Clinical Study of the Efficacy and Safety of MitoQ in Improving Cancer Cachexia

Study Protocol

Protocol No.	CHASE-019
Study Phase	Phase II
Study Drug	MitoQ Capsules
Version	V2.0
Version Date	June 29, 2026
Principal Investigator	Professor Yinghua Ji

Confidentiality Statement

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Study Site	The First Affiliated Hospital of Henan Medical University
Estimated Study Period	June 2026 - June 2027

Version History / Amendment History

Version	Version Date	Reason for Revision and Summary of Changes
V1.0	June 17, 2026	Initial version
V2.0	June 29, 2026	Revised version following scientific review comments

Protocol Synopsis

Study Title	Clinical Study of the Efficacy and Safety of MitoQ in Improving Cancer Cachexia
Protocol No.	CHASE-019
Version and Date	V2.0, June 29, 2026
Study Drug	MitoQ Capsules
Sponsor	The First Affiliated Hospital of Henan Medical University
Principal Investigator	Professor Yinghua Ji
Participating Center	Single center
Study Objectives	**Primary Objective** • To evaluate the preliminary efficacy of MitoQ in patients with cancer cachexia. **Secondary Objective** • To evaluate the safety of MitoQ in patients with cancer cachexia and explore the related mechanisms.
Study Endpoints	**Primary Efficacy Endpoint:** • To evaluate the preliminary efficacy of MitoQ in patients with cancer cachexia by comparing improvement in muscle function before and after MitoQ treatment at Weeks 7 and 13, as assessed by handgrip strength and the 6-minute walk test. **Key Secondary Efficacy Endpoints:** 1. Inflammatory and metabolic parameters: changes in C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-alpha); effects on oxidative stress markers (MDA, SOD, and GPx); and changes in

	prealbumin, serum albumin, etc. 2. Clinical benefit measures: changes in skeletal muscle mass before and after MitoQ treatment at Weeks 7 and 13 (skeletal muscle index at the third lumbar vertebral level measured by CT); changes in body weight, including total body weight, fat mass, and lean body mass; and quality of life and symptoms assessed using standardized scales, including the EORTC QLQ-C30, FAACT (Functional Assessment of Anorexia/Cachexia Therapy), Hospital Anxiety and Depression Scale (HADS), and Cancer Fatigue Scale (CFS). **Other Secondary Efficacy Endpoints:** 1. Tumor response and survival measures: objective response rate based on RECIST 1.1 and progression-free survival (PFS). 2. Safety assessments: liver function tests and blood lipid levels. 3. Exploratory assessments: exploratory metabolic and inflammatory biomarkers, etc. **Safety Endpoints:** • Vital signs, physical examinations, laboratory parameters, electrocardiogram (ECG), echocardiography, adverse events (AEs), etc.; AEs will be assessed according to NCI-CTCAE Version 5.0.
Efficacy Assessments	1) Muscle Strength (1) Handgrip Strength (HGS) Measured using a Jamar or equivalent hand dynamometer, with the participant seated and the elbow flexed at 90 degrees. The dominant hand will be measured three times and the mean value recorded. HGS is one of the most commonly used objective measures of physical function in cancer cachexia trials. A systematic review showed that HGS was a commonly used physical-function endpoint among 71 eligible cancer cachexia trials. 2) Physical Function (1) 6-Minute Walk Test (6MWT): A 30-m straight course will be marked on

