Document Coversheet

Study Title: Palliative Management of Inoperable Malignant Bowel Obstruction: A Prospective, Open Label, Phase-2 Study at an NCI Comprehensive Cancer Center

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1 OBJECTIVES

1.1 Primary Objective

- To identify role of palliative medical management of inoperable malignant bowel obstruction (MBO) with octreotide, dexamethasone and metoclopramide given together as triple therapy.

1.2 Secondary Objectives

- To examine the time to de-obstruction
- To assess how well patients with MBO tolerate the combination therapy regimens
- To measure the overall survival of patients who receive the triple therapy at 3 and 6 months post obstruction or de-obstruction

2 BACKGROUND

2.1 Malignant Bowel Obstruction

Bowel obstruction is defined as the failure of transit of contents through the intestinal lumen. Usually, a diagnosis is made based on clinical suspicion and confirmed radiographically. Malignant bowel obstruction as per consensus definition is based on clinical evidence of obstruction distal to the ligament of Treitz with presence of primary intra-abdominal malignancy or intra-peritoneal tumor with extra-abdominal primary tumor [1]

MBO is a frequent and challenging complication in patients with advanced malignancy especially in gynecological and gastrointestinal tract tumors. In general, prevalence of MBO is 5-15% in advanced malignancy. Prevalence of MBO is 20-50% in gynecological malignancies and 10-29% in colorectal malignancies. The higher overall frequency of MBO in women can be explained by the high incidence of this complication in ovarian cancers. Malignancy is responsible for the majority of cases but in about one-third of cases, presence of benign causes, such as adhesions from a previous bowel surgery, radiation enteritis and hernia have been implicated. MBO can be partial or complete. Obstruction could be at one level or multiple levels. Reported incidences of small bowel obstruction are higher (66%) than large bowel (33%), and both can occur simultaneously (20%). Nausea, abdominal pain, colic, and dry mouth may be present regardless of the level of obstruction. Occurrence of MBO is a poor prognostic sign. Besides portending a poor prognosis, MBO causes a heavy burden of distressing symptoms to the patient and emotional turmoil to the family [2 3].

The pathophysiology of malignant bowel obstruction involves a vicious cycle of distension due to gas and non-absorbed secretions, followed by increased fluid secretion, causing more distension in the bowel. The bowel mucosa, in turn via an inflammatory response and release of vasoactive intestinal peptide, becomes damaged by the hypertensive state of distension and produces even more secretions [3]. This cycle results in bloating, pain, cramping, nausea, and vomiting. The symptoms vary in severity and rapidity of onset, depending on the level of the obstruction [3]. For instance, in gastric outlet obstruction, there is early and severe nausea and vomiting. In small-bowel obstruction, there is pronounced cramping and nausea with vomiting. In large-bowel obstruction, symptoms appear later in the course of the obstruction, with considerable distension and occasional paradoxical diarrhea owing to bacterial overgrowth. There can be 2 types of pain—

a continuous one, from the distension and the tumor itself, and a cramping one, which can be episodic, and which occurs mostly after meals. The vomit might be feculent in large-bowel obstruction, whereas it is biliary in small-bowel and gastric outlet obstructions. In complete obstruction flatus and stool are absent [4].

Management

The management of MBO is difficult, complicated and involves a specific and individualized approach to each patient. Multiple studies have reported surgery as the best option to improve survival and management of symptoms, but not appropriate in all patients due to its high perioperative mortality and post-operative complications [5 6].

Placement of a self-expandable metal stent (SEMS) is an accepted therapeutic option for palliation of malignant obstruction involving the esophagus, gastro-duodenum, and colon. Introduction of stenting for palliative management has not improved survival but hospital stay is shortened. Despite high technical success with palliative stenting, it is feasible only in specific situations. Complications include perforation, migration, bleeding and obstruction [2 7]. Contraindications to stenting include poor performance status, poor prognosis (< 30 days), bowel perforation, bowel stenosis, multiple sites of obstruction, and peritoneal carcinomatosis [4].

Octreotide is a somatostatin analogue that inhibits vasoactive intestinal polypeptide activity in the gut, thereby reducing gastric and pancreatic juices and water and electrolyte excretion in the lumen.[3, 7] It also reduces splanchnic blood flow, indirectly decreasing gut wall edema, peristalsis (and secondary abdominal cramping), and bile excretion. Octreotide has been shown to improve bowel obstruction symptoms, sometimes eliminating the need for surgery, or improving the outcome of surgery by minimizing gut wall damage such as necrosis. Palliative patients might even have reversal of the subocclusive process [3 8 9].

Dexamethasone acts as an anti-inflammatory by decreasing gut wall edema, thereby relieving some of the stenosis and decreasing the excretion of water into the lumen [4]. Both of these actions can improve pain levels. It also has a central antiemetic effect.

Metoclopramide, a prokinetic of the stomach and small bowel and is often used first line to control nausea in the setting of partial bowel obstruction. Retrospectively, and clinically, when used in combination with octreotide and dexamethasone it is effective in patients achieving de-obstruction with low to minimal risk of perforation.

The use of the triple regimen together has not been yet done prospectively.

Evidence for Palliative Medical Management

Most cases of MBO are not surgical emergencies hence, medical therapy should always be considered initially as the picture becomes clear with passage of time. Baines et al [10] demonstrated successful management of 38 cases of MBO with medical treatment. Similar outcomes were demonstrated by several other authors [11]. In 1992, Mercedante et al. showed efficacy of octreotide in several cases of MBO in the resolution of intractable nausea and vomiting [12]. Since then multiple observational and case series support the efficacy of octreotide in the management of nausea and vomiting of MBO [13 14]. In a double-blinded, randomized placebo-controlled trial, there was no reduction in vomiting-free days with the addition of octreotide to a standardized regimen of dexamethasone, ranitidine and fluids in malignant bowel obstruction [15].

A retrospective study of MBO patients treated with octreotide, metoclopramide, and dexamethasone showed rapid improvement in nausea, and moderate/severe abdominal pain [16]. Metoclopramide has been studied in bowel obstruction in multiple studies but is usually recommended in partial obstruction and avoided in complete obstruction. Clinically, in the setting of MBO it is often difficult to decipher if a patient has complete or partial obstruction-imaging may not be accurate or reflective of the clinical picture. The general clinical rule of thumb is if there is flatus, it is a partial obstruction. In two retrospective studies when metoclopramide was given to patients with (complete or partial) MBO there was no incidence of perforation or increased colicky pain [8 16] Maximal effectiveness may not be reached until doses well in excess of 30 mg/day are given [5]. Due to a low risk of bowel perforation, especially in partial bowel obstruction, cautious use is recommended and the drug should be stopped immediately if pain worsens [4].

2.2 Rationale

Venting gastrostomies should be considered for patients with unresolved and symptomatic MBO depending on the clinical condition and patient's choice. They can be very effective at relieving nausea and vomiting, and usually better tolerated than nasogastric tubes. It may enable patients to eat and drink and to be cared for at home [17-20]. Contraindications to percutaneous gastrostomy include portal hypertension, massive ascites, active gastric ulceration and active bleeding [4].

Despite this progress there are few prospective studies and published guidelines for the medical management of inoperable MBO. Standard treatment involves bowel rest, intravenous fluids, pain medications and surgery if possible. The current proposed drug regimen has been studied retrospectively [16] but is not the standard of care for medical management. Metoclopramide has been traditionally avoided in the setting of complete bowel obstruction for concern for risk of perforation. However, in some retrospective studies and in years of clinical experience in the field, when using this drug in this population, the incidence is extremely rare [8 16].

We feel that the addition of metoclopramide to the other two drugs is a key for the efficacy of the medical management for MBO to be effective. The prognosis for patients who remain obstructed with venting G-tubes and TPN is often weeks to a few months; the benefits of de-obstruction is great, and the risks are minimal. The PI of this study surveyed five national palliative leaders who have studied MBO and work in oncology and they all use the triple regimen commonly, for many years with minimal adverse effects. The PI also discussed the use of the triple therapy with a three local GI medical oncologists, three GI surgical oncologists, a radiologist, 3 GYN oncologists and four hospitalists who all have been exposed to this regimen for the past 3 years at Roswell Park as we currently use it successfully for our patients who have MBO. We retrospectively examined data from 2015-2018 of 68 total patients: 34 who received the triple therapy compared to 34 who received no medications. Patients who received the triple therapy were twenty times more likely to reach de-obstruction, compared with patients who were given no medications (OR: 20.73 with 95% CI [1.99, 215.86], P=0.0112), after adjusting for related covariates. Only 3 patients in the triple therapy group had complete obstructions and there were no patients who had a reported bowel perforation after receiving the triple therapy.

We plan to study all three drugs for all patients with partial obstruction and exclude those with complete obstruction. If a patient develops worsened pain after administration of metoclopramide, this drug would be immediately discontinued.

The objectives of the current study are to analyze the rate of de-obstruction and effects on symptom control with use of medical regimens for malignant bowel obstruction prospectively.

3 INCLUSION AND EXCLUSION CRITERIA

NOTE: Patients requiring a gastrostomy tube insertion or with a prior gastrostomy tube will not be excluded.

3.1 Inclusion Criteria

To be included in this study, participants must meet the following criteria:

1 Age ≥ 18 years of age.

2 Diagnosis of partial bowel obstruction secondary to active or prior malignancy (primary or metastatic GI, GYN, and carcinomatosis) caused either by tumor itself or adhesions in the setting of active malignancy.

3 Cross-sectional imaging performed within 24 hours of clinical symptoms of bowel obstruction (nausea, vomiting, and constipation ± abdominal pain) during hospital admission.

4 Patient must have an inoperable MBO.

5 Participant must understand the investigational nature of this study and sign an Independent Ethics Committee/Institutional Review Board approved written informed consent form prior to receiving any study related procedure.

Refer to **Appendix A**: for the ***ELIGIBILITY VERIFICATION FORM: INCLUSION CRITERIA*** checklist.

