Study Protocol and Statistical Analysis Plan

Overall design	This study is a prospective, open-label, randomized controlled, multicenter study conducted in adult patients with non-dialysis chronic kidney disease (ND-CKD) anemia in China, aiming to explore the reasonable hemoglobin target value for the treatment of ND-CKD anemia patients with enarodustat. The study is divided into two phases: - Screening period (up to 4 weeks) - Treatment period (96 weeks).
Sample size	The sample size was calculated based on the primary safety endpoint MACE+. Supposing that the occurrence risk of MACE+ events in the high Hb target group and the low Hb target group was 10% per year, the non-inferiority margin for the hazard ratio (HR) was 1.3, the statistical power (1-β) was 0.85, the significance level (α) was 0.05, the recruitment period was 2 years, the total study duration was 4 years, the high Hb target group and the low Hb target group were allocated equally at a 1:1 ratio, and the dropout rate was 5% per year. The sample size required for each group was 835 cases, and the total sample size was approximately 1,670 cases. With respect to the primary efficacy endpoint, under the pre-determined sample size of 1,670, it was hypothesized that the change in the SF-36 vitality score from the baseline in the high Hb target group was 3.0 points higher than that in the low Hb target group, with an intra-group standard deviation of 21.0 points. With a one-sided test with $\alpha = 0.025$ and the high Hb target group and the low Hb target group being allocated equally at a 1:1 ratio, the statistical power (1-β) could reach 0.83.
Grouping	After screening, all eligible patients will be randomly assigned in a 1:1 ratio to: - The low Hb target group: Hb target value of 11 g/dL; - The high Hb target group: Hb target value of 13 g/dL.

Inclusion/Exclusion Criteria	Inclusion Criteria: 1. Aged 18-75 years at the time of consent to participate; 2. Body weight ranged from 45 to 100 kg; 3. Diagnosed with CKD stages 2-5 (10 ≤ eGFR < 90 mL/min/1.73m2) and were not dialysis dependent; 4. Diagnosed with renal anemia: 1) Hemoglobin level of 6 - 10 g/dL for those who have not received ESA or HIF-PHI treatment within 6 weeks at screening; 2)Hemoglobin level of 8 - 12 g/dL for those who are currently receiving ESA (ESA dosage ≤ 10,000 IU/week) or HIF-PHI (roxadustat dosage≤ 100 mg TIW) at screening; 5. Serum ferritin > 100 μg/L or transferrin saturation > 20% at screening; 6. Voluntary participation in the trial and signing of the informed consent form. 6.Voluntary participation in clinical trials and signing the informed consent form. Exclusion Criteria: 1. Uncontrolled hypertension identified as systolic blood pressure >160mmHg or diastolic blood pressure >100mmHg after 4 weeks of regular and adequate drug therapy prior to screening; 2. Uncontrolled proteinuria identified as UACR >3000mg/g or 24-hour urine protein >3.5g in non-diabetic patients and UACR of >5000mg/g or 24-hour urine protein >5.5g in diabetic patients; 3. Anemia due to other reasons except CKD including systemic hematological disorders (such as myelodysplastic syndrome, aplastic anemia, etc.), hemolytic anemia, hemorrhagic anemia or cancer-related anemia; 4. History of autoimmune diseases which could result in anemia such as systemic lupus erythematosus and ANCA vasculitis; 5. History of active bleeding within 4 weeks prior to screening; 6. History of serious thrombotic event such as a myocardial infarction, cerebral infarction, pulmonary embolism, unstable angina, or PCI or cardiac surgery within 6 months prior to screening; 7. Severe heart failure (NYHA class IV) at screening; 8. History of blood transfusion within 2 months prior to screening; 9. History of usage of immunosuppressants or other immune therapies within 6 months prior to screening;