	a flat, hard surface. Participants will be instructed to walk as far as possible within 6 minutes, and the total distance (m) will be recorded. The 6MWT reflects overall functional status in activities of daily living and has also been identified as an important physical-function endpoint in systematic reviews. 10.3.2 Secondary Study Endpoints 1) Change in Body Weight (Absolute and Percentage) At Week 13, body weight will be compared with baseline and measured using a calibrated electronic scale (precision: 0.1 kg) at a fixed time (in the morning after an overnight fast and voiding), with standardized clothing requirements (e.g., hospital gown). 2) Lean Body Mass (LBM) Assessed by dual-energy X-ray absorptiometry (DXA) or bioelectrical impedance analysis (BIA). DXA is preferred because it is the most widely used method in cachexia clinical trials and provides accurate regional muscle-mass data. If conditions are limited, BIA may be used as an alternative, provided that measurement conditions are kept consistent (e.g., fasting, voiding, and constant room temperature). 3) Blood Nutritional Parameters and Inflammatory Markers (ELISA) (1) High-sensitivity C-reactive protein (hs-CRP); (2) Tumor necrosis factor-alpha (TNF-alpha); (3) Interleukin-6 (IL-6); (4) Biochemical parameters including prealbumin, serum albumin, blood lipids, and liver function. The above parameters will be measured using fasting blood samples (at least 6 hours of fasting), collected between 08:00 and 10:00 to minimize circadian variation. 4) Quality of Life (1) EORTC QLQ-C30 (Core Quality-of-Life Questionnaire): global health status; functional domains (physical, role, emotional, cognitive, and social

	functioning); and symptom domains (fatigue, nausea/vomiting, pain, dyspnea, insomnia, appetite loss, constipation, and diarrhea). (2) FAACT (Functional Assessment of Anorexia/Cachexia Therapy): specifically designed to assess anorexia/cachexia-specific quality of life in patients with cachexia. Its Anorexia-Cachexia Subscale (ACSI) may be used to assess cachexia-related symptoms. (3) Hospital Anxiety and Depression Scale (HADS): primarily used to screen for anxiety and depression in general-hospital patients. HADS comprises 14 items, including 7 items assessing depression and 7 assessing anxiety. Six items are reverse-worded, including 5 in the depression subscale and 1 in the anxiety subscale. In the items and scoring criteria, A denotes the anxiety scale and D denotes the depression scale. Each item is scored on a 4-point scale from 0 to 3; a score of 0 indicates absence of the symptom. (4) Cancer Fatigue Scale (CFS): comprises 15 items across three domains (physical, affective, and cognitive), rated on a 5-point Likert scale (not at all = 1, very little = 2, a little = 3, quite a lot = 4, very much = 5). Item 5 is reverse-scored. A higher total score indicates greater fatigue severity. 5) Oxidative Stress Markers (Colorimetric Assay or ELISA) (1) Malondialdehyde (MDA; a marker of lipid peroxidation); (2) Superoxide dismutase (SOD); (3) Glutathione peroxidase (GPx); (4) Total antioxidant capacity (T-AOC). 6) Appetite and Nutritional Intake (1) Simplified Nutritional Appetite Questionnaire (SNAQ): assesses appetite status; a total score <14 indicates clinically significant appetite loss. (2) 3-day food diary: dietary intake will be recorded for 3 consecutive usual days (including one weekend day), and daily total energy and protein intake will be calculated. 7) Antitumor Efficacy and Safety Parameters (as Safety Monitoring)