3.2 Exclusion Criteria

Participants will be excluded from this study for the following:

1 Evidence of complete bowel obstruction by imaging.

2 Bacteremia/septicemia with a documented positive blood culture: If a blood culture comes back positive after study enrollment, patient will be excluded.

3 Patients already taking a steroid equivalent to 8 mg of dexamethasone per day for longer than 7 days prior to study enrollment.

4 Patients undergoing bowel surgery or stent placement for bowel obstruction.

5 Those patients with MBO in setting of incarcerated hernia.

6 Known history of QT prolongation syndrome or if QTc is > 500 msec on baseline EKG within 2 weeks of enrollment.

7 Lack of decision-making capacity/delirium.

8 Pregnant or nursing female participants.

9 Actively suicidal patients.

10 Acute cholecystitis.

11 History of seizure episode in the last 12 months or patient on a maintenance antiepileptic drug for seizure control.

12 Acute pancreatitis.

13 Bowel perforation.

14 Patients taking antipsychotic drugs.

15 History of dystonia or tardive dyskinesia.

16 Patients with pheochromocytoma.

17 Elevated blood pressure 180 mmHg systolic or 120 mmHg diastolic.

18 Immunocompromised patients.

19 Patients with latent tuberculosis history.

20 Incarcerated patients.

21 Patient already enrolled in a clinical trial.

22 Unwilling or unable to follow protocol requirements.

23 Any condition which in the Investigator's opinion deems the participant an unsuitable candidate to receive study treatment.

Refer to **Appendix B** for the ***ELIGIBILITY VERIFICATION FORM: EXCLUSION CRITERIA*** checklist.

3.3 Inclusion of Women and Minorities

Both men and women and members of all races and ethnic groups are eligible for this study.

4 LOCAL AND STUDY-WIDE NUMBER OF SUBJECTS

A maximum of 59 participants at Roswell Park will be enrolled prospectively. Accrual is expected to take 3 years.

5 LOCAL AND STUDY-WIDE RECRUITMENT METHODS

The Clinical Research Coordinator will be notified by the participating services (GYN, surgical and hospitalist) of any new admissions of patients presenting with bowel obstruction secondary to malignancy that may meet the study criteria (educational in-service will need to be conducted prior to study initiation on what criteria need to be met to identify potential study participants). Once a potential study participant is identified, a palliative care consult will be ordered, and the patient will be seen as usual in consultation by the palliative care service when a consult is ordered. They will remain as an inpatient under the primary service. The Clinical Research Coordinator will communicate with the primary team as well as the study personnel about study related changes to the treatment of the patient.

6 MULTI-SITE RESEARCH

Not applicable. This is a single-site study.

7 STUDY TIMELINES

Patients that are admitted with a bowel obstruction at Roswell Park and that meet the study eligibility requirements will be enrolled after signing an informed consent and, will be started on the drug regimen according to the type of bowel obstruction.

Day 1 will be identified as the day of start of treatment.

Patients will be followed for de-obstruction up to 7 days while on inpatient treatment.

If the patient de-obstructs within 7 days of starting treatment (as an inpatient), then they will continue the triple regimen for the full 7 days or until discharged. At that time, octreotide will be discontinued, and the metoclopramide and dexamethasone will be switched to oral for another 3 days, for a total of 10 days.

During the 3 days following discharge:

- Patients will be followed daily through phone calls by the Clinical Research Coordinator until they complete the 3-day post de-obstruction treatment (± 2 days) with the oral regimen. If the discharge occurs on a weekend day or holiday, the Clinical Research Coordinator will commence daily follow-up on the first business day following discharge and will continue until the patient has completed the 10 days of treatment. If completion of the 3-day post-de-obstruction treatment occurs on a weekend day or holiday, the Clinical Research Coordinator will follow-up with the patient within 2 days following the 3-day post-de-obstruction treatment completion time point.
    - Evaluation will include monitoring adverse events, treatment administration and recording the treatment administration data.

If the patient is discharged prior to 7 days, octreotide will be discontinued, and the metoclopramide and dexamethasone will be switched to oral until the 10-day treatment is complete.

If the patient is inpatient for over 7 days and up to 10 days, continue octreotide, metoclopramide, and dexamethasone treatment for up to 10 days. If the patient is then discharged prior to day 10, continue metoclopramide and dexamethasone orally until the 10-day treatment is complete.

If de-obstruction does not occur as inpatient, the clinician may choose to stop the drug regimen and a surgical/endoscopic consultation will be obtained to evaluate for possible venting G-tube placement.

8 STUDY ENDPOINTS

8.1 Primary Endpoint

- The primary efficacy endpoint is the proportion of eligible patients whose malignant bowel obstruction clears (de-obstruction) within 7 days of starting the protocol therapy. Patients meeting de-obstruction criteria within 7 days will be deemed treatment successes.
- De-obstruction is defined as:
    - Effective introduction of oral intake (yes/no)
        - Distinguished from small volumes of oral fluid that may be allowed with unresolved MBO

- Tolerating oral liquid diet (Day 1 of de-obstruction) that is able to be progressively more solid (oral or enteral)
- Cessation of vomiting or ability for NGT or venting G tube to remain clamped without vomiting
- The resumption of bowel movements

- Rate of de-obstruction is defined as:
  - From the date of study enrollment to the first observation of de-obstruction.

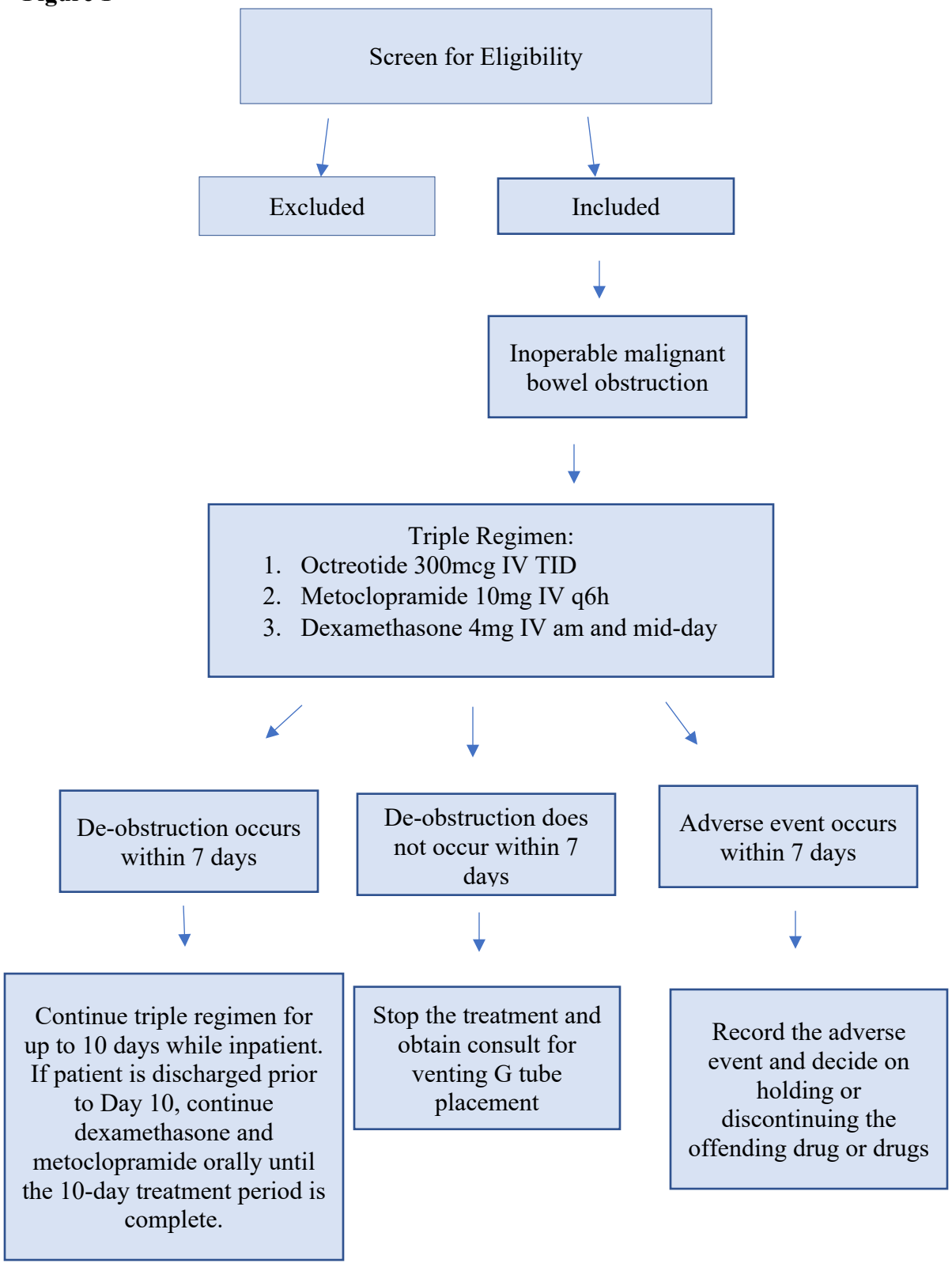
8.2 Secondary Endpoints

- Factors that may affect treatment with the treatment regimen will be determined by measuring/assessing the following:
  - Oral intake
  - NG/PEG output
  - Effect on symptom control:
    - pain
    - nausea
    - vomiting
    - constipation
  - Disposition upon discharge:
    - Discharged home
    - Hospice in any setting
    - LTC (Long Term care) or SAR (Sub-acute Rehabilitation)
- Overall survival (OS) will be measured from the date of study enrollment to the time of death from any cause in 6 months.

9 DESIGN

This is a prospective, open-label, single-center, Phase 2 study to identify the role of palliative management of inoperable malignant bowel obstruction. The study schema is depicted in Figure 1 on the next page.

