Clinical Trial Research Protocol

1. Declaration of Integrity

This study ensures that all procedures were carried out strictly in accordance with the trial protocol and that the authenticity of data recording was maintained. There are no conflicts of interest associated with this study.

2. Research Title

Research on the impact of stomach acid on the arrival of orally administered probiotics in the intestine and countermeasures

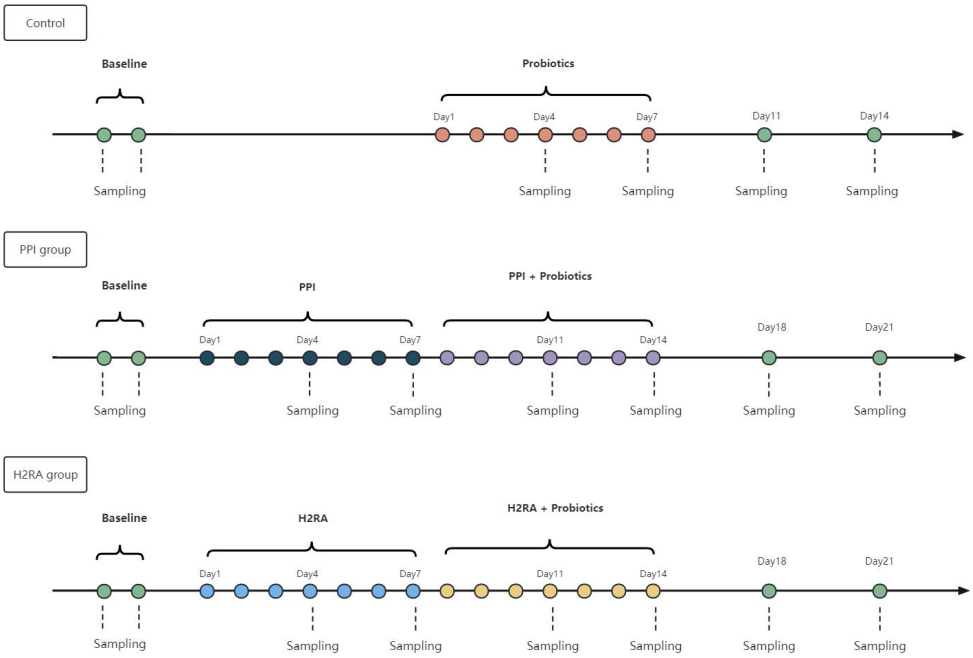
3. Research Protocol Version Number

Version 3 (March 17, 2022)

4. Funding

Thousand Talents Program - Gut Microbiota and Human Health (Project Number: 0214170083; Type: Talent Start-up Fund)

5. Flowchart (Table) of Research Procedures



In this study, the research subjects will be divided into three groups, each consisting of 50 participants, totaling 150 individuals. For the three groups of a total of 150 participants at baseline, two collections of oral saliva samples and intestinal fecal samples will be conducted, serving as the healthy control group. Subsequently, the control group will be administered probiotics approximately 1 hour after meals for seven consecutive days, with oral saliva and intestinal fecal samples collected on the 4th and 7th days after the start of the trial. The PPI

group will take PPI about 0.5 hours before meals for seven consecutive days. Starting from the 8th day, PPI group will be taken daily about 0.5 hours before meals, followed by the administration of probiotics approximately 1 hour after meals. The H2Blocker group will take H2Blocker about 0.5 hours after meals for seven consecutive days. Starting from the 8th day, H2Blocker will be taken daily about 0.5 hours after meals, followed by the administration of probiotics approximately 1 hour after meals. Both the PPI group and the H2 Blocker group will have oral saliva and intestinal fecal samples collected on the 4th, 7th, 11th, and 14th days after the start of the trial. Subsequently, each of the three groups will undergo two collections of oral saliva and intestinal fecal samples during the first and second weeks after discontinuing the intake of probiotics or gastric acid suppressants.

