MC200404

Phase Ib Open-label Study to Evaluate Safety, Tolerability, Immunogenicity and Efficacy of Multiple Subcutaneous Injections of PolyPEPI1018 Vaccine as an Add-on Immunotherapy to TAS-102 in Late-stage Metastatic Colorectal Cancer Subjects (OBERTO-201)

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RESEARCH PARTICIPANT CONSENT AND PRIVACY AUTHORIZATION FORM

Study Title: MC200404, Phase Ib Open-label Study to Evaluate Safety, Tolerability, Immunogenicity and Efficacy of Multiple Subcutaneous Injections of PolyPEPI1018 Vaccine as an Add-on Immunotherapy to TAS-102 in Late-stage Metastatic Colorectal Cancer Subjects (OBERTO-201)

IRB#: 20-013410

Principal Investigator: Joleen Hubbard, MD and Colleagues

Key Study Information

This section provides a brief summary of the study. It is important for you to understand why the research is being done and what it will involve before you decide. **Please take the time to read the entire consent form carefully and talk to a member of the research team before making your decision.** You should not sign this form if you have any questions that have not been answered.	
It's Your Choice	This is a research study. Being in this research study is your choice; you do not have to participate. If you decide to join, you can still stop at any time. You should only participate if you want to do so. You will not lose any services, benefits or rights you would normally have if you choose not to take part.
Research Purpose	The purpose of this research is to find out more about the combination of the standard of care treatment of TAS-102 and the experimental peptide vaccine, PolyPEPI1018 for patients with metastatic colon or rectal cancer. We want to learn more about the side effects of combination, and to collect information on how your cancer responds to this combination. The combination of TAS-102 and PolyPEPI1018 is investigational and is not approved by the Food and Drug Administration (FDA). However, TAS-102 is FDA approved for treatment of metastatic colorectal cancer.

What's Involved	To see if you can be in the study, you will need to have some screening tests and procedures. If you have already had some of these done at a recent doctor's office visit, then the tests may not need to be done again If you are a person of childbearing potential, a pregnancy test will be done before you start treatment. If you qualify for the study, you will take TAS-102 by mouth on Days 1-5 and 8-12 and PolyPEPI1018 is given every 2 weeks by an injection under your skin. You will receive treatment PolyPEPI1018 plus TAS-102 for up to 7 months. During the treatment, you will return to Mayo Clinic every 14 days. After treatment with PolyPEPI1018 is done, we will ask you to return in 14 days for some tests and procedures and to meet with your study doctor. After this, we will contact you every 3 months to see how you are doing until 1 year after going on the study. During these visits, your participation also includes physical exams; review of your side effects; routine blood tests; scans to follow your tumor size; mandatory research blood and tissue collections by Ultrasound or CT Guidance. If you are a female of childbearing potential, a pregnancy test will be required every 8 weeks. Both males and females will need to use an effective form of birth control during study and for 3 months after the last vaccination. These visits are similar to what you would have even if you aren't on the study.
Key Information	There are risks to the study drugs that are described later in this document. Some of the very common side effects of TAS-102 are nausea, vomiting, diarrhea, lowered white blood cell count, lowered red blood cell count (anemia), lowered platelet count, tiredness, loss of appetite, and fever. Some of the common side effects of the peptide vaccine, PolyPEPI1018, are redness and swelling at the injection sites. With this investigational treatment, some side effects may not be known. Side effects may range from mild to life-threatening. It is important to review the risk section carefully.

	The costs related to this research such as the peptide vaccine, PolyPEPI1018 and research blood and tissue collections will be paid for by the research study. However, you or your insurance company will need to pay for the tests, procedures, and any other medications that are a part of standard of care. If you get injured because of study participation, we will help you get treatment; however, the costs for this care will be billed to you or your insurance. We do not know whether this drug combination will make your colorectal cancer better or not. What we learn from this study will help doctors know more about TAS-102 and PolyPEPI1018 as a treatment for metastatic colon and rectal cancer. You do not need to be in this study to receive treatment for your colorectal cancer. Your doctor will discuss what your options are.
Learn More	If you are interested in learning more about this study, read the rest of this form carefully. The information in this form will help you decide if you want to participate in this research or not. A member of our research team will talk with you about taking part in this study before you sign this form. If you have questions at any time, please ask us.

