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Approved by the Beth Israel Deaconess Medical Center Committee on Clinical Investigations:

Consent Approval Date: 10/18/2017

Protocol Number: 2014P000375

BETH ISRAEL DEACONESS MEDICAL CENTER
APPROVED BY THE COMMITTEE ON CLINICAL INVESTIGATIONS
07/23/2018
APPROVAL EXPIRATION DATE

INFORMED CONSENT FORM TO TAKE PART IN A RESEARCH STUDY

SUBJECT'S NAME:
TITLE OF RESEARCH PROTOCOL: Pilot Study of the efficacy of pancreatic enzyme supplementation for symptom control in celiac disease not responding to the gluten free diet
PRINCIPAL INVESTIGATOR: Ciaran P. Kelly, MD
PROTOCOL NUMBER: 2014P000375

INTRODUCTION:

- This is a research study;
- Your participation is voluntary;
- A research study includes only people who choose to take part;
- You may or may not benefit from participating in the study. However, your participation may help others in the future as a result of knowledge gained from the research;
- You may leave the study at any time;
- If you choose not to take part, or if you leave the study, your decision will in no way harm your relationship with any member of the research team or any other individuals at Beth Israel Deaconess Medical Center.

Please read this consent form carefully and ask the investigators or study staff to explain any words or information that you do not clearly understand. Once you read this consent form and understand what your participation in this study will involve, you will be asked to sign this form if you wish to take part. You will be given a signed copy of the form to keep for your records.

DISCLOSURE OF SPECIAL INTERESTS OF BIDMC AND INVESTIGATORS

This study is being conducted by Dr. Kelly and is funded by Actavis plc. The funding agency in this study, Actavis, is paying Beth Israel Deaconess Medical Center and Dr. Kelly to perform this research.

WHOM TO CONTACT IF YOU HAVE QUESTIONS OR PROBLEMS

If you have any questions, concerns or complaints about this research or experience any problems, you should contact Dr. Kelly at [617] 667-1272.

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PURPOSE

Celiac disease is an inherited, life-long digestive disease affecting children and adults. When people with celiac disease eat *gluten*, there is a reaction that damages their small intestine and that can also harm the ability of their intestine to take in nutrients from food. Gluten is a plant protein found in foods like wheat, rye, and barley. It is also found in many everyday products like some medicines and vitamins. About 1 in every 100 people in the United States has celiac disease. There is no drug treatment or cure for celiac disease. The only available option for people with this disease is to follow a strict gluten-free diet.

However, for some people, following a strict gluten-free diet doesn't help their symptoms. Up to 1 in 3 patients with celiac disease continue to have symptoms despite following a gluten-free diet. One possible reason for this is poor production of enzymes by the pancreas. Enzymes are proteins that help chemical changes occur. The pancreas is an organ in your body that produces many molecules and enzymes that help you digest food. In this study we want to see whether taking a pancreatic enzyme supplement in addition to following a gluten-free diet will help your symptoms.

The pancreatic enzyme supplement that we are using is a FDA-approved drug called Viokace. The Viokace used in this study is investigational. This means that this particular investigational agent, Viokace, has been approved by the FDA for use in other diseases or conditions, but we do not yet know if it is useful or safe as a treatment for persistent symptoms in patients with Celiac Disease. In addition to Viokace, as a part of this study you will also be asked to take omeprazole. Omeprazole belongs to a group of drugs called proton pump inhibitors (PPIs). The omeprazole will help protect the Viokace from the acids in your stomach so that it can reach your intestines, which is where the Viokace becomes active. If you are already taking omeprazole or another proton pump inhibitor at enrollment you will be allowed to continue taking it as prescribed with no need to discontinue or switch over the course of the study.

Viokace contains three different enzymes that are normally produced by your pancreas. These enzymes are called lipase, protease, and amylase and are used by your body to break nutrients into smaller, easier to digest molecules. Lipase is an enzyme that helps your body digest fat. Protease is an enzyme that helps your body digest proteins. Amylase helps your body digest sugar.

