). They must be followed to comply with FDA regulations for the conduct and monitoring of clinical investigations.

Institutional Review

This study must be approved by an appropriate institutional review committee as defined by Federal Regulatory Guidelines (Ref. Federal Register Vol. 46, No. 17, January 27, 1981, part 56) and the Office for Protection from Research Risks Reports: Protection of Human Subjects (Code of Federal Regulations 45 CFR 46).

Monitoring

This study will be monitored by the Clinical Data Update System (CDUS) Version 3.0. Cumulative CDUS data will be submitted quarterly to CTEP by electronic means. Reports are due January 31, April 30, July 31 and October 31.

Confidentiality

Please note that the information contained in this protocol is considered confidential and should not be used or shared beyond the purposes of completing protocol requirements until or unless additional permission is obtained.

16.1 Adverse Event Reporting Requirements

a. Purpose

Adverse event data collection and reporting, which are required as part of every clinical trial, are done to ensure the safety of patients enrolled in the studies as well as those who will enroll in future studies using similar agents. Adverse events are reported in a routine manner at scheduled times during a trial. (Directions for routine reporting are provided in Section 14.0.) Additionally, certain adverse events must be reported in an expedited manner to allow for more timely monitoring of patient safety and care. The following guidelines prescribe expedited adverse event reporting for this protocol. See also Appendix 18.1 for general and background information about expedited reporting.

b. Reporting method

This study requires that expedited adverse events be reported using the Cancer Therapy Evaluation Program Adverse Event Reporting System (CTEP-AERS). CTEP's guidelines for CTEP-AERS can be found at http://ctep.cancer.gov. A CTEP-AERS report must be submitted to the SWOG Operations Office electronically via the CTEP-AERS Web-based application located at http://ctep.cancer.gov/protocolDevelopment/electronic_applications/adverse_events.htm.

In the rare event when internet connectivity is disrupted an electronic report MUST be submitted immediately upon re-establishment of internet connection.

c. When to report an event in an expedited manner

When the adverse event requires expedited reporting, submit the report within 10 calendar days of learning of the event.

d. Other recipients of adverse event reports

The SWOG Operations Office will forward reports and documentation to the appropriate regulatory agencies and drug companies as required.

Adverse events determined to be reportable to the Institutional Review Board responsible for oversight of the patient must be reported according to local policy and procedures.

e. Expedited reporting for commercial agents

Commercial reporting requirements are provided in Table 16.1. If there is any question about the reportability of an adverse event or if on-line CTEP-AERS cannot be used, please telephone or email the SAE Program at the Operations Office, 210/614-8808 or adr@swog.org, before preparing the report.

Table 16.1. Expedited reporting requirements for adverse events experienced by patients within 30 days of the last administration of the commercial agents and/or surgery.

ATTRIBUTION	Grade 4		Grade 5[a]	
	Unexpected	Expected	Unexpected	Expected
Unrelated or Unlikely			**CTEP-AERS**	**CTEP-AERS**
Possible, Probable, Definite	**CTEP-AERS**		**CTEP-AERS**	**CTEP-AERS**

CTEP-AERS: Indicates an expedited report is to be submitted via CTEP-AERS within 10 calendar days of learning of the event[b].

[a] This includes all deaths within 30 days of the last dose of treatment with a commercial agent(s) or within 30 days of the surgical procedure regardless of attribution. Any death that occurs more than 30 days after the last dose of treatment with a commercial agent(s) or within 30 days of the surgical procedure, and is attributed (possibly, probably, or definitely) to the agent(s) or surgery and is not due to cancer recurrence must be reported according to the instructions above.

[b] Submission of the on-line CTEP-AERS report plus any necessary amendments generally completes the reporting requirements. You may, however, be asked to submit supporting clinical data to the Operations Office in order to complete the evaluation of the event. If requested, the specified data should be sent within 5 calendar days by fax to 210-614-0006.

f. **Reporting Pregnancy, Fetal Death, and Death Neonatal**

1. **Pregnancy** Study participants who become pregnant while on study; that pregnancy should be reported in an expedited manner via CTEP-AERS as **Grade 3 "Pregnancy, puerperium and perinatal conditions – Other (pregnancy)"** under the **Pregnancy, puerperium and perinatal conditions** SOC.