<table>
<tr><td></td><td>10. Patients who are estimated to require dialysis, kidney transplantation, or major surgery within 6 months;
11. Severe liver and biliary system complications (AST or ALT >3 times the upper limit of normal, total bilirubin >2 times the upper limit of normal) at screening;
12. Receiving ESA combined with roxadustat treatment at screening;
13. History of proliferative retinopathy or diabetic retinopathy requiring ophthalmological treatment;
14. Severe hyperparathyroidism (iPTH ≥ 500 pg/mL);
15. Severe active infections (such as active tuberculosis, fungal infections, etc.);
16. Patients who are bedridden or have difficulty walking, or have a history of atrial fibrillation or deep vein thrombosis of the lower limbs;
17. History of active tumors;
18. Female patients who are pregnant or breastfeeding, or non-childbearing women who do not agree to effective contraception;
19. Patients with a history of severe drug allergies (such as anaphylactic shock), or known allergies to any of the active ingredients or excipients of enarodostat;
20. Patients who are currently participating in any other interventional clinical trial;
21. Other reasons determined by the investigator not suitable for participation in the study.</td></tr>
<tr><td>Intervention</td><td>The initial dose of both groups of enadutamide was 4 mg once daily. Dose adjustments were made in accordance with the instructions in the manual and the requirements of different hemoglobin value groups.
Reference Table for Dosage Ladder of Endastat
<table>
<tr><th colspan="6">Dosage Ladder of Endastat</th></tr>
<tr><td>Level</td><td>1</td><td>2</td><td>3</td><td>4</td><td>5</td></tr>
<tr><td>Daily dosage of medication</td><td>1mg</td><td>2mg</td><td>4mg</td><td>6mg</td><td>8mg</td></tr>
</table>
The treatment period involved oral administration for a total of 96 weeks. Patients would undergo a total of 14 study visits (including the baseline visit) at weeks 0, 2, 4, 8, 12, 16, 24, 32, 40, 48, 60, 72, 84, and 96 to assess safety and efficacy. Unscheduled visits would be conducted based on the clinical practice of the investigators. During the treatment period, the use of iron supplements was not restricted for patients in both groups and was determined based on iron metabolism indicators and clinical practice.</td></tr>
</table>

Exit criteria for the study	1. Subjects who experience serious adverse events and are considered by the investigator to be unsuitable to continue participating in the trial for safety reasons; 2. Subjects for whom the investigator determines that due to the poor efficacy of the investigational drug, other anemia rescue treatments (such as blood transfusion) are needed; 3. Subjects for whom the investigator determines that a kidney transplant is necessary; 4. Subjects who require surgical treatment within the first six months after enrollment and are judged by the doctor to be unsuitable to continue participating in the study; 5. Subjects who request to withdraw from the trial; 6. Subjects with poor compliance; 7. Female subjects who become pregnant during the study period; 8. Subjects who have participated in other clinical trials of the investigational drug or other types of medical research, and it is determined that such research is scientifically or medically incompatible with this study; 9. Other reasons for which the investigator determines that it is not suitable to continue the trial. 10. Subjects who withdraw from the study for any reason cannot re-enroll in the study.
Statistical analysis	**Statistical analysis data sets** 1.Full Analysis Set (FAS): This refers to the set of subjects that is as close as possible to the intention-to-treat principle (ITT). This data set is derived from all randomized subjects after the minimum and reasonable exclusions. It includes all subjects who were randomized and used the trial drug at least once. This analysis set is used for the analysis of baseline demographic data and efficacy data, etc. 2.Per Protocol Set (PPS): This is a subset of the FAS. It includes all randomized subjects who used the assigned study drug at least once and had no major protocol deviations. Major protocol deviations will be determined and recorded before the database lock for the primary analysis. This analysis set is mainly used for the analysis of efficacy data. 3.Safety Set (SS): This includes all randomized subjects who were enrolled and used the assigned study drug at least once and have safety data. This analysis set is used for safety analysis. During the treatment process, the dose of enadutamide was adjusted as much as possible to meet the Hb target requirements of both groups. Even if the target value was not

