Informed Consent

Optimized bismuth quadruple therapy vs triple standard therapy for Helicobacter pylori eradication:

Clinical efficacy randomized trial.

NCT: Not yet assigned

2022-08-12

INFORMED CONSENT DOCUMENT

Study Name: Optimized bismuth quadruple therapy vs triple standard therapy for *Helicobacter pylori* eradication: Clinical efficacy randomized trial.

Study Sponsor / Funding Source: AR Gastric Cancer Prevention Funding, Meridian BioScience, Maver Laboratories

Main Researcher: Patricio Medel

Contact phone: +56 9 4231 6715

Dept: Department of Public Health, Faculty of Medicine, Pontificia Universidad Católica de Chile

---

The purpose of this information is to help you make the decision to participate in medical research, which seeks to evaluate the effect of a treatment scheme for the eradication of *Helicobacter pylori*, which is a bacterium that infects humans and can cause gastroduodenal ulcers, gastric cancer, and a type of lymphoma (MALT).

Take the time you need to decide, read this document carefully, and ask your doctor or study staff any questions you want.

RESEARCH OBJECTIVES

- You have been invited to participate in this study because you have been diagnosed with *Helicobacter pylori* infection.
- The purpose of this study is to evaluate the effectiveness of an eradication scheme for *Helicobacter pylori* infection in the Chilean population, comparing it with the usual treatment in our country.
- The study will study a total group of 204 patients.
-

INVESTIGATION PROCEDURES

If you agree to participate in the study, you will/be asked to:

1. Answer a questionary, to record personal and health history.

Timbre, firma and date of approval
CEC-Salud UC

2. Two 5 ml blood samples, equivalent to one spoon of soup, will be taken to make measurements of *Helicobacter pylori* antibodies. One when you are recruited and another in the control to which you must go between 8 and 12 weeks after finishing the treatment.
3. You must go to control at the medical center to do an exhaled air test to confirm the effectiveness of the treatment received, and make a final survey and the second blood sample. This visit will last approximately 30 minutes. Your participation in this study will be around 15 weeks.
4. This study includes 2 groups, you will be assigned to one of them completely at random. If you are assigned to group 1, you will receive the usual treatment for Helicobacter pylori eradication. If you are assigned to group 2, you will receive the treatment being tested in this research. Both treatments consist of antibiotics and medications to decrease heartburn.
5. You can be assigned to the group that receives a placebo, this means that you will receive a tablet of the same characteristics as the study drug but without the active substance. For this study, only one of the four drugs you will receive may be a placebo.
6. In this study, neither you nor the researcher will know which group you have been assigned to.
7. The samples obtained will be used only for the purpose of this research. If in the future they are used for purposes other than this medical research, you will be asked for new consent.
8. In this study, genetic studies of Helicobacter pylori bacteria will be carried out through PCR.
9. The samples will be stored for *5 years*, in the Laboratory of experimental hepatology, under the responsibility of Dr. Marco Arrese.
10. The results obtained from eradication will be informed to you, as well as to your treating physician, you will also be informed of the most appropriate medical course of action for your condition.
11. You should know that in addition to the option to participate in this study, you may receive other eradication schemes in addition to those included in this study.

PROCEEDS

You will benefit from participating in this study by receiving free eradication treatment for *Helicobacter pylori* infection. In addition, confirmation of the eradication of the bacteria will be made at no cost to you. Finally, if your treatment fails to eradicate the infection, you will be referred at no cost to a doctor so that you can receive standard second-line treatment for eradication, as well as the test to confirm eradication on this second attempt at no cost for you.
In addition, the information that will be obtained will be useful to know more about your condition/disease (or the problem under study) and could eventually benefit other people with the same condition.

RISKS

Timbre, firma and date of approval
CEC-Salud UC

1.- This study has risks associated with taking blood samples such as pain, swelling, and bruising at the puncture site.
2.- Your participation in this study may cause you some kind of discomfort when answering the questions of the questionnaire / when completing the survey / with the topics covered in the interview.
3.- The drugs used have adverse reactions, with the following frequency:

Omeprazole:

Common: Between 1 and 10% or More than 1 and less than 10 people in 100	Rash Abdominal pain Constipation Diarrhea Flatulence Nausea Regurgitation Acidity Vomiting Asthenia Seasickness Headache Upper respiratory tract infection

Also reported, without frequency information: cutaneous lupus erythematosus, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, hypomagnesemia, atrophic gastritis, *Clostridium difficile* diarrhea, polyposis of the fundic glands of the stomach, pancreatitis, hemolytic anemia, hepatic encephalopathy, hepatic necrosis, liver failure, anaphylaxis, bone fracture, hip fracture, rhabdomyolysis, acute tubulointerstitial nephritis, angioedema.

Esomeprazole

Common: Between 1 and 10% or More than 1 and less than 10 people in 100	Constipation Diarrhea Flatulence Nausea Dry mouth Headache Sleepiness
Rare	Abdominal pain Diarrhea

Timbre, firma and date of approval
CEC-Salud UC

Between 0.1% and less than 1% or More than 1 and less than 10 people in 1000	

Also reported, without frequency information: cutaneous lupus erythematosus, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, *Clostridium difficile* diarrhea, fundic gland polyposis of the stomach, anaphylaxis, angioedema, bone fracture, rhabdomyolysis, acute tubulointerstitial nephritis

Amoxicillin:

Common: Between 1 and 10% or More than 1 and less than 10 people in 100	Rash Diarrhea Nausea Vomiting Headache

Erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, *Clostridium difficile* diarrhea, anaphylaxis, and hypersensitivity reaction has also been reported without frequency information.

