Medical Ethics Committee of Xiangya Hospital Central South University

Ethic Review Comment Letter

Review date: April 9, 2024 Censorship Section Brief No. (2024040396)

<table>
<tr><td>Project name</td><td colspan="4">Effect of TMAO on inter-individual differences of clopidogrel efficacy in patients with CAD and its mechanism</td></tr>
<tr><td>Classification</td><td>Research Project</td><td>Project source</td><td colspan="2">funded projects</td></tr>
<tr><td>Review form</td><td>Quick review</td><td>Review category</td><td colspan="2">Annual periodic follow-up review</td></tr>
<tr><td>Responsible department</td><td>Geriatrics Department of Xiangya Hospital Central South University</td><td>Principal investigator</td><td colspan="2">Bi-lian Chen</td></tr>
<tr><td>File and Version number</td><td colspan="4">See Annex 1 for details</td></tr>
<tr><td>Quick review</td><td colspan="4">Members: 2; Names: Xiao-xia Zuo, Xiao-shan Tian</td></tr>
<tr><td>Voting result</td><td>Consent（2）</td><td>Modified consent（0）</td><td>Disagree（0）</td><td>Pause or termination（0）</td></tr>
<tr><td rowspan="2">Review comment</td><td colspan="4">Review conclusion：The project was approved to continue the research in the geriatric department of our hospital, and the ethical approval of our hospital was extended for one year.</td></tr>
<tr><td colspan="3">(Chairman/Vice-Chairman)：
Xin Zhang</td><td>Issuing date：
April 17, 2024</td></tr>
<tr><td colspan="2">Annual/regular tracking frequency</td><td colspan="3">12 months</td></tr>
<tr><td colspan="2">Ethics Committee</td><td colspan="3">Clinical Medical Ethics Committee of Xiangya Hospital Central South University</td></tr>
<tr><td>Expiry date</td><td colspan="4">November 23,2024</td></tr>
</table>

The medical ethics committee's responsibilities,composition, operations and records are fully compliant with "Guidelines for ethical review of drug clinical trials"(2010),"Methods for ethical review of biomedical research involving human beings"(2016)、“Standard for quality control of clinical trials of medical devices" (2016)、GCP (2020)、ICH-GCP and other related regulations.

Address: No.87 Xiangya Road,Changsha(410008) Hunan Tel: 86-731-84327919
E-mail:xyyyllwyh@126.com

Medical Ethics Committee of Xiangya Hospital Central South University

Statement:

Please strictly adhere to medical ethical principles and the protocol approved by the Ethics Committee during clinical trials to ensure the rights and well-being of participants.

All studies must be reviewed and approved by the Ethics Committee before implementation. Please note:

(1) For research falling under the scope of the "Administrative Licensing Items for the Approval of Human Genetic Resources Collection, Acquisition, Sale, Export, and Exit" after obtaining ethical approval, submit the study to the China Human Genetic Resources Management Office for approval. Once approved, promptly submit the approval document to the Ethics Committee for filing before implementation.

(2) For clinical trials of medical devices listed in the "Catalog of Class III Medical Devices Requiring Clinical Trial Approval" after obtaining ethical approval, submit the study to the CFDA for approval. Once approved, promptly submit the approval document to the Ethics Committee for filing before implementation.

(3) For clinical studies within the scope of the "Scope and Procedures for the Filing of Chemical Drug Bioequivalence Trials," after obtaining ethical approval, promptly file with the NMPA. Within 30 days of completing the filing, notify the Ethics Committee in writing and obtain the Ethics Committee's filing receipt before initiation.

If changes are made to the principal investigator, protocol, informed consent form, or recruitment materials during the study, the applicant must submit an amendment review application.

If life-threatening or fatal serious adverse events occur during a trial at our hospital, a report must be submitted to our hospital's safety reporting system within 24 hours of the investigator's awareness.

In accordance with the annual/periodic follow-up review frequency specified in the approval document, the applicant must submit a study progress report to this committee one month before the deadline. If any situation arises that may significantly impact the trial or increase risks to participants, the applicant must promptly submit a written report to this committee.

For major and persistent protocol deviations, the investigator/sponsor must submit a protocol deviation report.

If the investigator/sponsor suspends or terminates the study prematurely, the applicant must promptly submit a suspension/termination report to this committee.

Upon completion of the clinical trial, the applicant must promptly submit a final study report and the sub-center summary form.