Making Your Decision

Taking part in research is your decision. Take your time to decide. Feel free to discuss the study with your family, friends, and healthcare provider before you make your decision. Taking part in this study is completely voluntary and you do not have to participate.

If you decide to take part in this research study, you will sign this consent form to show that you want to take part. We will give you either a printed or electronic copy of this form to keep. A copy of this form will be put in your medical record.

For purposes of this form, Mayo Clinic refers to Mayo Clinic in Arizona, Florida and Rochester, Minnesota; Mayo Clinic Health System; and all owned and affiliated clinics, hospitals, and entities.

Contact Information

If you have questions about …	You can contact …
▪ Study tests and procedures ▪ Materials you receive ▪ Research-related appointments ▪ Research-related concern or complaint ▪ Research-related injuries or emergencies ▪ Withdrawing from the research study	**Principal Investigator:** Joleen Hubbard, MD **Phone:** (507) 293-0487 **Institution Name and Address:** Mayo Clinic Rochester 200 First Street SW Rochester, MN 55905
▪ Rights of a research participant	**Mayo Clinic Institutional Review Board (IRB)** **Phone:** (507) 266-4000 **Toll-Free:** (866) 273-4681
▪ Rights of a research participant ▪ Any research-related concern or complaint ▪ Use of your Protected Health Information ▪ Stopping your authorization to use your Protected Health Information ▪ Withdrawing from the research study	**Research Subject Advocate (RSA)** **(The RSA is independent of the Study Team)** **Phone:** (507) 266-9372 **Toll-Free:** (866) 273-4681 **E-mail:** researchsubjectadvocate@mayo.edu
▪ Billing or insurance related to this research study	**Patient Account Services** **Toll-Free:** (844) 217-9591

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

A description of this research study will be available on https://www.mayoclinic.org and https://www.mayo.edu/research/clinical-trials. These Web sites will not include information that can identify you. You can search these Web sites at any time.

A description of this research study will also be available on https://www.treosbio.com.This Web site will not include information that can identify you. You can search this Web site at any time.

Why are you being asked to take part in this research study?

You are being asked to take part in this research study because you have metastatic colon or rectal cancer and you have received prior treatments for this cancer that have failed to work.

The plan is to have about 15 people take part in this study at Mayo Clinic.

Why is this research study being done?

In this study we want to find out more about the combination of the standard of care treatment of TAS-102 and the experimental peptide vaccine, PolyPEPI1018. We want to learn more about the side effects of combination, and to collect information on how your cancer responds to this combination.

PolyPEPI1018 peptide vaccine is used to immunize against proteins present on the surface of tumor cells. In a high number of patients, this vaccine will activate the body's immune cells, called T cells. T cells fight infections and can also kill cancer cells.

Everyone in this study will receive TAS-102 and PolyPEPI1018 which in combination is investigational and isn't approved by the U.S. Food and Drug Administration (FDA). However, TAS-102 is FDA approved for treatment of metastatic colorectal cancer. The FDA has allowed the use of this combination in this research study.

Information you should know

Who is Funding the Study?

The Department of Defense is funding this study and will pay the institution to cover costs related to running the study. Mayo Clinic is also funding the study and will cover some of the costs related to running the study. Treos Bio ZRT will supply the peptide vaccine, PolyPEPI1018, for the study.

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Information Regarding Conflict of Interest:

Your healthcare provider may be referring you to this research study. If your healthcare provider is also an investigator on this study, there is the chance that his or her responsibilities for the study could influence his or her recommendation for your participation. If you prefer, your healthcare provider will be happy to refer you to another investigator on the research study team for you to decide if you want to participate in the study and to see you for the research study activities while you are in the study.

How long will you be in this research study?

It will take you about 1 year to complete this research study. During treatment, we will ask you to return every 2 weeks (15 visits). After you finish treatment, we will ask you to return in 14 days from your last injection (1 visit).

After you finish treatment or your disease gets worse, we will review your medical record, contact you or your local physician every 3 months until 1 year from the time you enrolled on the study to see how you are doing.