6. Research Background

This study is conducted in the current context of flourishing research worldwide on the correlation between oral and gut microbiota. Positioned at opposite ends of the human digestive tract, the oral and gut regions constitute two major microbial ecological niches, and the interaction between their respective microbial communities has emerged as a focal point in recent human microbiome investigations. Existing studies have demonstrated a profound association between the composition and dynamics of oral and gut microbiota and human health and disease status (Wade 2013; Lynch and Pedersen 2016).

On a daily basis, humans ingest around 1.5L of saliva, carrying approximately 1011 oral microbial species into the gastrointestinal tract (RICHARDSON and JONES 1958). However, it has been observed that there are significant disparities in the composition of microbial communities between the oral and gut regions. A large proportion of orally ingested microbes fail to be detected in the gut. There is ongoing debate about whether oral microbes, especially probiotics taken orally, can successfully colonize the distal gut. Some studies suggest that most oral microbes from healthy individuals are killed by gastric acid, antibacterial bile acids, and other gastrointestinal barriers during transit through the digestive tract, preventing them from reaching and colonizing the gut (Martinsen et al. 2005; Ridlon et al. 2014).

Proton pump inhibitors (PPIs) are commonly used clinical drugs. Essentially, PPIs inhibit H + -K + -ATPase, a proton pump in gastric parietal cells, thus blocking the pathway of gastric acid secretion. On the other hand, H2 receptor antagonists primarily inhibit the H2 receptors of gastric parietal cells, reducing basal and nocturnal gastric acid secretion. These drugs also inhibit acid secretion stimulated by gastrin and M receptor agonists. H2 receptor antagonists are widely used in the treatment of peptic ulcers. PPIs can be used to treat peptic ulcers, gastroesophageal reflux disease, Zollinger-Ellison syndrome, and upper gastrointestinal bleeding, making them first-line drugs for disorders related to abnormal gastric acid secretion (Scarpignato et al. 2016). The short-term use of PPIs has minimal side effects, and some studies have reported that the effects of PPIs can be eliminated within two weeks after discontinuation (Mosli et al. 2012). Previous research has also explored the effects of PPIs on oral microbial changes by recruiting healthy volunteers for short-term PPI administration (Koo et al. 2019; Mishiro et al. 2018).

7. Research Objectives and Expected Outcomes

This study aims to investigate whether gastric acid serves as a major barrier for the colonization of orally administered probiotics in the gut and whether gastric acid inhibition drugs,

such as proton pump inhibitors (PPIs) and H2 receptor antagonists, can enhance the colonization of orally administered probiotics in the gut. This will be achieved by conducting metagenomic sequencing of oral and gut microbial communities before and after the administration of probiotics and gastric acid inhibition drugs in healthy individuals. Through bioinformatics analyses, we will compare the similarities and differences in the composition of oral and gut microbiome in response to different interventions. This approach will shed light on whether orally administered probiotics can successfully reach and colonize the gut under various interventions, allowing us to comprehend the barriers faced by probiotics in the human body. This understanding will facilitate the development of strategies for probiotic delivery, such as encapsulation in acid-resistant capsules, thus advancing probiotic research and their application in disease interventions.

8. Inclusion and Exclusion Criteria

Inclusion Criteria:

- Aged 18 - 45 years
- 19 kg/m^2 ≤ BMI ≤ 24 kg/m^2
- No smoking and no history of alcohol abuse
- Good physical health, without severe diseases such as cancer, cardiovascular diseases, or impaired liver and kidney function
- No severe oral diseases, no gastrointestinal diseases
- No use of antibiotics, probiotics, or gastric acid inhibitors within the previous three months.

Exclusion Criteria:

- Long-term smoking or a history of drug or alcohol abuse
- Use of antibiotics, probiotics, or gastric acid inhibitors within the previous three months
- Having cancer, cardiovascular diseases, and other related conditions
- Having long-term chronic oral or gastrointestinal diseases.

9. Study Design

Prospective, single-center, randomized controlled trial.