Figure 1


Screen for Eligibility
Excluded
Included
Inoperable malignant bowel obstruction
Triple Regimen:
1. Octreotide 300mcg IV TID
2. Metoclopramide 10mg IV q6h
3. Dexamethasone 4mg IV am and mid-day
De-obstruction occurs within 7 days
De-obstruction does not occur within 7 days
Adverse event occurs within 7 days
Continue triple regimen for up to 10 days while inpatient. If patient is discharged prior to Day 10, continue dexamethasone and metoclopramide orally until the 10-day treatment period is complete.
Stop the treatment and obtain consult for venting G tube placement
Record the adverse event and decide on holding or discontinuing the offending drug or drugs

Patents will be screened for eligibility on admission (i.e., presence of malignant bowel obstruction) and if eligible and agreeable to participate, will be enrolled.

Complete obstruction is diagnosed clinically (vomiting, pain, abdominal distention, anorexia, absence of stools or flatus) and verified with X-ray or CT scan. These patients would be excluded. Partial obstruction would be diagnosed clinically (with some of the same above symptoms but also passing flatus) along with CT scan findings.

Patients will receive a triple regimen consisting of IV octreotide + IV dexamethasone + IV metoclopramide. If the patient reports worsening severe abdominal pain after administration of metoclopramide they will be assessed, and it will be decided if the drug be discontinued.

Patients will be monitored throughout the course of hospitalization and time to de-obstruction will be recorded.

10 TREATMENT

10.1 Dosing and Administration

Triple drug regimen for bowel obstruction: IV octreotide 300 mcg TID + IV dexamethasone 4 mg BID (first dose 9am and second at 2pm) + IV metoclopramide 10 mg q6h.

- In patients with a creatinine clearance (CrCl) of < 40 mL/min, the metoclopramide dose will be reduced to 5 mg q6 hours.
- For patients ≥ 65 years of age, the metoclopramide dose will be reduced to 5 mg q6 hours.

The patient will continue on study treatment for up to 10 days or until de-obstruction (whichever occurs first), de-obstruction is defined in section **8.1**.

If de-obstruction occurs within 7 days of treatment initiation:

- Continue treatment regimen while inpatient for up to 10 days. If they are discharged before 7 days, octreotide would be discontinued, and they would continue metoclopramide and dexamethasone orally until the 10-day treatment period is complete.
- If the patient is inpatient for over 7 days up to 10 days continue octreotide, metoclopramide, and dexamethasone for up to 10 days. If the patient is discharged prior to Day 10, continue metoclopramide and dexamethasone orally until the 10-day treatment period is complete.

If de-obstruction <u>does not</u> occur within 7 days of treatment initiation:

- At the discretion of the clinician, treatment regimen can be stopped, and a surgical/IR consult obtained for possible venting g-tube placement

If an <u>adverse event</u> occurs within 7 days of treatment initiation:

- Decision will be made to hold or discontinue drug/drugs

Reported adverse events (AEs) and potential risks are described in Section **13**.

Treatment is intended for an inpatient setting.

10.2 Dose Modifications and Management of Adverse Events

10.2.1 Dexamethasone

Note: Starting dose of dexamethasone is 4 mg BID. For the management of adverse events the dose of dexamethasone can be reduced by one-half (e.g., the first dose reduction would be 2 mg BID: 2 mg in the morning and 2 mg in the afternoon).

- **Delirium:** Screen with Condensed Memorial Assessment Scale (CMAS) and Confusion Assessment Method-Short Form (CAM-S) daily (Acute onset and fluctuating course, inattention, disorganized thinking, altered level of consciousness) [21]. Nursing staff would screen for delirium over the weekend. ***Discontinue dexamethasone***.
- **Fever:** Monitor temperature daily. If there is a documented temperature of > 100.4°F, then ***stop dexamethasone*.**
- **Hyperglycemia:** Monitor blood sugar every day. If blood glucose is > 200 mg/dL, then activate sliding scale insulin protocol for insulin naïve patients. ***For patients already on insulin, increase the dose of insulin*** (clinical discretion of physician).
- **Increased risk of infections:** Monitor clinically and follow leukocyte count based on clinical discretion. The leukocyte count is expected to rise with the use of dexamethasone, and it would be up to the physician to pursue infectious work up if an infection is suspected. ***Stop dexamethasone if infection is suspected.***
- **Hypertension:** *May occur with dexamethasone*. Dose reduction or discontinuing the drug would be based on clinical discretion of the physician.
- **Body fluid retention or peripheral edema:** *May occur with dexamethasone*. Dose reduction or discontinuing the drug would be based on clinical discretion of the physician.
- **Depression:** *May occur with dexamethasone*. Dose reduction or discontinuing the drug would be based on clinical discretion of the physician.
- **Increased risk of tuberculosis:** *May occur with dexamethasone*. Discontinue dexamethasone if TB is suspected.
- **Skin irritation:** *May occur with dexamethasone*. Dose reduction or discontinuing the drug would be based on clinical discretion of the physician.
- **Cushing syndrome:** *May occur with dexamethasone*. Discontinue dexamethasone if Cushing's syndrome develops.
- **Cardiomyopathy:** *May occur with dexamethasone*. Dose reduction or discontinuing the drug would be based on clinical discretion of the physician.
- **Bowel perforation:** *May occur with dexamethasone*. Discontinue triple regimen and withdraw patient from the study.
- **Compression fracture:** *May occur with dexamethasone*. Dose reduction or discontinuing the drug would be based on clinical discretion of the physician.
- **Cerebrovascular accident:** *May occur with dexamethasone*. Discontinue triple regimen and withdraw patient from the study.

- **Infarction of spinal cord:** *May occur with dexamethasone*. Discontinue triple regimen and withdraw patient from the study.
- **Nerve injury:** *May occur with dexamethasone*. Discontinue dexamethasone.
- **Paraplegia:** *May occur with dexamethasone*. Discontinue triple regimen and withdraw patient from the study.
- **Raised intracranial pressure:** *May occur with dexamethasone*. Discontinue dexamethasone.
- **Seizure:** *May occur with dexamethasone*. Discontinue dexamethasone.
- **Tetraplegia:** *May occur with dexamethasone*. Discontinue triple regimen and withdraw patient from the study.
- **Blindness and/or vision impairment level:** *May occur with dexamethasone*. Discontinue triple regimen and withdraw patient from the study.
- **Cortical blindness:** *May occur with dexamethasone*. Discontinue triple regimen and withdraw patient from the study.

10.2.2 Metoclopramide

- **Extrapyramidal symptoms:** Monitor for development of involuntary movements, cog-wheel rigidity, severe irritability, personality change. If suspected, ***stop metoclopramide*** and if acute dystonic reaction, which is rare and may manifest with involuntary movements of limbs, facial grimacing, torticollis, rhythmic protrusion of tongue, dystonic reactions or difficulty breathing may give diphenhydramine 50 mg IV or IM.
- **QT prolongation:** Monitor EKG after 7 days on study. If QT is > 500 msec, then ***stop metoclopramide***.
- **Severe Abdominal Pain (Score of 7 or greater on Likert scale):** If abdominal pain occurs or worsens within 1-15 minutes of metoclopramide administration, then the drug would be withheld for the rest of the study. The onset of pharmacological action of metoclopramide is 1 to 3 minutes following an intravenous dose.
- **Bowel perforation:** *May occur with metoclopramide*. Discontinue triple regimen and withdraw patient from the study.
- **Neuroleptic malignant syndrome:** Neuroleptic malignant syndrome (NMS) may occur with metoclopramide. Discontinue the drug if NMS is suspected.
- **Tardive dyskinesia:** Tardive dyskinesia (TD) may occur with metoclopramide. Discontinue the drug if TD is suspected.
- **Seizure disorder:** This drug may lower the seizure threshold.

10.2.3 Octreotide:

Note: For the management of adverse effects, octreotide may be held for a minimum of 24 hrs and then followed by patient reassessment.

Dose Reduction: The starting dose of octreotide is 300 mcg TID. For the management of adverse events the dose of octreotide can be reduced by 100 mcg TID (e.g., the first dose reduction would be 200 mcg TID: 200 mcg in the morning, 200 mcg in the afternoon and, 200 mcg in the evening).

- **Hypoglycemia:** Monitor blood sugar every day. If blood glucose is < 60 mg/dL, then ***activate hypoglycemia protocol*** (refer to **Appendix E**:).
- **Nausea:** *May occur with octreotide*. Dose reduction or holding the drug would be based on clinical discretion of the physician.
- **Backache:** *May occur with octreotide*. Dose reduction or holding the drug would be based on clinical discretion of the physician.
- **Dizziness:** *May occur with octreotide.* Dose reduction or holding the drug would be based on clinical discretion of the physician.
- **Headache:** *May occur with octreotide*. Dose reduction or holding the drug would be based on clinical discretion of the physician.

Fatigue: *May occur with octreotide*. Dose reduction or holding the drug would be based on clinical discretion of the physician.

- **Flatulence:** *May occur with octreotide*. Dose reduction or holding the drug would be based on clinical discretion of the physician.
- **Hypothyroidism:** *May occur with octreotide*. Dose reduction or holding the drug would be based on clinical discretion of the physician.
- **Bradycardia:** Bradycardia may occur with octreotide. Dose reduction or holding the drug would be based on clinical discretion of the physician.

10.2.4 Allergic reaction to octreotide, dexamethasone, or metoclopramide

Dexamethasone: Signs of an allergic reaction to dexamethasone include hives; difficulty breathing, swelling of ace, lips, tongue, or throat.

Metoclopramide: Symptoms of an allergic reaction to metoclopramide can include rash, hives, trouble breathing, and swelling of tongue, lips, or throat.

Octreotide: Although urticaria, allergy/hypersensitivity reactions and anaphylaxis have been noted as possible adverse reactions, there is a lack of data showing a causal relationship between octreotide and hypersensitivity reactions and there is no information on management when continued use of this medication is essential.

Management of allergic reactions

Based on the specific symptoms of the reaction, *the identified offending medication would be discontinued,* and the allergic reaction would be treated as appropriate.

10.3 General Concomitant Medication and Supportive Care

Patients may receive anti-emetics, opioid pain medications for pain control and, antibiotics for infection, if necessary. If a patient develops a clinical condition unrelated to the study, then they may be withdrawn from the study (to be determined by the principal investigator).