What will happen to you while you are in this research study?

If you agree and you are eligible for the study, you will receive up to 7 cycles of treatment with TAS-102 and PolyPEPI1018. Each treatment cycle lasts for 28 days.

Screening Visit:
During the Screening visit, we will do some tests and procedures to see if you are eligible to take part in the research study. Your doctor will review the results of these tests and procedures. If you are not eligible, your doctor will tell you why. At this visit, we will:

- Ask you about your medical and medication history
- Give you a physical exam, including height and weight
- Ask you about your current medications
- Ask you about your activity level and symptoms
- Take your vital signs (blood pressure, pulse, respirations, and oral temperature)
- Collect a urine pregnancy test; if you are a person of childbearing potential. If this is positive or cannot be confirmed as negative, we will draw a blood pregnancy test
- Draw routine blood tests to check your hematology and chemistry blood counts

- Draw tumor biomarkers (CEA) found in your blood.
- Collect a urinalysis test
- Perform a CT, PET/CT, or MRI scan to record your tumor size.

If you have already had some of these tests and procedures as part of regular cancer care, it may not be necessary for them to be done again. Your doctor will let you know.

If you are eligible for the study, the following will be done for research purposes to help us understand how your immune system responds to the study treatment.

- Have a CT or Ultrasound (US) guided biopsy to collect mandatory research tissue samples to look for the presence of specific cells called tumor infiltrating lymphocytes or TILs. For this biopsy, x-rays are used to guide the needle placement during the biopsy procedure. The biopsy will be done during screening, prior to Cycle 4.
- Collect mandatory research blood samples (about 3 Tablespoons (45mLs) each time) prior to the first treatment, every 8 weeks, and at your last study visit.
- Collect research buccal swab to obtain DNA cells from the inside of your cheek. This is done prior to your first treatment.

Tests done only for research purposes are not meant to provide clinical information or help care for you. The results are only important for research. Therefore, the results of tests done with your information and samples will not be provided to you. In the rare event that a finding might affect the health of you or your family, we will contact you and you can choose whether to receive or refuse the information. If you decide to follow up and further medical testing or care is needed, the costs will be billed to you or your insurance.

All patients will receive PolyPEPI1018 injections every 2 weeks in the outpatient treatment area on Gonda 10. A needle is used to give the vaccine injection under your skin (subcutaneous). The vaccine will be given in 4 different areas of your body each time. We will ask you to watch for side effects at each of these sites and complete an adverse event diary. All patients will also take TAS102 twice a day by mouth on Days 1-5 and 8-12 of each treatment cycle. You will be given a prescription to fill prior to Day 1.

<u>During Treatment (Cycles 1-7)</u>:

Day 1 of each cycle, we will:

- Give you a physical exam, including weight
- Ask about your activity level and symptoms or side effects
- Ask about your current medications
- Take your vital signs (blood pressure, pulse, respirations, and oral temperature)
- Draw routine blood tests to check your hematology and chemistry blood counts

- Receive the study vaccine beneath your skin in 4 injection sites. You will need to stay at the clinic for at least 1 hour after the last injection to see if there are any changes in the areas where you received the vaccine.
- Take TAS-102 oral medication twice a day on Days 1-5 and 8-12 as instructed.
- Ask you to complete an adverse event diary and a medication diary and return them at your next doctor's appointment

In addition:
On Cycle 1 Day 1 only, we will:

- Collect a mandatory buccal swab for research
- Collect mandatory research blood samples (about 3 Tablespoons (45 mLs))
- If a CT, PET/CT or MRI scan hasn't been done within 21 days prior to Cycle 1 Day 1 treatment, another scan will need to be done and the study will pay for it. The CT scan uses X-rays to create images of the bones and internal organs of your body. The PET scan uses radioactive material to create images of your internal organs.
- If you are a person of childbearing potential, a urine pregnancy test will be collected within 48 hours prior to the CT or US guided biopsy, if needed. If this is positive or cannot be confirmed as negative, we will draw a blood pregnancy test.
- Collect a urine pregnancy test; if you are a person of childbearing potential. If this is positive or cannot be confirmed as negative, we will draw a blood pregnancy test
- Collect a urinalysis test
- Collect mandatory research blood samples (about 3 Tablespoons (45 mLs) each time)
- Perform a CT, PET/CT, or MRI scan to record your tumor size

