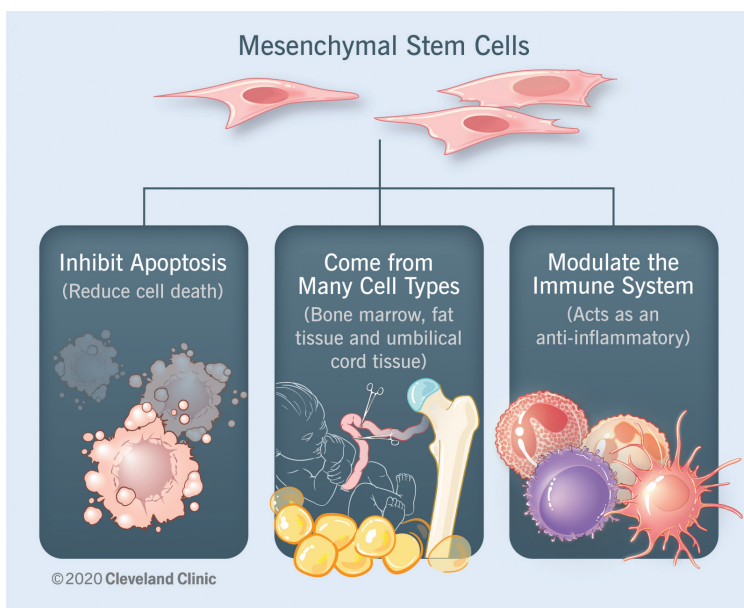


# Mesenchymal Stem Cells for the Treatment of Rectovaginal Fistulas in the Setting of Crohn's Disease

**Principal Investigator: Amy Lightner, MD**

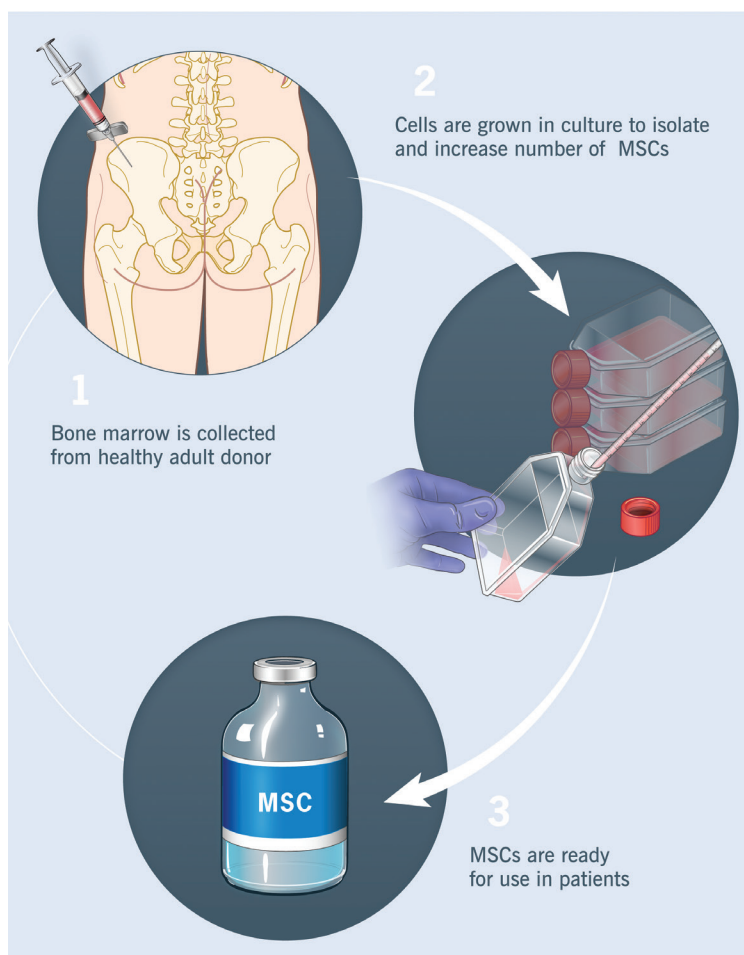
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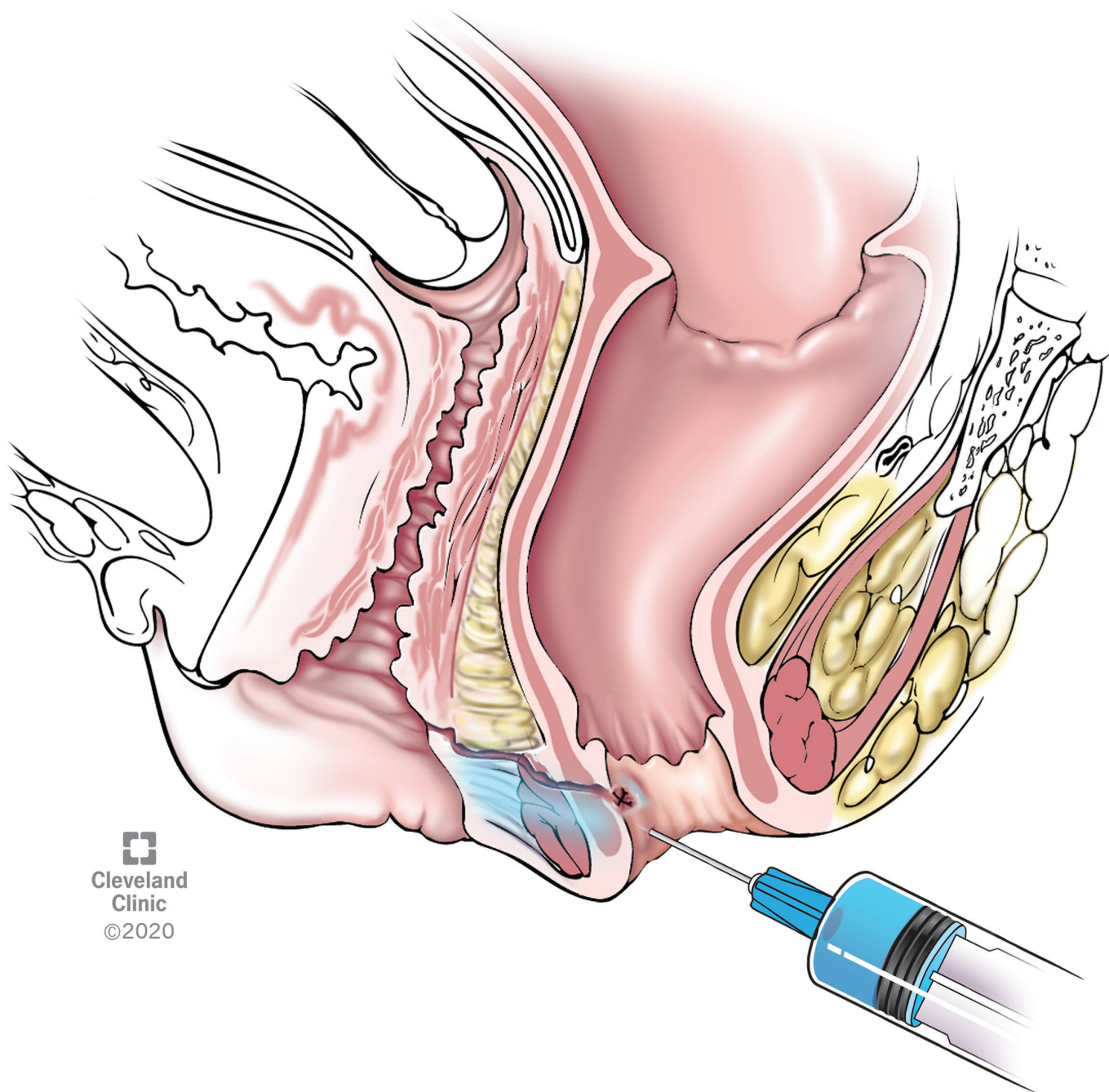
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**Inflammatory Bowel Disease (IBD)** is an idiopathic chronic inflammatory disease of the gastrointestinal tract which affects nearly one million people in the United States and millions more world-wide, and continues to increase in incidence for unknown reasons. Monoclonal antibodies have become the cornerstone of medical therapy for moderate to severe disease. However, their utility is limited by initial lack of response, loss of response over time, and significant side effects. Once monoclonal antibodies are no longer effective, patients may then undergo surgical intervention with risk of morbidity and life altering changes including the need for an ostomy. Therefore, we are passionately invested in developing novel improved therapeutic options for IBD patients.

The use of mesenchymal stem cells (MSCs) has recently emerged as a promising new therapeutic for perianal fistulizing Crohn's disease (CD), a phenotype of CD very difficult to treat. Several clinical trials including more than 400 patients have now demonstrated their safety and improved efficacy as compared to current medical and surgical options. MSCs come from multiple different tissue sources. Most commonly they are isolated from bone marrow aspirates, fat tissue harvest, or umbilical cord tissue. MSCs are able to travel to areas of inflammation and act as an anti-inflammatory and immunomodulating agent where they are most needed. The cells are adult cells, and do not have the ability to change into other cell types or become part of your body. Rather, they can be viewed as a type of strong anti-inflammatory medication that recruits your body's own immune cells to the area to help heal inflammation and repair tissue damage. Our team is working to deliver MSCs from healthy donors as a therapeutic for both Crohn's disease and ulcerative colitis. We have now established several clinical trials using MSCs to treat different types of fistulas and intestinal CD and ulcerative colitis. These clinical trials require a strong team well versed in regenerative medicine and inflammatory bowel disease, and include personnel from surgery, gastroenterology, radiology, pathology, laboratory medicine, cell manufacturing and regulatory medicine departments. This type of team is only available at a limited number of centers.





  
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Clinic  
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Injection of Mesenchymal Stem Cells



Amy Lightner MD





Mesenchymal stem cells in syringe

# Mesenchymal Stem Cells

## What is a mesenchymal stem cell?

Mesenchymal stem cells are adult stem cells that can be harvested from bone marrow or fat tissue. They are adult cells that your body uses to repair tissue that is injured. We are able to isolate these cells and deliver them in large numbers right to where the tissue is inflamed or injured to promote healing.