Appendix 1: List of Submission Documents

1 Cover Letter
2 Reporting Form
3 Delay Explanation
4 Clinical Research Project Approval Form,
5 Clinical Study Protocol (Version No.: V1.0, Version Date: October 10, 2022)
6 Informed Consent Form(Version No.: V1.0, Version Date: October 10, 2022)
7 Chen Bilian's Profile
8 Risk Prevention and Control Plan
9 Investigator's Statement of Responsibilities

Medical Ethics Committee of Xiangya Hospital Central South University

April 9, 2024

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中南大学湘雅医院医学伦理委员会

Medical Ethics Committee of Xiangya Hospital Central South University

伦理审查意见函

Ethic Review Comment Letter

审查日期 Review date：2024 年 04 月 09 日　　伦审科简第(2024040396) 号

项目名称 Project name	TMAO 对冠心病患者氯吡格雷药物疗效个体差异的影响及机制研究		
项目类别 Classification	科研项目	项目来源 Project source	其他基金资助项目
审查方式 Review form	简易审查	审查类别 Review category	年度定期跟踪审查
负责科室 Responsible department	中南大学湘雅医院老年病科	我院研究项目负责人 Principal investigator	陈碧莲
审查文件及版本号 File and Version number	详见附件一		
快速审查 Quick review	委员： 2 人 ； 姓名：左晓霞、田晓山		
投票结果 Voting result	批准（2） Consent	修改后批准（0） Modified consent	不批准（0） Disagree	暂停或终止已批准的研究（0） Pause or termination
评审意见 Review comment	审查决定（Review conclusion）：批准项目继续在我院老年病科开展研究，我院伦理批件展期一年。		
	主任委员/副主任委员（Chairman/Vice-Chairman）：	签发日期（Issuing date）：2024 年 4 月 17 日	
年度/定期跟踪审查频率 Annual /regular tracking frequency	12 个月		
伦理委员会 Ethics Committee	中南大学湘雅医院临床医学伦理委员会		
有效期： Expiry date	2024-11-23		

备注：本伦理委员会的职责、人员构成、运行和记录遵循《药物临床试验伦理审查工作指导原则》(2010)、《涉及人的生物医学研究伦理审查办法》(2016)、《医疗器械临床试验质量管理规范》(2016)、GCP（2020）、ICH-GCP、等相关法规。

The medical ethics committee's responsibilities, composition, operations and records are fully compliant with "Guidelines for ethical review of drug clinical trials"(2010)、"Methods for ethical review of biomedical research involving human beings"(2016)、"Standard for quality control of clinical trials of medical devices"(2016)、GCP（2020）、ICH-GCP and other related regulations.

地址：湖南省长沙市湘雅路 87 号　　邮编：410008　　电话号码：86-731-84327919
Address：No.87 Xiangya Road ,Changsha(410008) Hunan　　Tel：86- 731-84327919
E-mail:xyyyllwyh @126.com

2

中南大学湘雅医院医学伦理委员会

Medical Ethics Committee of Xiangya Hospital Central South University

中南大学湘雅医院临床医学伦理委员会声明：

请在临床试验过程中严格遵循医学伦理道德原则及本委员会批准的方案开展研究，确保受试者的权益。

所有研究需经伦理委员会审议同意并签署批准意见后方可实施。请注意：（1）对《人类遗传资源采集、收集、买卖、出口、出境审批行政许可事项》规定范畴内的研究，在获得伦理批准后请提交至中国人类遗传资源管理工作办公室进行审批，批准后及时将该批准文件交伦理委员会备案后方可实施。（2）对《需进行临床试验审批的第三类医疗器械目录》内医疗器械的临床试验，获得伦理批准后请提交至 CFDA 进行审批，批准后及时将该批准文件交伦理委员会备案后方可实施。（3）对《化学药生物等效性试验备案范围和程序》范围内的临床研究获得伦理批准后，应及时向 NMPA 备案，备案完成 30 天内书面告知伦理委员会，获得伦理委员会的备案回执后方可启动。

研究过程中若变更主要研究者、方案、知情同意书、招募材料的修改，请申请人提交修正案审查申请。

如果我院试验项目在过程中发生危及生命或死亡严重不良事件请在研究者获知的 24 小时内提交报告至我院的安全报告系统。

请按照批件中规定的年度/定期跟踪审查频率，申请人在截止日期前 1 个月向本委员会提交研究进展报告；当出现任何可能显著影响试验进行和增加受试者危险的情况时，申请人及时向本委员会提交书面报告。

重大及持续方案违背请研究者/申办者提交违背方案报告

研究者/申办者暂停/或提前终止研究，请申请人及时向本委员会提交暂停/终止研究报告。

临床试验结束，请申请人及时提交结题报告及分中心小结表。

附件一：送审文件清单

1. 递交信

2. 报告表

3. 延迟说明

中南大学湘雅医院临床医学伦理委员会

2024 年 04 月 09 日

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