   Additionally, the pregnancy outcome for patients on study should be reported via CTEP-AERS at the time the outcome becomes known, accompanied by the same Pregnancy Report Form used for the initial report.

   Fetal Death Fetal Death defined in CTCAE as "A disorder characterized by death in utero; failure of the product of conception to show evidence of respiration, heartbeat, or definite movement of a voluntary muscle after expulsion from the uterus, without possibility of resuscitation" should be reported expeditiously as **Grade 4 "pregnancy, puerperium and perinatal conditions – Other (pregnancy loss)" under the Pregnancy, puerperium and perinatal conditions** SOC.

2. **Death Neonatal** Neonatal death, defined in CTCAE as "A disorder characterized by cessation of life occurring during the first 28 days of life" that is felt by the investigator to be at least possibly due to the investigational agent/intervention should be reported expeditiously.

   A neonatal death should be reported expeditiously as **Grade 4 "General disorders and administration – Other (neonatal loss)"** under the **General disorders and administration** SOC.

   *Fetal death and neonatal death should **NOT** be reported as a Grade 5 event. If reported as such, the CTEP-AERS interprets this as a death of the patient being treated.*

NOTE: When submitting CTEP-AERS reports for "Pregnancy, "Pregnancy loss", or "Neonatal loss", the Pregnancy Information Form should also be completed and faxed with any additional medical information to 301-230-0159. The potential risk of exposure of the fetus to the investigational agent(s) or chemotherapy agent(s) should be documented in the "Description of Event" section of the CTEP-AERS report.

The Pregnancy Information Form is available at:
http://ctep.cancer.gov/protocolDevelopment/adverse_effects/htm

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18.0 APPENDIX

18.1 Dietary Recall Script

18.1 Dietary Recall

a. Script

The Arizona Diet, Behavior, and Quality of Life Assessment Lab NDSR- Phone Script (For use with the University of Minnesota's Nutritional Data System for Research). Interview may be conducted with the patient or designated care-giver/companion. The patient is the preferred respondent; if the patient's health makes it difficult for him/her to report, the surrogate caregiver will report. Documentation of who responded will be made on the call record by the interviewer. Contact will be made by telephone on randomly assigned days per protocol (days to call are generated from a randomization program used by the shared service at the University of Arizona Cancer Center). If the participant and his/her caregiver decline to complete the interview on a given day (as patients may feel ill or fatigued), the call will be rescheduled within 4 days.

INTRODUCTION:
Hello, my name is _____ and I am calling from the University of Arizona Diet lab for the malignant bowel obstruction study you are participating in through _____(fill in Site name from Contact sheet).

_____(Fill in Head Nurse/CRA's name, or if unavailable, say: The nurse who consented you to this study from the hospital) gave us your contact information so that we can begin the calls to collect information on what you are eating. You may remember that these calls were described in the study consent form. Today's call should not take more than 20 minutes and likely much less of your time. I need to ask you about what you ate yesterday.

(IF NEEDED: The length of time it takes varies greatly from person to person depending on whether you are eating or not.)

May I begin the diet recall with you now?

(IF NOW IS NOT CONVENIENT: When would be a good time to call you back to do the recall? It is important for the study that the recall is conducted within the next 24 hours.)

I am going to begin by asking you to answer a few brief questions about how you consume your food and with whom you share your meals:

3. In describing what you ate/consumed yesterday which of the following seems most accurate? I will read you 6 different options:

   a. I am not eating or drinking anything (except maybe water or ice)
   b. I am on tube feeding only
   c. I am on tube feeding but eat small amounts of food
   d. I am consuming only liquids (beverages including juice, milk, shakes, etc. as well as soups, Jell-O®, pudding, , ice cream, etc.) this may include liquid high calorie/protein beverages, but other liquids also)
   e. I am consuming only liquid nutritional supplements such as Boost®, Ensure® and no other solid food or liquids
   f. I am eating liquids and solids (such as fruit/vegetables, cereal, bread, meat, eggs, cheese, cottage cheese, pastries/sweets, etc.), but more liquids

g. I am eating both liquids and solids, but more solids

4. Did you share any meals yesterday with a family member, friend or care giver? Yes No

If Yes, which of your meals or snacks yesterday were eaten with others?
a. All
b. Breakfast
c. Lunch
d. Dinner/supper
e. Snacks

Based on response the interview will continue; response (a) from Questions 1 (tube feeding only) will trigger a closure of the interview at this point. I am now finished with the interview questions. Do you have any questions at this point? We plan to call you again in about 4 weeks. I hope you have a good day.