## Where do the mesenchymal stem cells come from?

Mesenchymal stem cells for our clinical trials are retrieved from the bone marrow from healthy donors. The donors are screened for several items just as blood donors are screened.

## How do mesenchymal stem cells work?

Mesenchymal stem cells act as a potent anti-inflammatory by secreting factors called cytokines into the tissue. These cytokines have anti-inflammatory properties. They also recruit immune cells that are normally in low levels that you need to heal these areas of injury. In late phases, they help regenerate, or repair, tissue to return to a healthy state.

## Do mesenchymal stem cells stay in my body after injection?

Mesenchymal stem cells likely in the body only 3-7 days, although we are unable to know for sure since we can't label these cells and see them. We have learned this information from animal studies that have been done. They are in the local area and secrete their cytokines, or signals, which change the local environment in the tissue and then lead to their anti-inflammatory and repair properties.

## Do mesenchymal stem cells turn into something else after injection?

Because mesenchymal stem cells are adult stem cells they don't turn into other cell types or tissues like 'embryonic stem cells'. These mesenchymal stem cells really serve as an anti-inflammatory and repair cell.

## Will my body react against the cells or be 'rejected'?

Mesenchymal stem cells don't have markers on their surface that would make your body recognize them as 'foreign'. Therefore, your body won't react against them or reject them.

## Are there any risks of these mesenchymal stem cells?

There do not appear to be any significant risks of mesenchymal stem cells. These cells have been used in inflammatory bowel disease since 2003. There have now been hundreds of patients treated without any reactions or infections or complications related to the cells. Thus, we now have several years of safety data of using these cells for inflammatory bowel disease and have strong evidence there are no clinical concerns.

## Clinical Information

### **What are the steps when I'm interested in learning more about the trial?**

Sometimes you will reach out via email ([ibdstemcell@ccf.org](mailto:ibdstemcell@ccf.org)) or your doctor will reach out to Dr. Lightner directly about your participation in a clinical trial. We then will contact you to register as a Cleveland Clinic patient. After you have registered, you can choose to 1) be seen in person in clinic with Dr. Lightner, or 2) do a virtual visit with Dr. Lightner from home. Before this visit, Dr. Lightner's clinic nurse, Amy, will reach out to ask you a few questions so we can understand your IBD history and what records we need to get before your clinic visit. Last, we will work on obtaining outside records such as labs, colonoscopy reports, CT and MRI imaging, and any prior operative reports from previous surgery.

### **What can I expect when I meet with Dr. Lightner?**

Dr. Lightner will review the notes taken by Amy and your outside records. She will then meet with you to discuss your IBD history and current symptoms to understand your IBD story. Then she will talk about treatment options which may or may not include participation in a stem cell trial. Sometimes, there are options that may help you before proceeding with a stem cell trial. Other times, it may be best to proceed right to a stem cell trial.

### **What might be some tests I need before enrolling into a clinical trial?**

Depending on which clinical trial, and when you last had these tests, you may need to get imaging of your intestine (MR enterography or CT enterography), a surveillance colonoscopy, pelvic MRI to look at fistula tracts, and blood tests done.

### **Do I need to stop my IBD medications before a clinical trial?**

This depends on which clinical trial you are participating in. If you are participating in a fistula study, you will remain on any IBD medications you are currently on. If you are participating in a trial for intestinal disease, then likely you will be discontinuing current medications for your inflammatory bowel disease prior to receiving any stem cell treatment. However, this will be discussed with

Dr. Lightner and the doctor prescribing your medication for inflammatory bowel disease.

### **Who can I contact with questions?**

There will be a team of people taking care of you during this process, and all of us are happy to answer any questions that arise. You will meet Amy, the nurse working with Dr. Lightner, study coordinators in charge of clinical trials, Dr. Lightner's assistant, and Dr. Lightner as well. The best way to reach us is through a MyChart message or by emailing [ibdstemcell@ccf.org](mailto:ibdstemcell@ccf.org)

### **How often will I have to come to Cleveland if I enroll into a clinical trial?**

The clinical trials require being seen in person multiple times over the course of the year as these are trial monitored by our institution and by the Food and Drug Administration (FDA) for both safety and how well cell therapy works. Thus, we are responsible for your safety and clinical care. That is why we have to see you in person here in Cleveland. We understand this may be difficult if you are coming from out of town, but we can try to work with your schedule the best we can and schedule visits far in advance.

### **What can I expect on the day of procedure when I receive mesenchymal stem cells?**

All stem cell deliveries are done in the operating room while you are asleep. You will report to the preoperative area and then when we are ready for your case to start you will be brought to the operating room. Dr. Lightner will see you outside the operating room to answer any questions and perform a team huddle with you, the anesthesiologist, the OR nurse and Dr. Lightner. Then you will go to sleep and the procedure will take about 30 minutes. After the procedure you will go to the recovery area where you will be monitored for a total of 4 hours. The 4 hours is required because you are receiving an investigational product and we have to make sure you don't have any reaction to the product before leaving the hospital. Dr. Lightner will see you and talk to the family member/friend of your choice if you want following the procedure.

## Where to Go – Based on Study Activity

### 1 Physical exams

#### Crile A Building: 3rd Floor

2049 E 100th St., A Building  
Cleveland, OH 44195

### 2 MRI

#### Q building: Basement level

2050 E 96th St., Q Building  
Cleveland, OH 44195

### 3 Exam under anesthesia

#### G building: 2nd floor

9800 Euclid Ave  
Cleveland, OH 44195

### 4 Labs

#### Crile A Building: 1st Floor

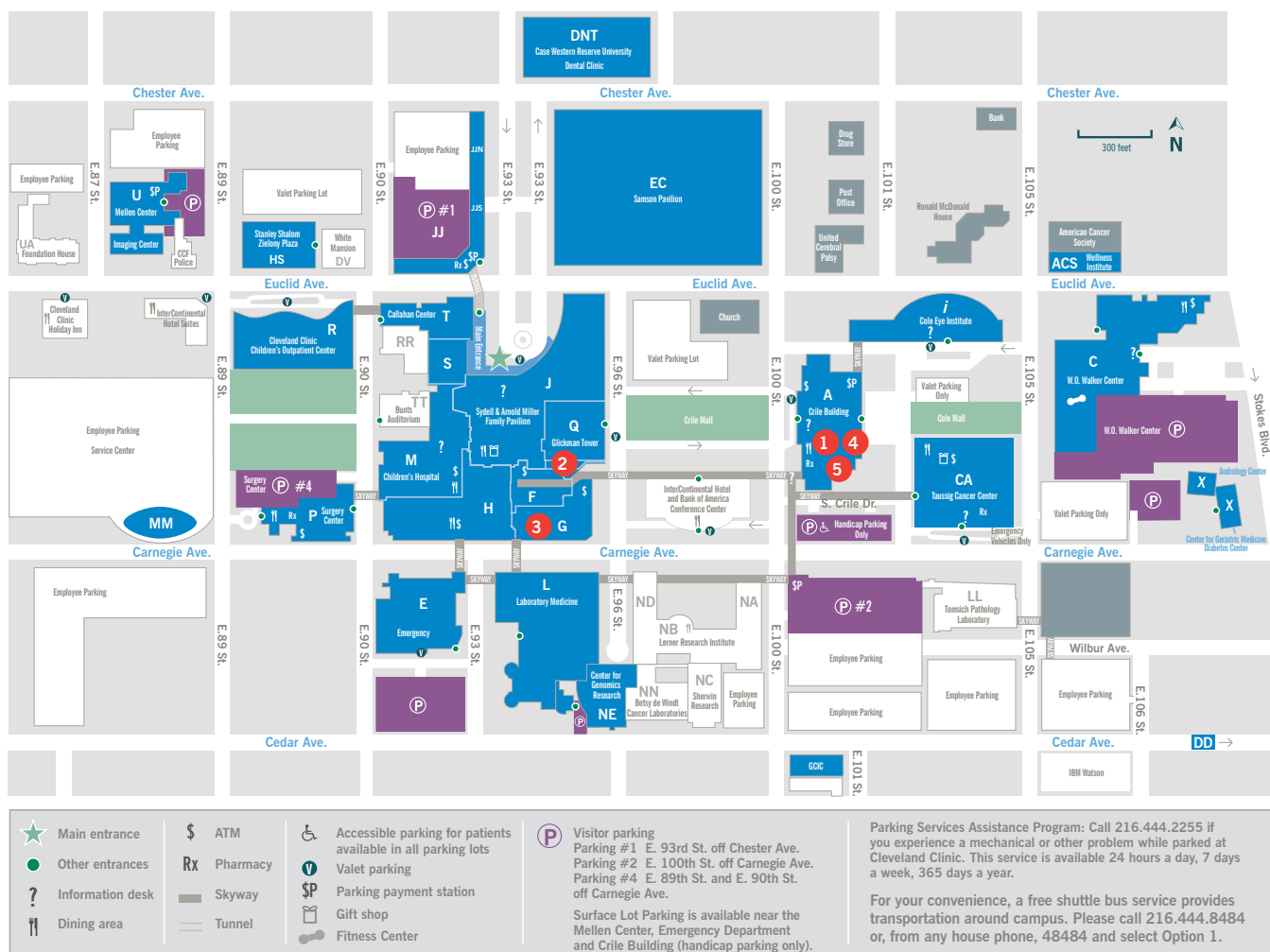
2049 E 100th St., A Building  
Cleveland, OH 44195

### 5 Endoscopy

#### Crile A Building: 3rd Floor

2049 E 100th St.,  
A Building, Cleveland, OH 44195

For onsite walking directions, use this link: [clevelandclinic.yourdirectroute.com/index.html#home](http://clevelandclinic.yourdirectroute.com/index.html#home)





## Parking, Lodging and Child Care

### Parking

Visit this link for additional details regarding parking:  
[my.clevelandclinic.org/patients/travel/parking](https://my.clevelandclinic.org/patients/travel/parking)

A Building - Crile Building  
P2 - Parking garage at E. 100th St. and Carnegie Ave. or Valet

J Building - Sydel & Arnold Miller Family Pavilion  
P1 - Parking garage at E. 93rd St. and Chester Ave. or Valet

P Building - Surgery Center  
P4 - Parking garage at E. 90th St. and Carnegie Ave.  
(Accessible only from the first floor main entrance on E. 89th St.)

