INFORMED CONSENT AND RESEARCH AUTHORIZATION

A 3 day open label, Pilot study followed by an-up to 21 day double-blind study to assess stool frequency of COVID + patients treated with oral bismuth subsalicylate (Pepto-Bismol): SABER-C (Specific Administration of Bismuth for Early Recovery of COVID-19)

Summary Information

The purpose of this study is evaluate the tolerance and efficacy of Bismuth subsalicylate (BSS) and Standard of Care (SOC) in mild/moderate severity COV+ population as defined by QRT-PCR (type of test for Covid-19) of saliva samples compared to SOC and placebo and compare this efficacy to patients treated with SOC (placebo) alone.

Participation in the first open-label group will last about 3 days. Participants in groups 2 and 3 will be in this study for about 3 weeks. Participants will provide medical history information, and provide stool samples and undergo Covid-19 testing.

There are risks to this study that are described in this document. The most common risks include anxiety, drowsiness and gastrointestinal problems.

Participation in this study may provide information in the treatment of Covid-19 for future patients.

If you are interested in learning more about this study, please continue to read below.

Introduction and Background Information

You are invited to take part in a research study because you have Covid-19.

This pilot study will be conducted in the United States at 1 study center. A total of 60 local participants are expected to be enrolled into the 3 arms of the study. Study one will consist of 10 open label (receive study drug) Covid-19 participants with mild/moderate disease. The second and third studies will be double-blind (participants will not know if they are receiving study drug or placebo) placebo controlled studies of 25 patients each, the first with mild/moderate disease and the third will consist of participants who are Covid-19 plus mild to moderate in severity with documented Covid-19 status by QRT-PCR testing for 14 days or more.

The study is being conducted under the direction of Dr. Bruce Yacyshyn at the University of Louisville. About 60 local participants will be invited to take part in this research. Procter & Gamble will supply the study medication.

Purpose

The primary purpose of this study is to see if treatment with the drug BSS such as pepto bismol given to participants with mild/moderate Covid-19 decreases daily stool frequency compared to participants taking placebo.

Procedures

If you are in the open-label group, your participation will last about 3 days, If you are in group 2 or 3, your participation in this study will last for about 3 weeks. If you consent to participate, you will have the following procedures while you are in this study.

Screening visit (Day -1 to 0)

For Groups 1 and 2, screening will occur at the time the diagnosis of Covid-19 is confirmed from a doctor's office, drive through location or hospital for the first study. For group 3, screening will occur at 2 weeks or more of documented Covid-19 status.

The first 10 participants will be treated with open label BSS for 3 days. For groups 2 and 3 (groups of 25) will be randomized to either placebo or BSS. The participants will be assigned by coin-toss, heads to placebo and tails to active treatment by a member of the research team not directly involved in the clinical trial.

The following will be obtained to determine patient eligibility:

- Written informed consent
- Demographic data
- Medication history for the previous 30 days
- Medical history including daily stool frequency;
- Social history (alcohol, tobacco, drugs)
- Height and Weight (self-reported)
- Vital signs (temperature, pulse, blood pressure measured after sitting for 5 minutes)
- Collection of serious, procedure-related non-treatment emergent AEs
- Reminder for patients to avoid the use of protocol excluded medications for the duration of the study

Baseline Visit/Dosing (Day 1)

The baseline visit should occur within 2 days after the screening assessment. The following procedures will be performed at this visit:

- Medical and medication history update to include any changes or new medications since screening
- Weight (self-reported)
- Recording of vital signs (temperature, pulse, oxygen saturation, blood pressure within 1 week of screening visit)
- Saliva sample
- Stool sample
- Collection of serious, study procedure-related, nontreatment-emergent AEs
- Review dosing instructions with the patient and stress the importance of compliance
- First dose of study medication
- Schedule all daily study visits
- Recording of daily stool frequency

Daily Visits (1+/-21 Days)

The visits may occur daily up to Day 21 (whichever comes first), or until the patient tests Covid-19 negative by QRT-PCR. The following procedures will be performed at this visit:

- Medication history updated to include any changes or new medications since baseline;
- Recording of daily stool frequency;
- Patient daily testing for COVID-19 via saliva;
- Assessment of adverse events
- Stool specimen collection at week 1 and week 2.