10.4 Duration of Treatment

Participants will be on the study drug combination for a maximum of 10 days as an inpatient in the absence of disease progression, unacceptable toxicity and withdrawal from study, intercurrent illness that prevents further administration of treatment, participant demonstrates an inability/refusal to comply with the medication regime or, participant withdraws from study.

If de-obstruction occurs within the 7 days, upon discharge, the patient will receive an additional 3 days of the treatment combination as an outpatient, for a total of 10 days of treatment.

11 PROCEDURES INVOLVED

11.1 Participant Registration

Eligibility of each participant will be established prior to registration

Informed consent **MUST** be completed prior to receiving any study related procedures.

11.2 Pre-treatment Screening

- Medical history (including all prior therapy related to malignant bowel obstruction)
    - Cancer stage and primary diagnosis date
    - Comorbidity index score
    - Surgical history
    - MBO symptoms
- Weight and BMI
- Blood draw to determine Plasma Creatinine clearance using the Cockcroft-Gault formula:

$$C_{Cr} = \frac{(140 - \text{age}) \times \text{weight (kg)}}{72 \times S_{Cr}} \quad [\times 0.85 \text{ if female}]$$

C_{Cr} = creatinine clearance (expressed in mL/min); S_{Cr} = serum creatinine (expressed in mg/dL)

- Smoking/ alcohol use history
- Prior use of steroids (include use for up to 1 month prior to hospitalization)
- Karnofsky score (refer to **Appendix D**)
- Concomitant Medications

Mandatory Pre-treatment Evaluations

- Baseline EKG (not necessary if one is available that was taken no later than 2 weeks prior to study registration)
- Pregnancy test (B-HCG) in females of childbearing potential

11.3 Evaluations Performed during Inpatient Treatment

The following research procedures will be performed up to Day 7 of Inpatient Treatment

- Condensed Memorial Assessment Scale
- Confused Assessment Method – Short Form
- Blood sugars will be performed **every day**
- Adverse event monitoring will be ongoing and recorded daily while on study treatment

The following standard of care procedures may be considered (depending on the clinical discretion of the physician) during the treatment, but are not mandatory:

- NG tube insertion
- IV line insertion
- G-tube insertion
- Venting G-tube insertion
- Imaging (CT scan or X-ray)

11.4 Evaluations Performed Prior to Discharge

The following evaluations will be performed at the end of 7 days (prior to discharge, ± 3 days) or at time of treatment discontinuation:

- EKG
- Concomitant medication
- Adverse events

11.5 Discharge Follow-up

Treatment continuation will be done as an outpatient if the patient is stable for discharge as determined by the physician. During the days following discharge:

- If the patient de-obstructs, the drug regimen will be transitioned to oral in the case of metoclopramide and dexamethasone while octreotide will be discontinued.
- Patients will be followed daily through phone calls by the Clinical Research Coordinator until they complete the post de-obstruction treatment (± 2 days) with the triple regimen. If the discharge occurs on a weekend day or holiday, the Clinical Research Coordinator will commence daily follow-up on the first business day following discharge and will continue until the patient has completed the triple regimen post-de-obstruction treatment. If completion of the post-de-obstruction treatment occurs on a weekend day or holiday, the Clinical Research Coordinator will follow-up with the patient within 3 days following the post-de-obstruction treatment completion time point.
- Evaluation will include monitoring adverse events, treatment administration and recording the treatment administration data.

11.6 Post-Treatment Follow-Up Evaluations

Follow-up safety evaluations will occur 30 days (± 3 days) after last dose of study drug or until resolution of any drug-related toxicity (telephone contact is acceptable).

- Concomitant medications: List any ongoing medications with dose changes, as applicable.
- Adverse events

11.7 Long Term Follow-Up Evaluations

Long-term follow up will be done at 3 month and 6 months from the time of discharge by follow-up phone call (to include tolerance of oral intake, bowel movements, hospitalizations).

Participants who are unavailable for follow-up evaluations should be classified as lost to follow-up for 1 of the following reasons:

- Lost to follow-up: For a participant to be considered lost to follow-up, the investigator must make two separate attempts to re-establish contact with the participant. The attempts to re-establish participant contact must be documented (e.g., certified letter).
- Death: Date and cause of death will be recorded for those participants who die within 30 days after last dose of study drug (telephone verification is acceptable).

12 WITHDRAWAL OF SUBJECTS

Participants will be withdrawn from the study if any of the following occurs:

- Allergic reaction to octreotide, dexamethasone, or metoclopramide
- Occurrence of any of the following while receiving the triple-drug regimen:
    - Bowel perforation
    - Cerebrovascular accident
    - Infarction of spinal cord
    - Paraplegia
    - Tetraplegia
    - Blindness and/or vision impairment level
    - Cortical blindness
- The patient can voluntarily withdrawal for any reason or, due to any unacceptable toxicity based on the PI’s decision.

12.1 Treatment Discontinuation

Upon treatment discontinuation all end of treatment evaluations and tests will be conducted. All participants who discontinue due to an AE must be followed until the event resolves or stabilizes. Appropriate medical care should be provided until signs and symptoms have abated, stabilized, or until abnormal laboratory findings have returned to acceptable or pre-study limits. The final status of the AE will be reported in the participant’s medical records and the appropriate eCRF.

Reasons for treatment discontinuation should be classified as follows:

- Death
- Progressive disease
- Toxicity: treatment related or unrelated
- Investigator judgment
    - The Investigator may discontinue a participant if, in his/her judgment, it is in the best interest of the participant to do so.
- Participant voluntary withdrawal
    - A participant may withdraw from the study at any time, for any reason. If a participant discontinues treatment, an attempt should be made to obtain information regarding the reason for withdrawal.

13 RISKS TO SUBJECTS

The drug regimens proposed for the study consist of octreotide, dexamethasone, and metoclopramide. These drugs are not experimental and have been FDA approved for various clinical conditions.

13.1 Dexamethasone

Dexamethasone sodium phosphate (dexamethasone) is an adrenocortical steroid anti-inflammatory drug.

Reported common adverse effects related to dexamethasone include:

- **Cardiovascular:** Hypertension (Diabetic macular edema, 13%)
- **Dermatologic**: Atrophic condition of skin, Finding of skin healing, Impaired
- **Endocrine metabolic**: Cushing's syndrome, Decreased body growth
- **Ophthalmic:** Abnormal vision (1% to 9%), Cataract (Diabetic macular edema, 68%; retinal vein occlusion and uveitis, 5%), Conjunctival edema (5%), Conjunctivitis (6%), Corneal edema (5% to 15%), Discomfort, Eye (10%), Dry eye syndrome (5%), Iritis (5% to 15%), Raised intraocular pressure (Diabetic macular edema, 35%; retinal vein occlusion and uveitis, 25% ; postoperative inflammation, 5% to 15%), Vitreous floaters (1% to 5%)
- **Psychiatric:** Depression, Euphoria
- **Respiratory**: Pulmonary tuberculosis

Reported serious adverse effects related to dexamethasone include:

- **Cardiovascular:** Cardiomyopathy
- **Endocrine metabolic:** Hyperglycemia, Primary adrenocortical insufficiency
- **Gastrointestinal:** Pancreatitis
- **Immunologic:** Infectious disease
- **Musculoskeletal:** Osteoporosis

- **Ophthalmic:** Conjunctival hemorrhage (Diabetic macular edema, 23%; retinal vein occlusion and uveitis, 22%), Glaucoma (Diabetic macular edema, 1.2%), Keratitis (2%), Posterior subcapsular cataract, Retinal tear (2%), Retinal vascular disorder (3%), Uveitis (2%)

13.2 Metoclopramide

Metoclopramide is classified as a dopamine-receptor antagonist. Metoclopramide stimulates motility of the upper gastrointestinal tract and, increases the tone and amplitude of gastric (especially antral) contractions, relaxes the pyloric sphincter and the duodenal bulb, and increases peristalsis of the duodenum and jejunum.

The most common adverse reactions reported for metoclopramide (> 10%) are restlessness, drowsiness, fatigue, and lassitude.

13.3 Octreotide

Octreotide exerts pharmacologic actions similar to the natural hormone, somatostatin and, is indicated for treatment of acromegaly, carcinoid tumors and, vasoactive intestinal peptide tumors (VIPomas).

The most common adverse reactions reported for octreotide, occurring in ≥ 20% of patients are:

- **Acromegaly**: diarrhea, cholelithiasis, abdominal pain, flatulence
- **Carcinoid Syndrome**: back pain, fatigue, headache, abdominal pain, nausea, dizziness

14 POTENTIAL BENEFITS TO SUBJECTS

- Patients who have inoperable MBO are not able to eat by mouth and often require a venting PEG tube and TPN to maintain nutrition which is associated with increased morbidity and mortality, with reduced prognosis and quality of life.
- If we are able to relieve the MBO, preventing them from having a venting PEG tube and/or TPN, they would be able to eat food by mouth for pleasure and nutrition. They would have reduced risk for infections due to TPN and pain from PEG tube insertion and discomfort at the site.

15 DATA AND SPECIMEN BANKING

Not Applicable.

16 MEASUREMENT OF EFFECT

Rate of de-obstruction:

- Defined date of study enrollment to the first observation of clearance or de-obstruction.

Patients meeting de-obstruction criteria within 7 days will be deemed treatment successes.

17 SAFETY EVALUATION

17.1 Adverse Events

An adverse event or adverse experience (AE) is any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug related. Therefore, an AE can be ANY unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not considered related to the medicinal (investigational) product (attribution of 'unrelated', 'unlikely', 'possible', 'probable', or 'definite').

An AE is considered "unexpected" if it is not listed in the investigator brochure or is not listed at the specificity or severity that has been observed; or if an investigator brochure is not required or available, is not consistent with the risk information described in the general investigational plan in other study-related documents.