	reached, the patient's data would still be included in the analysis. **Statistical analysis methods** Statistical analysis will be conducted using SAS 9.4 or a higher version. For quantitative data, the number of observations, mean, standard deviation, median, upper and lower quartiles, maximum, and minimum values will be listed. For qualitative data, the number of cases and percentages will be used for statistical description. When necessary, 95% confidence intervals can be added. Generally, missing values will not be included in the percentage calculation. Unless otherwise specified, all statistical inferences will be based on a two-sided test with $\alpha = 0.05$. A P value < 0.05 will be considered statistically significant. Confidence intervals will be at a 95% confidence level. We adopted a sequential test for the dual endpoints, first testing the efficacy endpoint. When the null hypothesis (H0) is rejected for the efficacy endpoint, we will proceed to the next safety endpoint hypothesis test. Descriptive statistical methods will be used to separately describe the number and proportion of subjects in each statistical analysis set by randomization group, the number and proportion of subjects who completed the study and those who withdrew from the study, and the categories of reasons for withdrawal (e.g., number, proportion). Demographic and other baseline characteristics will be described separately by randomization group. 1. Primary endpoint analysis (1) The change in SF-36 vitality score from baseline at 24 weeks after enrollment. This primary endpoint will be statistically described using descriptive methods for the high Hb target value group and the low Hb target value group at 24 weeks (e.g., number of cases, mean, standard deviation, median, maximum, minimum, etc.). Covariance analysis will be used, with the intervention as a fixed effect and the baseline SF-36 vitality score as a covariate, to estimate the least squares mean (LS mean), standard error, 95% confidence interval, and corresponding P value of the change in SF-36 vitality score from baseline at 24 weeks for the high Hb target value group and the low Hb target value group. (2) The risk of the first occurrence of MACE+ events within 96 weeks after enrollment.

	This primary endpoint will be statistically described using descriptive methods for the high Hb target value group and the low Hb target value group within 96 weeks (e.g., frequency, percentage, etc.). Kaplan-Meier curves will be used to plot the survival curves of MACE+ events for the two groups. The hazard ratio (HR) and its 95% confidence interval for the first occurrence of MACE+ events within 96 weeks for the two groups will be calculated in the Cox proportional hazards model. 1. When the upper limit of the 95% confidence interval of HR is less than the non-inferiority margin of 1.3, it can be concluded that the risk of the first occurrence of MACE+ within 96 weeks in the high Hb target group is non-inferior to that in the low Hb target group. 2. Secondary endpoint analysis For quantitative secondary endpoint indicators (such as the change in eGFR from baseline), summary statistical descriptions will be provided for each group, including the number of observations, mean, standard deviation, median, upper and lower quartiles, minimum and maximum values. Group comparisons will be conducted using a repeated measures mixed-effects model. For qualitative indicators, the number of cases and percentages will be used for statistical description, and chi-square tests or Fisher's exact probability test will be used for comparisons between two groups. For time-to-event indicators (the risk of the first occurrence of MACE risk events, the risk of thromboembolic events [excluding cardiovascular and cerebrovascular events], and the risk of cardiovascular death events), Kaplan-Meier curves will be used to plot the survival curves for the two groups, and the hazard ratio (HR) and its 95% confidence interval will be calculated in the Cox proportional hazards model. 3. Exploratory analysis For quantitative data (such as iron agent dosage, treatment duration; changes in ferritin, serum iron, and transferrin saturation from baseline at weeks 12, 24, 48, 72, and 96; average dose of ruxolitinib in the first 24 weeks), summary statistical descriptions will be provided for each group, including the number of observations, mean, standard deviation, median, upper and lower quartiles, minimum and maximum values. Group comparisons will be conducted using t-tests, Wilcoxon rank sum tests, or repeated measures mixed-effects models. For types of iron agents, the number of cases and percentages will be used for statistical description, and chi-square tests or Fisher's exact probability test will be

	used for comparisons between two groups. 4. Safety analysis In the safety analysis set, adverse events will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) and classified and summarized according to the System Organ Class (SOC) and Preferred Term (PT) based on the randomization group. Additionally, all adverse events, drug-related adverse events, serious adverse events, and adverse events leading to premature withdrawal from the study will be summarized separately.

