

知情同意书 Informed Consent

尊敬的先生/女生：

Dear Sir/ Madam

您好！我们邀请您参加“不同疗法治疗胃幽门螺杆菌感染的疗效对比及对胃和肠道菌群分布影响的随机对照前瞻性研究”的随机对照临床研究。在您决定是否参加这项研究之前，请您仔细阅读以下内容，帮助您了解该项研究。如果您愿意，您可以向医生询问，以确定您理解有关内容。

You will be invited to participate in a randomized controlled clinical study. Please read the informed consent to help you understand the study before you decide whether to participate in the study or not. If you have any questions, please consult the doctor to make sure you understand the study.

1. 研究目的

1. Objectives

以传统治疗四联铋剂方案为对照，观察含聚普瑞锌四联疗法对胃幽门螺杆菌（HP）的根除效果；进行 HP 抗生素耐药突变位点检测，探索含聚普瑞锌四联疗法疗效与耐药位点之间的关系；探索采用不同治疗方法前后，患者胃以及肠道菌群分布情况；探索治疗后，采用不同方案的患者其胃以及肠道菌群分布情况。

The three objectives of the study are as follows. The first is to evaluate the efficacy of polaprezinc-containing quadruple therapy for eradication of *H. pylori* infection. The second is to detect the antibiotic drug-resistance mutation sites of *H. pylori* and explore the association between the therapy and the drug-resistance sites. The third is to compare the distribution of gastral and intestinal flora, before and after the treatments and between the different therapies.

2. 研究背景

2. Background

幽门螺杆菌感染是慢性胃炎的重要病因，根除 HP 是治疗慢性胃炎和预防复发的重要手段。HP 根除治疗方案主要包括三联和四联疗法。随着时间变迁，长时间和频繁应用抗生素出现 HP 对抗生素耐药现象，导致 HP 根除率越来越低，目前阿莫西林和克拉霉素是临床中较为常用的两个抗生素。

H. pylori infection is an important etiology of chronic gastritis, and eradication of *H. pylori* is an essential approach to treat chronic gastritis and prevent its relapse. Therapeutic regimens mainly include triple and quadruple regimens at present. *H. pylori* eradication rates are constantly decreasing, due to secular and frequent use of antibiotics resulting in antibiotic-resistance of *H. pylori* over time.

聚普瑞锌颗粒（商品名：瑞莱生）是唯一一个 L-肌肽与锌的螯合剂，具有多途径阻断幽门螺杆菌的独特药理作用，通过阻断幽门螺杆菌定植、抑制其活性、清除尿素酶及一氯胺、抑制炎症反应达到提高幽门螺杆菌根除率的目的。由吉林省博大伟业制药有限公司研制的聚

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普瑞锌颗粒于 2012 年在中国上市。本着严谨、科学循证的态度，在上市后将对其进行深入研究，验证其提高 HP 根除率的有效性。

Polaprezinc, a chelating agent of L-carnosine and zinc, can pharmacologically block the colonization of *H. pylori* by inhibiting its activity and the correlated inflammatory chain reaction, and removing urea, enzymes, monochloramines to eradicate *H. pylori*. Polaprezinc Granules produced by Jilin Broadwell Pharmaceutical Co., Ltd was approved in China in 2012. Post-marketing study should be conducted to monitoring its performance in improving *H. pylori* eradication rate.

随着生活质量的提高，生活节奏的加快，HP 阳性的胃炎患者逐年增多，严重者可发展为溃疡甚至胃癌，严重影响患者的生活质量甚至危及患者生命，因而，应及时采取有效的手段进行治疗。目前治疗 HP 阳性胃炎的常用方法为质子泵抑制剂联合两种抗生素，但近年抗生素耐药性明显增加，HP 根除率有所下降。因此，探索 HP 耐药性也是本项目的研究目的之一。

As the quality of life improves, the pace of life accelerates, the number of patients with *H. pylori* positive gastritis increases by years, and the severe cases can develop into ulcers or gastric cancer, which affects the quality of life or even endangers the lives of patients seriously. Therefore, effective means should be taken for *H. pylori* eradication. At present, the commonly used therapy of *H. pylori* positive gastritis is proton pump inhibitor (PPI) combined with two antibiotics, but antibiotic-resistance has been increased recently, and the rate of *H. pylori* eradication has decreased. Hence, exploring *H. pylori* drug-resistance is also one of the objectives of this study.