R Building - Cleveland Clinic Children's Outpatient Center  
P1 - Parking garage at E. 93rd St. and Chester Ave. or Valet

i Building - Cole Eye Institute  
Valet or P2 - Parking garage at E. 100th St. and Carnegie Ave. (Please note, using the P2 garage will require you to walk 4 streets blocks, so plan accordingly.)

CA Building - Taussig Cancer Center  
P2 - Parking garage at E. 100th St. and Carnegie Ave. or Valet

N Building - Education Building & Lerner Research Institute  
P2 - Parking garage at E. 100th St. and Carnegie Ave.

X Building - Centers for Geriatric and Diabetes Care  
Surface parking lot accessible from Carnegie Ave.

### Lodging on Cleveland Clinic Main Campus

Visit this link to review the most updated details regarding lodging: [my.clevelandclinic.org/patients/travel/lodging](https://my.clevelandclinic.org/patients/travel/lodging)

### Center-based childcare

These centers offer childcare services operating with approved pandemic licenses

#### Kindercare contact:

Danielle Corbin [dcorbin@kindercare.com](mailto:dcorbin@kindercare.com)

**YMCA contact:** 216.263.6860 or [children@ymca.org](mailto:children@ymca.org)

**JDN Early Childhood Center contact:** Jill Sadowsky at 216.320.8483 or [sadowskyj@bellefairejcb.org](mailto:sadowskyj@bellefairejcb.org)

## Bowel Preparation Instructions for: Miralax-Gatorade Preparations

**IF YOU DO NOT FOLLOW THESE DIRECTIONS, YOUR COLONOSCOPY WILL BE CANCELLED.**

### Key Instructions:

- Your bowel must be empty so that your doctor can clearly view your colon. Follow all of the instructions in this handout EXACTLY as they are written.
- **Do NOT eat any solid food the ENTIRE day before your colonoscopy.**
- Buy your bowel preparation at least 5 days before your colonoscopy.
- Four (4) Dulcolax laxative tablets containing 5mg of bisacodyl each (NOT Dulcolax stool softener)
- One (1) 8.3oz. bottle Miralax (238 grams) or generic equivalent
- 2 x 32oz. Bottles of Gatorade (NOT RED)
- **Diabetic Patients: Use G2 (Gatorade 2)**

### TRANSPORTATION on the Day of Your Exam

A responsible adult **MUST** be present with you at Check In prior to your colonoscopy and REMAIN in the endoscopy area until you are discharged. You are **NOT ALLOWED** to drive, take a taxi or bus, or leave the Endoscopy Center **ALONE**. If you do not have a responsible driver (family member or friend) with you to take you home, your exam cannot be done with sedation and will be cancelled.

Please bring a list of all of your current medications, including any over-the-counter medications with you.

### Medications

If you take insulin, diabetic medications or blood thinners such as Coumadin (warfarin), Plavix (clopidogrel), Ticlid (ticlopidine hydrochloride), Agrylin (anagrelide), Xarelto (Rivaroxaban), Pradaxa (Dabigatran), Eliquis (Apixaban), and Effient (Prasugrel). You **MUST** call the doctors who orders those medicines for instructions on altering the dosage before your colonoscopy.

All other medications should be taken the day of the exam with a sip of water including ASPIRIN.

### Five (5) Days Before Your Colonoscopy

- Do **NOT** take medicines that stop diarrhea – such as Imodium, Kaopectate, or Pepto Bismol.
- Do **NOT** take fiber supplements – such as Metamucil, Citrucel, or Perdiem.
- Do **NOT** take products that contain iron – such as multi-vitamins (the label lists what is in the products).

### Three (3) Days Before Your Colonoscopy

- Do **NOT** eat high-fiber foods – such as popcorn, beans, seeds (flax, sunflower, quinoa), multigrain bread, nuts, salad/vegetables, or fresh and dried fruit.

### One (1) Day Before Your Colonoscopy

- **Only drink clear liquids the ENTIRE DAY before your colonoscopy. Do NOT eat any solid foods.** Drink at least **8 ounces** of clear liquids every hour after waking up. The clear liquids you can drink include:

Clear Liquid (NO RED LIQUIDS)	DO NOT DRINK
Gatorade, Pedialyte or Powerade	Alcohol
Clear broth or bouillon	Milk or non-dairy creamers
Coffee or tea (no milk or non-dairy creamer)	Noodles or vegetables in soup
Carbonated and non-carbonated soft drinks	Juice with pulp
Kool-Aid or other fruit flavored drinks	Liquid you cannot see through
Strained fruit juices (no pulp)	
Jell-O, popsicles, hard candy	
Water	

Mix 1/2 of Miralax bottle (119 grams) in each 32 ounces of Gatorade bottle until dissolved. Keep cool in the refrigerator. DO NOT ADD ICE.

Between 2-5 p.m., you will begin to drink the Gatorade/Miralax mixture. It is best to drink 8oz, wait 15 mins then drink another 8oz. Drink the mixture until you have completed all 64oz.

One hour after you are done drinking, take all four dulcolax tablets at once. This will complete your prep.

You can continue drinking clear liquids up until midnight.

## Home Going Instructions After an Anorectal Operation

Thank you for choosing the Cleveland Clinic for your health care needs. As part of the Digestive Disease Center, the Department of Colorectal Surgery is honored to serve you. Thank you again for trusting us with your care and being part of our clinical trials. The following guidelines have been developed to help better assure a successful recovery following surgery.

- 1. Diet:** Your previous diet can be resumed after surgery.
- 2. Alcohol:** Alcoholic beverages should be avoided until the day after surgery, or while using narcotics.
- 3. Activity:** Walking and climbing stairs is acceptable, but strenuous activity (e.g., lifting objects weighing over 30 lbs, sit-ups, press-ups) should be avoided for 2 weeks.
- 4. Driving:** Do not drive a vehicle while still uncomfortable or while taking narcotic pain medications. When you return to driving, do not go alone the first time.
- 5. Wound care:** The wound usually heals in 6-10 weeks and should be kept generally clean with a daily shower. Please avoid soaking in hot water until your 2 week postoperative visit. This includes baths, sitz baths, hot tubs, etc.
- 6. Vaginal care:** For fistulas involving the vagina, please avoid insertion of any item or creams in the vagina, or sexual intercourse, for the first two weeks after surgery.
- 7. Medications:** These should be taken as instructed by your surgeon including:
  - **Anti-diarrheal medications:** If you do not currently have liquid-like stool and do not have an ileal J pouch, please take MiraLAX to keep your stool loose and liquid-like for the first 5 days after surgery.
  - **Antibiotics:** Please take your prescribed Ciprofloxacin/Flagyl, Augmentin, or alternative for 2 weeks following your procedure
  - **Pain medications:** Tylenol, Darvocet, Vicodin, Oxycodone, or Percocet are permitted as instructed.
  - **Prior medications:** Resume these medications unless otherwise instructed.
- 8. Bowel function:** Bowel function should return to normal following the procedure. There may be some discomfort with bowel movements for the first few days.

### 9. Potential problems:

- **Anal irritation:** Vigorous wiping after bowel motions can cause irritation that can be minimized by using cotton balls, medicated wipes, or a shower nozzle attachment instead of toilet paper to clean the area followed by gentle drying. An absorbent pad or cotton ball placed between the buttock cheeks can remove irritating moisture or seepage. Please avoid baths, sitz baths, or ointments to the perianal area for the first two weeks following surgery.
- **Bleeding:** A small amount of bleeding may occur and is normal. If you experience large amounts of bleeding or the passing of clots, you must call your surgeon for advice.
- **Drainage:** Heavy pus-like drainage or passage of gas or stool more than prior to surgery should prompt communication with our study team via MyChart or email.
- **Surgical infections:** Difficulty urinating, fever over 101° F, or worsening pain, may indicate a life-threatening infection, and you must immediately call your surgeon for advice.

- 10. Office visits:** Follow-up appointments should be made in your MyChart already. If you need to change the time, please call the colorectal surgery appointment line at 216.444.5404 or contact the study team.

### For other questions or concerns, please

1. Send a MyChart Message
2. Email: [ibdstemcell@ccf.org](mailto:ibdstemcell@ccf.org)
3. During office hours: call Dr. Amy Lightner's office at 216.445.9715
4. After hours/weekends: call the colorectal surgery resident on-call at 216.444.2200.

# Your Visits and Test Schedule

## Treatment Group

	Visit 1.0	Visit 1.1 <sup>a</sup>	Visit 2 Day 0	Visit 3 Day 1	Visit 4 Week 2	Visit 5 Week 6	Visit 6 Month 3	Visit 6.1 Month 3 Day 0	Visit 6.2 Month 3 Day 1	Visit 6.3 Month 3 Week 2	Visit 6.4 Month 3 Week 6	Visit 7 Month 6	Visit 9 Month 12
Visit Window (Days)	-30 days	0	0	0	+/- 3	+/-5	+/-7	within 3 days of visit 6	+/- 3	+/-5	+/-7	+/-14	+/-14
Eligibility	X		X					X					
Informed Consent	X												
Medical Surgical History	X		X	X	X	X	X	X	X	X	X	X	X
General, Perianal, and Vaginal Exam W/Vital Signs	X			X	X	X	X		X	X	X	X	X
Patient Reported Outcomes Surveys	X				X	X	X			X	X	X	X
MRI	X <sup>b</sup>						X					X	X
Exam Under Anesthesia	X	X <sup>d</sup>	X					X					
Seton		X <sup>d</sup>											
MSC Delivery			X					X <sup>e</sup>					
Pregnancy Test <sup>f</sup>	X	X	X					X					
Creatinine Test <sup>g</sup> (Blood Draw)	X						X					X	X
CBC W/ Diff (Blood Draw)	X				X	X	X			X	X	X	X
CRP (Blood Draw)	X				X	X	X			X	X	X	X
Acute Hepatitis Panel (Blood Draw)	X												
HIV (Blood Draw)	X												
AST/ALT (Blood Draw)	X												
Concomitant Medications	X	X	X	X	X	X	X	X	X	X	X	X	X
Adverse Events	X	X	X	X	X	X	X	X	X	X	X	X	X

a = Only if there are indications of active sepsis

b = If not done clinically in the last 30 days

c = Only if patient has no active pelvic sepsis. Baseline biopsies will occur at Visit 1 or Visit 1.1, not both.