知情同意书

受试者须知页

方案名称：恩那度司他治疗非透析慢性肾脏病贫血患者合理血红蛋白目标值的前瞻性、开放标签、随机对照、多中心研究
本中心主要研究者：丁小强
本中心：复旦大学附属中山医院
申办者：复旦大学附属中山医院

尊敬的受试者：

您被邀请参加恩那度司他治疗非透析慢性肾脏病贫血患者合理血红蛋白目标值的前瞻性、开放标签、随机对照、多中心研究。请仔细阅读本知情同意书并慎重做出是否参加本项研究的决定。参加这项研究完全是您自主的选择，但您只有在签署过本知情同意书后方可有可能进入研究。当您的研究医生或者研究人员和您讨论知情同意书的时候，您可以让他/她给您解释您看不明白的地方。我们鼓励您在做出参与此项研究的决定之前，和您的家人及朋友进行充分讨论。您有权拒绝参加本研究，也可随时退出研究，且不会受到处罚，也不会失去您应有的权利。若您正在参加别的研究，请告知您的研究医生或者研究人员。本研究的背景、目的、研究过程及其他重要信息如下：

一、 研究背景

慢性肾脏病（CKD）已经成为我国的一个重要公共健康问题，而贫血是 CKD 患者最常见的并发症之一。肾性贫血是指各种肾脏疾病导致红细胞生成素（EPO）绝对或相对生成不足，以及尿毒症毒素影响红细胞生成及其寿命而发生的贫血。

贫血将降低患者生活质量，增加心血管疾病及死亡风险。贫血患者氧分压降低，致心脏负荷增加，呈现高输出状态，久之将导致左心室肥大，乃至全心扩大和心力衰竭，增加患者病死率。因此，在 CKD 早期就重视贫血的诊断和治疗，对降低心血管并发症及死亡率均有重要意义。

肾性贫血治疗目的是避免患者输血，减少心血管事件发生，改善认知功能和提高生活质量。肾性贫血的治疗包括 ESAs 治疗、铁剂治疗、缺氧诱导因子脯氨酰羟化酶抑制剂（HIF-PHI）治疗等。肾性贫血治疗涉及 ESAs、铁、营养状态以及透析充分性等多方面，其中应用 ESAs 补充 EPO，或者通过 HIF-PHI 调控内源性 EPO 为肾性贫血治疗的关键。ESAs/HIF-PHI 治疗过程中，应依据 Hb 变化幅度调整剂量，避免 Hb 波动幅度过大。

目前 HIF-PHI 的治疗 Hb 靶目标是基于 ESAs 类的相关研究推荐。但是，HIF-PHI 类药物是在生理范围内提高 EPO 水平，不存在大剂量 ESAs 时体内 EPO

水平的过度升高。目前建议 HIF-PHI 治疗肾性贫血的 Hb 靶目标参考 ESAs，维持 Hb≥110 g/L，但不超过 130g/L。

HIF-PHI 治疗肾性贫血的 Hb 靶目标能否提高？是否能带来生活质量获益还有待于深入研究。恩那度司他治疗 ND-CKD 贫血患者，EPO 浓度始终保持在 50IU/L 以内，保持生理浓度。基于既往针对 Hb 靶目标和生活质量的研究结果，研究者计划开展本项临床试验，拟进一步探索 HIF-PHI（恩那度司他）治疗 ND-CKD 贫血患者在较高目标 Hb 下，不增加心血管等风险并提升患者生活质量，以期为 ND-CKD 贫血患者的治疗提供更有效的选择，为临床诊疗实践提供指导。