3. 研究内容和步骤

3. Procedures

如果您是近期诊断为 HP 阳性的患者，同意参加本研究并签署本知情同意书，您将会接受一些检查，包括一般体格检查、心电图、C13/C14 尿素呼气试验、肝肾功、血常规、尿常规、粪便 HP 抗原等，以确定您是否适合参加本项研究，这些检查都是免费的。如果您经过检查，符合入选标准，您将被随机分入治疗组或对照组接受相应治疗。如果您符合本研究入组条件，医生将建议您参与本研究。您将免费得到本品和三联药品的治疗，研究期间医生将严密观察您的治疗情况，让您得到有效的医学治疗和服务。

If you agree to participate in this study when you are recently diagnosed *H. pylori* positive, you will be invited to several examinations including general physical examination, electrocardiogram (ECG), C13/C14 urea breath test, blood test for liver and kidney function, urine test, *H. pylori* stool antigen, etc. These will determine whether you are suitable for this study which are free of charge. If you meet the inclusion criteria, you will be randomized into the treatment/control group. You will receive free treatment of quadruple therapy under the guidance of the doctors during the study.

本研究为随机、对照试验设计。158 例患者有相同可能性分入治疗组（奥美拉唑、阿莫西林、克拉霉素联合聚普瑞锌颗粒）或对照组（奥美拉唑、阿莫西林、克拉霉素联合枸橼酸

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铋钾），分别服用试验药或对照药连续治疗 2 周后停药。在接受药物治疗前后，您将进行 2 次免费的无痛胃镜检查，以了解您胃部的疾病或健康状态变化情况；在接受药物治疗的期间，要求您每周定期来医院接受相应的检查，并按要求填写日记卡，交由您的主管医生检查，同时领取您下一周期服用的药物。你必须将在研究期间自行服用的其他药物，以及您打算在该项研究期间使用的药物和疑问告知您的医生。这一点非常重要，如果您不便按照上述要求或者为了您的安全，医生也可能让您退出该项研究，接受其他替代治疗。特别提醒的是，如果您是妊娠妇女，则不宜参加本项研究。育龄妇女应该在试验期间采取有效避孕措施。

This study is a randomized, controlled trial. 158 patients have the same possibility to be assigned into treatment group (esomeprazole, amoxicillin, clarithromycin combined with polaprazinc granules) or control group (esomeprazole, amoxicillin, clarithromycin combined with bismuth potassium citrate). Before and after the therapy, you will have free painless gastroscopy examinations respectively, to observe the stomach. During the course of medication, you are required to come to the hospital after one week for a corresponding examination, and fill in the diary card to submit it to your doctor, and receive the medicine for the next cycle. You should inform the doctor of any other drug you take on your own or intend to use during the study. This is very important, and if you do not follow the requirements above, for your safety, you may be asked to withdraw from the study, and receive alternative treatment. In particular, it is not appropriate to participate if you are pregnant currently. Reproductive women should take effective contraception during the study.

4. 参与本研究的风险

4. Risk

对于 HP 阳性患者，临床主要的治疗方法为质子泵抑制剂联合两种抗生素，本研究中所应用的质子泵抑制剂为阿斯利康制药有限公司生产的奥美拉唑，所选用的抗生素分别为西安利君制药有限责任公司生产的克拉霉素及联邦制药生产的阿莫西林，以及丽珠医药生产的枸橼酸铋钾胶囊。在服用奥美拉唑期间可能出现头痛和腹泻、恶心、便秘等胃肠道症状，其发生率在 1~3%。对成年患者，克拉霉素每天总剂量为 1 克时的最常见不良反应是恶心、呕吐、味觉失调、腹泻、皮疹、胃气胀、头痛、便秘、听觉障碍、白细胞和血小板数减少等。在服用阿莫西林期间，可能发生的不良反应为恶心、呕吐、腹泻及假膜性肠炎等胃肠道反应；皮疹、药物热和哮喘等过敏反应；贫血、血小板减少、嗜酸性粒细胞增多等；血清氨基转移酶可轻度增高；由念珠菌或耐药菌引起的二重感染；偶见兴奋、焦虑、失眠、头晕以及行为异常等中枢神经系统症状。