d = If there is no drainage of active sepsis and a seton is placed at Visit 1.1, the patient will be sent home and will return in 4 weeks (+/-3 days) and be re-evaluated with exam, vitals, labs, Exam under Anesthesia. If there is sufficient drainage of sepsis, pt. will be scheduled for MSC injection (Visit 2 Day 0). If there is not sufficient drainage of sepsis a, patient will screen fail from the study.

e = Repeat MSC delivery if there is no clinical healing and no allergic reaction to the first treatment (follow-up visit 6.1 to 6.4 -Day 1, Week 2, Week 6 and Months 6, Month 12)

f = Women of child bearing potential only

g = Creatinine is obtain only when performing MRI





## Control Group

	Visit 1	Visit 1.1 <sup>a</sup>	Visit 2 Day 0	Visit 3 Day 1	Visit 4 Week 2	Visit 5 Week 6	Visit 6 Month 3	Visit 6.1 Month 3 Day 0	Visit 6.2 Month 3 Day 1	Visit 6.3 Month 3 Week 2	Visit 6.4 Month 3 Week 6	Visit 7 Month 6
Visit Window (Days)	-30	0	0	0	+/- 3	+/-5	+/-7	within 3 days of visit 6	0	+/-3	+/-5	+/-7
Eligibility	X		X					X				
Informed Consent	X											
Medical Surgical History	X		X	X	X	X	X	X	X	X	X	X
General, Perianal, and Vaginal Exam W/Vital Signs	X			X	X	X	X		X	X	X	X
Patient Reported Outcomes Surveys	X				X	X	X			X	X	X
MRI	X <sup>b</sup>						X					X
Exam Under Anesthesia		X <sup>d</sup>	X					X				
Seton		X <sup>d</sup>										
Normal Saline			X					X <sup>e</sup>				
MSC Delivery												
Pregnancy Test <sup>f</sup>	X	X	X					X				
Creatinine Test <sup>g</sup> (Blood Draw)	X						X					X
CBC W/Diff (Blood Draw)	X				X	X	X			X	X	X
CRP (blood draw)	X				X	X	X			X	X	X
Acute Hepatitis Panel (Blood Draw)	X											
HIV (Blood Draw)	X											
AST/ALT (Blood Draw)	X											
Concomitant Medications	X	X	X	X	X	X	X	X	X	X	X	X
Adverse Events	X	X	X	X	X	X	X	X	X	X	X	X

Continued on next page

## Control Group, continued

	Visit 7.1 Month 6 Day 0	Visit 7.2 Month 6 Day 1	Visit 7.3 Month 6 Week 2	Visit 7.4 Month 6 Week 6	Visit 8 Month 9	Visit 8.1 Month 9 Day 0	Visit 8.2 Month 9 Day 1	Visit 8.3 Month 9 Week 2	Visit 8.4 Month 9 Week 6	Visit 9 Month 12	Visit 10 Month 15	Visit 11 Month 18
Visit Window (Days)	within 3 days of visit 7	0	+/-3	+/-5	+/-7	within 3 days of visit 7	0	+/-3	+/-5	+/-14	+/-14	+/-14
Eligibility	X					X						
Informed Consent												
Medical surgical history	X	X	X	X	X	X	X	X	X	X	X	X
General, Perianal, and Vaginal Exam W/Vital Signs		X	X	X	X		X	X	X	X	X	X
Patient Reported Outcomes Surveys			X	X	X			X	X	X	X	X
MRI					X					X	X	X
Exam Under Anesthesia	X					X						
Seton												
Normal Saline												
MSC Delivery	X					X						
Pregnancy Test <sup>f</sup>	X					X						
Creatinine Test <sup>g</sup> (Blood Draw)					X					X	X	X
CBC W/Diff (Blood Draw)			X	X	X			X	X	X	X	X
CRP (blood draw)			X	X	X			X	X	X	X	X
Acute Hepatitis Panel (Blood Draw)												
HIV (Blood Draw)												
AST/ALT (Blood Draw)												
Concomitant Medications	X	X	X	X	X	X	X	X	X	X	X	X
Adverse Events	X	X	X	X	X	X	X	X	X	X	X	X

a = Only if there are indications of active sepsis

b = If not done clinically in the last 30 days

c = Only if patient has no active pelvic sepsis. Baseline biopsies will occur at Visit 1 or Visit 1.1, not both.

d = If there is no drainage of active sepsis and a seton is placed at Visit 1.1, the patient will be sent home and will return in 4 weeks (+/-3 days) and be re-evaluated with exam, vitals, labs, Exam under Anesthesia. If there is sufficient drainage of sepsis, pt. will be scheduled for injection (Visit 2 Day 0). If there is not sufficient drainage of sepsis a, patient will screen fail from the study.

e = Repeat delivery if there is no clinical healing and no allergic reaction to the first treatment (follow-up visit 6.1 to 6.4 -Day 1, Week 2, Week 6 and Months 6, Month 12)

f = Women of child bearing potential only

g = Creatinine is obtained only when performing MRI

h = Cross over

## Visit 1 – Screening Visit

After signing this consent form, you will be evaluated for eligibility. This screening test will consist of:

- A general physical exam which will include measurement of your vital signs (blood pressure, heart rate, and temperature) and a rectal and vaginal exam
- Surveys about your perianal disease
- A review of your medications including blood products
- Medical and surgical history since your last visit
- Blood sample taken to measure your Complete Blood Count (CBC), liver functions (AST/ALT), C-Reactive Protein (CRP), Acute Hepatitis Panel, and HIV.

**Approximately 3 tablespoons of blood will be drawn.**

If your HIV and/or your Acute Hepatitis Panel tests are positive, you will need to have a second test done to make sure the results are the same. The researcher will tell you how to find medical help and counseling as needed, and you may not be able to take part in the study.

Your health insurer or you will have to pay for the cost of the repeat test, any follow-up medical care, or counseling.

If the HIV and/or Acute Hepatitis Panel test results are positive, it is state law that they be reported to the Ohio Department of Health. The test results will also be put in your medical record.

- If you are able to become pregnant, a urine pregnancy test will be performed.
- A creatinine level and MRI of the pelvis will be performed to assess your fistula if this has not already been performed clinically in the last 30 days.
- An Exam Under Anesthesia (EUA) for examination of the fistula anatomy will be conducted prior to study drug administration. If it is found at this visit that you have active sepsis, you will be scheduled for Visit 1.1 where a colorectal surgeon will drain the sepsis and place a seton as part of your clinical care for your fistula.

A seton is a small suture or vessel loop that is placed in the fistula track to allow the fistula to remain open to allow for drainage and prevent the development of an abscess. This allows the fistula to heal over time.

- If a seton was placed, 4 weeks later you will undergo a EUA to assess the fistula tract

**(Visit 1.2).** If there is not sufficient drainage of sepsis, you will not be able to continue to participate in the study. If there is adequate drainage of sepsis, you will be scheduled to return for the next study visit.

## Visit 2 – Treatment Visit

After being determined eligible for the study, you will come to **Visit 2**. At this visit you will undergo the following:

- Review of your medications including blood products
- Medical and surgical history since your last visit
- Blood sample taken to measure CBC and CRP
- If you are able to become pregnant, a urine pregnancy test will be performed
- You will then be randomized to receive either injection of investigational study drug MSCs (**Treatment**) or injection of study drug placebo normal saline (**Control**). You will be blinded, meaning you will not know which study drug (treatment or control) you are receiving. The investigator will know which study drug (treatment or control) you are receiving, and will unblind you to your treatment (treatment or control) at **Visit 7**.
- You will then undergo a scheduled EUA to assess the fistula tract. The study drug will be injected into the fistula tract.

Your vital signs, including blood pressure, heart rate, and temperature will be monitored after the procedure at regular intervals for 4 hours in the recovery area. If your vital signs remain stable and you remain free of adverse events, you will be discharged to home. If your vital signs go outside of the acceptable range, it is possible that you could be admitted over night to the Clinic for observation.

## Visit 3 – Day 1

The day after the injection of the study drug, you will report to the outpatient Colorectal Surgery clinic for a follow-up visit where a brief physical exam and measurement of your vitals will be performed.



### Visit 4 (Week 2; +/- 3 days)

Two weeks after the injection of study drug, you will report to the outpatient Colorectal Surgery clinic for a follow-up visit where the following will be performed:

- A general physical exam, a measurement of your vital signs, as well as a rectal and vaginal exam to assess the fistula
- Review of your medications including blood products
- Medical and surgical history since your last visit
- Surveys about your perianal disease
- Blood sample taken to measure CBC and CRP

### Visit 5 (Week 6; +/- 5 days)

Six weeks after the injection of the study drug, you will report to the outpatient Colorectal Surgery clinic for a follow-up visit where the following will be performed:

- A general physical exam, a measurement of your vital signs, as well as a rectal and vaginal exam to assess the fistula
- Review of your medications including blood products,
- Medical and surgical history since your last visit
- Surveys about your perianal disease
- Blood sample taken to measure CBC and CRP

### Visit 6 (Month 3; +/- 7 days)

Three month after the injection of study drug, you will report to the outpatient Colorectal Surgery clinic for a follow-up visit where the following will be performed:

- A general physical exam, a measurement of your vital signs, as well as a rectal and vaginal exam to assess the fistula
- Review of your medications including blood products
- Medical and surgical history since your last visit
- Surveys about your perianal disease
- Blood sample taken to measure CBC and CRP and creatinine
- Pelvic MRI

If complete healing has not been achieved, and you did not experience an allergic reaction to the first treatment, you will return to the operating room for a EUA, MRI, and a repeat injection of investigational study drug MSCs or normal saline in the same way as before at Visit 2.

### Visit 6.1 (Month 3, Day 0; within 3 days of Visit 6.0)

At this visit, you will undergo the following:

- Review of your medications including blood products
- Medical and surgical history since your last visit
- If you are able to become pregnant, a urine pregnancy test will be performed
- You will then undergo a scheduled EUA to assess the fistula tract. The study drug will be injected into the fistula tract.