On Day 1 of Cycles 3, 5, and 7, we will:

- Collect a urine pregnancy test; if you are a person of childbearing potential. If this is positive or cannot be confirmed as negative, we will draw a blood pregnancy test
- Collect a urinalysis test
- Collect mandatory research blood samples (about 3 Tablespoons (45 mLs) each time)
- Perform a CT, PET/CT, or MRI scan to record your tumor size
- Draw tumor biomarkers (CEA) found in your blood

On Cycle 4 Day 1, we will:

- Perform a mandatory CT or US guided biopsy performed for research

Day 15 of each cycle, we will:

- Ask about your current medications
- Take your vital signs (blood pressure, pulse, respirations, and oral temperature)
- Draw routine blood tests to check your hematology blood counts

- Receive the study vaccine beneath your skin in 4 injection sites. You will need to stay at the clinic for at least 1 hour after the last injection to see if there are any changes in the areas where you received the vaccine.
- Bring back your completed adverse event diary and medication diary

End of Treatment Visit:
14 days from the last vaccine administration, we will

- Give you a physical exam, including weight
- Ask about your activity level and side effects
- Ask about your current medications
- Take your vital signs (blood pressure, pulse, respirations, and oral temperature)
- Draw routine blood tests to check your hematology and chemistry blood counts
- Bring back your completed adverse event diary and medication diary to your doctor's appointment

What are the possible risks or discomforts from being in this research study?

With this investigational treatment, some side effects may not be known. Side effects may range from mild to life-threatening. Other drugs may be given to make side effects less serious and less uncomfortable. Talk to your healthcare provider about side effects and ask any other questions. All drugs may cause certain side effects and discomforts. As with any medication, allergic reactions are possible. There may also be a risk of death

PolyPEPI1018 risks:
The following list includes effects that both may or may have not been related to PolyPEPI1018 and were reported in the previous clinical trial when patients got parallel cytostatic and PolyPEPI1018 vaccine treatment. You may experience some other side effects that are not listed. However, this is not a complete list because rare events of a non-severe nature are not listed; however, rare events of a severe nature are listed. Though many of the side effects reported were mild to moderate in nature, some side effects may become severe and life-threatening and could potentially worsen, leading to death.

Likely risks, occurring in > 20% of participants:

- Injection site reactions (some pain, redness, swelling, burning sensation etc.) and fatigue.

Common risks, occurring in 3 -20% of participants:

- Anemia (lowering of your red blood cells. Red blood cells are important for carrying oxygen in the blood and decreased amounts can lead to symptoms such as tiredness or shortness of breath
- Arthralgia (joint pain)
- Constipation
- Erythema-multiforme (skin reaction often caused by an infection or medication)
- Myalgia (muscle pain)
- Noninfective encephalitis (inflammation of the brain)
- Superficial thrombophlebitis (blood clot just below the surface of your skin)
- Vomiting

Severe, occurring in <20% of participants:

- Non-infectious acute encephalitis (inflammation of the brain)
- Pulmonary embolism (blood clot in your lung)
- Abdominal pain
- Metastatic colon cancer progression
- Intestinal obstruction (blocking of your small or large colon)
- Neutrophil count decreased (lowering of your blood cell counts that are important in helping people fight off or prevent infections)
- Syncope (fainting or losing consciousness)
- Anemia (lowering of your red blood cells. Red blood cells are important for carrying oxygen in the blood and decreased amounts can lead to symptoms such as tiredness or shortness of breath)

The first case of severe events the non-infectious acute encephalitis (inflammation of the brain) considered by the study investigator as related to the vaccine, the other events were reported as severe, but the investigator physician reported these events as not related to the vaccine.

TAS-102 risks:
The following list includes effects that both may or may have not been related to TAS-102 and you may experience some other side effects that are not listed. However, this is not a complete list because rare events of a non-severe nature are not listed; however, rare events of a severe nature are listed. Though many of the side effects reported were mild to moderate in nature, some side effects may become severe and life-threatening and could potentially worsen, leading to death.