恩那罗®（恩那度司他片）由深圳信立泰药业股份有限公司生产，于 2023 年 6 月在中国获批，用于治疗非透析的成人慢性肾脏病（CKD）患者的贫血，是国内上市的新一代缺氧诱导因子脯氨酰羟化酶抑制剂（HIF-PHI）药物。恩那罗®对 HIF 靶点的调控更加合理适度，刺激生成的内源性 EPO（促红细胞生成素）更贴近生理浓度，平稳可控升高血红蛋白，整体安全性良好；一天一次的口服给药，用药依从性好，无需按体重调整，药物相互作用风险低。2023 年 12 月 13 日，恩那罗®被纳入国家医保，本次纳入医保目录后，将覆盖更多肾性贫血患者，为其带来全新的用药选择。恩那度司他中国说明书中起始剂量为 2mg/天，本研究参考恩那度司他治疗 ND-CKD 贫血患者的 3 期研究应用起始剂量为 4mg/天，在本研究中恩那度司他片起始剂量为 4mg，在整个研究期间会由研究医生根据患者实际状态和方案要求进行药物调整。

二、 研究目的

探索恩那度司他治疗的不同血红蛋白（Hb）目标值对非透析慢性肾脏病贫血患者生活质量和心血管风险的影响。

三、研究过程

1. 多少人将参与这项研究？

大约 1670 人将参与在约 52 个不同的研究机构/医疗机构开展的本项研究，其中计划至少 40 人会在本院参与本研究，本研究为竞争入组，最终实际入组数根据实际情况记录。

2. 研究步骤

如果您同意参加本研究，请您签署这份知情同意书。在整个研究观察 96 周共有 14 次随访，包括筛选期（第 1 次随访，V1）及治疗期（第 2 次-第 14 次随访，v2-v14），每次随访均进行血常规检查，每次抽血约 2ml，此后 2-6 个月不等，进行血生化、凝血功能及铁代谢检查采血研究期间总采血量约 90ml。

本研究分为 2 个阶段：

筛选期（-4 周）

在签署知情同意书后您需要进行筛选检查，在此期间您将被问询一些关于您过去疾病的病史、当前疾病情况以及您正在服用的药物等问题。您的研究医生将检测您的心率、血压、身高和体重、体格检查、12-导联心电图检查、血常规、血生化（包括：丙氨酸转氨酶、天冬氨酸转氨酶、尿素氮、血肌酐、钾，钠）、Hs-CRP 检测（高敏感 C-反应蛋白）、NT-proBNP（N 末端 B 型利钠肽原）、尿常规、UACR（尿白蛋白/肌酐比值）或 24 小时尿蛋白定量、铁代谢、甲状旁腺激素 iPTH、凝血功能、胸部 X 片、腹部 B 超、心脏 B 超、生活质量评估(SF-36 量表评估)等，如果您是育龄期女性将会进行妊娠试验检测。

治疗期（96 周）

符合筛选条件后，您会被随机分配到不同的研究组，分别为：

- 低 Hb 目标值组：Hb 目标值 11g/dL；
- 高 Hb 目标值组：Hb 目标值 13g/dL。

两组恩那度司他片的起始剂量均为 2mg qd，参考说明书及不同 Hb 值组别要求进行剂量调整。您的研究医生和您均知晓您所在的研究组，随机分配后您将接受相应治疗并随访 96 周，其间通过规律访视确保您的安全性，直至治疗期结束或您退出研究。

整个用药期间，您必须配合您的研究医生按期进行检测。在治疗后的第 2 周、4 周、8 周、12 周、16 周、24 周、32 周、40 周、48 周、及随后的每 12 周各访视一次直至 2 年。每次访视进行疗效及安全性评价，每次访视您的化验项目均由研究提供不会增加您的任何不必要的经济负担。

在治疗期间您将被问询一些关于您过去一段时间内的用药情况、当前疾病情况以及您正在服用的药物等问题，还会根据方案要求，根据每次随访时间检测不同的指标，包含心率、血压、血常规、血生化（包括：丙氨酸转氨酶、天冬氨酸转氨酶、尿素氮、血肌酐、钾，钠）、NT-proBNP、12-导联心电图检查、铁代谢、凝血功能、心脏 B 超、生活质量评估 SF-36 量表等。治疗期间两组患者铁剂使用不受限制，铁剂的使用根据铁代谢指标及临床诊疗常规而定。