17.1.1 Diagnosis Versus Signs and Symptoms

If known, a diagnosis should be recorded on the CRF rather than individual signs and symptoms (e.g., record only liver failure or hepatitis rather than jaundice, asterixis, and elevated transaminases). However, if a constellation of signs and/or symptoms cannot be clinically characterized as a single diagnosis or syndrome at the time of reporting, each individual event should be recorded as an AE or SAE on the CRF. If a diagnosis is subsequently established, it should be reported as follow-up information.

17.1.2 Adverse Events Occurring Secondary to Other Events

In general, AEs occurring secondary to other events (e.g., cascade events or clinical sequelae) should be identified by their primary cause. For example, if severe diarrhea is known to have resulted in dehydration, it is sufficient to record only diarrhea as an AE or SAE on the CRF.

However, clinically significant AEs occurring secondary to an initiating event that are separated in time should be recorded as independent events on the CRF. For example, if a severe gastrointestinal hemorrhage leads to renal failure, both events should be recorded separately on the CRF.

17.1.3 Abnormal Laboratory Values

Only clinically significant laboratory abnormalities that require active management will be recorded as AEs or SAEs on the CRF (e.g., abnormalities that require study drug dose modification, discontinuation of study treatment, more frequent follow-up assessments, further diagnostic investigation, etc.).

If the clinically significant laboratory abnormality is a sign of a disease or syndrome (e.g., alkaline phosphatase and bilirubin 5 x the upper limit of normal associated with cholecystitis), only the diagnosis (e.g., cholecystitis) needs to be recorded on the Adverse Event CRF.

If the clinically significant laboratory abnormality is not a sign of a disease or syndrome, the abnormality itself should be recorded as an AE or SAE on the CRF. If the laboratory abnormality can be characterized by a precise clinical term, the clinical term should be recorded as the AE or SAE. For example, an elevated blood potassium level of 7 mEq/L should be recorded as "hyperkalemia".

Observations of the same clinically significant laboratory abnormality from visit to visit should not be repeatedly recorded as AEs or SAEs on the CRF, unless their severity, seriousness, or etiology changes.

Preexisting Medical Conditions (Baseline Conditions)
A preexisting medical condition should be recorded as an AE or SAE only if the frequency, severity, or character of the condition worsens during the study. When recording such events on an Adverse Event CRF, it is important to convey the concept that the preexisting condition has changed by including applicable descriptors (e.g., "more frequent headaches").

17.2 Grading and Reporting Adverse Events

17.2.1 Grading and Relationship to Drug

The descriptions and grading scales found in the CTEP Version 5 of the NCI Common Terminology Criteria for Adverse Events (CTCAE) will be utilized for AE reporting. CTEP Version 5.0 of the CTCAE is identified and located at:

http://ctep.cancer.gov/protocolDevelopment/electronic_applications/ctc.htm.

AEs not covered by specific terminology listed should be reported with common medical terminology and documented according to the grading scales provided in the CTCAE Version 5.

The relationship of event to study drug will be documented by the Investigator as follows:

- **Unrelated:** The event is clearly related to other factors such as the participant's clinical state, other therapeutic interventions or concomitant drugs administered to the participant.
- **Unlikely:** The event is doubtfully related to investigational agent(s). The event was most likely related to other factors such as the participant's clinical state, other therapeutic interventions, or concomitant drugs.
- **Possible:** The event follows a reasonable temporal sequence from the time of drug administration but could have been produced by other factors such as the participant's clinical state, other therapeutic interventions, or concomitant drugs.
- **Probable:** The event follows a reasonable temporal sequence from the time of drug administration and follows a known response pattern to the study drug. The event cannot be reasonably explained by other factors such as the participant's clinical state, therapeutic interventions, or concomitant drugs.
- **Definite:** The event follows a reasonable temporal sequence from the time of drug administration, follows a known response pattern to the study drug, cannot be reasonably explained by other factors such as the participant's condition, therapeutic interventions or concomitant drugs; AND occurs immediately following study drug administration, improves upon stopping the drug, or reappears on re-exposure.

17.3 Reporting Adverse Events

Routine AEs occurring between the start date of intervention until 30 days after the last intervention, or until the event has resolved, the study participant is lost to follow-up, the start of a new treatment, or until the study investigator assesses the event(s) as stable or irreversible, will be reported. New information will be reported after it is received.

Guidelines for Routine Adverse Event Reporting for Pilot, Phase 2, and Phase 3 Studies (Regardless of Expectedness)

Attribution	Grade 1	Grade 2	Grade 3	Grade 4
Unrelated			X	X
Unlikely			X	X
Possible	X	X	X	X
Probable	X	X	X	X
Definite	X	X	X	X

17.4 Serious Adverse Events

A serious adverse event (SAE) is any adverse event (experience) that in the opinion of either the investigator or sponsor results in **ANY** of the following:

- Death.
- A life-threatening adverse event (experience). Any AE that places a participant or participants, in the view of the Investigator or sponsor, at immediate risk of death from the reaction as it occurred. It does NOT include an AE that, had it occurred in a more severe form, might have caused death.
- Inpatient hospitalization or prolongation of existing hospitalization (for > 24 hours).
- A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions.
- A congenital anomaly or birth defect.
- Important Medical Event (IME) that, based upon medical judgment, may jeopardize the participant, and may require medical or surgical intervention to prevent one of the outcomes listed above.

17.4.1 Reporting Serious Adverse Events

All new SAEs occurring from the date the participant signs the study consent until 30 days after the last intervention or a new treatment is started, whichever comes first, will be reported. The Roswell Park SAE Source Form is to be completed with all available information, including a brief narrative describing the SAE and any other relevant information.

SAEs occurring after the 30-day follow-up period that the investigator determines to be possibly, probably, or definitely related to the study intervention should be reported.

SAEs that are unexpected and possibly, probably, or definitely related must be reported as an Unanticipated Problem. Please refer to Section 17.6 for details on reporting Unanticipated Problems.

17.5 Follow-Up for Serious Adverse Events

All related SAEs should be followed to their resolution, until the study participant is lost to follow-up, the start of a new treatment, or until the study investigator assesses the event(s) as stable or irreversible. New information will be reported when it is received.

17.6 Unanticipated Problems

An Unanticipated Problem (UP) is any incident, experience, or outcome that meets all of the following criteria:

- Unexpected (in terms of nature, severity, or frequency) given:
  - The research procedures that are described in the study-related documents, including study deviations, as well as issues related to compromise of participant privacy or confidentiality of data.
  - The characteristics of the participant population being studied.
- Related or possibly related to participation in the research (possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research).
- Suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized or if in relation to an AE is deemed Serious per Section 17.3.

17.6.1 Reporting Unanticipated Problems

The Reportable New Information (RNI) Form will be submitted to the CRS Quality Assurance (QA) Office within 1 business day of becoming aware of the Unanticipated Problem. After review, CRS QA Office will submit the RNI to the IRB.

When becoming aware of new information about an Unanticipated Problem, submit the updated information to CRS QA Office with an updated Reportable New Information Form. The site Investigator or designated research personnel will report all unanticipated problems to the IRB in accordance with their local institutional guidelines.

18 DATA MANAGEMENT AND CONFIDENTIALITY

18.1 Data Collection

A unique code will be assigned to each patient on the data collection sheet. The codes will not correspond to any patient identifiers. The data collection sheet will be saved and maintained in the SharePoint site which is password protected. A copy of the data collection sheet is attached (**Appendix C**:). Study data (for analysis) will be provided to the statistician in a SAS-compatible EXCEL file.

The research data will not contain any patient identifiers. It will be secured from improper use and disclosures by granting access to data files to only personnel involved in the study, namely principal investigator, and the co-investigators. Any paper files containing identifiers will not be taken off Roswell Park premises. Subject identity will not be disclosed in the event of publication or sharing of data.

A “basic build” will be used to collect the required information for grant, DSMB and continuing review reporting.

18.2 Maintenance of Study Documents

Essential documents will be retained per Roswell Park policy for 6 years from the study termination date. These documents could be retained for a longer period, however, if required by the applicable local regulatory requirements or by an agreement with Roswell Park.

18.3 Revisions to the Protocol

Roswell Park may make such changes to the protocol as it deems necessary for safety reasons or as may be required by the U.S. FDA or other regulatory agencies. Revisions will be submitted to the IRB/ERC for written approval before implementation.

18.4 Termination of the Study

It is agreed that, for reasonable cause, either the Roswell Park Investigators or the Sponsor, may terminate this study, provided a written notice is submitted within the time period provided for in the Clinical Trial Agreement. In addition, Roswell Park may terminate the study at any time upon immediate notice if it believes termination is necessary for the safety of participants enrolled in the study.

18.5 Confidentiality

All information provided to the Investigator by Roswell Park including preclinical data, protocols, CRFs, and verbal and written information, will be kept strictly confidential and confined to the clinical personnel involved in conducting this study, and no disclosure shall be made except in accordance with any right of publication granted to the Investigator. This information may be related in confidence to the IRB/ERC or other committee functioning in a similar capacity. No report or information about the study will be provided to anyone not involved in the study without consent of Roswell Park except if required by law.

19 STATISTICAL PLAN

This is a single arm, one-stage Phase II trial evaluating the role of palliative management of inoperable malignant bowel obstruction in palliative care patients presenting with bowel obstruction secondary to malignancy.

Statistical analysis will be performed by the Roswell Park Biostatistics & Bioinformatics Department.

Sample Size Determination

The sample size calculations are based on the primary analysis, which compares the clearance rate for the prospective cohort to a historic control using one-sided binomial exact tests.

The historic control rate using the standard of care for this patient population (i.e. patient presenting with inoperable bowel obstruction secondary to malignancy) is approximately 0.7. The study design has 80.9% power to detect a 0.85 clearance rate with the proposed triple therapy, while controlling to 5% the probability of erroneously finding a truly ineffective treatment as worthy of further research.

To account for patients that may be non-evaluable (i.e., survival outcome occurs prior to the 7-day evaluation for clearance), up to n=59 patients may be accrued for the prospective cohort.

Demographics and Baseline Characteristics

Descriptive statistics (as appropriate: n, percent, mean, median, min and max) will be used to summarize demographic and baseline characteristics in the overall sample.