Your vital signs, including blood pressure, heart rate, and temperature will be monitored after the procedure at regular intervals for 6 hours in the recovery area. If your vital signs remain stable and you remain free of adverse events, you will be discharged to home. If your vital signs go outside of the acceptable range, it is possible that you could be admitted overnight for observation to the Cleveland Clinic.

### Visit 6.2 (Month 3, Day 1)

**For patients who received a repeat injection of study drug,** you will be seen the day after the second injection of the study drug at the outpatient Colorectal Surgery clinic for a follow-up visit where a brief physical exam and measurement of your vitals will be performed.

### Visit 6.3 (Month 3, Week 2; +/- 3 days)

**For patients who received a repeat injection of study drug,** you will be seen two weeks after the second injection of the study drug at the outpatient Colorectal Surgery clinic where you will undergo the following:

- A general physical exam, a measurement of your vital signs, as well as a rectal and vaginal exam to assess the fistula
- Review of your medications including blood products
- Medical and surgical history since your last visit
- Surveys about your perianal disease
- Blood sample taken to measure CBC and CRP

### Visit 6.4 (Month 3, Week 6; +/- 5 days)

For patients who received a repeat injection of study drug, you will be seen six weeks after the second injection of the study drug at the outpatient Colorectal Surgery clinic where you will undergo the following:

- A general physical exam, a measurement of your vital signs, as well as a rectal and vaginal exam to assess the fistula
- Review of your medications including blood products
- Medical and surgical history since your last visit
- Surveys about your perianal disease
- Blood sample taken to measure CBC and CRP

### Visit 7 (Month 6 +/- 14 days)

Six months after enrolling in the study, you will report to the outpatient Colorectal Surgery clinic for a follow-up visit where the following will be performed:

- A general physical exam, a measurement of your vital signs, as well as a rectal and vaginal exam to assess the fistula
- Review of your medications including blood products
- Medical and surgical history since your last visit
  - Surveys about your perianal disease
  - Blood sample taken to measure CBC, CRP, and Creatinine
- Pelvic MRI
- At this visit, you will be unblinded to your study drug therapy (MSCs or normal saline control). If you are a MSC patient, you will continue on to **Visit 8**. If you are a control patient and you have not experienced complete healing, you will then crossover to receive the investigational study drug MSC. You will return to the operating room for a EUA, a pelvic MRI, and receive an injection of the MSC product in the same fashion as previously done at **Day 0** and **Month 3 visits**.

### Visit 7.1 (Month 6, Day 0; within 3 days of Visit 7.0)

If you are a control patient who did not experience complete healing, you will come to Visit 7.1 to receive the injection of MSCs. The following will be completed at this visit:

- Review of your medications including blood products
- Medical surgery, and surgical history since your last visit
- If you are able to become pregnant, a urine pregnancy test will be performed
- You will then undergo a scheduled EUA to assess the fistula tract. The investigational study drug MSCs will be injected into the fistula tract.

Your vital signs (including blood pressure, heart rate, and temperature) will be monitored after the procedure at regular intervals for 6 hours in the recovery area. If your vital signs remain stable and you remain free of adverse events, you will be discharged to home. If your vital signs go outside of the acceptable range, it is possible that you could be admitted over night to the Clinic for observation.

### Visit 7.2 (Month 6; Day 1)

If you are a control-crossover patient, you will be seen the day after the MSC injection at the outpatient Colorectal Surgery clinic for a follow-up visit where a brief physical exam and measurement of your vitals will be performed.

### Visit 7.3 (Month 6, Week 2; +/- 3 days)

If you are a control-crossover patient, you will be seen two weeks after the MSC injection in the outpatient Colorectal Surgery clinic where the following will be performed:

- A general physical exam, a measurement of your vital signs, as well as a rectal and vaginal exam to assess the fistula
- Review of your medications including blood products
- Medical and surgical history since your last visit
- Surveys about your perianal disease
- Blood sample taken to measure CBC and CRP

### Visit 7.4 (Month 6, Week 6; +/-5 days)

If you are a control-crossover patient, you will be seen six weeks after the MSC injection in the outpatient Colorectal Surgery clinic where the following will be performed:

- A general physical exam, a measurement of your vital signs, as well as a rectal and vaginal exam to assess the fistula
- Review of your medications including blood products
- Medical and surgical history since your last visit
- Surveys about your perianal disease
- Blood sample taken to measure CBC and CRP

### Visit 8 (Month 9; +/- 7 days)

If you are a control-crossover patient, three months after the MSC injection you will be seen in the outpatient Colorectal Surgery Clinic where the following will be performed:

- A general physical exam including vital signs as well as a rectal and vaginal exam to assess the fistula
- Review of your medications including blood products
- Medical and surgical history since your last visit
- Surveys about your perianal disease
- Blood sample taken to measure your CBC, CRP, and Creatinine
- Pelvic MRI

If complete healing has not been achieved, and you did not have an allergic reaction to the first MSC injections, you will return to the operating room for a EUA and repeat injections of the investigational study drug MSC in the same way as before at **Visit 7.1**.

### Visit 8.1 (Month 9, Day 0; within 3 days of Visit 8.0)

**For control-crossover patients who did not experience complete healing and are receiving a repeat injection of MSC**, you will come to **Visit 8.1** where you will undergo the following:

- Review of your medications including blood products
- Medical and surgical history since your last visit
- If you are able to become pregnant, a urine pregnancy test will be performed
- You will then undergo a scheduled EUA to assess the fistula tract. The investigational study drug MSCs will be injected into the fistula tract.

Your vital signs (including blood pressure, heart rate, and temperature) will be monitored after the procedure at regular intervals for 6 hours in the recovery area. If your vital signs remain stable and you remain free of adverse events, you will be discharged to home. If your vital signs go outside of the acceptable range, it is possible that you could be admitted over night to the hospital for observation.

### Visit 8.2 (Month 9; Day 1)

**If you are a control-crossover patient**, you will be seen the day after the repeat MSC injection at the outpatient Colorectal Surgery clinic for a follow-up visit where a brief physical exam and measurement of your vitals will be performed.

### Visit 8.3 (Month 9, Week 2; +/- 3 days)

If you are a control-crossover patient, you will be seen two weeks after the repeat MSC injection in the outpatient Colorectal Surgery clinic where the following will be performed:

- A general physical exam, a measurement of your vital signs, as well as a rectal and vaginal exam to assess the fistula
- Review of your medications including blood products
- Medical and surgical history since your last visit
- Surveys about your perianal disease
- Blood Sample taken to measure your CBC and CRP

### Visit 8.4 (Month 9, Week 6; +/-5 days)

If you are a control-crossover patient, you will be seen six weeks after the repeat MSC injection in the outpatient Colorectal Surgery clinic where the following will be performed:

- A general physical exam, a measurement of your vital signs, as well as a rectal and vaginal exam to assess the fistula
- Review of your medications including blood products
- Medical and surgical history since your last visit
- Surveys about your perianal disease
- Blood Sample taken to measure your CBC and CRP

### Visit 9 (Month 12; +/- 14 days)

**All patients will complete this visit.** Twelve months after enrolling in the study, you will be seen in the outpatient Colorectal Surgery Clinic where you will undergo the following:

- A general physical exam, a measurement of your vital signs, as well as a rectal and vaginal exam to assess the fistula
- Review of your medications including blood products
- Medical and surgical history since your last visit
- Surveys about your perianal disease
- Blood sample taken to measure CBC, CRP, and creatinine
- If you are able to become pregnant, a urine-pregnancy test will be performed
- An MRI of the pelvis will be performed to assess the rectovaginal fistula

**Treatment Patients – Visit 9** completes your participation in the study

**Control-crossover Patients** – You will continue on to be seen at Visit 10 and Visit 11.

### Visit 10 - Month 15 (+/- 14 days)

Nine months after the initial injection of MSCs, you will report to the outpatient Colorectal Surgery Clinic for a follow-up visit where the following will be performed:

- A general physical exam including vital signs and a rectal exam to assess the fistula and vital signs
- Review of your medications including blood products, medical surgery, and surgical history since your last visit
- Surveys about your perianal disease
- An MRI of the pelvis to assess fistula healing
- Blood sample taken to measure your CBC, CRP, and creatinine

### Visit 11 (Month 18; +/- 14 days)

Twelve months after the initial injection of MSCs, you will report to the outpatient Colorectal Surgery clinic for a follow-up visit where the following will be performed:

- A general physical exam including vital signs and a rectal exam to assess the fistula and vital signs
- Review of your medications including blood products, medical surgery, and surgical history since your last visit
- Surveys about your perianal disease
- Blood sample taken to measure your CBC and CRP and creatinine
- An MRI of the pelvis to assess fistula healing





## My Visits

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### VISIT 1 Screening for eligibility visit

Date \_\_\_\_\_

Notes:

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### VISIT 6 3 months after treatment visit

Date \_\_\_\_\_

Notes:

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### VISIT 1.1 (Only for patients with active pelvic sepsis at screening)

Date \_\_\_\_\_

Notes:

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### VISIT 6.1 0-3 days within visit 6

(Retreatment day for patients with incomplete healing at visit 6)

Date \_\_\_\_\_

Notes:

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### VISIT 2 Treatment Day visit

Date \_\_\_\_\_

Notes:

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### VISIT 6.2 Day after retreatment visit

Date \_\_\_\_\_

Notes:

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### VISIT 3 Day after treatment visit

Date \_\_\_\_\_

Notes:

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### VISIT 6.3 2 weeks after retreatment (month 3, week 2)

Date \_\_\_\_\_

Notes:

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### VISIT 4 2 weeks after treatment visit

Date \_\_\_\_\_

Notes:

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### VISIT 6.4 6 weeks after retreatment (month 3, week 6)

Date \_\_\_\_\_

Notes:

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### VISIT 5 6 weeks after treatment visit

Date \_\_\_\_\_

Notes:

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### VISIT 7 6 months mark since initial treatment day

Date \_\_\_\_\_

Notes:

## My Visits, continued

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**VISIT 7.1** 0-3 days within visit 7

(Crossover for controls: Patients who received normal saline will crossover to receive investigational MSCs)