3. 这项研究会持续多久？

研究整体计划持续约 4 年，对您个人来说参与本研究持续约 96 周。

您可以在任何时间选择退出研究而不会失去您本应获得的任何利益。然而，如果在研究途中您决定退出本研究，我们鼓励您先和您的医生商议。如果您出现严重的不良事件，或者您的研究医生觉得继续参加研究不符合您的最佳利益，他/她会决定让您退出研究。申办者或者监管机构也可能在研究期间要求终止研究。但您的退出不会影响您的正常医疗待遇与权益。

如果您因为审核医院从研究中退出，如果医生认为需要您也可能被要求进行退出前的最后一次实验室检查和体格检查以确保您的安全。

4. 研究中收集的生物标本

在研究过程中，研究步骤所描述的您的 14 次血液和 1 次尿液生物样本及样本检测产生的数据将会是为了本试验告知的目的而被采集和使用，研究结果产生的知识产权或潜在商业价值不会分享给您。

四、风险与受益

1. 参加本研究的风险是什么？

参加本研究可能给您带来的风险如下。您应该和您的研究医生，或者您愿意，与您平日照看您的医生讨论一下这些风险。

在参与研究过程中，可能会有因对药物不耐受或者身体伴发疾病等自身身体条件而产生的少数不良反应，对于您来说，与我们进行沟通、交谈可能会减轻心里不适。

如果在研究期间您出现任何不适，或病情发生新的变化，或任何意外情况，不管是否与研究有关，均应及时通知您的研究医生。

您在研究期间需要按时到医院随访，做一些检查，这将会占用您的一些时间，也可能给您造成麻烦或带来不方便。

2. 参加研究有什么受益？

直接受益：如果您同意参加本研究，您将有可能通过服用恩那度司他提高您的血红蛋白水平，改善肾性贫血带来的部分症状，如疲乏无力等，此外，可以减少肾性贫血加重带来的输血及其他风险，但我们不能对此作出承诺。

潜在受益：我们希望从您参与的本研究中得到的信息在将来能够使您或与您病情相同的患者获益。

五、备选的治疗方案

除了参与本研究，您可以接受您的医生提供的常规治疗：ESAs 治疗、铁剂治疗、其他类 HIF-PHI 治疗。请您和您的医生讨论一下这些及其他可能的选择。

六、个人信息的保密

本研究期间，出于本研究目的，研究团队可能需要接触您的病史，收集您过去必要的医疗记录和检测结果等个人信息。 在您签署本知情同意书后，就代表您允许研究团队去联系给您提供其他医疗帮助的提供者，以获得在他们为您提供医护服务期间的关于您必要的医疗信息。只有研究团队的成员能接触您的医疗信息，并识别您的身份。在不违反保密原则和相关法规的情况下，申办者授权的监查员；伦理委员会；监管部门会可以查阅您的原始医学记录以核实临床试验数据。

研究过程中，我们将收集您的个人信息和研究数据，为保证隐私我们将姓名、联系方式等可以直接识别您的这部分数据编码，以便任何人无法确定您的身份。如果在医学期刊上发表或在科学会议上汇报本研究的结果，也不会披露可识别您身份

的信息。

您许可的个人信息使用和分享权限，在任何时候都可以收回，如有需要，可通联系您的研究医生。如果这样做，您将无法继续停留在研究中。在这之后，研究者将不会再收集能识别出您个人信息的新健康数据。然而，对于已经收集到的健康数据，将可能会被继续使用和分享给其他研究者，正如该知情同意书中描述的一样。为了确保这项研究的科学性和可信度，在该研究结束之前，您可能不能够查看到一些与研究相关的记录。当研究结束时，您可以向研究医生提出查看健康数据的要求，这些健康数据就是研究过程中收集的，在您查看之后，可以提出任何关于您个人信息的错误。在本研究期间收集或产生的个人信息和研究过程产生的数据会进行编码后保存（“研究数据”），保存在（复旦大学附属中山医院肾内科）10 年后销毁。