Metronidazole:

Common: Between 1 and 10% or More than 1 and less than 10 people in 100	Abdominal discomfort Abnormal taste in the mouth Diarrhea Nausea Seasickness Headache Candidiasis in genital area

Stevens-Johnson syndrome, toxic epidermal necrolysis, leukopenia, acute liver failure, hepatotoxicity, aseptic meningitis, encephalopathy, peripheral neuropathy, seizures, optic nerve disorder, ototoxicity, hemolytic uremic syndrome have also been reported without frequency information.

Clarithromycin

Common: Between 1 and 10% or	Abdominal pain Diarrhea Abnormal taste in the mouth

Timbre, firma and date of approval
CEC-Salud UC

More than 1 and less than 10 people in 100	Indigestion Nausea Vomiting Headache Hepatitis
Rare Between 0.1% and less than 1% or More than 1 and less than 10 people in 1000	QT prolongation

It has also been reported, without frequent information: cardiovascular disease, immunoglobulin A vasculitis, Stevens-Johnson syndrome, toxic epidermal necrolysis, *Clostridium difficile* diarrhea, liver failure, anaphylaxis, drug reaction with eosinophilia and systemic symptoms, cerebrovascular disease.

Bismuth subsalicylate:

Common: Between 1 and 10% or More than 1 and less than 10 people in 100	Mane Darkening of bowel movements Darkening of the tongue
Rare Between 0.1% and less than 1% or More than 1 and less than 10 people in 1000	Nauseas Diarrhoea Gastralgia

It has also been reported, without frequency information, or

4.- The drugs under study can have negative effects on an unborn child. Therefore, if you are a woman and are pregnant, plan to become pregnant, or are open to becoming pregnant for the duration of the study, you should not participate in this research.
If during the study you believe you are pregnant, you should immediately contact the responsible researcher, who will give you the most appropriate recommendations to take the best care of your pregnancy, protecting both your health and the health of your child.
For any previous case, the elements oblige us to ask you to avoid pregnancy for the entire duration of the study and up to three months after the end of it.

COSTS

Timbre, firma and date of approval
CEC-Salud UC

Your participation in this study will not mean any additional cost to that already associated with the procedure/condition for which you are being treated at this center.

DAMAGE COVERAGE

Digestive endoscopy and biopsy (urease test) are medical procedures that you will undergo at the direction of your treating physician, which is why this study does not cover the costs of possible complications derived from these procedures. However, in the event that an adverse event directly associated with a patient's participation in this protocol occurs after recruitment, the research team will respond with immediate care and follow-up. Treatment costs will be covered by the project through grant funds 3888-308.

COMPENSATION

You will benefit from free eradication treatment, and free eradication confirmation and if the treatment is not effective with the randomly assigned scheme, you will be treated under the usual practice, at no cost to you.

ALTERNATIVES TO STUDY

Alternatives to participation in the study are as follows:

1. Not participating in this study
2. Receive standard treatment

CONFIDENTIALITY OF INFORMATION

1.- The information obtained will be kept confidential. Your name, RUN, test results or any identifiable information, will be encoded in a database, by computer code/system. This information will be stored for 10 years under the responsibility of the Responsible Researcher, Patricio Medel, whose tutor is Dr. Arnoldo Riquelme Perez
2.- It is possible that the results obtained are presented in journals and medical conferences, however, your name will not be known.

VOLUNTARISM

1.- Your participation in this research is entirely voluntary. You have the right not to agree to participate or to withdraw your consent and to withdraw this research at any time you deem appropriate. By doing so, you do not lose any rights to you as a patient of this institution and the quality of medical care you deserve will not be affected.

Timbre, firma and date of approval
CEC-Salud UC

2.- If you withdraw your consent, your samples will be deleted and the information obtained will not be used.
3.- If you withdraw your consent, for security reasons it may be necessary for us to analyze your data obtained until that moment. We will do this by ensuring your confidentiality.

QUESTIONS

If you have questions about this medical research you can contact or call Patricio Andrés Medel Jara, Principal Investigator of the study, at +56 9 4231 6715 and e-mail: pamedel@uc.cl.

If you have questions about your rights as a participant in medical research, you can call Ms. Ivonne Vargas., President of the Scientific Ethics Committee on Health Sciences of the Pontificia Universidad Católica de Chile, at 223542397-223548173, or send an email to: eticadeinvestigacion@uc.cl

DECLARATION OF CONSENT

- I have been explained the purpose of this medical research, the procedures, the risks, the benefits, and the rights that assist me and that I can withdraw from it at any time.
- I signed this document voluntarily, without being forced/forced to do so.
- I am not giving up any rights that assist me.
- I will be informed of any new information related to the study/study drug/that comes up during the study and that may have direct relevance to my health condition.
- I have been informed that I have the right to re-evaluate my participation in this medical research at my discretion and at any time I wish.
- I authorize the responsible investigator and his collaborators to access and use the data contained in my clinical record for the purposes of this medical research.
- At the time of signing, I was given a signed copy of this document.

Timbre, firma and date of approval
CEC-Salud UC

MANDATORY SIGNATURES:

_____

Participant: name, signature and date

_____

Researcher: name, signature and date

_____

Director of the institution or its Order: name, signature and date

Timbre, firma and date of approval
CEC-Salud UC