One of the enzymes that your pancreas produces is called elastase. Elastase helps your body digest proteins that you eat. The amount of elastase in your bowel movement (stool) tells us how well your pancreas is producing enzymes and other molecules involved in digestion. In this study, we'll measure the amount of elastase in your stool to:

- Get a sense of how well your pancreas is producing enzymes and other molecules.
- See whether the amount of elastase in your stool helps predict whether the study therapy works.

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This study will include people who have been diagnosed with Celiac Disease who are following a gluten free diet and are actively experiencing symptoms. If you choose to take part in the study, you will continue to follow your current diet during the trial and will receive Viokace or placebo (a dummy pill that looks like the study medication but doesn't contain medication). You may also receive omeprazole, if you aren't currently taking it or another PPI. Various measurements will be made throughout the study including looking at samples of your blood, stool, and (for women) urine. You will also be asked to provide answers to questions about your symptoms.

STUDY PARTICIPANTS

You have been asked to be in the study because you have celiac disease and your symptoms haven't gone away despite following a gluten-free diet.

Approximately 40 people will take part in this study at Beth Israel Deaconess Medical Center. A total of 40 people will take part in this study at all study sites.

DESCRIPTION OF STUDY DETAILS

If you agree to be in this study, you will be asked to read and sign this consent form. After you sign the consent form, the following things will happen:

1. <u>Randomization Procedures:</u>

   In this study, you will take omeprazole (or the PPI you're currently on) in addition to Viokace pills or placebo pills for a total of 34 days. At certain points during the study you will take Viokace pills with omeprazole/your PPI, and at other points you will take placebo pills with omeprazole/your PPI:
   - You will not take Viokace pills for longer than 10 days during the 34-day study treatment period,
   - You will not be able to tell the Viokace pills apart from the placebo pills,
   - You won't know when you're taking Viokace or placebo pills,
   - You won't be able to choose when you take the Viokace or the placebo pills,
   - You will know when you're taking omeprazole/PPI pills, and
   - If you aren't currently on omeprazole, you won't be able to choose whether you take the omeprazole.

   In case of an emergency we will be able to find out whether you have been taking Viokace or placebo. We will refer to the Viokace and placebo pills as the "study medication" throughout the rest of this form.

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Study Medication

You must take the study medication with major meals and snacks, with a maximum of 3 major meals and 3 snacks per day. Here is how you will take the study medication:

How much study medication you take will be based on your weight.

If you weigh 59 kg or greater you will take:
- 6 pills with breakfast
- 6 pills with lunch
- 6 pills with dinner
- 4 pills with snacks; maximum of 3 snacks
- A maximum of 30 pills in one day

If you weigh between 53 kg and 58 kg you will take:
- 5 pills with breakfast
- 5 pills with lunch
- 5 pills with dinner
- 4 pills with snacks; maximum of 3 snacks
- A maximum of 27 pills in one day

If you weigh between 47 kg and 53 kg you will take:
- 5 pills with breakfast
- 5 pills with lunch
- 5 pills with dinner
- 3 pills with snacks; maximum of 3 snacks
- A maximum of 24 pills in one day

If you weigh between 40 kg and 46 kg you will take:
- 4 pills with breakfast
- 4 pills with lunch
- 4 pills with dinner
- 3 pills with snacks; maximum of 3 snacks
- A maximum of 21 pills in one day

If you take less than the maximum number of pills because you don't eat 3 major meals and 3 snacks, that's ok. We just ask that you record this in your daily study medication log.

You should allow at least 3 hours in-between meals, and at least 1 hour between a meal and a snack. Make sure that you drink water when you take your study medication.

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Omeprazole
If you have **ALREADY** been prescribed omeprazole or another PPI by your doctor you should continue to take it as prescribed. Do not change how you take your medication.

If you have **NOT ALREADY** been prescribed omeprazole or anther PPI by your doctor, you must take the omeprazole before breakfast each day that you are in the study. Here is how you will take the omeprazole:

- 1 pill before breakfast

We will ask you to track when you take the omeprazole in your daily study medication log.