除本次研究外，将来不会再次利用到您的这些信息。

七、研究结果的反馈

研究的整体结果（不包含您的个人信息）将在研究结束后在 http://www.ClinicalTrials.gov 进行描述，您根据研究题目关键词可自行检索。

八、关于研究费用及相关补偿

1. 研究所用的药物/器械及相关检查费用

您参与本试验后将不会有额外费用产生。您将获赠免费检查直至您退出研究。研究药物为常规诊疗用药，在整个研究期间所服用的试验药物恩那度司他片都由深圳信立泰药业股份有限公司免费提供，对于您同时合并的其他疾病所需的常规治疗和检查，将不在免费的范围之内。

2. 参加研究的补偿

为参与本研究所花费的开支（如交通费和额外采血的营养费），您将得到 1400 元人民币的补偿。

3. 发生损伤后的补偿/赔偿

如果发生与该项研究相关的伤害，您可以获得由复旦大学附属中山医院提供的免费治疗，或按中国有关法律进行补偿/赔偿。为了进一步保障您的权益，本研究为参加研究的受试者购买了保险。保险覆盖了整个研究期间，每次事故每人赔偿限额 10 万，累计赔偿限额 2000 万。

九、受试者的权利和相关注意事项

1. 您的权利

在参加研究的整个过程中，您都是自愿的。如果您决定不参加本研究，也不会影响您应该得到的其他治疗。您有权在试验的任何阶段随时退出试验而不会遭到歧视或受到不公平的待遇，您相应医疗待遇与权益不受影响。如果有可能影响您权益

和安全的信息更新时，再次签署更新版本知情同意书获得新信息。

2. 注意事项

作为受试者，您需要提供有关自身病史和当前身体状况的真实情况；告诉研究医生自己在本次研究期间所发现的任何不适；不得服用医生已告知的受限制药物、食物等；告诉研究医生自己最近是否参与其他研究，或目前正参与其他研究。

十、获知信息的相关联系方式

如果在研究过程中有任何重要的新信息，可能影响您继续参加研究的意愿时，您的医生将会及时通知您。如果您对自己的研究数据，或研究结束后您希望知道本研究的发现，您可以在任何时间提出有关本项研究的任何问题，并得到相应的解答，请通过电话 13816209067 与项方方联系。

伦理委员会已经审查通过该研究，如果您有与自身权利/权益相关的任何问题，或者您想反映参与本研究过程中遭遇的困难、不满和忧虑，或者想提供与本研究有关的意见和建议，请联系复旦大学附属中山医院医学伦理委员会，联系电话：021-31587871，电子邮件：ec@zs-hospital.sh.cn。

受试者签字页

知情同意声明：

我已被告知此项研究的目的、背景、过程、风险及获益等情况。我有足够的时间和机会进行提问，问题的答复我很满意，同意参加本研究。

我也被告知，当我有问题、想反映困难、顾虑、对研究的建议，或想进一步获得信息，或为研究提供帮助时，应当与谁联系。

我知道我可以选择不参加此项研究，或在研究期间的任何时候无需任何理由退出本研究。

我已知道如果我的状况更差了，或者我出现严重的不良事件，或者我的研究医生觉得继续参加研究不符合我的最佳利益，他/她会决定让我退出研究。无需征得我的同意，资助方或者监管机构也可能在研究期间终止研究。如果发生该情况，研究医生将及时通知我，研究医生也会与我讨论我的其他选择。

我将得到这份知情同意书的副本，上面包含我和研究者的签名。

我了解参与本研究必须要使用我的个人信息，我同意按照本知情同意书所述的目的使用和处理我的个人信息和/或生物样本。

☐同意　　☐不同意，无法参与本研究。

受试者签名：_____　　日期：_____

监护人签字：_____与受试者关系（　　） 日期：_____

（适用于受试者无行为能力/限制行为能力时，则需监护人签名和签署日期）

公正见证人签字：_____ 日期：_____

（适用于受试者不能阅读该知情同意书时，则需一名公正见证人见证研究者已将知情同意书的所有内容告知了受试者，受试者表示了同意参加的意愿，公正见证人需签名和签署日期）

研究者签名：_____ 日期：_____