Likely, occurring in > 20% of participants:

- Nausea
- Vomiting
- Diarrhea
- Lowered white blood cell count/neutrophils (white blood cells are important in helping people fight off or prevent infections)
- Lowered red blood cell count (anemia). Red blood cells are important for carrying oxygen in the blood and decreased amounts can lead to symptoms such as tiredness or shortness of breath
- Fatigue (tiredness)
- Loss of appetite
- Infections, e.g. blood, lung, pelvis, eye, urinary tract, intestinal tract, skin, liver/biliary tract

Common, occurring in 3 -20% of participants:

- Sores in mouth (stomatitis)
- Constipation
- Abdominal pain
- Indigestion
- Lowered platelet count (platelets are important in helping a person's blood to clot when they are bleeding)
- Hair loss
- Rash (changes in the color or texture of the skin, possible blistering and peeling)
- Loss of protein through the urine
- Changes in sense of taste
- Headache
- Back pain
- Joint pain
- Fever
- Weakness
- Decreased blood protein
- Anxiety
- Abnormally high levels of enzymes produced by the liver (meaning that your liver is not working properly)

Rare but severe, occurring in < 3% of participants:

- Heart attack
- Heart muscle damage
- Chest pain

- The heart beats too fast or too slow
- Liver damage - yellow color of skin or eyes (jaundice)
- Kidney damage - blood in urine
- Effects on brain or nerve function
- Seizure
- Decreased level of consciousness
- Blood clot
- Inflammation of large bowel (symptoms with abdominal pain, diarrhea, and bloody stool)
- Abnormal connection between digestive system and other areas (fistula)
- Colonic Perforation (hole in colon wall)
- Blockage of small or large bowel
- Accumulation of fluid in abdomen
- Bleeding (including urinary track)
- Intestinal ulcer
- Blood clot in lung
- Difficulties in or cessation of breathing
- Inflammation of lung
- Nosebleed
- Gout (high levels of uric acid with symptoms of red, tender, hot and swollen joints)
- Dehydration
- Fainting
- Blood clot in leg
- Decreased blood pressure
- Blood clotting disorder
- Hot flushes
- Shock
- Dizziness
- Numbness
- Tingling
- Muscle pain
- Flu like symptoms
- Hyperglycemia (high blood sugar)
- Hypokalemia (low blood potassium)
- Hyperkalemia (high blood potassium)
- Hypomagnesium (low magnesium)
- Cardiac failure
- Heart muscle damage (leading to heart attack)
- Edema (fluid accumulation) abdomen, extremities, face
- Bleeding (including gastrointestinal tract)

Pregnancy Risk-Females:
The effect of TAS-102 and PolyPEPI1018 on a fetus (developing baby still in the womb), or on a breastfeeding infant, is unknown and may be harmful. Because of these risks, women cannot take part in this study if they are pregnant or breastfeeding.

If you are a woman who are sexually active and able to become pregnant, you must agree to use an effective form of birth control while on the study and for 3 months after the last vaccination. You will also need to have a negative pregnancy test before starting the study and every 8 weeks while in the study.

An effective form of contraception is defined as:

- Hormonal contraceptives (such as birth control pills, patches, injections, vaginal ring, or implants) or an intrauterine device
- Combined with at least 1 of the following:
    - Diaphragm
    - Cervical cap
    - Condom

If you become pregnant while on this study, please notify your study doctor immediately.

Pregnancy Risk –Men:
If you are sexually active, and able to father a child, you must agree to use an effective form of birth control while on the study and for 3 months after the last vaccination. In addition, you cannot donate sperm during this same time frame as well.

An effective form of contraception is defined as:

- Hormonal contraceptives used by your partner (such as birth control pills, patches, injections, vaginal ring, or implants) or an intrauterine device used by your partner
- Combined with at least 1 of the following:
    - Diaphragm used by your partner
    - Cervical cap used by your partner
    - Condom

If your partner thinks she might have become pregnant while you are in the study or for 3 months afterwards, you must tell the Principal Investigator immediately. The Principal Investigator may ask for your partner's permission to collect information about the outcome of her pregnancy and her newborn. You won't have to stop taking the study drug or stop taking part in the study if your partner becomes pregnant.