Since you are taking in foods by mouth, I am next going to have you tell me when and what you ate yesterday. After midnight the day before yesterday (state day of week), what was the first time after waking that you recall having something to eat or drink?

What did you have to eat or drink at that time?

Did you have anything else to eat or drink at that time?

When was the next time you had something to eat or drink?

What did you have at that time?

Did you have anything else at that time?

(THE LAST THREE QUESTIONS ARE REPEATED UNTIL THE PARTICIPANT SAYS THAT HAD NOTHING ELSE TO EAT OR DRINK YESTERDAY. THEN THE QUICK LIST IS REVIEWED WITH THE PARTICIPANT).

At (at time) you had (read recorded food items). Can you think of anything else you had at that time?

IF NEEDED PROBE: Did you have a beverage with that meal?
IF NEEDED PROBE: Did you have any snacks between meals or did you sample foods as you prepared the meal?

How much did you eat/drink?
(THE SECTION ABOVE IS REPEATED FOR EACH INDIVIDUAL FOOD ITEM)
We are almost done, but I'd like to review the day with you once more just to make sure I have entered everything correctly.

At (time) you had (amount) of (food). Is this correct?
Did you have anything else at that time?
(REPEAT FOR ALL FOODS)

ADDITIONAL QUESTIONS FOR MBO

5. Was this a typical day in relation to your eating pattern over the past week (in terms of your diet habits)?
   a. Yes,
   b. No, (SPECIFY REASON)

6. Please tell me if the amount of food you consumed yesterday was
   a. close to the amount you usually have
   b. a lot more than usual (SPECIFY REASON) or
   c. a lot less than usual (SPECIFY REASON)?

7. Did you experience any problems that may have altered your eating or food choices yesterday such as:

Symptom	IF YES, ATE MORE OR LESS
a. Sore stomach,	More / Less
b. Bloating/gas,	More / Less
c. No appetite,	More / Less
d. Significant constipation,	More / Less
e. Diarrhea, or	More / Less
f. Too tired to eat?	More / Less
g. OTHER PROBLEM (SPECIFY)	More / Less

Please tell me of any foods you are avoiding and why:
(no raw foods, no dairy, no gluten, etc. [SPECIFY]; can't digest, constipated, too much gas, etc.) (Rationale)

I have finished the interview questions. Do you have any questions at this time? We plan to call you again in about 4 weeks. I hope you have a good day.

b. Quality Control

Quality control procedures have been established and are fully implemented for the 24-hour dietary recall data collection, coding, and entry process. Regular meetings are held to discuss and solve problems to ensure that the quality of dietary data provided by study participants is excellent. Complete sets of checked and corrected recalls are sent to The Arizona Diet, Behavior, and Quality of Life Assessment Lab where they are coded and entered. The 24-hour dietary recall quality control/quality assurance (QC/QA) procedures include a 25% duplicate entry of recalls by a different coder, followed by a comparison of entered recalls and reconciliation. Discrepancies attributable to coder error are addressed by closer surveillance and retaining when necessary. Whenever differing interpretations of a subject's data set are identified, the entire 4-day recall set is reviewed to provide consistency of coding. In general, the differences found in the quality control process are minor.

Informed Consent Model for **S1316**

*NOTES FOR LOCAL INSTITUTION INFORMED CONSENT AUTHORS:

This model informed consent form has been reviewed by the DCTD/NCI and is the official consent document for this study. Local IRB changes to this document are allowed. (Institutions should attempt to use sections of this document that are in bold type in their entirety.) Editorial changes to these sections may be made as long as they do not change information or intent. If the institutional IRB insists on making deletions or more substantive modifications to the risks or alternatives sections, they may be justified in writing by the investigator and approved by the IRB. Under these circumstances, the revised language, justification and a copy of the IRB minutes must be forwarded to the SWOG Operations Office for approval before a patient may be registered to this study.