Primary Analyses

The primary objective is to evaluate the role of palliative medical management of inoperable MBO with as the proposed triple therapy in patients presenting with inoperable bowel obstruction secondary to malignancy. The primary outcome is obstruction clearance, where the malignant bowel obstruction clears within 7 days of starting the protocol therapy, which is treated as a dichotomous variable. Clearance will be summarized using frequencies and relative frequencies, with the clearance rate estimated using a 90% confidence interval obtained by Jeffrey's prior method.

The efficacy of the proposed triple therapy will be assessed using a one-sided, one-sample binomial exact test about the following hypotheses:

$$H_0: \pi \leq \pi_0 \text{ versus } H_A: \pi > \pi_0,$$

where π is the true clearance rate of the proposed triple therapy and π_0 is the historic clearance rate for the standard of care.

For this patient population, we expect the clearance rate for the standard of care to be approximately 0.7 ($= \pi_0$). If the true clearance rate of the proposed triple therapy is 0.85, then we'd consider the therapy promising.

Based on these characteristics, a sample size of n=49 evaluable patients with inoperable bowel obstructions secondary to malignancy will be enrolled. If 39 or fewer of these patients have clearance, the triple therapy will be declared ineffective, and the study terminated. If 40 or more patients have clearance, the triple therapy will be considered interesting for further study.

Secondary Analyses

The secondary objectives are to compare the time to clearance and OS in patients treated with the proposed therapies, and the safety and tolerability of the proposed therapies.

Time to clearance and OS will be treated as bivariate time-to-event outcomes. Time to clearance will be measured from the date of study enrollment to the first observation of clearance. OS will be measured from the date of study enrollment to the time of death from any cause. The time-to-event outcomes will be summarized by cohort using standard Kaplan-Meier (KM) methods. Estimates of the median times will be obtained with 95% confidence intervals. The 3- and 6-month OS rates will be estimated with 95% confidence intervals.

The adverse events and toxicities will be summarized by grade using frequencies and relative frequencies.

The additional factors that may affect or be related to treatment regimen (such as symptom control, discharge disposition, etc.) will be summarized using the appropriate descriptive statistics. As exploratory analyses, associations between these factors and time to clearance or OS may be evaluated using Cox regression models, while associations with toxicity may be evaluated using logistic regression models.

Exploratory Analysis

As exploratory analyses, sub-group analyses may be performed on the set of patients that present with A) complete and B) partial obstructions. The analyses described in the primary and secondary analyses would be performed in these sub-groups. Additionally, a comparison of clearance and toxicity rates may be performed using Fisher's exact test; and a comparison of time to clearance or OS may be performed using the log-rank test.

Safety Analysis

All participants who receive any study treatment will be considered evaluable for toxicity using the revised NCI Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. Adverse events and toxicities will be summarized by grade using frequencies and relative frequencies.

Interim Analyses and Criteria for Early Termination

No formal interim analysis is included in the design, given the severity of the condition and the limited number of alternative treatment options. The study will be monitored by the Roswell Park Data Safety and Monitoring Committee (DSMC), who may make recommendations about study continuation and termination.

20 PROVISIONS TO MONITOR THE DATA TO ENSURE THE SAFETY OF SUBJECTS

As per the Roswell Park Data Safety Monitoring Plan, the Roswell Park Data and Safety Monitoring Committee will assess the progress of the study, the safety data, and critical efficacy endpoints. The DSMC will review the study and will make recommendations that include but not limited to; (a) continuation of the study, (b) modifications to the design (c) suspension of or, (d) termination of the study.

21 VULNERABLE POPULATIONS

Not Applicable.

22 COMMUNITY-BASED PARTICIPATORY RESEARCH

Not Applicable.

23 SHARING OF RESULTS WITH SUBJECTS

Individual response data is shared with the participant as a part of their clinical care.

24 SETTING

Inpatients at Roswell Park, a tertiary cancer care center.

25 PROVISIONS TO PROTECT THE PRIVACY INTERESTS OF SUBJECTS

Any data, specimens, forms, reports, video recordings, and other records that leave the site will be identified only by a participant identification number (Participant ID, PID) to maintain confidentiality. All records will be kept in a limited access environment. All computer entry and

networking programs will be done using PIDs only. Information will not be released without written authorization of the participant.

Data collection will not contain patient identifiers – these will be removed by the Clinical Research Coordinator assigned to the study and will be replaced with a unique code that is assigned to each patient on the data collection sheet.

26 RESOURCES AVAILABLE

Study funding: Alliance Foundation of Roswell Park.

27 PRIOR APPROVALS

Not Applicable.

28 COMPENSATION FOR RESEARCH-RELATED INJURY

If the subject believes they have been injured as a direct result of their participation in this research study, they will be advised to notify the Roswell Park Patient Advocate at (716) 845-1365 or the Study Doctor at (716) 845-8675.

Medical diagnosis and treatment for the injury will be offered, and a determination will be made regarding appropriate billing for the diagnosis and treatment of the injury. A financial counselor (716-845-3161) will be able to provide an explanation of coverage and to answer questions the subject may have regarding study related billing.

The subject is not prevented from seeking to collect compensation for injury related to malpractice, fault, or blame on the part of those involved in the research.

29 ECONOMIC BURDEN TO SUBJECTS

The participants will not be subject to any economic burden. Any mandatory tests, including EKG and B-HCG, will be covered by the study.

30 CONSENT PROCESS

This study will not be initiated until the protocol and informed consent document(s) have been reviewed and approved by a properly constituted Institutional Review Board (IRB) or Independent Ethics Committee (IEC). Each participant (or legal guardian) shall read, understand, and sign an instrument of informed consent prior to performance of any study-specific procedure. It is the responsibility of the investigator to ensure that the participant is made aware of the investigational nature of the treatment and that informed consent is given.

The Investigator is responsible for the retention of the participant log and participant records; although personal information may be reviewed by authorized persons, that information will be treated as strictly confidential and will not be made publicly available. The investigator is also responsible for obtaining participant authorization to access medical records and other applicable study specific information according to Health Insurance Portability and Accountability Act regulations (where applicable).

This study will be conducted in compliance with all applicable laws and regulations of the state and/or country and institution where the participant is treated. The clinical trial should be conducted in accordance with the ethical principles embodied in the Belmont Report: Ethical

Principles and Guidelines for the Protection of Human Subjects of Research, consistent with good clinical practice and the applicable regulatory requirements and according to the guidelines in this protocol, including attached appendices.

31 PROCESS TO DOCUMENT CONSENT IN WRITING

Eligible patients would be screened electronically prior to study enrollment and informed consent would be obtained if patient agrees to participate in the study.

Consent will also be obtained from the primary service admitting the patient.

The Investigator (or IRB specified designee) is responsible for obtaining written consent from each participant or the participant's legally authorized representative in accordance with GCP guidelines using the approved informed consent form, before any study specific procedures (including screening procedures) are performed. The informed consent form acknowledges all information that must be given to the participant according to applicable GCP guidelines, including the purpose and nature of the study, the expected efficacy and possible side effects of the treatment(s), and specifying that refusal to participate will not influence further options for therapy. Any additional information that is applicable to the study must also be included. Additional national or institutionally mandated requirements for informed consent must also be adhered to. The participant should also be made aware that by signing the consent form, processing of sensitive clinical trial data and transfer to other countries for further processing is allowed.

The Investigator shall provide a copy of the signed consent form to the participant and the signed original shall be maintained in the Investigator File. A copy of the signed consent form must be filed in the participant file. At any stage, the participant may withdraw from the study and such a decision will not affect any further treatment options.

32 DRUGS OR DEVICES

Dexamethasone, metoclopramide, and octreotide are used singly or in different combination depending on the type of obstruction for the medical management of malignant bowel obstruction. All drugs are commercially available.

Drugs will not be provided for the study. Dexamethasone, metoclopramide, and octreotide will be paid for by the patient’s insurance carrier as part of the standard of care treatment.

33 REFERENCES

1. Anthony T, Baron T, Mercadante S, et al. Report of the clinical protocol committee: development of randomized trials for malignant bowel obstruction. J Pain Symptom Manage 2007;**34**(1 Suppl):S49-59 doi: 10.1016/j.jpainsymman.2007.04.011[published Online First: Epub Date]|.

2. Tuca A, Guell E, Martinez-Losada E, Codorniu N. Malignant bowel obstruction in advanced cancer patients: epidemiology, management, and factors influencing spontaneous resolution. Cancer Manag Res 2012;**4**:159-69 doi: 10.2147/CMAR.S29297[published Online First: Epub Date]|.

3. Ripamonti C, Easson A, Gerdes S. Bowel Obstruction. In: Cherny N, Fallon M, Kaasa S, Portenoy R, Currow D, eds. Oxford Textbook of Palliative Medicine. 5th ed. Oxford: Oxford University Press, 2015:9119-930.

4. Tradounsky G. Palliation of gastrointestinal obstruction. Can Fam Physician 2012;**58**(6):648-52, e317-21

5. Ripamonti CI, Easson AM, Gerdes H. Management of malignant bowel obstruction. Eur J Cancer 2008;**44**(8):1105-15 doi: 10.1016/j.ejca.2008.02.028[published Online First: Epub Date]|.

6. Ferguson HJ, Ferguson CI, Speakman J, Ismail T. Management of intestinal obstruction in advanced malignancy. Ann Med Surg (Lond) 2015;**4**(3):264-70 doi: 10.1016/j.amsu.2015.07.018[published Online First: Epub Date]|.

7. Esha B, and Louis MWKS. Palliative enteroscopic stent placement for malignant mid-gut obstruction. Gastrointestinal Intervention 2014;**3**(1):30-34

8. Mercadante S, Ferrera P, Villari P, Marrazzo A. Aggressive pharmacological treatment for reversing malignant bowel obstruction. J Pain Symptom Manage 2004;**28**(4):412-6 doi: 10.1016/j.jpainsymman.2004.01.007[published Online First: Epub Date]|.