Other Research Related Risks:

Blood Draw Risks:
The risks of drawing blood include pain, bruising, lightheadedness, and/or fainting, or rarely, infection at the site of the needle stick.

CT or Ultrasound Guided tumor biopsy:
The CT or Ultrasound guided tumor biopsy risks include bleeding, infection, the need for additional procedures, or organ damage. All of these risks are very rare, <1 in 100 to 1000.

If the tumor biopsy is done by CT guidance, you will be exposed to radiation from this procedure. The amount of radiation from this has a low risk of harmful effects. If you are a person of childbearing potential and the biopsy is done in the abdominal/pelvic area, you will also need to have a pregnancy test done prior to the procedure.

CT or PET/CT risks
If a CT or PET/CT scan has not been done within 21 days prior to Cycle 1 Day 1 treatment, another scan will need to be done. Your doctor will discuss this with you. Since this scan is extra scan is being done for research only, you will be exposed to additional radiation from the x-rays or radioactive material during the CT or PET/CT scan done for this study. The amount of radiation from these studies has a low risk of harmful effects.

Genetic Testing:
This study involves testing your DNA, which is the genetic information you inherited from your parents (also known as genetic testing). This testing will not include whole genome sequencing (mapping your entire genetic code). You will not be notified of the genetic test results and they will not be put into your medical record.

A Federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information when making a decision to hire, promote, or fire you or when setting the terms of your employment.

All health insurance companies and group health plans must follow this law.

Be aware that this new Federal law doesn't protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

Standard of Care Risks:
Your doctor will discuss the risks of routine blood tests, and PET/CT, CT, or MRI scans as these tests and procedures are part of your standard clinical care.

Taking Study Drugs with Other Medications:
For your safety during this study, call the Principal Investigator BEFORE you take any:

- New medications prescribed by your doctor
- Other medications sold over-the-counter without a prescription
- Dietary or herbal supplements

Additional Costs:
Taking part in this research study may lead to added costs to you. In some cases, insurance will not pay for services ordinarily covered because these services were performed in a research study. You should check with your insurance company to see what services will be covered and what you will be responsible to pay.

Confidentiality:
As with all research, there is a chance that confidentiality could be compromised; however, we take precautions to minimize this risk.

Are there reasons you might leave this research study early?

You may decide to stop at any time. You should tell the Principal Investigator if you decide to stop and you will be advised whether any additional tests may need to be done for your safety.

In addition, the Principal Investigator or Mayo Clinic may stop you from taking part in this study at any time:

- If it is in your best interest,
- If you don't follow the study procedures,
- If the study is stopped.

If you leave this research study early, or are withdrawn from the study, no more information about you will be collected; however, information already collected about you in the study may continue to be used.

We will tell you about any new information that may affect your willingness to stay in the research study.

What if you are injured from your participation in this research study?

Where to get help:

If you think you have suffered a research-related injury, you should promptly notify the Principal Investigator listed in the Contact Information at the beginning of this form. Mayo Clinic will offer care for research-related injuries, including first aid, emergency treatment and follow-up care as needed.

Who will pay for the treatment of research related injuries:

Care for such research-related injuries will be billed in the ordinary manner, to you or your insurance. You will be responsible for all treatment costs not covered by your insurance, including deductibles, co-payments and coinsurance.

What are the possible benefits from being in this research study?

This study may or may not make your colorectal cancer better. While doctors hope that the study drugs will be more useful against colorectal cancer compared to the usual treatment, there is no proof of this yet. We do know that the information from this study will help doctors learn more about vaccines as a treatment for colorectal cancer. This information could help future colon or rectal cancer patients.

What alternative do you have if you choose not to participate in this research study?

You don't have to be in this study to receive treatment for your condition. Your other choices may include TAS-102 alone outside of the study, regorafenib, or another clinical trial. Talk to the Principal Investigator or your doctor if you have any questions about any of these treatments or procedures.