Date \_\_\_\_\_

Notes:

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**VISIT 7.2** Day after crossover visit

Date \_\_\_\_\_

Notes:

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**VISIT 7.3** 2 weeks after crossover visit (month 6, week 2)

Date \_\_\_\_\_

Notes:

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**VISIT 7.4** 6 weeks after crossover visit (month 6, week 6)

Date \_\_\_\_\_

Notes:

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**VISIT 8** 3 months after crossover visit (month 9)

Date \_\_\_\_\_

Notes:

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**VISIT 8.1** 0-3 days within visit 8

(Retreatment day for crossover patients with incomplete healing at visit 8)

Date \_\_\_\_\_

Notes:

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**VISIT 8.2** Day after crossover retreatment visit

Date \_\_\_\_\_

Notes:

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**VISIT 8.3** 2 weeks after crossover retreatment visit

(month 9, week 2)

Date \_\_\_\_\_

Notes:

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**VISIT 8.4** 6 weeks after crossover retreatment visit

(month 9, week 6)

Date \_\_\_\_\_

Notes:

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**VISIT 9** One year from visit 2: All patients will complete this visit. (month 12) \*This is the last visit for treatment patients

Date \_\_\_\_\_

Notes:

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**VISIT 10** 6 months after crossover visit (month 15)

Date \_\_\_\_\_

Notes:

---

**VISIT 11** 9 months after crossover visit (month 18)

Date \_\_\_\_\_

Notes:

## JANUARY

SU	MO	TU	WE	TH	FR	SA
					1	2
3	4	5	6	7	8	9
10	11	12	13	14	15	16
17	18	19	20	21	22	23
24	25	26	27	28	29	30
31						

## FEBRUARY

SU	MO	TU	WE	TH	FR	SA
	1	2	3	4	5	6
7	8	9	10	11	12	13
14	15	16	17	18	19	20
21	22	23	24	25	26	27
28						

## MARCH

SU	MO	TU	WE	TH	FR	SA
	1	2	3	4	5	6
7	8	9	10	11	12	13
14	15	16	17	18	19	20
21	22	23	24	25	26	27
28	29	30	31			

## APRIL

SU	MO	TU	WE	TH	FR	SA
				1	2	3
4	5	6	7	8	9	10
11	12	13	14	15	16	17
18	19	20	21	22	23	24
25	26	27	28	29	30	

## MAY

SU	MO	TU	WE	TH	FR	SA
						1
2	3	4	5	6	7	8
9	10	11	12	13	14	15
16	17	18	19	20	21	22
23	24	25	26	27	28	29
30	31					

## JUNE

SU	MO	TU	WE	TH	FR	SA
		1	2	3	4	5
6	7	8	9	10	11	12
13	14	15	16	17	18	19
20	21	22	23	24	25	26
27	28	29	30			

## JULY

SU	MO	TU	WE	TH	FR	SA
				1	2	3
4	5	6	7	8	9	10
11	12	13	14	15	16	17
18	19	20	21	22	23	24
25	26	27	28	29	30	31

## AUGUST

SU	MO	TU	WE	TH	FR	SA
1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28
29	30	31				

## SEPTEMBER

SU	MO	TU	WE	TH	FR	SA
			1	2	3	4
5	6	7	8	9	10	11
12	13	14	15	16	17	18
19	20	21	22	23	24	25
26	27	28	29	30		

## OCTOBER

SU	MO	TU	WE	TH	FR	SA
					1	2
3	4	5	6	7	8	9
10	11	12	13	14	15	16
17	18	19	20	21	22	23
24	25	26	27	28	29	30
31						

## NOVEMBER

SU	MO	TU	WE	TH	FR	SA
	1	2	3	4	5	6
7	8	9	10	11	12	13
14	15	16	17	18	19	20
21	22	23	24	25	26	27
28	29	30				

## DECEMBER

SU	MO	TU	WE	TH	FR	SA
			1	2	3	4
5	6	7	8	9	10	11
12	13	14	15	16	17	18
19	20	21	22	23	24	25
26	27	28	29	30	31	

## Survey: Perianal Crohn's Disease Activity Index (PCDAI)

Patient Study ID Number: \_\_\_\_\_

Visit Number: \_\_\_\_\_

Visit Date: \_\_\_\_ / \_\_\_\_ / \_\_\_\_ (mm/dd/yyyy)

☐ Not Done

### Discharge

---

- 0 No discharge
- 1 Minimal mucous discharge
- 2 Moderate mucous or purulent discharge
- 3 Substantial discharge
- 4 Gross faecal soiling

Discharge Total \_\_\_\_\_

### Pain and Restriction of Activities

---

- 0 No activity restriction
- 1 Mild discomfort, no restriction
- 2 Moderate discomfort, some limitation activities
- 3 Marked discomfort, marked limitation
- 4 Severe pain, severe limitation

Pain and Restriction of Activities Total \_\_\_\_\_



## Survey: PCDAI, continued

### Restriction of Sexual Activity

---

- 0 No restriction sexual activity
- 1 Slight restriction sexual activity
- 2 Moderate limitation sexual activity
- 3 Marked limitation sexual activity
- 4 Unable to engage in sexual activity

Restriction of Sexual Activity Total \_\_\_\_\_

### Type of Perianal Disease

---

- 0 No perianal disease or skin tags
- 1 Anal fissure or mucosal tear
- 2 <3 Perianal fistulas
- 3 >3 Perianal fistulas
- 4 Anal sphincter ulceration of fistula with significant undermining of skin

Type of Perianal Disease Total \_\_\_\_\_

### Degree of Induration

---

- 0 No induration
- 1 Minimal induration
- 2 Moderate induration
- 3 Substantial induration
- 4 Gross fluctuance or abscess

Degree of Induration Total \_\_\_\_\_

**Grand Total** \_\_\_\_\_

## Survey: Wexner Incontinence Score

Patient Study ID Number: \_\_\_\_\_

Visit Number: \_\_\_\_\_

Visit Date: \_\_\_\_ / \_\_\_\_ / \_\_\_\_ (mm/dd/yyyy)

☐ Not Done

	Frequency				
Type of incontinence	<i>Never</i>	<i>Rarely</i>	<i>Sometimes</i>	<i>Usually</i>	<i>Always</i>
Solid	0	1	2	3	4
Liquid	0	1	2	3	4
Gas	0	1	2	3	4
Wears pad	0	1	2	3	4
Lifestyle alteration	0	1	2	3	4

- Never: 0
- Rarely: < 1/month
- Sometimes: < 1/week or ≥ 1/month
- Usually: < 1/day or ≥ 1/week
- Always: ≥ 1/day

## Survey: EuroQol Five Dimensions Questionnaire (EQ-5D-5L)

Patient Study ID Number: \_\_\_\_\_

Visit Number: \_\_\_\_\_

Visit Date: \_\_\_\_ / \_\_\_\_ / \_\_\_\_ (mm/dd/yyyy)

☐ Not Done

### Mobility

- ☐ 1 - I have no problems in walking about
- ☐ 2 - I have slight problems in walking about
- ☐ 3 - I have moderate problems walking about
- ☐ 4 - I have severe problems walking about
- ☐ 5 - I am unable to walk about

### Self-Care

- ☐ 1 - I have no problems with washing or dressing myself
- ☐ 2 - I have slight with washing or dressing myself
- ☐ 3 - I have moderate with washing or dressing myself
- ☐ 4 - I have severe with washing or dressing myself
- ☐ 5 - I am unable to wash or dress myself

### Usual Activities

(e.g. work, study, house work, family or leisure activities)

- ☐ 1 - I have no problems performing my usual activities
- ☐ 2 - I have slight problems with my usual activities
- ☐ 3 - I have moderate problems with my usual activities
- ☐ 4 - I have severe problems with my usual activities
- ☐ 5 - I am unable to perform my usual activities

### Pain/discomfort

- ☐ 1 - I have no pain or discomfort
- ☐ 2 - I have slight pain or discomfort
- ☐ 3 - I have moderate pain or discomfort
- ☐ 4 - I have severe pain or discomfort
- ☐ 5 - I have extreme pain or discomfort

### Anxiety/depression

- ☐ 1 - I am not anxious or depressed
- ☐ 2 - I am slightly anxious or depressed
- ☐ 3 - I am moderately anxious or depressed
- ☐ 4 - I am severely anxious or depressed
- ☐ 5 - I am extremely anxious or depressed

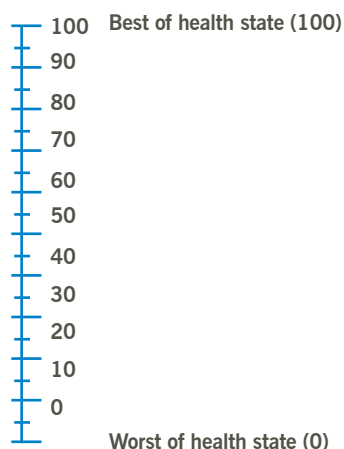
Score \_\_\_\_

### Visual Analog Scale (VAS)

Your own health state today

We have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst scale you can imagine mark 0.

We would like you to indicate on this scale how good or bad your own health is today, in your option. Please do this by drawing a line from the box below to whichever point on the scale indicates how good or bad your health state is today.



\_\_\_\_ Vas Score

# Survey: Inflammatory Bowel Disease Patient-Reported Treatment Impact

Patient Study ID Number: \_\_\_\_\_

Visit Number: \_\_\_\_\_

Visit Date: \_\_\_\_ / \_\_\_\_ / \_\_\_\_ (mm/dd/yyyy)

☐ Not Done

## 1. Overall, how satisfied are you with the drug that you received since you entered this trial?

- ☐ 1 - Extremely satisfied
- ☐ 2 - Satisfied
- ☐ 3 - Neither satisfied nor dissatisfied
- ☐ 4 - Dissatisfied
- ☐ 5 - Extremely dissatisfied

## 2. Before enrolling in this clinical trial, what treatment were you receiving for your bowel condition?

- ☐ 1 - Injectable prescription medicines
- ☐ 2 - Prescription medicines taken by mouth
- ☐ 3 - Surgery
- ☐ 4 - Prescription medicines and surgery
- ☐ 5 - No treatment

**Preface question for question number 3;**  
**Overall, do you prefer the drug that you received since you entered this trial to the treatment you received before this clinical trial?**

- ☐ Yes, I definitely prefer the drug that I am receiving now
- ☐ I have a slight preference for the drug that I am receiving now
- ☐ I have no preference either way
- ☐ I have a slight preference for my previous treatment
- ☐ No, I definitely prefer my previous treatment

## 3. In the future, would you be willing to use the same drug that you have received since you entered this trial for your bowel condition?