10. Sample Size Estimation

According to the principles of clinical statistics, recruiting at least 30 individuals per group is necessary to potentially achieve statistical significance. However, ensuring a sufficiently large and representative sample size to appropriately detect the effects of the research hypothesis requires consideration of various factors, such as effect size, expected direction of effect, and statistical methods. Therefore, we intend to recruit 50 individuals per group, totaling 150 individuals, to account for these factors.

11. Methods for Randomization and Concealment

Random number sequences generated using the "sample" function in R language by a researcher who was not involved in the analysis and interpretation of this study.

12. Blinding

Not applicable.

13. Outcome Measures

- Gut microbiota: Metagenomic sequencing, performed uniformly after completion of sample collection.
- Oral microbiota: Metagenomic sequencing, performed uniformly after completion of sample collection.
- Body mass index (BMI): Self-reported, obtained through questionnaires during participant recruitment.
- Health status: Self-reported, obtained through questionnaires during participant recruitment.
- Dietary habits: Self-reported, obtained through questionnaires during participant recruitment.

14. Definition of Participant Validity Determination

(A) Participants have the right to withdraw from the clinical trial at any stage. Researchers are also obligated to take necessary measures, including proactively making decisions for participants to exit the clinical trial, to ensure participant safety and rights.

(B) In the following circumstances, the researcher should proactively consider allowing participants to exit the clinical trial:

- Poor participant compliance, where participants cannot adhere to the clinical trial protocol during visits or research interventions.
- Occurrence of severe adverse reactions related to the study intervention.
- Other situations that may increase participant risk or compromise the reliability of study results.

(C) Participants voluntarily withdrawing from the clinical trial:

- Participants should not face any discrimination or retaliation, and their medical treatment and rights should not be affected.
- Researchers should strive to understand the reasons for participants' voluntary withdrawal from the clinical trial and document this information in the source documents.
- Post-withdrawal follow-up should be conducted as required by the protocol. If the protocol does not explicitly describe follow-up requirements, the research team can discuss and decide.
- Researchers should provide their contact information to participants and actively obtain the latest contact information from participants to ensure timely follow-up.

(D) If participants withdraw due to allergies, adverse reactions, or ineffective treatment, researchers should take appropriate treatment measures based on the participants' actual situation.

(E) If participants withdraw from the trial due to any adverse events, researchers should conduct follow-up according to the protocol or until the adverse event is resolved, and the follow-up information should be recorded and archived in the source documents.

(F) Information related to participants' withdrawal from the clinical trial should be documented in the source documents and regularly submitted to the ethics committee (e.g., in annual reports).

(G) Upon learning or deciding that a participant is withdrawing from the clinical trial, researchers should complete all evaluative items and data collection that can be completed.
(H) Participant withdrawal from the trial does not mean the participant's trial data obtained up to that point should be withdrawn from the clinical trial. Trial data acquired up to the participant's withdrawal should be retained as part of the trial database and should not be ignored or deleted.

15. Definition, Identification, and Management System for Adverse Events and Adverse Reactions

(A) Researchers should actively collect safety information from participants through methods such as open communication, proactive inquiries, detailed physical examinations, and review of laboratory data. This will enable timely and accurate identification of adverse events occurring during the study.
(B) An adverse event (AE) refers to any unfavorable medical occurrence in a patient or clinical trial participant undergoing research intervention, which may not necessarily have a causal relationship with the treatment. Adverse events can encompass any unfavorable and unexpected signs (including abnormal laboratory findings), symptoms, or diseases related or unrelated to the research intervention.
(C) Serious adverse events are adverse events that occur under any dose of the intervention or at any time during the observation period, including events that result in prolonged hospitalization, disability, impairment of work capacity, life-threatening situations, or death, and events resulting in congenital abnormalities.
(D) After confirming an adverse event, a determination should be made whether it is a serious adverse event. Regular adverse events should be clinically managed as appropriate based on the actual situation, and the adverse event record form in the Case Report Form (CRF) should be completed.
(E) If an adverse event can be definitively attributed to a specific drug reaction, it should be reported based on the center's adverse reaction reporting procedure.
(F) Handling of Serious Adverse Events:

- In case of a life-threatening serious adverse event threatening the participant's life, prompt and sufficient medical treatment should be provided to ensure participant safety and alleviate anxiety.
- Reporting of Serious Adverse Events:
  - Must be reported to the center's responsible person within 12 hours of first knowledge and to the ethics committee of the center.
  - Reported to the coordinating unit within 24 hours or no later than the second working day.
  - Communication and follow-up with the participant and their family should be conducted.