What tests or procedures will you need to pay for if you take part in this research study?

You won't need to pay for tests and procedures which are done just for this research study. These tests and procedures are:

- Collection, processing, and analyzing of research blood samples, buccal swabs, and research tissue specimens
- Study drug: PolyPEPI108 medication and injection
- CT or US guided biopsy for research tissue collection: after registration but before Cycle 1 Day 1; and before Cycle 4 Day 1
- Repeat CT, PET/CT, or MRI, if screening scan was not done within 21 days prior to Cycle 1 Day 1 treatment.

However, you and/or your insurance will need to pay for all other tests and procedures that you would have as part of your clinical care, including other drugs or treatments to help control side effects. These tests and procedures are:

- Physical exams
- Urine or serum pregnancy tests
- Standard of care blood tests such as Hematology, Chemistry, and tumor biomarker (CEA) tests
- Standard of care urinalysis
- Standard of care CT, PET/CT, or MRI to follow your cancer
- Commercially available TAS-102 medication

You will also be responsible for any co-payments and deductibles.

If you have billing or insurance questions call Patient Account Services at the telephone number provided in the Contact Information section of this form.

Will you be paid for taking part in this research study?

You won't be paid for taking part in this study.

There is a very small chance that some commercial value may result from the use of your sample. This could include new products like a drug or a test to diagnose a disease. If that happens, you will not be offered a share in any profits.

Will your information or samples be used for future research?

Your samples will be sent to the LabCorp, HalioDx and ImmunXpert for in a coded format which protects your identity. They will process, analyze, and store your samples for research purposes as described in the research study and this consent form. The results will be shared with Treos Bio ZRT and Mayo Clinic.

Unless you give your permission below, your information or samples collected for this study will not be used or shared for future research, even if the identifiable information such as your name, Mayo Clinic number or date of birth is removed.

We would like to keep your information and samples for future research. You can still take part in this current study even if you don't want your information or samples used for future research.

Researchers at Mayo Clinic who aren't involved with this study may ask to use your information and/or samples for future research. Researchers at other institutions may also ask for a part of your information and/or samples for future studies. Unless you indicate otherwise, the future research will be related to understanding patients' reactions to the vaccine. No direct benefits to you are expected from the future research. Your information and/or samples will only be shared consistent with your consent, and with all applicable laws and regulations.

If you approve release of your information and/or samples by checking 'yes' below, Mayo may send the information and/or samples to researchers who request them, but Mayo will not send your name, address, phone number, social security number, or any other identifying information with the information and/or samples. Your information and/or samples may be sent with a code, and only the researchers for this study at Mayo Clinic would be able to link the code to you.

Some future studies may examine your DNA, the genetic information you inherited from your parents (genetic testing). If there are findings which may be useful for your health care, the researchers may contact Mayo Clinic, so Mayo Clinic can give you the option of learning the results. You would be given general information on the potential risks, benefits, and costs of choosing to learn about the findings.

To support future research, de-identified genetic information may be placed in databases accessible by the internet. Some of the information may be available to anyone using the internet, and some will be released only to approved researchers. Combined study information (including genomic summary results) may be published, but the information will not identify you.

Even though information traditionally used to identify you will not be shared, people may develop ways in the future to allow someone to link your genetic information back to you. For this reason, confidentiality cannot be guaranteed. It is also possible that reidentified information could be used in discriminating ways, and there could be additional unknown risks. We will make every effort to protect your confidentiality.

Please read the following statements and mark your choices:

1. I permit my information and samples to be stored and used in this study's future research to better understand patients' reaction to the vaccine.

☐ Yes ☐ No Please initial here: _____Date: _____

You may withdraw your consent for future use of your information and/or samples at any time, by writing to the Principal Investigator at the address provided in the "Contact Information" section of this consent form.

Your information and/or samples would be removed from any repository where they are stored, if possible. Information and/or samples already distributed for research use will not be retrieved.

How will your privacy and the confidentiality of your records be protected?

Mayo Clinic is committed to protecting the confidentiality of information obtained about you in connection with this research study. Information collected during the study will be coded and stored in a room with restricted access and/or on a computer that is password protected.