Please particularly note that the questions related to banking of specimens for future study are in bolded type and may not be changed in any way without prior approval from the SWOG Operations Office.

Readability Statistics:	
Flesch Reading Ease	61.3 (targeted above 55)
Flesch-Kincaid Grade Level	8.8 (targeted below 8.5)

- Instructions and examples for informed consent authors are in *[italics]*.
- A blank line, _____, indicates that the local investigator should provide the appropriate information before the document is reviewed with the prospective research participant.
- The term "study doctor" has been used throughout the model because the local investigator for a cancer treatment trial is a physician. If this model is used for a trial in which the local investigator is not a physician, another appropriate term should be used instead of "study doctor".
- The dates of protocol updates in the header and in the text of the consent is for reference to this model only and should not be included in the informed consent form given to the prospective research participant.
- The local informed consent must state which parties may inspect the research records. This includes the NCI, the drug manufacturer for investigational studies, any companies or grantors that are providing study support (these will be listed in the protocol's model informed consent form) and SWOG.

  "SWOG" must be listed as one of the parties that may inspect the research records in all protocol consent forms for which patient registration is being credited to SWOG. This includes consent forms for studies where all patients are registered directly through the SWOG Data Operations Office, all intergroup studies for

which the registration is being credited to SWOG (whether the registration isthrough the SWOG Data Operations Office or directly through the other group), as well as consent forms for studies where patients are registered via CTSU and the registration is credited to SWOG.

- When changes to the protocol require revision of the informed consent document, the IRB should have a system that identifies the revised consent document, in order to preclude continued use of the older version and to identify file copies. An appropriate method to identify the current version of the consent is for the IRB to stamp the final copy of the consent document with the approval date. The stamped consent document is then photocopied for use. Other systems of identifying the current version of the consent such as adding a version or approval date are allowed as long as it is possible to determine during an audit that the patient signed the most current version of the consent form.

*NOTES FOR LOCAL INVESTIGATORS:

- The goal of the informed consent process is to provide people with sufficient information for making informed choices about participating in research. The consent form provides a summary of the study, the individual's rights as a study participant, and documents their willingness to participate. The consent form is, however, only one piece of an ongoing exchange of information between the investigator and study participant. For more information about informed consent, review the "Recommendations for the Development of Informed Consent Documents for Cancer Clinical Trials" prepared by the Comprehensive Working Group on Informed Consent in Cancer Clinical Trials for the National Cancer Institute. The Web site address for this document is http://cancer.gov/clinicaltrials/understanding/simplification-of-informed-consent-docs/
- Suggestion for Local Investigators: An NCI pamphlet explaining clinical trials is available for your patients. The pamphlet is titled: "Taking Part in Cancer Treatment Research Studies". This pamphlet may be ordered on the NCI Web site at *https://cissecure.nci.nih.gov/ncipubs* or call 1-800-4- CANCER (1-800-422-6237) to request a free copy.
- Optional feature for Local Investigators: Reference and attach drug sheets, pharmaceutical information for the public, or other material on risks. Check with your local IRB regarding review of additional materials.

*These notes for authors and investigators are instructional and should not be included in the informed consent form given to the prospective research participant.

Consent Form

Study Title for Study Participants: Testing surgery versus non-surgical management for malignant bowel obstruction

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: **S1316**, "Prospective Comparative Effectiveness Trial for Malignant Bowel Obstruction"

What is the usual approach to treating malignant bowel obstruction?

You are being asked to take part in this study because you have a malignant bowel obstruction (MBO) and your doctor is not sure if surgery or non-surgical treatment will be better for your condition. MBO means you have a blockage of the bowels due to cancer or its treatment, and you likely still have cancer inside of you. People who have MBO and choose not to participate in a study are treated with either abdominal surgery or non-surgical treatment. Both of these options are commonly used, considered standard of care, and will be described to you by your physician.

What are my other choices if I do not take part in this study?