(G) Follow-up for Adverse Events:
All adverse reactions/events should be followed up to confirm their outcomes and ensure appropriate resolution or stabilization of the condition.

16. Ethical Considerations

- Ethics Committee: Clinical Trial Ethics Committee of Huazhong University of Science and Technology
- Approval Process: Fill out the ethics approval application form and attach relevant approval materials.
- Informed Consent: Before each participant is included in this study, the researcher has the responsibility to provide a comprehensive and complete introduction of the study's purpose, drug properties, potential adverse reactions, and possible risks. Participants should be informed about their rights, risks, and benefits. Participants should sign an informed consent form before enrollment.
- Ethical Standards: This clinical trial must adhere to the Helsinki Declaration, the "Guidelines for the Quality Management of Clinical Trials of Drugs" (GCP) issued by SFDA, and relevant regulations. The study can only commence after approval by the coordinating unit's ethics committee. Any modifications to the trial protocol during the clinical study must be reported to and documented by the ethics committee.
- Registration Date: January 26, 2022
- Registration Institution: Clinical Trial Ethics Committee of Huazhong University of Science and Technology; Chinese Clinical Trial Registry (ChiCTR).

17. Participant Recruitment

- Recruitment Location: Huazhong University of Science and Technology
- Recruitment Method: Open recruitment
- Screening Process: Screening according to inclusion and exclusion criteria of the study
- Screening Personnel: Dr. Hu Desheng, Professor Chen Weihua

18. Collection of General Participant Information

- Implementing Researcher for Collection: Zhu Jiaying
- Contents: Age, height, weight, gender, sleep habits, dietary status, medical history, recent physical examination results, gastrointestinal health status, oral health status, self-assessment of health status

19. Baseline Indicators and Observation Items

- Baseline Indicators: Age, height, weight, gender, sleep habits, dietary status, medical history, recent physical examination results, gastrointestinal health status, oral health status, self-assessment of health status
- Observation Items: Oral microbiota, gut microbiota

20. Standard Operating Procedures

- As per the official instructions of Omeprazole Enteric-coated Capsules and professional guidance from doctors, this medication should be taken orally 30 minutes before a meal, once daily, one capsule each time, with each capsule containing 20mg.
- As per the official instructions of Famotidine and professional guidance from doctors, this medication should be taken orally after a meal, once daily, one capsule each time, with each capsule containing 20mg.

21. Statistical Analysis Methods

- Descriptive statistics for quantitative indicators will include means, standard deviations, medians, minimum values, maximum values, and quartiles.
- For categorical indicators, the number and percentage of each category will be described.
- Statistical differences will be assessed using t-tests and Wilcoxon rank-sum tests.

22. Participant Management System

- Before the study, all participants must sign written informed consent.
- Patients will be enrolled based on the inclusion and exclusion criteria.
- Attention will be given to protecting patient privacy and safety.

23. Specimen Management System

- Collection: Collect saliva and feces samples from patients for relevant indicator tests. Unused samples will be destroyed.
- Storage: Stored in a -80°C freezer
- Submission: Transported using dry ice

24. Drug and Equipment Management System

Refer to the drug instructions for storage. Check and confirm before administering medication.

25. Data Management System

All data will be recorded in specific forms, entered by Chuqing Sun, verified by Min Li, and analyzed by Jiaying Zhu. The database will be managed by Wei-Hua Chen.

26. Data Safety and Monitoring Committee's Composition and Responsibilities

None

27. Research Team

Professor Wei-Hua Chen's Research Group, College of Life Science and Technology, Huazhong University of Science and Technology:

Wei-Hua Chen, Professor, PhD supervisor, Project leader; Provides research guidance; Contact: 15827354263.