2. Screening Procedures: Screening procedures are tests and procedures that will be done to determine if you are eligible to take part in the research study. For this research study, the screening procedures include:

Visit 1 – This visit should take about 2 1/2 hours. At this visit:

- You will have an interview. We will ask about:
  - You: your date of birth, race and ethnicity;
  - Your medical history including diseases or medical conditions you have been diagnosed with, surgeries you have had, and any medications that you are currently taking or have taken recently.

- You will have a brief physical examination.

- Your vital signs (heart rate, blood pressure, temperature, and breathing rate) will be measured.

- You will undergo a dietary assessment with a Celiac Center dietician. Note: This assessment will happen either in-person at study visit 1, or over the phone following your visit 1 but before you start your study treatment. How and when you will start the study treatment is described below.

- You will have a blood sample (about 2 tablespoons or 30 milliliters) collected. This will be used to check:
  - Counts of your red, white and clotting blood cells;
  - Your kidney function, blood acid/base balance, and blood sugar level;
  - How active your Celiac Disease is.

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- You will have a urine pregnancy test if you are a woman who is able to get pregnant.

- You will also be asked to provide a sample of a bowel movement (a stool sample). If you can't produce the bowel movement at Visit 1 we will ask you to collect a stool sample at home and bring it back at Visit 2. We will give you all of the supplies and instructions that you will need to do this.

- We will give you a **take-home Bowel Movement Diary** and explain how to complete it.
  - You will use it to keep track of all of the bowel movements during the study;
  - You will bring this log to each of your visits so the study staff can review it.

- We will give you a **take-home Study Medication Log** and explain how to complete it.
  - You will use it to keep track of when you take the omeprazole/your PPI and your study medication during the study;
  - You will bring this log to each of your visits so the study staff can review it.

- You will complete three study questionnaires:

Celiac Disease Gastrointestinal Symptom Rating Scale (CeD-GSRS)
  - This survey asks you to rate how uncomfortable your gastrointestinal symptoms have been.
  - It is 15 questions long.
  - It should take 5 minutes.

Celiac Symptom Index (CSI)
  - This survey asks about gastrointestinal symptoms and more general symptoms like feeling tired or having headaches.
  - It is 16 questions long.
  - It should take 5 minutes.

Celiac Dietary Adherence Test (CDAT)
  - This survey asks you about your general symptoms and about any potential recent exposures to gluten.
  - It is 7 questions long.
  - It should take 3 minutes

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Study Treatment START

If we find that you qualify for this study and if you decide that you would like to participate, you will be given your first batch of omeprazole and of the study medication at visit 1.

You will NOT begin to take the omeprazole and study medication immediately following the screening visit, NOR will you begin to complete the questionnaires, bowel movement diary, or study medication log immediately following the screening visit. (Note that if you are already taking omeprazole or another PPI as prescribed by your doctor, you may continue to take that as prescribed following the visit 1.)

Instead, we will give you a call within the few days following your screening visit to let you know when you can begin to take your study medication. When we call you, we will instruct you to begin to take your study medication the following day. On the day that you start your study medication you will also begin to complete your study medication log, bowel movement diary, and study questionnaires. The day that you begin to take your study medication and complete your take-home materials will be called, "Day 1."

You will receive your next batch of the study medication at study Visit 2.

3. Research Procedures: If you qualify to take part in this research study, you will undergo these research procedures:

Visit 2 (Day 14-21) – This visit should take about 1 hour. At this visit:

- If you come to Visit 2 after Day 17 we will ask you to stop taking the study medication, omeprazole (ONLY if you are taking it just for the study), and the questionnaires on Day 17. We will tell you when this is. You will begin taking the medication and questionnaires after Visit 2.

- You will return the bottles of study medication that you used up over the first half of the study.

- You will have an interview during which we will:
  - Review your take-home questionnaires;
  - Review your Bowel Movement Diary;
  - Review your Study Medication Log;
  - Ask you about your symptoms.

- You will have a brief physical examination.