- ☐ 1 - Yes, I would definitely want to use the same drug again
- ☐ 2 - I might want to use the same drug again
- ☐ 3 - I am not sure
- ☐ 4 - I might not want to use the same drug again
- ☐ 5 - No, I definitely would not want to use the same drug again

## Survey: Quality of Life in the Inflammatory Bowel Disease Questionnaire (IBDQ)

Patient Study ID Number: \_\_\_\_\_

Visit Number: \_\_\_\_\_

Visit Date: \_\_\_\_ / \_\_\_\_ / \_\_\_\_ (mm/dd/yyyy)

☐ Not Done

**1. How frequently have your bowel movements been during the last two weeks?**

- ☐ 1 - Bowel movements as or more frequent than they have ever been
- ☐ 2 - Extremely frequent
- ☐ 3 - Very frequent
- ☐ 4 - Moderate increase in frequency of bowel movements
- ☐ 5 - Some increase in frequency of bowel movements
- ☐ 6 - Slight increase in frequency of bowel movements
- ☐ 7 - Normal, no increase in frequency of bowel movements

**2. How often has the feeling of fatigue or of being tired and worn out been a problem for you during the last two weeks?**

- ☐ 1 - All of the time
- ☐ 2 - Most of the time
- ☐ 3 - A good bit of the time
- ☐ 4 - Some of the time
- ☐ 5 - A little of the time
- ☐ 6 - Hardly any of the time
- ☐ 7 - None of the time

**3. How often during the last two weeks have you felt frustrated, impatient, or restless?**

- ☐ 1 - All of the time
- ☐ 2 - Most of the time
- ☐ 3 - A good bit of the time
- ☐ 4 - Some of the time
- ☐ 5 - A little of the time
- ☐ 6 - Hardly any of the time
- ☐ 7 - None of the time

**4. How often during the last two weeks have you been unable to attend school or do to your work because of your bowel problem?**

- ☐ 1 - All of the time
- ☐ 2 - Most of the time
- ☐ 3 - A good bit of the time
- ☐ 4 - Some of the time
- ☐ 5 - A little of the time
- ☐ 6 - Hardly any of the time
- ☐ 7 - None of the time

**5. How much of the time during the last two weeks have your bowel movements been loose?**

- ☐ 1 - All of the time
- ☐ 2 - Most of the time
- ☐ 3 - A good bit of the time
- ☐ 4 - Some of the time
- ☐ 5 - A little of the time
- ☐ 6 - Hardly any of the time
- ☐ 7 - None of the time

## Survey: IBDQ, continued

### 6. How much energy have you had during the last two weeks?

- ☐ 1 - No energy at all
- ☐ 2 - Very little energy
- ☐ 3 - A little energy
- ☐ 4 - Some energy
- ☐ 5 - A moderate amount of energy
- ☐ 6 - A lot of energy
- ☐ 7 - Full of energy

### 7. How often during the last two weeks did you feel worries about the possibility if needing to have surgery because of your bowel problem?

- ☐ 1 - All of the time
- ☐ 2 - Most of the time
- ☐ 3 - A good bit of the time
- ☐ 4 - Some of the time
- ☐ 5 - A little of the time
- ☐ 6 - Hardly any of the time
- ☐ 7 - None of the time

### 8. How often during the last two weeks have you had a delay or cancel a social engagement because of your bowel problems?

- ☐ 1 - All of the time
- ☐ 2 - Most of the time
- ☐ 3 - A good bit of the time
- ☐ 4 - Some of the time
- ☐ 5 - A little of the time
- ☐ 6 - Hardly any of the time
- ☐ 7 - None of the time

### 9. How often during the last two weeks have you been troubled by cramps in your abdomen?

- ☐ 1 - All of the time
- ☐ 2 - Most of the time
- ☐ 3 - A good bit of the time
- ☐ 4 - Some of the time
- ☐ 5 - A little of the time
- ☐ 6 - Hardly any of the time
- ☐ 7 - None of the time

### 10. How often during the last two weeks have you felt generally unwell?

- ☐ 1 - All of the time
- ☐ 2 - Most of the time
- ☐ 3 - A good bit of the time
- ☐ 4 - Some of the time
- ☐ 5 - A little of the time
- ☐ 6 - Hardly any of the time
- ☐ 7 - None of the time

### 11. How often during the last two week have you been troubled because of fear of not finding washroom?

- ☐ 1 - All of the time
- ☐ 2 - Most of the time
- ☐ 3 - A good bit of the time
- ☐ 4 - Some of the time
- ☐ 5 - A little of the time
- ☐ 6 - Hardly any of the time
- ☐ 7 - None of the time

### 12. How much difficulty have you had, as a result of your bowel problems, doing leisure or sports activities you would have liked to have done during the last two weeks?

- ☐ 1 - A great deal of difficulty; activities made impossible
- ☐ 2 - A lot of difficulty
- ☐ 3 - A fair bit of difficulty
- ☐ 4 - Some difficulty
- ☐ 5 - A little difficulty
- ☐ 6 - Hardly any difficulty
- ☐ 7 - No difficulty; the bowel problems did not limit sports or leisure activities

### 13. How often during the last two weeks have you been troubled by pain in the abdomen?

- ☐ 1 - All of the time
- ☐ 2 - Most of the time
- ☐ 3 - A good bit of the time
- ☐ 4 - Some of the time
- ☐ 5 - A little of the time
- ☐ 6 - Hardly any of the time
- ☐ 7 - None of the time



## Survey: IBDQ, continued

**14. How often during the last two weeks have you had problems getting a good night's sleep, or been troubled by waking up during the night?**

- ☐ 1 - All of the time
- ☐ 2 - Most of the time
- ☐ 3 - A good bit of the time
- ☐ 4 - Some of the time
- ☐ 5 - A little of the time
- ☐ 6 - Hardly any of the time
- ☐ 7 - None of the time

**15. How often during the last two weeks have you felt depressed or discouraged?**

- ☐ 1 - All of the time
- ☐ 2 - Most of the time
- ☐ 3 - A good bit of the time
- ☐ 4 - Some of the time
- ☐ 5 - A little of the time
- ☐ 6 - Hardly any of the time
- ☐ 7 - None of the time

**16. How often during the last two weeks have you had to avoid attending events where there was no washroom close at hand?**

- ☐ 1 - All of the time
- ☐ 2 - Most of the time
- ☐ 3 - A good bit of the time
- ☐ 4 - Some of the time
- ☐ 5 - A little of the time
- ☐ 6 - Hardly any of the time
- ☐ 7 - None of the time

**17. Overall, in the last two weeks, how much of a problem have you had with passing large amounts of gas?**

- ☐ 1 - A major problem
- ☐ 2 - A big problem
- ☐ 3 - A significant problem
- ☐ 4 - Some trouble
- ☐ 5 - A little trouble
- ☐ 6 - Hardly any trouble
- ☐ 7 - No trouble

**18. Overall, in the last two weeks, how much of a problem have you had maintaining or getting to the weight you would like to be at?**

- ☐ 1 - A major problem
- ☐ 2 - A big problem
- ☐ 3 - A significant problem
- ☐ 4 - Some trouble
- ☐ 5 - A little trouble
- ☐ 6 - Hardly any trouble
- ☐ 7 - No trouble

**19. Many patients with bowel problems often have worries and anxieties related to their illness. These include worries about getting cancer, worries about never feeling better, and worries about having a relapse. In general, how often during the last two weeks have you felt worries or anxious?**

- ☐ 1 - All of the time
- ☐ 2 - Most of the time
- ☐ 3 - A good bit of the time
- ☐ 4 - Some of the time
- ☐ 5 - A little of the time
- ☐ 6 - Hardly any of the time
- ☐ 7 - None of the time

**20. How much of the time during the last two weeks have you been troubled by the feeling in abdominal bloating?**

- ☐ 1 - All of the time
- ☐ 2 - Most of the time
- ☐ 3 - A good bit of the time
- ☐ 4 - Some of the time
- ☐ 5 - A little of the time
- ☐ 6 - Hardly any of the time
- ☐ 7 - None of the time

## Survey: IBDQ, continued

**21. How often during the last two weeks have you felt relaxed and free of tension?**

- ☐ 1 - None of the time
- ☐ 2 - A little of the time
- ☐ 3 - Some of the time
- ☐ 4 - A good bit of the time
- ☐ 5 - Most of the time
- ☐ 6 - Almost all of the time
- ☐ 7 - All of the time

**22. How much of the time during the last two weeks have you had problem with the rectal bleeding with your bowel movements?**

- ☐ 1 - All of the time
- ☐ 2 - Most of the time
- ☐ 3 - A good bit of the time
- ☐ 4 - Some of the time
- ☐ 5 - A little of the time
- ☐ 6 - Hardly any of the time
- ☐ 7 - None of the time

**23. How much of the time during the last two weeks you felt embarrassed as a result of your bowel problem?**

- ☐ 1 - All of the time
- ☐ 2 - Most of the time
- ☐ 3 - A good bit of the time
- ☐ 4 - Some of the time
- ☐ 5 - A little of the time
- ☐ 6 - Hardly any of the time
- ☐ 7 - None of the time

**24. How much of the time during the last two weeks have you been troubled by a feeling of having to go to the bathroom even though your bowels were empty?**

- ☐ 1 - All of the time
- ☐ 2 - Most of the time
- ☐ 3 - A good bit of the time
- ☐ 4 - Some of the time
- ☐ 5 - A little of the time
- ☐ 6 - Hardly any of the time
- ☐ 7 - None of the time

**25. How much of the time during the last two weeks have you felt fearful or upset?**

- ☐ 1 - All of the time
- ☐ 2 - Most of the time
- ☐ 3 - A good bit of the time
- ☐ 4 - Some of the time
- ☐ 5 - A little of the time
- ☐ 6 - Hardly any of the time
- ☐ 7 - None of the time