Jiaying Zhu, PhD student; Responsible for participant recruitment, sample transport and storage, data analysis; Contact: 15827572512.

Yingjian Wu, PhD student; Responsible for participant recruitment, sample transport, and storage; Contact: 15527185702.

Guoru Hu, Master student; Responsible for participant recruitment, sample transport, and storage; Contact: 15827595161.

Hanbo Jin, Master student; Responsible for participant recruitment, sample transport, and storage; Contact: 15533005035.

Professor Desheng Hu's Research Group, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology:

Desheng Hu, Professor, Doctoral Supervisor, Chief Physician, Project Collaborator in Charge;

Providing medication guidance; Contact: 18040597967.
Mengling Yang, Research Assistant; Responsible for recruiting study participants, sample collection; Contact: 13164172931.

28. Intellectual Property Rights

All intellectual property rights of the study belong to Huazhong University of Science and Technology, and authorship will be determined based on contributions to the research.

29. Publication Plan

Expect to publish 2 papers by the end of 2023.

30. Data Sharing Plan

Original data has been uploaded to the GSA database (https://ngdc.cncb.ac.cn/gsa/) and ResMan (http://www.medresman.org.cn/login.aspx), and will be made publicly available immediately after the publication of study results.

31. Treatment and Management of Participants After the End of the Trial

None

临床试验研究计划书

1. 诚信申明

本研究保证操作严格按照试验规程和数据记录的真实性；本研究不存在任何利益冲突。

2. 研究题目

胃酸对口服益生菌到达肠道的影响及对策研究

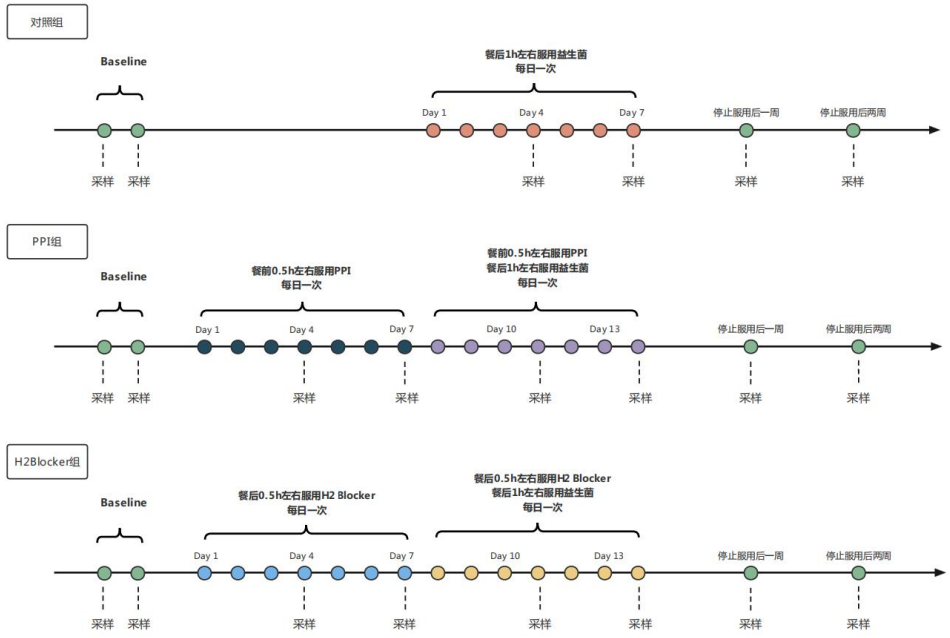
3. 研究计划书版本号

版本 3（2022 年 03 月 17 日）

4. 经费来源

千人计划肠道微生物组与人体健康(项目编号:0214170083;类型:人才启动经费)

5. 研究事项执行流程图（表）



6. 研究背景

本研究是在目前全世界对口腔微生物与肠道微生物相关研究进展的如火如荼的情况下展开的。口腔和肠道分别位于人体消化道的两端,但却是人体最主要的两大微生物生态位点,两者定植微生物群落间的相互关系已经成为近年来人体微生物组研究的热点。现有研究表明口腔微生物和肠道微生物的组成和动态变化与人体的健康和疾病状况息息相关 (Wade 2013; Lynch and Pedersen 2016) 。