Treatment Group	Dose Regimen
BSS open label	Take 2 chewable tablets up to 4 times a day by mouth for 3 days.
Mild/Moderate Covid-19 newly diagnosed BSS or Placebo	Take 2 chewable tablets by mouth up to 4 times a day for up to 21 days or until Covid-19 is negative by QRT-PCR test
Mild/Moderate Covid-19, diagnosed at least 14 days prior, and still Covid-19 positive BSS or Placebo	Take 2 chewable tablets by mouth up to 4 times a day for up to 21 days or until Covid-19 is negative by QRT-PCR test

- Each tablets contain 262 mg; two tablets should be taken every 6 hours up to 4 times a day
- The maximum dose of BSS is 8 tablets per day – do not take more than 8 tablets a day
- Chew or dissolve in mouth
- Store study medication in a closed container at room temperature away from heat, moisture, and direct light out of reach of children and pets. Do not freeze.

Do not begin any new medications including prescription and over the counter medications without first tell your study doctor.

The following is a list of prohibited medications while participating in this study:

- Corticosteroids (including oral, IV, IM, or rectally administered) except those used in the treatment of COVID-19 infection
- Chemotherapy agents
- Anti-diarrheals and anti-spasmodics (excluding prescribed opiates)
- Any investigational or marketed drugs that are known to interfere with the evaluation of the study medication. Vaccines are not exclusionary as they do not interfere with the mechanism of the study drug.

Your research test results will be shared with you.

The use of your samples may result in commercial profit. You will no longer have any ownership in the samples. You will not be compensated for the use of your samples other than what is described in this consent form nor will you be able to have the samples returned to you.

Future Research

Your samples and/or data will be stored and shared for future research without additional informed consent if identifiable private information, such as your name and medical record number, are removed. If identifying information is removed from your samples and/or data, the samples and/or data may be used for future research studies or given to another investigator for future research studies without additional consent from you.

Potential Risks

The following details the known risks related to Bismuth Subsalicylate:

Very Common (10% or more): Black stool (this is temporary and will go away when medication is stopped)
Common (1% to 10%): Black tongue (this is temporary and will go away when medication is stopped)

<table>
<tr><td colspan="2">Rare (less than 0.1%): Myclonic encephalopathy (a rare epilepsy syndrome seen in neonates and infants)</td></tr>
<tr><td>Frequency not reported:
Weakness
Fatigue
Depression
Anxiety
Irritability
Insomnia
Unsteady gait
Loss of memory
Jerky movements</td><td>Mental confusion
Disorientation
Difficulty in walking and speaking
Tremor
Myoclonic jerks
incontinence
Motor incoordination
Salicylism (a toxic condition produced by the excessive intake of salicylic acid or salicylates and marked by ringing in the ears, nausea, and vomiting)</td></tr>
<tr><td>Signs of Overdose:
Loss of hearing
Extreme drowsiness
Fast breathing
Confusion</td><td>Uncommon and serious:
Ringing in ears – stop taking and call study doctor</td></tr>
</table>

Reye's syndrome

Although Reye's has never been shown to be caused by BSS children and teenagers who have or are recovering from chicken pox or flu-like symptoms should not use this product. When using this product, if changes in behavior with nausea and vomiting occur, consult a doctor because these symptoms could be an early sign of Reye's syndrome, a rare but serious illness.

In addition, you may suffer harms that we have not seen before.

Possible Pregnancy Risks

You should discuss pregnancy risks with your doctor before signing this consent form. It is not known whether bismuth subsalicylate is a hazard to a pregnant woman, the developing (unborn) child, or nursing infant. You may not take part in this study if you are breastfeeding, are pregnant, or think that you may be pregnant, or are trying to get pregnant. Before starting this research study, females able to have children will be asked if to the best of their knowledge they are or could be pregnant.

Benefits

You may or may not benefit personally by participating in this study. The information collected may not benefit you directly; however, the information may be helpful to others.

Alternatives

Instead of taking part in this study, you could choose not to participate

Research Related Injury

If you are injured by being in this research study, the study doctor will arrange for you to get medical treatment. The sponsor, the study site, or your study doctor has not set aside money to pay for treatment of any injury. You and your insurance will be billed for the treatment of these injuries.

Before you agree to take part in this research study you should find out whether your insurance will cover an injury in this kind of research. You should talk to the study doctor or staff about this. If you are injured, there is no money set aside for lost wages, discomfort, disability, etc. You do not give up your legal rights by signing this form. If you think you have a research related injury, please call your study doctor at 502-588-4600.

Payment

You will receive a prepaid card for your time, inconvenience or expenses while you are in this study. You will receive a card each week of your participation as follows:

- $50.00 for Screening through Day 7
- $50.00 Day 8 through 14
- $50.00 Day 15 through 21

The maximum you may receive during the study is $150.00. You will only be paid for those visits which have been completed.

Additional reimbursement for travel costs may also be provided. You should ask your study doctor if you have any questions about what additional travel costs might be reimbursed.