If you decide not to take part in this study, you have other choices. For example:

- you may choose to have either of the usual approaches described above without being on the study
- you may choose to take part in a different study, if one is available
- or you may choose not to be treated for MBO

Why is this study being done?

For many patients with MBO, it is not known whether surgery or non-surgical treatment will give you a better quality of life. Both approaches are commonly used and considered standard of care. The purpose of this study is to use two groups of study participants to compare the quality of life of patients with MBO who are treated with surgery to that of similar patients who are treated with the best medical management (non-surgical treatment). There will be about 220 people taking part in this study.

What are the study groups?

This study has two components; a randomized clinical trial and a non-randomized study. As of 6/6/19, if you are eligible, you may only join the randomized component.

Randomized clinical trial

Randomized clinical trials are studies that provide the most reliable information for improving medical practice. If you agree to participate in this part of the study, you will be randomized to one of the two standard MBO treatments.

- Group 1 will receive the usual abdominal surgery for MBO which will involve an incision in the abdomen. There are multiple procedures that are possible, and these will be described in more detail by your surgical team.
- Group 2 will receive the usual non-surgical treatment for MBO which include intravenous hydration, often naso-gastric tube decompression, and medications to prevent pain or nausea. You may also receive an agent (somatostatin analogue) to decrease the swelling of the bowels. These medications may be given by injection of the skin two or three times a day.

A computer will assign one of these two treatment groups to you at random, like a flip of a coin. This is done to make the treatment groups comparable on other factors that might affect quality of life measures.

Your doctors will provide the assigned treatment and follow you closely to track your health status and quality of life. You will be provided with the care that your own circumstances require, no matter which group you were assigned to. For example, if you are randomized to non-surgical treatment and your condition changes to indicate that surgery is needed, you will be offered that surgery.

Non-randomized study *(Closed to accrual on 6/6/19)*

If you or your doctor do not choose for you to be randomly assigned to a treatment group, you may still participate in the non-randomized surgical component of this study. You will receive the usual abdominal surgery for MBO, which will involve an incision in the abdomen. There are multiple procedures that are possible, and these will be described in more detail by your surgical team. Your treatment will be recorded and we will follow you closely for your health status and quality of life.

How long will I be in this study?

You will receive the study treatment soon after starting the study. After you finish treatment and are discharged from the hospital, your doctor will continue to follow you for one year from the start of the study.

What extra tests and procedures will I have if I take part in this study?

All of the exams, tests, and procedures you will have are part of the usual approach for MBO. However, the study team will contact you more often to track your health status and quality of life.

If the exams, tests, and procedures show that you can take part in the study, and you choose to take part, then you will have the following extra contact with the study team.

During the study:

- Weekly telephone call (or hospital visits if you are in the hospital) for 13 weeks from the start of the study and then monthly telephone calls for up to 1 year. Each telephone call or hospital visit will last for about 15 minutes. These telephone calls will include questions about your quality of life, recent hospitalizations, and MBO-related problems.
- Monthly telephone calls from the Arizona Diet, Behavior, and Quality of Life Assessment Lab to find out what you are eating. Each telephone call will last for about 15-20 minutes. When the study team collects your contact information for the Arizona Diet, Behavior, and Quality of Life Assessment Lab, you will be asked if a text message can be sent to your phone for scheduling these calls. You may agree or decline to receive such texts.

You have the option to allow a family member or caregiver to answer these calls and questions on your behalf. In the event that you no longer want to or are able to continue the follow-up phone calls, we will continue to collect your medical history until 1 year from beginning the study.

What possible risks can I expect from taking part in this study?

If you choose to take part in this study, there is a risk that:

- **You may be asked sensitive or private questions which you normally do not discuss**
- **The study approach that you receive, may or may not be better, and could possibly be worse than the study approach that you did not receive for MBO.**

There is also a risk that you could have side effects from the treatment.

Here are important points about side effects:

- **The study doctors do not know who will or will not have side effects.**
- **Some side effects may go away soon, some may last a long time, or some may never go away.**
- **Some side effects may be serious and may even result in death.**

Here are important points about how you and the study doctor can make side effects less of a problem:

- **Tell the study doctor if you notice or feel anything different so they can see if you are having a side effect.**
- **The study doctor may be able to treat some side effects.**
- **The study doctor may adjust the study drugs to try to reduce side effects.**

If you are going to receive surgery, you will be informed of all risks associated with the surgery in a separate consent form from your surgical center prior to the surgery. *)*

The tables below show the most common and the most serious side effects that researchers know about.