人类每一天大约要咽下大约 1.5L 的唾液,约有 1011 种口腔微生物也随之进入胃肠消化道 (RICHARDSON and JONES 1958)。然而研究发现,口腔微生物和肠道微生物在群落组成上存在着显著的差异,大部分被咽下的口腔微生物种类并没有在肠道中被发现。口腔微生物尤其是

口服益生菌是否可以到达并成功定植远端肠道目前为止仍存在争议。有研究认为,健康人群中大部分口腔微生物在经过胃肠消化道时被作为胃肠屏障的胃酸、抗菌胆汁酸等杀死,导致最终无法到达肠道并定植 (Martinsen et al. 2005; Ridlon et al. 2014)。

质子泵抑制剂(PPI)是临床常用药物之一,其本质是 H + -K + -ATP 酶抑制剂,抑制胃壁细胞内质子泵驱动的 H + 分泌,从而阻断胃酸分泌的通道。而 H2 受体阻断药主要是通过阻断胃壁细胞的 H2 受体,抑制基础胃酸和夜间胃酸分泌,同时对胃泌素及 M 受体激动药引起的胃酸分泌也有抑制作用,是治疗消化性溃疡较为广泛的一类药物。临床上质子泵抑制剂可以用于治疗消化性溃疡、胃食管反流性疾病、卓艾综合征以及上消化道出血,现已成为胃酸分泌异常及相关疾病的一线药物 (Scarpignato et al. 2016)。短期服用质子泵抑制剂的副作用非常小,有研究报道服用 PPI 两周后 PPI 效应即可消除 (Mosli et al. 2012)。先前亦有研究通过招募健康志愿者短期服用 PPI 以研究 PPI 对口腔菌群变化的影响 (Koo et al. 2019; Mishiro et al. 2018)。

7. 研究目的

本研究拟通过对健康人口服益生菌、胃酸抑制剂(如质子泵抑制剂、H2 受体阻断剂)前后口腔菌群和肠道菌群的宏基因组测序,研究胃酸是否是口服益生菌到达肠道定植的主要障碍、胃酸抑制类药物是否可促进口服益生菌在肠道内的定植以及胃酸抑制类药物对口腔和肠道菌群的影响。通过生物信息学手段分析健康人口腔菌群与肠道菌群组成和结构的异同,比较在不同干预手段下口服益生菌是否能成功到达肠道并定植,以理解益生菌使用的人体障碍,用于后续开发相应的对策(比如用抗酸的胶囊对口服益生菌进行包裹等),以推动益生菌研究及在疾病干预中的应用。

8. 纳入和排除标准

纳入标准:

1. 年龄在 18~45 岁之间
2. 体重 BMI 指数在 19-24kg/m2 之间
3. 不抽烟、不酗酒
4. 身体健康,无癌症、心脑血管、肝肾功能不全等严重疾病;
5. 无严重口腔疾病、无肠道疾病;
6. 三个月内没使用过胃酸抑制剂、抗生素及益生菌类药物

排除标准:

1. 长期抽烟或饮酒
2. 最近三月或者长期服用胃酸抑制剂、抗生素和益生菌类药物;
3. 有癌症、心脑血管等疾病;
4. 有长期慢性口腔疾病或肠道疾病

9. 设计方案，设计模式图，附 SPIRIT 模版

前瞻、单中心、随机对照研究

10. 样本量估算

根据临床统计学原则，为了达到统计显著性每组需要至少招募 30 名个体。然而，确保一个足够大和代表性的样本量以适当地检测研究假设的效应需要考虑各种因素，如效应大小、预期效应方向和统计方法。因此，我们计划每组招募 50 名个体，总计 150 名个体，以考虑这些因素。