Because you will be paid to be in the study, the University of Louisville may collect your name, address, social security number, and keep records of how much you are paid. You may or may not be sent a Form 1099 by the University. This will only happen if you are paid $600 or more in one year by the University. This will not include payments you may receive as reimbursement, for example mileage reimbursement. We are required by the Internal Revenue Service to collect this information and you may need to report the payment as income on your taxes.

You can still be in the study even if you don't want to be paid.

Costs

You will not be billed for the following visits, tests, medications, and procedures that are done for this research study: The charges for these items will be paid for by the Sponsor.

- Covid-19 testing and stool sample testing
- Study medications

You or your insurance company will be billed for all office visits, tests, medications and procedures that are part of your routine medical care. You will be responsible for paying your co-pay that is associated with any office visit, test, medication or procedure. Some insurance companies will not pay for medical bills for people who participate in a research study. It is your responsibility to find out what costs, if any, your insurance company will cover before taking part in the study. If you need help finding out what your insurance company will cover, please ask your study doctor for assistance. If your insurance company does not pay for your bills associated with this study, you will be responsible for paying them.

HIPAA Research Authorization

The Health Insurance Portability and Accountability Act of 1996 (HIPAA) provides federal safeguards for your protected health information (PHI). State and federal privacy laws also may also require your health information to be protected. By signing this form you provide your permission, called your "authorization," for the use and disclosure of PHI.

If you sign this form, the research team working on this study will use and share your health information to answer the research questions described in this document, and to make sure that the

research was done correctly. This includes things learned from the procedures described in this consent form. They may also collect other information including your name, address, date of birth, medical history, and other information from your medical records from this institution and other institutions involved with this research, as well as from your other healthcare providers (which may include information about HIV status, drug, alcohol or sexually transmitted disease treatment, genetic test results, or mental health treatment). Those persons who receive your health information may not be required by Federal privacy laws (such as the HIPAA Privacy Rule) to protect it and may share your information with others without your permission, if permitted by laws governing them.

In most cases, the health information that identifies you can be used or shared by the research team only if you give your permission by signing this form. Your health information may be shared with a public health authority that is authorized by law to collect or receive such information for the purpose of preventing or controlling disease, injury, or disability, and conducting public health surveillance, investigations or interventions.

The time period when information can be used or shared ends when all activities related to this study are completed.

Some information collected about you only for this research study may be kept in a research study record separate from your medical record, and some research information may also be part of your medical record. You will not have access to this research information until the end of the study. However, it will be available to your physicians if needed for your care.

You do not have to sign this form. If you do not sign this form, you may not participate in the study and health information that identifies you will not be shared for research purposes.

Revocation of Research Authorization

You may withdraw the authorization you have given to use and share your protected health information at any time. This means you can tell us to stop using and sharing your protected health information. If you withdraw/revoke your authorization:

- We will stop collecting information about you.
- You may not withdraw information that we had before you told us to stop.
    - We may already have used it or shared it.
    - We may need it to complete the research.
    - We may need it to search records that are available to the public.
- Staff may ask your permission to follow-up with you if there is a medical reason to do so.

To withdraw your authorization, you will be requested to complete a written "Revocation of Research Authorization" form located at the end of this document. You may also obtain a copy from your study doctor, designated personnel or from the Human Subjects Protections Program Office website (https://louisville.edu/research/humansubjects/templates/biomedical-forms).

Information Available on ClinicalTrials.gov

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. The website will include a summary of the results of the clinical trial.

Confidentiality

Total privacy cannot be guaranteed. We will protect your privacy to the extent permitted by law. If the results from this study are published, your name will not be made public. Once your information leaves our institution, we cannot promise that others will keep it private.

Your information may be shared with the following:

- The sponsor, Dr. Bruce Yacyshyn and others hired by the sponsor to oversee the research
- Organizations that provide funding at any time for the conduct of the research.
- The University of Louisville Institutional Review Board, Human Subjects Protection Program Office, Privacy Office, others involved in research administration and research and legal compliance at the University, and others contracted by the University for ensuring human participants safety or research and legal compliance
- The local research team
- People who are responsible for research, compliance and HIPAA/privacy oversight at the institutions where the research is conducted
- People responsible for billing, sending and receiving payments related to your participation in the study
- Applicable government agencies, such as:
    - Office for Human Research Protections
    - Office of Civil Rights
    - Food and Drug Administration
- Those responsible for data safety monitoring related to the study

Security

The data collected about you by Institution will be kept private and secure in a secured location. The information will be kept in a limited access area in a locked office. All computers in the office are password protected and enabled with encryption programs.

Voluntary Participation

Taking part in this study is completely voluntary. You may choose not to take part at all. If you decide not to be in this study, you won't be penalized or lose any benefits for which you qualify. If you decide to be in this study, you may change your mind and stop taking part at any time. If you decide to stop taking part, you won't be penalized or lose any benefits for which you qualify. You will be told about any new information learned during the study that could affect your decision to continue in the study.