The esomeprazole used in this study is produced by AstraZeneca Pharmaceutical Co., Ltd., clarithromycin produced by Xi'an Lijun Pharmaceutical Co., Ltd., amoxicillin produced by United Laboratories Co., Ltd., and bismuth potassium citrate capsule produced by Livzon Pharmaceutical Group Inc. Headache, diarrhea, nausea, constipation and other gastrointestinal symptoms may occur by esomeprazole administration, with the occurrence rate of 1~3%. For adults, the most

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common adverse effects of clarithromycin at a total daily dose of 1 g are nausea, vomiting, taste disorders, diarrhea, rash, stomach bloating, headache, constipation, hearing impairment, leukopenia, and thrombocytopenia. During the administration of amoxicillin, the possible adverse reactions are gastrointestinal reactions such as nausea, vomiting, diarrhea and pseudomembranous enteritis; allergic reactions such as rash, drug fever and asthma; anemia, thrombocytopenia, eosinophilia, etc.; serum aminotransferase may be slightly elevated; secondary infections caused by candida or drug-resistant bacteria; and occasional symptoms of the central nervous system include excitement, anxiety, insomnia, dizziness, and behavioral abnormalities, etc.

任何药物均可能产生一定的不良反应，故不能排除本研究参与者研究期间发生不良反应的可能。内镜检查及活检后极少发生上消化道出血。活检后出血是内镜检查的常见并发症，凝血功能正常的情况下，绝大多数无需处理均能自凝。在研究中发现任何可能影响您健康的情况，医生会及时告知您，并积极采取有效的治疗措施。

Adverse reactions may be caused by any drug. Upper gastrointestinal bleeding rarely occurs after endoscopy and biopsy. Bleeding after biopsy is a common complication of endoscopic examination, most of them can self-coagulate without treatment when coagulation function is normal. Any situation that may affect your health founded in the study, the doctor will inform you in time and take effective treatment measures.

5. 研究可能的获益

5. Benefits

本研究将为您提供目前临床用于治疗 HP 感染的药品和相关的检查费用。研究期间，您将获得 2 次免费的高质量无痛胃镜检查，可帮助您及时掌握胃部健康状况。本研究所涉及到的 HP 相关治疗可能有效，也可能无效。根据前期研究，如您完成本项研究的全过程，很可能将得到较好的 HP 根除效果。

This project will provide you with drugs for *H. pylori* eradication and associated examination costs. You will receive 2 free high-quality painless gastroscopy tests. *H. pylori* related treatment involved in this study may be effective or ineffective. According to the previous studies, if you complete the process of this study, it is likely that *H. pylori* eradication should be effective.

6. 研究相关费用及补偿

6. Expense and Compensation

在您参与本研究期间，您所使用的试验药物（聚普瑞锌、奥美拉唑、阿莫西林、克拉霉素药品、铋剂）由研究者免费提供，本研究规定的C13/C14尿素呼气试验、血常规、尿常规、肾功能、肝功能、心电图、尿妊娠检查及粪便HP抗原检查，亦由申办单位支付相关检查费用。与本项研究无关的费用（如：除胃以外的其他部位的病理诊断费用及非HP感染的

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其他疾病治疗费用），则由您或您的医疗保险机构负担。在研究期间，如果您发生与本研
究药物相关的不良事件或严重不良事件时，医生会采取积极的措施及时进行处理。如发生
健康损害时，依据国家法律法规，研究者将对您进行相应的补偿。

The drugs (polaprozinc, esomeprazole, amoxicillin, clarithromycin, bismuth) are free of
charge. The $^{13}\text{C}/^{14}\text{C}$ UBT, blood test for renal function and liver function, urine test, ECG, urine
pregnancy test and *H. pylori* stool antigen examination are also paid by the investigators. Expenses
irrelated to this study (e.g., the cost of pathological diagnosis of sites other than the stomach and
the cost of treatment of other diseases that are not *H. pylori* infection) should be paid by yourself or
the medical insurance. If you have adverse events or serious adverse events related to the drugs
during the study period, the doctor will take measures in time. In the event of health damage,
according to national laws and regulations, researchers will compensate you accordingly.