<table>
<tr><td></td><td>(1) Objective response rate (ORR): assessed according to RECIST 1.1;
(2) Disease control rate (DCR);
(3) Progression-free survival (PFS).</td></tr>
<tr><td>Study Estimand</td><td>The attributes of the primary estimand for the primary study endpoint are as follows:
1. Treatment:
Dosing regimen: During the study, concomitant use of antioxidants such as vitamin C, selenium, N-acetylcysteine (NAC), melatonin, vitamin E, or coenzyme Q10 is not permitted.
<table>
<tr><th>Study Phase</th><th>StudyGroup</th></tr>
<tr><td>Treatment Period (12 weeks)</td><td>MitoQ 20 mg/day (one 20-mg capsule), orally once daily in the morning on an empty stomach.</td></tr>
</table>
2. Population: participants with malignant solid tumors and cachexia.
3. Variable: change in muscle strength after 12 weeks of treatment in patients with cachexia.
4. Intercurrent events and handling strategies: the intercurrent events for the primary estimand are premature treatment discontinuation and study withdrawal.
<table>
<tr><td>Intercurrent Event</td><td>Handling Strategy</td></tr>
<tr><td>Premature treatment discontinuation</td><td>Treatment-policy strategy
Participants who discontinue treatment prematurely will be encouraged to continue scheduled visits according to the protocol; analyses will be performed using the data collected.</td></tr>
<tr><td>Study withdrawal</td><td>Composite strategy</td></tr>
</table>
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Study Population	Participants with malignant solid tumors and cachexia.
Study Design	This is a single-center, single-arm study planned to enroll 20 participants. Enrolled participants will be stratified by: (1) tumor type (pancreatic cancer vs. other); (2) baseline CRP level (>=10 mg/L vs. <10 mg/L); and (3) age (<65 years vs. >=65 years). Subgroup analyses will use interaction tests, with P<0.10 considered indicative of an interaction. The study consists of a screening period, a treatment period, and a safety follow-up period. Eligible participants will receive study treatment according to the protocol and subsequently complete the required follow-up visits and examinations according to the Schedule of Assessments. During the study, if the investigator determines that rescue antiemetic medication is clinically necessary, rescue treatment may be administered as appropriate; the specific drug, route, dose, and frequency will be determined by the investigator.
Method of Administration	➢ MitoQ Capsules 20 mg/day (one 20-mg capsule; 60 capsules/bottle), orally once daily for the 12-week treatment period.
Inclusion Criteria	Participants must meet all of the following inclusion criteria at screening to be enrolled in this study: (1) Age >=18 years at screening; (2) Willing and able to comply with all scheduled visits, treatment plans, laboratory tests, and other study procedures; (3) Able to sign the informed consent form; (4) ECOG performance status of 0, 1, or 2; (5) Life expectancy >3 months; (6) Histologically or cytologically confirmed malignant solid tumor (clinical diagnosis is acceptable for patients with liver cancer); (7) Medically documented cachexia or pre-cachexia (patient-reported weight-loss information is acceptable at initial treatment): • Cachexia: involuntary weight loss >5% within the 6 months before

	screening; • Pre-cachexia: involuntary weight loss <=5% within the 6 months before screening, accompanied by anorexia or metabolic changes; (8) Adequate organ function, including: • Serum total bilirubin <=1.5 x the upper limit of normal (ULN), unless the participant has confirmed Gilbert syndrome; • Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) <=2.5 x ULN, or <=5.0 x ULN if the liver is involved by tumor; • Creatinine <=2 mg/dL, or glomerular filtration rate (GFR) >=30 mL/min/1.73 m², calculated using the Modification of Diet in Renal Disease (MDRD) formula; (9) Participants of reproductive potential must agree to use at least one medically accepted effective method of contraception during sexual activity throughout the study and for 6 months after the last dose, and must have no plans for conception or sperm/oocyte donation. (10) Fully understands the study, voluntarily agrees to participate, and personally signs the informed consent form.
Exclusion Criteria	Participants meeting any of the following criteria at screening may not be enrolled in this study: (1) Known allergy to MitoQ Capsules or any excipient; (2) Known symptomatic brain metastases requiring regular steroid use. Participants with asymptomatic or previously diagnosed brain metastases may be enrolled if treatment has been completed, they have recovered from the acute effects of radiotherapy or surgery before screening, steroid therapy for brain metastases has been discontinued, and neurological status is stable before the first dose of study drug; (3) Known active hepatitis B virus (HBV) or hepatitis C virus (HCV) infection (participants with HBV DNA <10^4 IU/mL may be enrolled); (4) Known positive human immunodeficiency virus (HIV) test or positive