11. 随机和隐蔽分组的方法
由不参与研究分析的研究人员用 R 语言的 sample 函数产生随机数字序列，保密到干预开始前

12. 盲法
无

13. 测量指标
肠道菌群，宏基因组测序，所有样本采集完成后统一进行测序
口腔菌群，宏基因组测序，所有样本采集完成后统一进行测序
体质指数，自我报告，招募志愿者时填写问卷
健康状况，自我报告，招募志愿者时填写问卷
饮食状况，自我报告，招募志愿者时填写问卷

14. 对参试者有效性认定的定义
(一) 受试者有权在临床试验的任何阶段随时退出试验。研究者也有义务采取必要措施，包括主动做出让受试者退出临床试验的决定,以保障受试者安全和权益。
(二) 本研究在以下情况下,研究者应主动考虑让受试者退出临床试验:
1. 受试者依从性差,在接受访视、研究干预等方面不能依从临床试验方案执行:
2. 出现严重不良研究干预相关反应;
3. 可能增加受试者风险或损害研究结果可靠性的其他情况。
(三) 受试者主动退出临床试验
1.不应因此受到任何歧视或报复,其医疗待遇与权益也不应受到任何影响。
2.研究者应尽可能了解受试者主动退出临床试验的原因,并将相关信息记录到原始文件中。
3.退出后的随访应根据方案的要求进行。如在方案中未明确描述随访要求,可以通过研究团队讨论决定。
(四) 研究者应该将自己的联系方式主动告知受试者,并主动获取受试者的最新联系方式以确保受试者的按时随访。
(五) 如果受试者因过敏、不良反应、治疗无效而退出,研究者应根据受试者实际情况积极采取相应的治疗措施。
(六) 如果受试者因为任何不良事件而退出试验,研究者应该根据方案随访或直到不良事件解决,并将随访的信息记录在原始文件中存档。
(七) 受试者退出临床试验的相关信息应记录在原始文件中,并定期(比如在年度报告中)提交伦理委员会。
(八) 研究者在获知或决定受试者退出临床试验后,应完成所有能够完成的评价项目和数据采集。
(九) 受试者退出试验不意味着已获得的受试者试验数据退出临床试验。截止到受试者退出的时点,已经获得的试验数据应该保留作为试验数据库的一部分提交不应忽略或者删除。
包括退出、剔除、失访、混杂、中止、暂停的定义

15. 不良事件和不良反应的定义、鉴定方法和管理制度
(一) 研究者应当主动的方式,比如与受试者充分交流、主动询问、详尽的体格检查、审核实

验室检查数据等,充分收集受试者的安全性信息,及时准确的判断研究过程中出现的不良事件。

(二) 不良事件(AE,adverse event) 指患者或临床研究受试者在接受研究干预时发生的不必一定与该治疗干预有因果联系的任何不利的医学事件。不良事件因此可以是与研究干预实施时间上相关的任何不利和意想不到的迹象(比如,包括异常的实验室发现)、症状或疾病,无论是否考虑其与研究干预相关。

(三) 严重不良事件是指在试验干预任何剂量下或在观察期间任何时候出现的以下不良事件,包括:需延长住院时间、伤残、影响工作能力、危及生命或死亡导致先天畸形的事件。

(四) 确认不良事件后,应首作出是否为严重不良事件的判断。普通不良事件根据实际情况,给予相应的临床处理,并填写 CRF 中的不良事件记录表。

(五) 不良事件可以明确确认为某种药物不良反应的,依据本中心不良反应报告程序上报。

(六) 严重不良事件的处理

1.如严重不良事件威胁到受试者或病人的生命时,需第一时间进行充分的救治。保护受试者安全,缓解对立情绪。

2.严重不良事件报告

(1)必须在首次获悉 12 小时之内报告研究单位的中心负责人和本中心伦理委员公。

(2)24 小时内或不迟于第二个工作日向组长单位报告。

(3)做好受试者及其家属的沟通善后工作。

(七) 不良事件的随访

所有不良反应/事件都应当追踪随访,确认其发展结局,相关事宜到得到妥善解决或病情稳定。

16. 伦理考量

伦理委员会: 华中科技大学同济医学院医学伦理委员会

报批程序: 填写伦理审批申请表,并附上相关审批材料

知情同意:每一位受试者入选本研究前, 研究医师有责任向患者完整、全面地介绍本研究的目的、药物的性能及其可能出现的毒副反应和可能的风险, 应让受试者知道他们的权利、所要承担的风险和受益。入选前受试者应签署知情同意书。