Possible Side Effects of Abdominal Surgery

COMMON, SOME MAY BE SERIOUS **In 100 people receiving abdominal surgery, more than 20 and up to 100 may have:**
• **Scar on abdomen**

OCCASIONAL, SOME MAY BE SERIOUS **In 100 people receiving abdominal surgery, from 4 to 20 may have:**
• **Wound problems** • **Gastrointestinal leak** • **Unable to fix obstruction or blockage** • **Return to operating room to correct problem** • **Deep vein blood clots or fluid around lung** • **Blood transfusion for blood loss** • **Hernia** • **Infection** • **Death**

RARE, AND SERIOUS **In 100 people receiving abdominal surgery, 3 or fewer may have:**
• **Bleeding** • **A hole between the intestines and the skin or other organ or structure, such as colon** *(6/29/15)* • **Injury to intra-abdominal structures** • **Pneumonia** • **Nerve damage** • **Heart attack** • **Stroke**

Possible Side Effects of Non-surgical Management (somatostatin analogues)

COMMON, SOME MAY BE SERIOUS **In 100 people receiving non-surgical management (somatostatin analogues), more than 20 and up to 100 may have:**
• **Abnormal heartbeat** • **Diarrhea, nausea, passing gas** • **Tiredness** • **Pain** • **Headache** • **Pain at injection site**

OCCASIONAL, SOME MAY BE SERIOUS **In 100 people receiving non-surgical management (somatostatin analogues), from 4 to 20 may have:**
• **Blockage of the liver which may cause belly pain** • **Dizziness** • **Thyroid changes** • **Change in stool color** • **Chest pain** • **Constipation** • **Hair loss** • **Lung infection** • **Need for surgery** • **Death**

RARE, AND SERIOUS **In 100 people receiving non-surgical management (somatostatin analogues), 3 or fewer may have:**
• **Bowel perforation** • **Pneumonia** • **Heart attack** • **Stroke** • **Heart failure which may cause shortness of breath, swelling of ankles, and tiredness**

Let your study doctor know of any questions you have about possible side effects. You can ask the study doctor questions about side effects at any time.

Reproductive risks: You should not get pregnant, breastfeed, or father a baby while in this study. The treatment used in this study could be very damaging to an unborn baby. Check with the study doctor about what types of birth control, or pregnancy prevention, to use while in this study.

What possible benefits can I expect from taking part in this study?

Both treatment approaches treat your MBO, but there is no added benefit to you participating in the study. This study will help researchers learn which treatment approach improves quality of life and will help people in the future.

Can I stop taking part in this study?

Yes. You can decide to stop at any time. If you decide to stop for any reason, it is important to let the study doctor know. If you stop, you can decide whether or not to let the study doctor continue to provide your medical information to the organization running the study.

The study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

The study doctor may take you out of the study:

- **If your health changes and the study is no longer in your best interest**
- **If new information becomes available**
- **If you do not follow the study rule**
- **If the study is stopped by the sponsor, Institutional Review Board or Food and Drug Administration.**

What are my rights in this study?

Taking part in this study is your choice. No matter what decision you make, and even if your decision changes, there will be no penalty to you. You will not lose medical care or any legal rights.

For questions about your rights while in this study, call the _____ *(insert name of center)* Institutional Review Board at _____ *(insert telephone number). (Note to Local Investigator: Contact information for patient representatives or other individuals at a local institution who are not on the IRB or research team but take calls regarding clinical trial questions can also be listed here.)*

What are the costs of taking part in this study?

You and/or your health plan/insurance company will need to pay for all of the costs of treating your MBO while in this study, including the cost of tests, procedures, somatostatin analogue, or medicines to manage any side effects, unless you are told that certain tests are supplied at no charge. Before you decide to be in the study, you should check with your health plan or insurance company to find out exactly what they will pay for. There will be no treatment or test that is offered that is not standard of care.

You will not be paid for taking part in this study.