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- Your vital signs (heart rate, blood pressure, temperature, and breathing rate) will be measured.

- You will receive the second batch of study medication.

Visit 3 (Day 35-40) – This visit should take about 1 hour. At this visit:

- You will return the bottles of study medication that you used up over the second half of the study.

- You will have an interview during which we will:
  - Review your take-home questionnaires;
  - Review your Bowel Movement Diary;
  - Review your Study Medication Log;
  - Ask you about your symptoms.

- You will have a brief physical examination.

- Your vital signs (heart rate, blood pressure, temperature, and breathing rate) will be measured.

- You will have a blood sample (about 2 tablespoons or 30 milliliters) collected. This will be used to check:
  - Counts of your red, white and clotting blood cells;
  - Your kidney function, blood acid/base balance, and blood sugar level
  - How active your Celiac Disease is.

4. Monitoring/Follow-Up Procedures. Procedures performed to evaluate the effectiveness and safety of the research procedures are called "monitoring" or "follow-up" procedures. For this research study, the monitoring/follow-up procedures include:

Questionnaires

After Visit 1, you will be asked to complete the CSI questionnaire once on each day that you are taking the study treatment.

You will also be asked to complete the CeD-GSRS and a modified CSI 4 more times, once on Day 7, 17, 24 and 34.

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Daily Bowel Movement Diary

To measure your bowel symptoms, you will also be asked to record every bowel movement that you have during the study.

- You will be required to write down each bowel movement that you have over the entire study period.
- You will also be asked rate each bowel movement using the Bristol Stool Form Scale (BSFS). The BSFS is a 7 point picture/text reference for identifying stool form and consistency. We will show you how to use the BSFS.

Study Medication Log

To keep track of when you take omeprazole/your PPI and your study medication we will ask you to complete a study medication log throughout the study.

- You will be required to record each time that you take omeprazole/your PPI during the study period.
- You will be required to record each time that you take the study medication during the study period.

You will begin to complete the study medication log on the day that you begin taking your study medication (i.e. Day 1).

Phone Calls

You will be called by the study coordinator once every 2-4 days throughout the study. These phone calls will be brief and are meant to help you remember to complete your daily bowel movement diary and questionnaires, and to take your study medication.

A chart with the study procedures is shown below:

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Procedures	**Visit 1 (Day 0)**	**Visit 2 (Day 17-21)**	**Visit 3 (Day 35-40)**
BIDMC Visit	X	X	X
Medical History	X		
Physical Exam	X	X	X
Interview	X	X	X
Vital Signs, Height, Weight	X	X	X
Blood Draw	X		X
Stool Test	X		
Pregnancy Test (if necessary)	X		
Get Study Drug	X	X	
Dietary Assessment	X		
Complete CDAT	X		
Complete CeD-GSRS and CSI	X	←	→
Complete Bowl Movement Diary daily	X	←	→
Complete Study Medication Log daily	X	←	→
Phone Contacts Every 2-4 Days	X	←	→

RISKS AND DISCOMFORTS

As a result of your participation in this study, you are at risk for side effects listed in this section. You should discuss these with the investigator and with your regular doctor if you choose.

Viokace

As a participant in this study you will receive no more than 10 days of Viokace. The common, non-serious potential side-effects associated with Viokace include:

- Diarrhea (experienced by up to 10% of patients)
- Indigestion (experienced by up to 10% of patients)
- Cough (experienced by 6% to 10% of patients)

Serious and rare potential side effects include:

- Distal intestinal obstruction syndrome (rare) – This refers to when thickened stool blocks the intestines causing symptoms that include crampy abdominal pain, vomiting, and a palpable mass in the abdomen.
- Fibrosing colonopathy (rare) – Symptoms of fibrosing colonopathy include abdominal pain, distension, vomiting, and constipation. Fibrosing colonopathy is rare and has been seen in patients on long-term, high-dose administration of Viokace.
- Stricture of the colon (rare) – This refers to when scar tissue forms in a circle around the colon. As it ages and tightens the scar tissue can narrow the intestine and eventually cause blockage. Stricture of the colon is rare and has been seen in patients on long-term, high-dose administration of Viokace.