7. 遵从的义务

7. Obligation

在整个研究期间，您必须遵守本品研究方案的有关规定，配合医护人员，详细记录试
验相关的信息资料，保证研究资料的真实性。如果您未经负责医生的同意使用其他药物，
或有妨碍研究完成的行为，研究人员可要求您退出试验，或提前终止试验。

During the whole research period, you must abide by the relevant regulations of the research
protocol, cooperate with the medical staff, record the relevant information of the study in detail,
and ensure the authenticity of the data. If you use other drugs without the consent of the doctor, or
if there is an act that hinders the completion of the study, the researcher may ask you to withdraw
from the study or terminate the study in advance.

8. 可能获得的其他备选治疗方案及其受益和风险

8. Alternative therapeutic regimens, risks and benefits

HP感染目前临床多采用联合用药来清除HP感染，本研究中含铋剂四联疗法为首选的一
线治疗方案。此外，其他备选的治疗方案包括：不包含铋剂的四联疗法、序贯疗法、三联
疗法以及包含喹诺酮的治疗方案等。若您不愿意参加本研究，您也可以选择自行咨询医
生，针对您的个体情况选择治疗方案。不同治疗方案对清除HP感染均可能有效或无效的。
目前临床上HP治疗后的根除率大约在80%。

Combination drugs, usually, are adopted to eradicate *H. pylori* infection at present. The
bismuth-containing quadruple therapy is the first-line treatment. In addition, alternative treatment
options include quadruple therapy without bismuth, sequential therapy, triple therapy, and
treatment with quinolone, etc. If you are not willing to participate in this study, you can also
consult the doctor and choose regimen. Different treatments may effective or ineffective in
eradicating *H. pylori* infection. At present, the eradication rate in clinical is about 80%.

9. 自愿参加/退出研究

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9. Voluntary

参与本研究以自愿为原则，您可以拒绝参与或在任何时候均可退出，您将不会因此受到任何惩罚或受到任何不公正待遇。如果您计划退出研究，必须通知研究医生。如果继续参加本研究对您不利，医生有权在任何时候终止您参与本研究。伦理委员会及申办单位也有可能终止本研究。如果提前退出研究，医生将要求您做最后一次检查和评估。在相关法律/法规允许范围内，退出之前已获得的研究资料仍可能会被采用。如果您对本研究有疑问，请联系四川省肿瘤医院医学伦理委员会，电话028-85420681。

Participation in this study is voluntary and you could refuse to participate or withdraw at any time and there will not be any punishment or unfair treatment. You should inform the doctor if you plan to withdraw the study. If this study is detrimental to you for continuing to participate in, the physician has the right to terminate your participation in this study at any time. The ethics committee and the investigators may also stop this study. The doctor will ask you to do the exit examinations before you withdraw from the study. Data obtained prior to withdrawal may still be used under the relevant laws/regulations. If you have any questions about this study, please contact the Medical Ethics Committee of Sichuan Cancer Hospital at 028-85420681.

10. 医疗记录的公开及保密

10. Privacy issue

在有关法律规定下，您的医疗记录将被编码后妥善保存，但研究人员、监查人员、伦理委员会成员或药政管理人员可能查阅您的医疗记录。如果研究结果需要公开发表，您的身份不会被公开。签署本文件表示您已经授权研究人员可以使用您研究相关的医疗记录。

Your personal data in and during the study are confidential, but researchers, inspectors, members of the ethics committee or drug administration may refer to your personal data in the research unit as required. No information about you will be disclosed if the results of this study are published. Signing this document indicates that you have authorized the researchers to use your medical data.