9. Prommer EE. Established and potential therapeutic applications of octreotide in palliative care. Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer 2008;**16**(10):1117-23 doi: 10.1007/s00520-007-0399-4[published Online First: Epub Date]|.

10. Baines M, Oliver DJ, Carter RL. Medical management of intestinal obstruction in patients with advanced malignant disease. A clinical and pathological study. Lancet 1985;**2**(8462):990-3

11. Ventafridda V, Ripamonti C, Caraceni A, Spoldi E, Messina L, De Conno F. The management of inoperable gastrointestinal obstruction in terminal cancer patients. Tumori 1990;**76**(4):389-93

12. Mercadante S, Maddaloni S. Octreotide in the management of inoperable gastrointestinal obstruction in terminal cancer patients. J Pain Symptom Manage 1992;**7**(8):496-8

13. Mercadante S, Porzio G. Octreotide for malignant bowel obstruction: twenty years after. Critical reviews in oncology/hematology 2012;**83**(3):388-92 doi: 10.1016/j.critrevonc.2011.12.006[published Online First: Epub Date]|.

14. Mercadante S, Ripamonti C, Casuccio A, Zecca E, Groff L. Comparison of octreotide and hyoscine butylbromide in controlling gastrointestinal symptoms due to malignant inoperable bowel obstruction. Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer 2000;**8**(3):188-91

15. Currow DC, Quinn S, Agar M, et al. Double-blind, placebo-controlled, randomized trial of octreotide in malignant bowel obstruction. J Pain Symptom Manage 2015;**49**(5):814-21 doi: 10.1016/j.jpainsymman.2014.09.013[published Online First: Epub Date]|.

16. Berger J, Lester P, Rodrigues L. Medical Therapy of Malignant Bowel Obstruction With Octreotide, Dexamethasone, and Metoclopramide. Am J Hosp Palliat Care 2016;**33**(4):407-10 doi: 10.1177/1049909115569047[published Online First: Epub Date]|.

17. Cannizzaro R, Bortoluzzi F, Valentini M, et al. Percutaneous endoscopic gastrostomy as a decompressive technique in bowel obstruction due to abdominal carcinomatosis. Endoscopy 1995;**27**(4):317-20 doi: 10.1055/s-2007-1005700[published Online First: Epub Date]|.

18. Kawata N, Kakushima N, Tanaka M, et al. Percutaneous endoscopic gastrostomy for decompression of malignant bowel obstruction. Dig Endosc 2014;**26**(2):208-13 doi: 10.1111/den.12139[published Online First: Epub Date]|.

19. Pothuri B, Montemarano M, Gerardi M, et al. Percutaneous endoscopic gastrostomy tube placement in patients with malignant bowel obstruction due to ovarian carcinoma. Gynecologic oncology 2005;**96**(2):330-4 doi: 10.1016/j.ygyno.2004.09.058[published Online First: Epub Date]|.

20. Brooksbank MA, Game PA, Ashby MA. Palliative venting gastrostomy in malignant intestinal obstruction. Palliat Med 2002;**16**(6):520-6 doi: 10.1191/0269216302pm590oa[published Online First: Epub Date]|.

21. Hall WH, Ramachandran R, Narayan S, Jani AB, Vijayakumar S. An electronic application for rapidly calculating Charlson comorbidity score. BMC cancer 2004;**4**:94 doi: 10.1186/1471-2407-4-94[published Online First: Epub Date]|.

22. Karnofsky DA, Burchenal JH. The Clinical Evaluation of Chemotherapeutic Agents in Cancer. In: MacLeod CM, ed. Evaluation of Chemotherapeutic Agents: Symposium Held at the New York Academy of Medicine. New York: Columbia University Press, 1949:191-205.

20. Clark K., Lam L., Currow D. Reducing gastric secretions–a role for histamine 2 antagonists or proton pump inhibitors in malignant bowel obstruction? 2009;17:1463–1468.

34 APPENDICES/ SUPPLEMENTS

Appendix A: ELIGIBILITY VERIFICATION FORM:
INCLUSION CRITERIA

Participant Name: _____

Medical Record No: _____

Title: Palliative Management of Inoperable Malignant Bowel Obstruction: A Prospective, Open Label, Phase-2 Study at an NCI Comprehensive Cancer.

INCLUSION CRITERIA				
Yes	**No**	**N/A**	**All answers must be "Yes" or "N/A" for participant enrollment.**	**Date**
☐	☐	☐	1. Age ≥ 18 years of age.	
☐	☐	☐	2. Diagnosis of partial bowel obstruction secondary to active or prior malignancy (primary or metastatic GI, GYN, and carcinomatosis) caused either by tumor itself or adhesions in the setting of active malignancy.	
☐	☐	☐	3. Cross-sectional imaging performed within 24 hours of clinical symptoms of bowel obstruction (nausea, vomiting, and constipation ± abdominal pain) during hospital admission.	
☐	☐	☐	4. Patient must have an inoperable MBO.	
☐	☐	☐	5. Participant must understand the investigational nature of this study and sign an Independent Ethics Committee/Institutional Review Board approved written informed consent form prior to receiving any study related procedure.	

Investigator Signature: _____ **Date:** _____

Printed Name of Investigator: _____

Appendix B: ELIGIBILITY VERIFICATION FORM: EXCLUSION CRITERIA

Participant Name: _____

Medical Record No.: _____

Title: Palliative Management of Inoperable Malignant Bowel Obstruction: A Prospective, Open Label, Phase-2 Study at an NCI Comprehensive Cancer.

EXCLUSION CRITERIA				
Yes	**No**	**N/A**	**All answers must be "No" or "N/A" for participant enrollment.**	**Date**
☐	☐	☐	1. Evidence of complete bowel obstruction by imaging.	
☐	☐	☐	2. Bacteremia/septicemia with a documented positive blood culture: If a blood culture comes back positive after study enrollment, patient will be excluded.	
☐	☐	☐	3. Patients already taking a steroid equivalent to 8 mg of dexamethasone per day for longer than 7 days prior to study enrollment.	
☐	☐	☐	4. Patients undergoing bowel surgery or stent placement for bowel obstruction.	
☐	☐	☐	5. Those patients with MBO in setting of incarcerated hernia.	
☐	☐	☐	6. Known history of QT prolongation syndrome or if QTc is > 500 msec on baseline EKG within 2 weeks of enrollment.	
☐	☐	☐	7. Lack of decision-making capacity/delirium.	
☐	☐	☐	8. Pregnant or nursing female participants.	
☐	☐	☐	9. Actively suicidal patients.	
☐	☐	☐	10. Acute cholecystitis.	
☐	☐	☐	11. History of seizure episode in the last 12 months or patient on a maintenance antiepileptic drug for seizure control.	
☐	☐	☐	12. Acute Pancreatitis.	
☐	☐	☐	13. Bowel perforation.	
☐	☐	☐	14. Patients taking antipsychotic drugs.	
☐	☐	☐	15. History of dystonia or tardive dyskinesia.	
☐	☐	☐	16. Patients with pheochromocytoma.	
☐	☐	☐	17. Elevated blood pressure 180 mmHg systolic or 120 mmHg diastolic.	
☐	☐	☐	18. Immunocompromised patients.	
☐	☐	☐	19. Patients with latent tuberculosis history.	
☐	☐	☐	20. Incarcerated patients.	
☐	☐	☐	21. Patient already enrolled in a clinical trial.	
☐	☐	☐	22. Unwilling or unable to follow protocol requirements.	

EXCLUSION CRITERIA				
Yes	**No**	**N/A**	**All answers must be "No" or "N/A" for participant enrollment.**	**Date**
☐	☐	☐	23. Any condition which in the Investigator's opinion deems the participant an unsuitable candidate to receive study treatment.	

Participant meets all entry criteria: ☐ **Yes** ☐ **No**
If "NO", do not enroll participant in study.

Investigator Signature: _____ **Date:** _____

Printed Name of Investigator: _____

Appendix C: Study Data Collection Sheet: <u>Standardized Data Entry Protocol</u>

1. Code
   - This is the assigned patient number.
2. Age at diagnosis
   - Enter age at diagnosis of bowel obstruction in years
3. Date of birth (mm/dd/yyyy)
4. Date of diagnosis of bowel obstruction
5. Patient characteristics
   1. Gender

      Select options from drop-down menu.
   2. Ethnicity

      Select options from drop-down menu.
   3. Malignancy

      Manually enter the type of malignancy
   4. Cancer stage

      Enter the stage at the time of diagnosis of bowel obstruction
   5. Date of cancer diagnosis (mm/dd/yyyy): primary diagnosis
   6. BMI

      Enter the BMI on admission at the time of diagnosis of bowel obstruction
   7. BMI Class

      Select options from drop-down menu (where BMI = kilograms/ meters^2).

BMI	Classification
< 18.5	underweight
18.5–24.9	normal weight
25.0–29.9	overweight
30.0–34.9	class I obesity
35.0–39.9	class II obesity
≥ 40.0	class III obesity

   8. Smoking

      Select options from drop-down menu.
   9. Alcohol

      Select options from drop-down menu.

10. Prior use of steroids (include use for up to 1 month prior to hospitalization)
    a. If yes, manually enter the details (name and dosing schedule)
11. Comorbidities
    a. Cardiovascular: Select options from drop-down menu.
    b. Pulmonary: Select options from drop-down menu.
    c. Renal: Select options from drop-down menu.
    d. Neurological: Select options from drop-down menu.
    e. Endocrine: Select options from drop-down menu.
    f. Infectious Disease: Select options from drop-down menu.
    g. Hematologic/Oncologic: Select options from drop-down menu.
    h. Liver/Gastrointestinal: Select options from drop-down menu.
12. Comorbidity index score [21]: Calculate the score according to the table:

Comorbidity	Score
CAD	1
CHF	1
PAD	1
COPD	1
CVA with no deficits	1
Dementia	1
PUD	1
Mild liver disease	1
DM without end-organ damage	1
DM with end-organ damage	2
Leukemia/Lymphoma	2
Moderate-severe renal disease	2
Hemiplegia	2
Moderate-severe liver disease	3
Metastatic solid tumor	6
AIDS (not just HIV)	6

13. Personal history of bowel obstruction

    Select options from drop-down menu.