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- Recurrence of pre-existing cancer – Patients with a prior history of cancer are excluded from this study.
- Allergic reaction/anaphylaxis (rare) – Severe allergic reactions have rarely occurred in adults taking pancreatic enzyme supplements. Symptoms of a severe allergic reaction can include difficulty breathing, dizziness, rash, and itching. Please notify us or your health care provider or call 911 immediately if you experience any of these symptoms.
- Viral exposure (rare) - There is a theoretical risk that Viokace may transmit viruses to humans. This is because Viokace is made using pig pancreatic tissue. This risk has been reduced by testing for and inactivating certain viruses during manufacturing. No cases of transmission of an infectious illness associated with use of medical products made from pig pancreas have been reported to-date.

It is very important that you let us know about any side effects or changes in your health that you experience, whether or not you think they are related to the study medication.

Omeprazole
As a participant in this study you will receive 34 days of omeprazole. The common, non-serious potential side-effects associated with omeprazole include:

- Gastrointestinal:
  - Abdominal pain (experienced by at least 5.2% of patients)
  - Diarrhea (experienced by at least 3.7% of patients)
  - Flatulence (experienced by at least 2.7% of patients)
  - Nausea (experienced by at least 4% of patients)
  - Vomiting (experienced by at least 3.2% of patients)
- Neurologic:
  - Headache (experienced by at least 6.9% of patients)

Serious and rare potential side effects of omeprazole include:

- Skin: Erythema multiforme (skin rash with lesions), Stevens-Johnson syndrome (life threatening skin condition causing a painful rash), Toxic epidermal necrolysis (life threatening skin condition causing skin death)
- Hormones and Metabolsim: Hypomagnesemia (abnormally low level of magnesium in the blood)
- Digestive Tract: Clostridium difficile diarrhea (bacterial infection causing diarrhea, bloating and abdominal pain), Pancreatitis (inflammation of the pancreas)
- Blood: Agranulocytosis (decrease in white blood cells causing chronic bacterial infections), Hemolytic anemia (red blood cell destruction)
- Live: Hepatic encephalopathy (loss of brain function), Hepatic necrosis (acute liver failure), Liver failure

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- Immune System: Anaphylaxis (severe, life threatening allergic reaction)
- Muscles and Skeleton: Fracture of bone, Hip fracture, Rhabdomyolysis (death of muscle fibers which can lead to kidney failure)
- Kidneys: Interstitial nephritis, acute (disorder causing swelling in kidneys)

Risk of Blood Draw
The risks and discomforts of blood drawing from a vein include the possibility of pain or bruising at the site of the blood draw, occasional feeling of lightheadedness, and rarely, infection at the site of the blood draw.

Risks Associated With Surveys/Questionnaires
Some of the questions we will ask as part of this study may make you feel uncomfortable. You may refuse to answer any of the questions and you may take a break at any time during the study. You may stop your participation in the study at any time.

PREGNANCY
Because of the effects of Viokace on the developing fetus is not known, you may not participate in this study if you are pregnant. You will be required to take a pregnancy test to verify that you are not pregnant before receiving your first dose of the study medication at Visit 1.

Furthermore, if you are a woman capable of becoming pregnant, you must agree to use adequate birth control. For the purpose of this study, use of adequate birth control includes one of the following:

1. oral hormonal contraceptives;
2. implanted hormonal contraceptives
3. diaphragm with spermicide;
4. condoms;
5. intra-uterine device;
6. abstinence;
7. male partner vasectomy.

If you believe you have become pregnant while participating in this study, you must inform your study investigators immediately. They will have you take a pregnancy test. If the results demonstrate that you are pregnant, you must withdraw from the study, and the study investigators will ask to monitor your pregnancy. To monitor your pregnancy may include (but not limited to) office visits, blood work, and questionnaires.