Termination

You may decide to stop taking part in this study at any time. Your study doctor or the study sponsor has the right to stop this study at any point. Your study doctor may take you out of this study with or without your okay. Reasons why this may occur include:

- Patient's request
- Complicated COVID-19 infection that requires intubation;
- The Investigator determines that continued participation may cause harm. The Investigator always has the right to withdraw patients in the event of adverse events (AEs), intercurrent illnesses, protocol violations, laboratory abnormalities, treatment failure, or for administrative or other reasons
- The patient becomes pregnant the treatment code will be revealed and the patient will be referred to an obstetrician and followed throughout the remainder of the study period

If you are withdrawn from the study during the treatment period you will be asked to undergo all end-of-treatment (Week 12) procedures at the time of withdrawal, regardless of the length of treatment received. Participants withdrawn from the study for medical reasons will remain under medical supervision until the Investigator deems the condition to be resolved or stabilized.

Participation in Other Research Studies

You may not take part in this study if you are currently in another research study. It is important to let your doctor know if you are in another research study.

Research Participant's Rights

If you have any questions about your rights as a research participant, you may call the Human Subjects Protection Program Office at (502) 852-5188. You may discuss any questions about your rights as a research participant, in private, with a member of the Institutional Review Board (IRB). The IRB is an independent committee made up of people from the University community, staff of the institutions, as well as people from the community not connected with these institutions. The IRB has approved the participation of human participants in this research study.

Questions, Concerns and Complaints

If you have any questions about the research study, please contact **(502-588-4600)**

If you have concerns or complaints about the research or research staff and you do not wish to give your name, you may call this toll free number: 1-877-852-1167. This is a 24 hour hot line answered by people who do not work at the University of Louisville.

Acknowledgment and Signatures

This document tells you what will happen during the study if you choose to take part. Your signature and date indicates that this study has been explained to you, that your questions have been answered, and that you agree to take part in the study. You are not giving up any legal rights to which you are entitled by signing this informed consent document though you are providing your authorization as outlined in this informed consent document. You will be given a copy of this consent form to keep for your records.

Participant Name (Please Print)	Signature of Participant	Date Signed
Printed Name of Person Explaining Consent Form	Signature of Person Explaining Consent Form (if other than the Investigator)	Date Signed
Printed Name of Investigator (PI, Sub-I, or Co-I)	Signature of Investigator (PI, Sub-I, or Co-I)	Date Signed

24 hour phone number for participants to call for questions: 502-588-4600

Industry Contracts/Grant number: G3282

Investigator(s) name & address:

Dr. Bruce Yacyshyn
University of Louisville
MedCenter One
501 E. Broadway, Suite 210
Louisville, KY 40202

Dr. James Collins
CTRB
Microbiology & Immunology
505 S. Hancock, Room 607
Louisville, KY 40202

Site(s) where study is to be conducted:

University of Louisville Hospital
530 S. Jackson St.
Louisville, KY 40202

U of L Health – Jewish Hospital
200 Abraham Flexner Way
Louisville, KY 40202

UofL 620 Garage
620 E. Mohammad Ali (entrance on Clay Street)
Louisville, KY 40202

University of Louisville Clinical Trials Unit (drug storage)
401 E. Chestnut St., Suite 460
Louisville, KY 40202

REVOCATION OF AUTHORIZATION FOR USE AND DISCLOSURE OF YOUR HEALTH INFORMATION FOR RESEARCH

Return To:
PI Address: Clinical Trials Unit, 501 E. Broadway, Suite 210, Louisville, KY 40202
PI Phone: 502-852-6189

OR

Institutional Review Board
MedCenter One, Suite 200
501 E. Broadway
Louisville, KY 40202

Do not sign this letter unless you are withdrawing from this research.

To Whom It May Concern:

I would like to discontinue the use of my data in this research study. I understand that health information already collected will continue to be used as discussed in the Authorization I signed when joining the study.

Your options are (***choose one***):

☐ **Withdraw from Study & Discontinue Authorization:**
Discontinue my authorization for the future use and disclosure of protected health information. In some instances, the research team may need to use your information even after you discontinue your authorization, for example, to notify you or government agencies of any health or safety concerns that were identified as part of your study participation.

☐ **Withdraw from Study, but Continue Authorization:**
Allow the research team to continue collecting information from me and my personal health information. This would be done only as needed to support the goals of the study and would not be used for purposes other than those already described in the research authorization.

_____

Printed Name and Signature of Participant — Date Signed

_____

Participant's Address — Participant's Phone Number

Optional:
I am ending my participation in this study because: _____

_____