14. History of bowel surgery

    Select options from drop-down menu.

15. Partial vs complete obstruction

    Enter data based on the imaging description

16. Location

    Enter data based on the imaging description

17. Symptoms on admission
    a. Nausea
    b. Vomiting
    c. Abdominal pain
    d. Constipation
    e. Others: Manually enter other symptoms present on admission

18. Imaging type

Select options from drop-down menu.

19. Karnofsky score on admission

    Enter Karnofsky score at admission

20. Drug Regimen
    a. Octreotide
    b. Dexamethasone
    c. Metoclopramide

21. Inpatient Anti-emetics Drug Names
22. Inpatient Pain Regimen Drug Names
23. NG tube
    a. Inserted
    b. If yes, enter the day of bowel obstruction when it was inserted
    c. Average output in mL per day
    d. Total number of NG-inserted-days
    e. Removed before discharge
    f. If yes, enter the day of bowel obstruction when it was removed

24. G-tube
    a. Present prior to study
    b. Inserted during study

c. If yes, enter the date when it was inserted
d. Average output in mL per day

25. De-obstruction
    a. Yes
        i. Time to de-obstruction in days
        ii. Follow up number of days post de-obstruction
        iii. Discharged post de-obstruction
        iv. Completed outpatient treatment regimen
    b. No
        i. Venting PEG Placed
26. Adverse effects during trial
27. 30-day Follow Up in clinic
28. Phone Call Follow Up
    a. 3 months
    b. 6 months
29. Disposition
    a. Home
    b. Hospice
    c. LTC (long-term care) or SAR (sub-acute rehabilitation)

Appendix D: Karnofsky Performance Scale

Karnofsky Performance Scale [22]	
Percent	**Description**
100	Normal, no complaints, no evidence of disease.
90	Able to carry on normal activity, minor signs, or symptoms of disease.
80	Normal activity with effort, some signs, or symptoms of disease.
70	Cares for self. Unable to carry on normal activity or to do active work.
60	Requires occasional assistance but is able to care for most of his needs.
50	Requires considerable assistance and frequent medical care.
40	Disabled, requires special care and assistance.
30	Severely disabled, hospitalization is indicated although death not imminent.
20	Hospitalization necessary, very sick, active supportive treatment necessary.
10	Moribund, fatal processes progressing rapidly.
0	Dead.

Karnofsky, D.A., and Burchenal, J.H. (1949). The Clinical Evaluation of Chemotherapeutic Agents in Cancer. In Evaluation of Chemotherapeutic Agents: Symposium Held at the New York Academy of Medicine, C.M. MacLeod, ed. (New York, Columbia University Press), pp. 191-205.

Appendix E: Assessment Sheet
I-70418 Assessment Sheet / PI: Dr. Amy Case

Directions for Nursing Staff: Please complete once during your shift and file in designated folder.

Date:_____ MRN: _____

Time:_____ Nurse Performing Assessment:_____

CAM-S Short Form Scoring Worksheet: Circle appropriate score for each question.

Feature	Severity Score
1. Acute Onset and Fluctuating Course Is there evidence of an acute change in mental status from patient's baseline? *OR* Did the (abnormal) behavior fluctuate during the day, that is – tend to come and go, or increase and decrease in severity?	Either present: No: 0 Yes 1
2. Inattention Did the patient have difficulty focusing attention, for example, being easily distractible or having difficulty keeping track of what was being said?	No: 0 Yes (mild): 1 Yes (marked): 2
3. Disorganized Thinking Was the patient's thinking disorganized and incoherent, such as rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable switching from subject to subject?	No: 0 Yes (mild): 1 Yes (marked): 2
4. Altered Level of Consciousness Overall, how would you rate the patient's level of consciousness? • Alert (normal • Vigilant (hyperalert) • Lethargic (drowsy, easily aroused) • Stupor (difficult to arouse)	No: 0 Mild (vigilant or lethargic): 1 Marked: (stupor or coma): 2
Severity Score Total*: (Add the score in rows 1-4) **Notify provider if total score equals 2 or greater.*	

Condensed Memorial Symptom Assessment Scale (cMSAS): Ask patient "*How much does this symptom bother you today?*" If symptom present, circle patient's score.

Symptom	Present	Not at all	A little bit	Somewhat	Quite a bit	Very much
Abdominal pain due to cancer/obstruction	Y N	0	1	2	3	4
Constipation	Y N	0	1	2	3	4
Nausea	Y N	0	1	2	3	4
Vomiting	Y N	0	1	2	3	4
Has patient had a bowel movement in last 24 hours?	Y N			Is patient able to tolerate oral intake?		Y N

For questions, please contact Sarah Chatley, Research Coordinator, at x. 5055 or Sarah.Chatley@RoswellPark.org.

Appendix F: Hypoglycemia Protocol

The following (modified) Hypoglycemia Protocol is taken from the Roswell Park Cancer Institute *CLINICAL GUIDELINES FOR GLUCOSE MANAGEMENT IN ADULT ACUTE CARE INPATIENTS (Section 6: Hypoglycemia Treatment)*:

Hypoglycemia Protocol for Patients NOT on an Insulin Infusion

Blood glucose > 40 mg/ dL but < 60 mg/ dL:

Nursing Orders:

1 If patient can take PO: administer 15 grams of carbohydrate (4 oz of fruit juice-orange or apple, or regular soda)
2 If patient unable to take PO: administer 12.5 grams of dextrose 50% IV (25 mL) or 1 mg of glucagon IM
3 Check blood glucose every 15 minutes and repeat above treatment until blood glucose is ≥ 80 mg/ dL
4 Notify MD if blood glucose is ≤ 70mg/ dL

Blood glucose < 40 mg/ dL:

Nursing Orders:

1 If patient can take PO: administer 30 grams of carbohydrate (8 oz of fruit juice-orange or apple, or regular soda)
2 If patient unable to take PO: administer 25 grams of dextrose 50% IV (50 mL) or 1 mg of glucagon IM
3 Check blood glucose every 15 minutes and repeat above treatment until blood glucose is ≥ 80 mg/ dL
4 Notify MD if blood glucose is ≤ 40mg/ dL

Hypoglycemic signs and symptoms:

1 Trembling or Shaking, Cold Clammy Skin
2 Diaphoresis, Palpitations, Tachycardia
3 Hunger, Nausea, Headache, Tiredness, Weakness
4 Sudden Visual Changes, Paresthesia around Lips & Tongue
5 Slurred Speech, Lack of Coordination
6 Mental Dullness, Inability to process information
7 Behavior Changes, Confusion, Hallucinations
8 Amnesia, Seizures, Convulsions, Coma

Appendix G: Schedule of Procedures and Observations

Time Point	Pre-treatment Screening[1]	Day 1-7	Discharge/End of Treatment (±3 days)	Outpatient Treatment [2]	Post-Treatment Follow-Up 30 days after study drugs (±3 days)[3]	Long Term Follow-Up- 3 Mos. And 6 Mos. Post-discharge[7]
Clinical Procedures						
Medical/Surgical History	X					
Co-Morbidity Index Score	X					
Physical Examination[4]	X					
Vital Signs[5]	X					
Karnofsky Score	X					
Concomitant Medications[6]	X[6]		X	X	X	
Adverse Events[7]	X	X	X	X	X	
Smoking and Alcohol History	X					
cMSAS[8]		X				
CAMS-S[9] (Delirium Screen while on Decadron)		X				
De-obstruction Assessment[10]		X			X	X
Laboratory Procedures						
Chemistry	X	X				
BMP	X	X				

Time Point	Pre-treatment Screening[1]	Day 1-7	Discharge/End of Treatment (±3 days)	Outpatient Treatment [2]	Post-Treatment Follow-Up 30 days after study drugs (±3 days)[3]	Long Term Follow-Up- 3 Mos. And 6 Mos. Post-discharge[7]
Pregnancy Test (Urine or Serum) in women of child-bearing potential	X					
Imaging Procedures						
EKG (within 2 weeks of study registration)[11]	X	X	X			
Cross sectional imaging[12]		X				
Surgical Consult (if needed)[13]		Day 7 only				
Treatment Regimen/Drug Administration						
Octreotide[14]		X	X			
Dexamethasone[15]		X	X	X (Change to Oral)		
Metoclopramide[15]		X	X	X (Change to Oral)		

1. Performed with 48 hours to treatment start (ideally 24 hours).
2. If de-obstruction occurs in 7 days or less, patient continues regimen until the 10-day treatment period is complete. If the patient de-obstructs the drug regimen will be transitioned to oral for metoclopramide and dexamethasone, and IV or sub-cutaneous for octreotide is discontinued. If patient discharged home the CRC will contact the patient daily for 3 days following discharge to monitor adverse events and treatment administration (including missed doses).
3. Participants will be followed for 30 days ±3 days after last dose of study drug, telephone contact is acceptable.
4. PE must include physical symptoms of MBO.
5. Vital signs (temperature, heart rate, respiratory rate, and blood pressure), body weight, and height.
6. Medications ongoing, or discontinued, with 1 week prior to first dose of study drug. Steroid use for up to 1 month prior to hospitalization.
7. After patient discharge AE and con med assessments can be collected by phone. At Post-Treatment Follow-Up, CRC will assess regularity of bowel movements and toleration of oral intake.
8. Condensed Memorial Symptom Assessment Scales assessed by inpatient nurses using study form (Appendix E).

9. Confusion Assessment Method-Short Form assessed by inpatient nurses using study form (Appendix E).
10. De-obstruction defined as effective introduction of oral intake as per study.
11. EKGs will be performed prior to discharge (±3 days) or at the time of treatment discontinuation (±3 days).
12. Performed within 24 hours of clinical symptoms of bowel obstruction (nausea, vomiting, and constipation ± abdominal pain) during hospital admission.
13. At the discretion of the clinician, surgical consult can be obtained for possible venting G-tube placement if de obstruction does not occur within 7 days of treatment initiation.