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LOSS OF CONFIDENTIALITY

There is the potential for loss of confidentiality by participating in this study. Every effort will be made to protect the confidentiality of your identifiable information. However, if your participation becomes known, it could create a problem or hardship for you depending upon the type of information disclosed.

CONFIDENTIALITY

Information learned from your participation in this study and from your medical record may be reviewed and photocopied by the Food and Drug Administration (FDA) and/or other federal and state regulatory agencies, and by the drug manufacturer, Actavis, accreditation agencies, the Committee on Clinical Investigations, the Human Subjects Protection Office and others involved in research administration of the Beth Israel Deaconess Medical Center with protection of confidentiality so far as permitted by applicable law. Information resulting from this study and from your medical record may be used for research purposes and may be published; however, you will not be identified by name in such publications.

POSSIBLE BENEFITS

It is not possible to predict whether you will benefit directly from participation in this study. However, your participation may help others in the future as a result of knowledge gained from the research.

OTHER AVAILABLE OPTIONS

Taking part in this study is voluntary. Instead of being in this study, you have the following options:

Not participating.

It is important to note that it is possible to get Viokace even if you do not take part in the study. Viokace has not been approved by the FDA for treatment of your condition, however, many doctors in the community commonly prescribe the drug to treat pancreas problems. Please be aware that not all doctors may agree to prescribe this drug for you, and that not all health insurance companies will pay for the drug when it is prescribed for celiac disease.

This research study is not meant to diagnose or treat medical problems not specifically stated in this informed consent document. Participation in this research study does not take the place of routine physical examinations or visits to your regular doctor.

We recommend that you discuss these and other options with the investigator and your regular doctor so that you can make a well-informed decision about participating in this study.

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FUTURE STUDIES

Our research group will do other studies in the future that you may qualify for. We would like your permission to keep your name, phone number, address, and email address on file so that we can contact you about these studies. Please initial one of the lines below to say if you will allow us to do this.

_____ Yes, please keep my name and contact information and contact me about future studies.

_____ No, please do not contact me about future studies.

Even if you say yes you can tell us any time that you don't want to be contacted about studies any more. We will stop right away.

IF YOU DECIDE NOT TO TAKE PART IN THE STUDY

Participation in this study is voluntary. You have the right to decide not to take part in this study. If you choose to participate, you have the right to leave the study at any time. Your decision to not participate will not result in any penalties or loss of benefits to you. The investigators will tell you about new information that may affect your willingness to stay in this study.

If you decide not to participate in the study or decide to leave the study early, your decision will not affect your relationship with the research team or any other individual at Beth Israel Deaconess Medical Center.

INVESTIGATORS RIGHT TO STOP THE STUDY

The investigators have the right to end your participation in this study if they determine that you no longer qualify to take part, or if it would be dangerous for you to continue, or if you do not follow study procedures as directed by the investigators. Beth Israel Deaconess Medical Center or the funding source may stop the study at any time.

COSTS AND/OR PAYMENTS TO YOU

COSTS COVERED BY STUDY

You will not be charged for any tests, procedures, or medications that are part of this research study.

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PAYMENTS TO YOU:

You will receive a voucher for three free hours of parking for each visit that you attend.

COST OF RESEARCH RELATED INJURY:

If you are injured as a direct result of your participation in this study, you should contact the Investigator at the number provided under the section "Who to Call if You Have Questions" in this form. You will be offered the necessary care to treat your injury. We reserve the right to bill your insurance company or the sponsor, if appropriate, for the care you get for the injury. We will try to get these costs paid for, but you may be responsible for some of them. You may be responsible for all co-payments and deductibles required under your insurance. At this time there is no plan to reimburse you for items such as lost wages or lost time from work. By signing this consent form you have not given up any legal rights.

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

AUTHORIZATION FOR USE AND DISCLOSURE OF YOUR PROTECTED HEALTH INFORMATION

As part of this study, we will be collecting, using and sharing with others information about you. Please review this section carefully as it contains information about the federal privacy rules and the use and disclosure of your information.