您同意在本研究中获得资料，包括所有检查结果保存在研究者的计算机和书面文档系统中，研究资料中不会出现您的姓名。您也同意将这些试验资料用于在我国或其它国家药品注册的目的，在此过程中申办单位将使用这些记录，并按有关法律法规规定予以保存。

Your file obtained in this study, including all examination results, is kept in the researcher's computer and paper documents, and your name will be covered in data. These data may be used for registration in China or other countries. In the process, the sponsors will use these data and save them in accordance with the relevant laws and regulations.

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我们将储存本项目所采取的活检标本及胃液，粪便等样本，并可能在以后的研究中使用，所有活检标本及胃液，粪便样本上贴有带编码的标签，不会出现您的姓名，您的所有信息将会保密。

The biopsy specimens, gastric juices, stools and other samples collected in this study will be stored and may be used in future studies. All specimens are labeled with codes not appear your name. All your information will be kept confidential.

如果您对本项目还有其他的疑问，可以联系您当地_____医院的医生_____, 电话: _____, 您也可以联系本研究的负责人, _____医院_____, 教授, 电话:_____。

If you have any question about this study, you can contact_____ hospital doctor_____ at: _____, you can also contact the principal investigator(PI), _____ hospital professor_____ at: _____.

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患者（或代理人）姓名：

Patient's (or Patient's Families) name:

- 我在此确定医生已向我告知了聚普瑞锌颗粒临床研究的目的是、方法、获益和可能的风险。
 - I confirm that the doctor informed me the purposes, methods, benefits and risks of the polaprezinc granules clinic study.
 - 我已经阅读并理解了关于受试者资讯的说明。
 - I have read an informed consent form.
 - 我已经知道研究的结果将在临床研究总结报告中进行分析，但个人资料如：姓名、生日和诊断结果等会保密。
 - I know that the results of the study will be analyzed in clinic research report, but personal data such as name, birthday and results of diagnosing are confidential.
 - 我可以在任何时候退出该项研究。
 - I can choose to quit this study at any time.
 - 我有足够的机会提出问题并表明我是否自愿参加该项研究。
 - I have the opportunity to ask questions and to indicate whether I volunteered to participate in the study.
 - 我已被告知口服该药可能发生不良反应，如在试验过程中发生与试验有关的不良反应研究单位和申办者将给予积极的治疗。
 - I have been told that oral administration of the drug may have adverse reactions, research institution and the applicant will take active treatment measures if the adverse reactions related to the trial occurred during the study.
 - 我同意在试验期间采取适当的避孕措施（育龄妇女）。
 - I agree to take appropriate contraception during the trial (reproductive women)
 - 我已知道本项研究已经得到本医院伦理委员会讨论批准。
 - I know that this project has been approved by the ethics committee of Sichuan Cancer hospital.
- 本知情同意书一式两份，请受试者和研究中心妥善保管，以备药品注册审评部门审查。

This informed consent form is in duplicate and should be kept properly by the subject and the research center for review by the drug registration review department

患者（或代理人）：我已阅读并完全理解上述的有关医学研究的资料，我确认已有充足的时间考虑，有关疑问已经得到圆满解答，我自愿同意参加本临床研究。

Patient's (or Patient's Families): I have read and fully understood the above information on medical research, I confirm that all questions have been answered, and I voluntarily agree to participate in this clinical study after consideration.

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患者（或代理人）姓名：

与患者关系：

Patient's (or Patient's Families) name:

Kinship:

日期： 年 月 日

Date:

联系电话：1、手机： 2、宅电：

Telephone:

家庭住址：

Address:

主管医生：我确认已向患者解释了本项研究的详细情况，包括其权利及可能的获益和风险；并且保证随时解答患者关于本项临床研究信息的咨询。

Doctor: I confirm that I have explained to the patient the details of this study, including its rights, possible benefits and risks; and assure to answer the patient's consult on this clinical study at any time.

医生签名：

Doctor Name:

日期： 年 月 日

Date:

联系电话：

Telephone:

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