During this research, information about your health will be collected. Under Federal law called the Privacy Rule, health information is private. However, there are exceptions to this rule, and you should know who may be able to see, use and share your health information for research and why they may need to do so. Information about you and your health cannot be used in this research study without your written permission. If you sign this form, it will provide that permission (or "authorization") to Mayo Clinic.

Your health information may be collected from:

- Past, present and future medical records.
- Research procedures, including research office visits, tests, interviews and questionnaires.

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Not to be used after: **October 7, 2022**

Your health information will be used and/or given to others to:

- Do the research.
- Report the results.
- See if the research was conducted following the approved study plan, and applicable rules and regulations.

Your health information may be used and shared with:

- Mayo Clinic research staff involved in this study.
- Other Mayo Clinic staff involved in your clinical care.
- The sponsor(s) of this study and the people or groups hired by the sponsor(s) to help perform this research.
- The Mayo Clinic Institutional Review Board that oversees the research.
- Federal and State agencies (such as the Food and Drug Administration, the Department of Health and Human Services, the National Institutes of Health and other United States agencies) or government agencies in other countries that oversee or review research.
- The medical monitor who oversees the data (study information) and safety of this research.
- Treos Bio ZRT, the company providing the study medication, PolyPEPI1018, and funding for this study, and Treos Bio ZRT's current and future collaborators.

How your information may be shared with others:

While taking part in this study, you will be assigned a code that is unique to you, but does not include information that directly identifies you. This code will be used if your study information is sent outside of Mayo Clinic. The groups or individuals who receive your coded information will use it only for the purposes described in this consent form.

If the results of this study are made public (for example, through scientific meetings, reports or media), information that identifies you will not be used.

In addition, individuals involved in study oversight and not employed by Mayo Clinic may be allowed to review your health information included in past, present, and future medical and/or research records. This review may be done on-site at Mayo Clinic or remotely (from an off-site location). These records contain information that directly identifies you. However, the individuals will not be allowed to record, print, or copy (using paper, digital, photographic or other methods), or remove your identifying information from Mayo Clinic.

Is your health information protected after it has been shared with others?

Mayo Clinic asks anyone who receives your health information from us to protect your privacy; however, once your information is shared outside Mayo Clinic, we cannot promise that it will remain private and it may no longer be protected by the Privacy Rule.

MAYO CLINIC

Name and Clinic Number

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Your Rights and Permissions

Participation in this study is completely voluntary. You have the right not to participate at all. Even if you decide to be part of the study now, you may change your mind and stop at any time. You do not have to sign this form, but if you do not, you cannot take part in this research study.

Deciding not to participate or choosing to leave the study will not result in any penalty. Saying 'no' will not harm your relationship with your own doctors or with Mayo Clinic.

If you cancel your permission for Mayo Clinic to use or share your health information, your participation in this study will end and no more information about you will be collected; however, information already collected about you in the study may continue to be used.

You can cancel your permission for Mayo Clinic to use or share your health information at any time by sending a letter to the address below:

Mayo Clinic
Office for Human Research Protection
ATTN: Notice of Revocation of Authorization
201 Building 4-60
200 1st Street SW
Rochester, MN 55905

Alternatively, you may cancel your permission by emailing the Mayo Clinic Research Subject Advocate at: researchsubjectadvocate@mayo.edu.

Please be sure to include in your letter or email:

- The name of the Principal Investigator,
- The study IRB number and /or study name, and
- Your contact information.

Your permission for Mayo Clinic to use and share your health information lasts forever, unless you cancel it.

LabCorp, HalioDx, and ImmunXpert will store your coded samples for a maximum of 1 year. After 1 year, the samples will be destroyed.

MAYO CLINIC

Name and Clinic Number

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Enrollment and Permission Signatures

Your signature documents your permission to take part in this research.

Printed Name Date (mm/dd/yyyy) Time (hh:mm am/pm)

Signature

Person Obtaining Consent

- I have explained the research study to the participant.
- I have answered all questions about this research study to the best of my ability.

Printed Name Date (mm/dd/yyyy) Time (hh:mm am/pm)

Signature