PROTECTED HEALTH INFORMATION [PHI]

By signing this informed consent document, you are allowing the investigators and other authorized personnel to use [internally at BIDMC] and disclose [to people and organizations outside the BIDMC workforce identified in this consent] health information about you. This may include information about you that already exists (for example: your medical records and other sources of health information, demographic information, the results of any laboratory tests, and mental health records if applicable as well as any new information generated as part of this study. This is your Protected Health Information.

PEOPLE/GROUPS AT BIDMC WHO WILL SHARE AND USE YOUR PROTECTED HEALTH INFORMATION

Your Protected Health Information may be shared with and used by investigators working on this study, including the supporting research team (such as research assistants and coordinators, statisticians, data managers, laboratory personnel, pharmacy personnel, and administrative assistants), and may also be shared and used by other health care providers at BIDMC who have

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PRINCIPAL INVESTIGATOR'S NAME: Ciaran P. Kelly, MD
PROTOCOL #: 2014P000375

treated you in the past and have information relevant to the research, or who provide services to you in connection with the research. Your Protected Health Information may also be shared with the members and staff of the Committee on Clinical Investigations of Beth Israel Deaconess Medical Center, which is responsible for reviewing studies for the protection of the research subjects.

PEOPLE/GROUPS OUTSIDE OF BIDMC WITH WHOM YOUR PROTECTED HEALTH INFORMATION WILL BE SHARED

We will take care to maintain confidentiality and privacy about you and your Protected Health Information. We may share your Protected Health Information with the following groups so that they may carry out their duties related to this study:

- The funding source and/or sponsor of this study (Actavis) and, where applicable, the people and companies that the funding source and/or sponsor use to oversee, administer, or conduct the research (for example, clinical research organizations are companies that are sometimes hired by research sponsors to help manage and run a clinical research study)
- The other hospitals and medical centers taking part in this study and research collaborators at those institutions
- Any external health care providers who provide services to you in connection with this research
- Laboratories not affiliated with BIDMC that are involved in conducting tests related to the research
- Statisticians and other data monitors not affiliated with BIDMC
- The members and staff of any other IRBs (beyond the BIDMC Committee on Clinical Investigations) that oversee the research
- Centralized data collectors
- Your health insurance company
- The Food and Drug Administration [FDA], the Department of Health and Human Services [DHHS], the National Institute of Health [NIH], the Office for Human Research Protections [OHRP], and other federal and state agencies that may have jurisdiction over the research
- Hospital and Clinical Research Accrediting Agencies
- Data and Safety Monitoring boards that oversee this study (if applicable)

Those who receive your Protected Health Information during the course of the research may not be required by the federal privacy regulations to protect it, and they may make further disclosures to others and use your information without being subject to penalties under those laws.

WHY WE ARE USING AND SHARING YOUR PROTECTED HEALTH INFORMATION

The main reason for using and sharing your Protected Health Information is to conduct and oversee the research as described in this Informed Consent Document. There are many other reasons

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beyond the research for which BIDMC may use or disclose your Protected Health Information. Not all of these reasons require your express written authorization. For example, we will use and share your Protected Health Information to ensure that the research meets legal, institutional and accreditation requirements and to conduct public health activities. The various ways in which BIDMC may use and disclose your protected health information without your authorization are explained in a document called the Notice of Privacy Practices. If you have not received a copy of BIDMC's Notice of Privacy Practices, please ask us for one and review it before signing this form. In addition to signing this document, you may also be asked to sign a BIDMC General Agreement form acknowledging that you have received the BIDMC Notice of Privacy Practices.

NO EXPIRATION DATE – RIGHT TO WITHDRAW AUTHORIZATION

Your authorization for the use and disclosure of your Protected Health Information in this Study shall never expire. However, you may withdraw your authorization for the use and disclosure of your Protected Health Information at any time provided you notify the Principal Investigator in writing. If you would like to take back your authorization so that your Protected Health Information can no longer be used in this study, please send a letter notifying the Principal Investigator of your withdrawal of your authorization to

Dr. Ciaran Kelly
330 Brookline Ave.
Boston, MA 02215.