伦理规范:本临床试验必须遵循赫尔辛基宣言、SFDA 颁布的《药物临床试验质量管理规范》(GCP) 以及相关的法规。在试验开始之前,由组长单位伦理委员会批准该方案后方可开始本项研究。在临床研究期间试验方案做任何修改均应向伦理委员会报告并备案。

注册时间: 2022.01.26

注册机构: 华中科技大学同济医学院医学伦理委员会

17. 参试者的征募

征募地点:华中科技大学

征募方法:公开招募

筛选过程:根据研究的纳入、排除标准进行筛选

筛选的研究人员: 胡德胜主任医师、陈卫华教授

18. 参试者一般信息的收集

实施收集的研究人员: 竺嘉滢

内容: 年龄、身高、体重、性别、作息规律、饮食状况、既往疾病史、最近一次的体检状况、胃肠道健康状况、 口腔健康状况、 自我健康状况评估

19. 基线指标和观测项目

基线指标: 年龄、身高、体重、性别、作息规律、饮食状况、既往疾病史、最近一次的体检状况、 胃肠道健康状况、 口腔健康状况、 自我健康状况评估
观测项目: 口腔菌群、肠道菌群

20. 标准操作规程
根据奥美拉唑肠溶胶囊的官方说明书和医生的专业指导,该药品需在餐前30 min口服,一日一次,一次一粒,一粒 20mg。
根据法莫替丁的官方说明书和医生的专业指导,该药品需在餐后口服,一日一次,一次一粒,一粒 20mg。

21. 统计分析方法
定量指标的描述将计算均数、标准差、中位数、最小值、最大值、四分位数、
分类指标将描述各类的例数及百分数
统计学差异检验采用 t-test 和 wilcox 秩和检验

22. 参试者管理制度
1. 在进行研究之前,所有患者必须签署书面的知情同意;
2. 根据纳入及排除标准入组患者;
3. 注意保护患者隐私及安全。

23. 标本管理制度
采集: 采集患者唾液和粪便标本,进行相关指标的检测,使用后剩余样本进行销毁。
保管: -80℃冰箱储存
送检: 干冰运输

24. 药品和器材管理制度
参照药品说明书对药品进行储存, 给药前进行核对、确认。

25. 数据管理制度
所有资料将会录入至具体的表格, 由孙楚晴统一录入, 李敏核对, 竺嘉滢分析; 数据库由陈卫华管理。

26. 数据安全与监察委员会的组成和工作职责
无

27. 研究团队
华中科技大学生命科学与技术学院,陈卫华教授课题组:
陈卫华,教授,博士生导师,项目主要负责人;提供研究指导;15827354263。
竺嘉滢,博士研究生;负责样本运输与保存、数据分析;15827572512。
吴英健,博士研究生;负责招募研究对象、样本运输与保存;15527185702。
胡国茹,硕士研究生;负责招募研究对象、样本运输与保存;15827595161。
靳瀚博,硕士研究生;负责招募研究对象、样本运输与保存;15533005035。

华中科技大学同济医学院附属协和医院,胡德胜教授课题组:

胡德胜,教授,博士生导师,主任医师,项目合作方负责人;提供用药指导;18040597967。
杨梦灵,科研助理;负责招募研究对象、样本收集;13164172931。

28. 知识产权
研究的所有知识产权归于华中科技大学, 根据研究者对研究的贡献大小进行署名。

29. 发表计划
预计 2023 年底发表论文 2 篇。

30. 原始数据共享计划
原始数据已上传至 GSA 数据库 (https://ngdc.cncb.ac.cn/gsa/) 和 ResMan(http://www.medresman.org.cn/login.aspx), 在研究结果发表后立刻公开。

31. 试验结束后对参试者的治疗和管理
无