What happens if I am injured or hurt because I took part in this study?

If you are injured or hurt as a result of taking part in this study and need medical treatment, please tell your study doctor. The study sponsors will not offer to pay for medical treatment for injury. Your insurance company may not be willing to pay for study-related injury. If you have no insurance, you would be responsible for any costs.

If you feel this injury was a result of medical error, you keep all your legal rights to receive payment for this even though you are in a study.

Who will see my medical information?

Your privacy is very important to us. The study doctors will make every effort to protect it. The study doctors have a privacy permit to help protect your records if there is a court case. However, some of your medical information may be given out if required by law. If this should happen, the study doctors will do their best to make sure that any information that goes out to others will not identify who you are.

Some of your health information, such as your response to cancer treatment, results of study tests, and medicines you took, will be kept by the study sponsor in a central research database. However, your name and contact information will not be put in the database. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

There are organizations that may inspect your records. These organizations are required to make sure your information is kept private, unless required by law to provide information. Some of these organizations are:

- The study sponsor supporting the study
- The Institutional Review Board, IRB, is a group of people who review the research with the goal of protecting the people who take part in the study.
- The Food and Drug Administration and the National Cancer Institute.
- Arizona Diet, Behavior, and Quality of Life Assessment Lab will receive minimal contact information in order to call you for monthly diet assessments.

Where can I get more information?

You may visit the NCI Web site at http://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Who can answer my questions about this study?

You can talk to the study doctor about any questions or concerns you have about this study or to report side effects or injuries. Contact the study doctor _____ *(insert name of study doctor[s])* at _____ *(insert telephone number).*

Randomization

I agree to participate and allow the study to randomly select my treatment (surgery or non-surgical treatment).

Yes No

(If no) I agree to participate and be a part of the non-randomized study in which I will receive standard surgical treatment:

Yes No

Future Contact

I agree to allow my study doctor, or someone approved by my study doctor, to contact me regarding future research involving my participation in this study.

Yes No

My Signature Agreeing to Take Part in the Study

I have read this consent form or had it read to me. I have discussed it with the study doctor and my questions have been answered. I will be given a signed copy of this form. I agree to take part in the main study.

Participant's signature_____
(or their legally authorized representative)

Date of signature_____

Signature of person(s) conducting the informed consent discussion_____

Date of signature_____

S1316 Dietary Recall Contact Form

Instructions: This form will be used by the Arizona Diet, Behavior, and Quality of Life Assessment Lab to contact the patient to conduct the **S1316** 24-hour dietary recalls.

Email this form to the Arizona Diet, Behavior, and Quality of Life Assessment Lab within 24 hours after registration to S1316. **Always follow your institutional HIPAA policies for emailing PHI.**

You must use the following address to submit this form: UACC-MBO@uacc.arizona.edu

Patient First Name and Last Name Initial: _____

Site Name _____ SWOG Site # or NCI code: _____

Name of Nurse/CRA who will be contacting this patient for weekly site calls: Patient's preferred language:

_____ English Spanish

SWOG ID: __ __ __ __ __ __ __ __ __ __ Registration Date:_____

Phone # (best): (_ _ _) _ _ _ – _ _ _ _ Cell / Land Time Zone (Please circle): ET CT MT PT

Phone Number (alt): (_ _ _) _ _ _ – _ _ _ _ Cell / Land Time Zone (Please circle): ET CT MT PT
□ Okay to text the patient *for scheduling purposes only* if this box is marked

Full name of an authorized alternate contact who could respond to dietary questions (always provide):

_____

Alternate's contact phone number (best): (_ _ _) _ _ _ – _ _ _ _ Cell / Land

Alternate's Email address:_____

NOTES re: Alternate Contact: _____

□ **DO NOT CALL THE PATIENT if this box is marked**; use the authorized alternate contact for the information.

Preferred time to call (place "yes" in available times):

Time	Mon	Tue	Wed	Thu	Fri	Sat	Sun
Morning - Anytime							
7 - 9 AM							
9 - 11 AM							
11 - noon							
Afternoon - Anytime							
Noon - 2 PM							
2 - 4 pm							
4 – 6 pm							
Evening							
6 – 8 pm							
Other							