Please be aware that the investigators in this study will not be required to destroy or retrieve any of your Protected Health Information that has already been used or disclosed before the Principal Investigator receives your letter, and they are permitted to continue to use and disclose your previously collected information as necessary to complete the research.

REFUSAL TO SIGN

Your clinical treatment may not be conditioned upon whether you sign the Authorization for Research. However, if you choose not to sign this informed consent document and authorization for the use and disclosure of your Protected Health Information, you will not be allowed to take part in the research study.

RIGHT TO ACCESS AND COPY YOUR PHI

If you wish to review or copy your Protected Health Information as it is made part of your medical record, you may do so after the completion or termination of the study by sending a letter to the Principal Investigator requesting a copy of your Protected Health Information. You may not be allowed to inspect or copy your Protected Health Information until this study is completed or terminated.

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ADDITIONAL CONTACT FOR QUESTIONS OR CONCERNS

You may contact the Human Subjects Protection Office at [617] 975-8500 in the event that you would like to obtain information or to offer input about the research study. This office is independent of the investigator or investigator's research staff and can also assist with questions relating to your rights as a participant in research, which may include questions, concerns or complaints about your participation in the study.

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BETH ISRAEL DEACONESS MEDICAL CENTER
APPROVED BY THE
COMMITTEE ON CLINICAL INVESTIGATIONS
07/23/2018
APPROVAL EXPIRATION DATE

THE FOLLOWING PARAGRAPHS CONTAIN SOME STANDARD INFORMATION WHICH GENERALLY APPLIES TO INDIVIDUALS PARTICIPATING IN A RESEARCH STUDY.

CONSENT FORM FOR CLINICAL RESEARCH

I have read the previous page[s] of the consent form and the investigator has explained the details of the study. I understand that I am free to ask additional questions.

If I wish additional information regarding this research and my rights as a research subject, or if I believe I have been harmed by this study, I may contact the Human Subjects Protection Office (HSPO).

I am aware that this is a research project and that unforeseen side effects may occur.

I understand that the Beth Israel Deaconess Medical Center has no formal program for compensating patients for medical injuries arising from this research. Medical treatment will be provided for injuries at the usual charge to me or to my insurer unless payment is otherwise provided for in this consent form.

I understand that participation in this study is voluntary and I may refuse to participate or may discontinue participation at any time without penalty, loss of benefits, or prejudice to the quality of care which I will receive.

I acknowledge that no guarantees have been made to me regarding the results of the treatment involved in this study, and I consent to participate in the study and have been given a copy of this form.

_____ _____

Signature of Subject or Legally Authorized Representative (Parent if the subject is a minor) — Date

_____

Relationship of Legally Authorized Representative to Subject

The subject has been given the opportunity to read this consent form and to ask questions before signing, and has been given a copy.

_____

SIGNATURE OF INVESTIGATOR/Co-Investigator DATE

_____

PRINT INVESTIGATOR'S/Co-Investigator's NAME

A signing co-investigator must be listed on the study's approved Research Staffing Form at the time of consent.

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THE FOLLOWING SECTIONS ARE NOT NEEDED FOR ALL STUDIES AND SHOULD BE UTILIZED AS INDICATED:

If the subject is able to speak and understand English but is not able to read or write

I was present during the entire oral presentation of the informed consent and witnessed the subject's agreement to participate in the study.

Signature of Witness: _____

Printed Name of Witness: _____

Date: _____

If the subject is able to understand English but is not physically able to read or write or see

I was present during the entire oral presentation of the informed consent and witnessed the subject's agreement to participate in the study.

Signature of Witness: _____

Printed Name of Witness: _____

Date: _____

If the subject is not English speaking and signed the translated Short Form in lieu of the English consent document.

As someone who understands both English and the language spoken by the subject, I interpreted, in the subject's language, the researcher's presentation of the English consent form. The subject was given the opportunity to ask questions.

Signature of Interpreter: _____

Printed name of Interpreter: _____

Date: _____