**26. How much of the time during the last two weeks have you had trouble by accidental soiling of your underpants?**

- ☐ 1 - All of the time
- ☐ 2 - Most of the time
- ☐ 3 - A good bit of the time
- ☐ 4 - Some of the time
- ☐ 5 - A little of the time
- ☐ 6 - Hardly any of the time
- ☐ 7 - None of the time

**27. How much of the time during the last two weeks have you felt anger as a result of your bowel movement problem?**

- ☐ 1 - All of the time
- ☐ 2 - Most of the time
- ☐ 3 - A good bit of the time
- ☐ 4 - Some of the time
- ☐ 5 - A little of the time
- ☐ 6 - Hardly any of the time
- ☐ 7 - None of the time

**28. To what extent has your bowel problem limited sexual activity during the last two weeks?**

- ☐ 1 - No sex as a result of bowel disease
- ☐ 2 - Major limitation as a result of bowel disease
- ☐ 3 - Moderate limitation as a result of bowel disease
- ☐ 4 - Some limitation as a result of bowel disease
- ☐ 5 - A little limitation as a result of bowel disease
- ☐ 6 - Hardly any limitation as a result of bowel disease
- ☐ 7 - No limitation as a result of bowel disease

## Survey: IBDQ, continued

**29. How much of the time during the last two weeks have you been troubled by nausea or feeling sick to the stomach?**

- ☐ 1 - All of the time
- ☐ 2 - Most of the time
- ☐ 3 - A good bit of the time
- ☐ 4 - Some of the time
- ☐ 5 - A little of the time
- ☐ 6 - Hardly any of the time
- ☐ 7 - None of the time

**30. How much of the time during the last two weeks have you felt irritable?**

- ☐ 1 - All of the time
- ☐ 2 - Most of the time
- ☐ 3 - A good bit of the time
- ☐ 4 - Some of the time
- ☐ 5 - A little of the time
- ☐ 6 - Hardly any of the time
- ☐ 7 - None of the time

**31. How often during the past two weeks have you felt a lack of understanding from others?**

- ☐ 1 - All of the time
- ☐ 2 - Most of the time
- ☐ 3 - A good bit of the time
- ☐ 4 - Some of the time
- ☐ 5 - A little of the time
- ☐ 6 - Hardly any of the time
- ☐ 7 - None of the time

**32. How satisfied, happy, or pleased have you been with your personal life during the past two weeks?**

- ☐ 1 - Vary dissatisfied, unhappy most of the time
- ☐ 2 - Generally dissatisfied, unhappy
- ☐ 3 - Somewhat dissatisfied, unhappy
- ☐ 4 - Generally satisfied, pleased
- ☐ 5 - Satisfied most of the time, happy
- ☐ 6 - Very satisfied most of the time, happy
- ☐ 7 - Extremely satisfied, could not have been more happy or pleased

**Score** \_\_\_\_

## Survey: The Short Form 36 Health Survey (SF-36)

Patient Study ID Number: \_\_\_\_\_

Visit Number: \_\_\_\_\_

Visit Date: \_\_\_\_ / \_\_\_\_ / \_\_\_\_ (mm/dd/yyyy)

☐ Not Done

Choose one option for each questionnaire item

**1. In general, would you say your health is**

- ☐ Excellent (100)
- ☐ Very good (75)
- ☐ Good (50)
- ☐ Fair (25)
- ☐ Poor (0)

**2. Compared to one year ago, how would you rate your health in general now?**

- ☐ Much better now than one year ago (100)
- ☐ Somewhat better now than one year ago (75)
- ☐ About the same (50)
- ☐ Somewhat worse now than one year ago (25)
- ☐ Much worse now than one year ago (0)

The following items are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

**3. Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports**

- ☐ Yes, limited a lot (0)
- ☐ Yes, limited a little (50)
- ☐ No, not limited at all (100)

**4. Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, playing golf**

- ☐ Yes, limited a lot (0)
- ☐ Yes, limited a little (50)
- ☐ No, not limited at all (100)

**5. Lifting or carrying groceries**

- ☐ Yes, limited a lot (0)
- ☐ Yes, limited a little (50)
- ☐ No, not limited at all (100)

**6. Climbing several flights of stairs**

- ☐ Yes, limited a lot (0)
- ☐ Yes, limited a little (50)
- ☐ No, not limited at all (100)

**7. Climbing one flight of stairs**

- ☐ Yes, limited a lot (0)
- ☐ Yes, limited a little (50)
- ☐ No, not limited at all (100)

**8. Bending, kneeling, or stooping**

- ☐ Yes, limited a lot (0)
- ☐ Yes, limited a little (50)
- ☐ No, not limited at all (100)

**9. Walking more than a mile**

- ☐ Yes, limited a lot (0/50)
- ☐ Yes, limited a little (50)
- ☐ No, not limited at all (100)

**10. Walking several blocks**

- ☐ Yes, limited a lot (0)
- ☐ Yes, limited a little (50)
- ☐ No, not limited at all (100)

**11. Walking one block**

- ☐ Yes, limited a lot (0)
- ☐ Yes, limited a little (50)
- ☐ No, not limited at all (100)

## Survey: SF-36, continued

### 12. Bathing or dressing yourself

- ☐ Yes, limited a lot (0)
- ☐ Yes, limited a little (50)
- ☐ No, not limited at all (100)

During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

### 13. Cut down the amount of time you spent on work or other activities

- ☐ Yes (0)
- ☐ No (100)

### 14. Accomplished less than you would like

- ☐ Yes (0)
- ☐ No (100)

### 15. Were limited in the kind of work or other activities

- ☐ Yes (0)
- ☐ No (100)

### 16. Had difficulty performing the work or other activities (for example, it took extra effort)

- ☐ Yes (0)
- ☐ No (100)

During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

### 17. Cut down the amount of time you spent on work or other activities

- ☐ Yes (0)
- ☐ No (100)

### 18. Accomplished less than you would like

- ☐ Yes (0)
- ☐ No (100)

### 19. Didn't do work or other activities as carefully as usual

- ☐ Yes (0)
- ☐ No (100)

### 20. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?

- ☐ Not at all (100)
- ☐ Slightly (75)
- ☐ Moderately (50)
- ☐ Quite a bit (25)
- ☐ Extremely (0)

### 21. How much bodily pain have you had during the past 4 weeks?

- ☐ None (100)
- ☐ Very mild (80)
- ☐ Mild (60)
- ☐ Moderate (40)
- ☐ Severe (20)
- ☐ Very severe (0)

### 22. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

- ☐ Not at all (100)
- ☐ A little bit (75)
- ☐ Moderately (50)
- ☐ Quite a bit (25)
- ☐ Extremely (0)

These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks...

### 23. Did you feel full of pep?

- ☐ All of the time (100)
- ☐ Most of the time (80)
- ☐ A good bit of the time (60)
- ☐ Some of the time (40)
- ☐ A little of the time (20)
- ☐ None of the time (0)

## Survey: SF-36, continued

### 24. Have you been a very nervous person?

- ☐ All of the time (0)
- ☐ Most of the time (20)
- ☐ A good bit of the time (40)
- ☐ Some of the time (60)
- ☐ A little of the time (80)
- ☐ None of the time (100)

### 25. Have you felt so down in the dumps that nothing could cheer you up?

- ☐ All of the time (0)
- ☐ Most of the time (20)
- ☐ A good bit of the time (40)
- ☐ Some of the time (60)
- ☐ A little of the time (80)
- ☐ None of the time (100)

### 26. Have you felt calm and peaceful?

- ☐ All of the time (100)
- ☐ Most of the time (80)
- ☐ A good bit of the time (60)
- ☐ Some of the time (40)
- ☐ A little of the time (20)
- ☐ None of the time (0)

### 27. Did you have a lot of energy?

- ☐ All of the time (100)
- ☐ Most of the time (80)
- ☐ A good bit of the time (60)
- ☐ Some of the time (40)
- ☐ A little of the time (20)
- ☐ None of the time (0)

### 28. Have you felt downhearted and blue?

- ☐ All of the time (0)
- ☐ Most of the time (20)
- ☐ A good bit of the time (40)
- ☐ Some of the time (60)
- ☐ A little of the time (80)
- ☐ None of the time? (100)

### 29. Did you feel worn out?

- ☐ All of the time (0)
- ☐ Most of the time (20)
- ☐ A good bit of the time (40)
- ☐ Some of the time (60)
- ☐ A little of the time (80)
- ☐ None of the time (100)

### 30. Have you been a happy person?

- ☐ All of the time (100)
- ☐ Most of the time (80)
- ☐ A good bit of the time (60)
- ☐ Some of the time (40)
- ☐ A little of the time (20)
- ☐ None of the time (0)

### 31. Did you feel tired?

- ☐ All of the time (0)
- ☐ Most of the time (20)
- ☐ A good bit of the time (40)
- ☐ Some of the time (60)
- ☐ A little of the time (80)
- ☐ None of the time (100)

### 32. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)?

- ☐ All of the time (0)
- ☐ Most of the time (25)
- ☐ Some of the time (50)
- ☐ A little of the time (75)
- ☐ None of the time (100)



## Surveys: SF-36, continued

How **TRUE** or **FALSE** is each of the following statements for you.

**33. I seem to get sick a little easier than other people**

- ☐ Definitely true (0)
- ☐ Mostly true (25)
- ☐ Don't know (50)
- ☐ Mostly false (75)
- ☐ Definitely false (100)

**34. I am as healthy as anybody I know**

- ☐ Definitely true (100)
- ☐ Mostly true (75)
- ☐ Don't know (50)
- ☐ Mostly false (25)
- ☐ Definitely false (0)

**35. I expect my health to get worse**

- ☐ Definitely true (0)
- ☐ Mostly true (25)
- ☐ Don't know (50)
- ☐ Mostly false (75)
- ☐ Definitely false (100)

**36. My health is excellent**

- ☐ Definitely true (100)
- ☐ Mostly true (75)
- ☐ Don't know (50)
- ☐ Mostly false (25)
- ☐ Definitely false (0)

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