	Treponema pallidum antibody (TP-Ab) test; (5) Current reversible reduction in food intake, as determined by the investigator, including but not limited to: National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) Grade 3 or 4 oral mucositis; NCI CTCAE Grade 3 or 4 gastrointestinal (GI) disorders (e.g., nausea, vomiting, diarrhea, and constipation); or mechanical obstruction preventing oral intake; (6) Receiving tube feeding or parenteral nutrition (either total or partial parenteral nutrition) at screening; (7) Major surgery within 4 weeks before the first dose of study drug (central venous access placement and tumor biopsy are not considered major surgery); participants must have adequately recovered from the acute effects of surgery before screening, and no major surgery should be planned during the study; (8) Severe gastrointestinal disease (including esophagitis, gastritis, or malabsorption); (9) History of subtotal gastrectomy or small-bowel resection (>1/3); (10) Cachexia due to other causes, as determined by the investigator, including but not limited to: Severe chronic obstructive pulmonary disease (COPD); New York Heart Association (NYHA) Class III or IV heart failure; Acquired immunodeficiency syndrome (AIDS); (11) Any of the following within the past 3 months: myocardial infarction, congenital long QT syndrome, torsades de pointes, arrhythmia (including sustained ventricular tachycardia and ventricular fibrillation), unstable angina, coronary or peripheral arterial bypass grafting, symptomatic congestive heart failure (CHF; NYHA Class III or IV), severe cerebrovascular accident, symptomatic pulmonary embolism, or other clinically significant cardiovascular/thromboembolic disease;

	(12) Persistent NCI CTCAE Grade >=2 malignant arrhythmia; (13) Initiation of new systemic glucocorticoid therapy within 4 weeks before the first dose of study drug. Stable steroid therapy (i.e., no significant change in dose or dosing frequency within 4 weeks before the first dose) is permitted, such as dexamethasone used as premedication or daily oral prednisone; (14) Antitumor treatment to be received during the study includes agents associated with weight gain, such as ALK inhibitors, ROS1 inhibitors, or docetaxel, within 4 weeks or 5 half-lives of the drug (whichever is longer) before the first dose of study drug; (15) Use of any prescription medication intended to increase appetite or improve weight loss within 4 weeks or 5 half-lives of the drug (whichever is longer) before the first dose of study drug, including but not limited to anamorelin, medroxyprogesterone acetate, cannabidiol, or medical cannabis; (16) Currently receiving another investigational drug, or use of another investigational drug within 4 weeks before the first dose of study drug or within 5 half-lives of the previous investigational drug (whichever is longer); (17) Female participants who are pregnant or breastfeeding; (18) Other acute or chronic medical or psychiatric conditions, including recent (within the past year) or ongoing suicidal ideation or behavior, laboratory abnormalities that may increase the risks associated with study participation or study-drug use, or conditions that may interfere with interpretation of study results; participants may be excluded if the investigator considers them unsuitable for participation on this basis.
Study Discontinuation Treatment Discontinuatio	Participants have the right to discontinue study treatment at any time for any reason. Reasons for discontinuation of study treatment also include, but are not limited to: 1) The participant requests discontinuation of treatment;

n Criteria	2) Pregnancy occurs during the study; 3) The investigator determines that treatment should be discontinued, including: a) Any adverse event, laboratory abnormality, or other medical condition indicating that continued treatment may no longer provide benefit or may pose a substantial risk to the participant's health or safety; b) A significant protocol deviation is identified such that continued participation is no longer appropriate; c) Any other circumstance in which continued participation would significantly affect the participant's health or safety.
Study Withdrawal Criteria	1) The participant voluntarily withdraws and refuses further follow-up; 2) Lost to follow-up; 3) Death; 4) Premature termination of the study by the sponsor.
Efficacy Evaluation	● 1) Primary Objective: ● To evaluate the preliminary efficacy of MitoQ in patients with cancer cachexia by comparing improvement in muscle function before and after MitoQ treatment at Weeks 7 and 13, as assessed by handgrip strength and the 6-minute walk test. ● 2) Secondary Objectives: ● 1. Inflammatory and metabolic parameters: changes in C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-alpha); effects on oxidative stress markers (MDA, SOD, and GPx); and changes in prealbumin, serum albumin, etc. ● 2. Clinical benefit measures: changes in skeletal muscle mass before and after MitoQ treatment at Weeks 7 and 13 (skeletal muscle index at the third lumbar vertebral level measured by CT); changes in body weight, including total body weight, fat mass, and lean body mass; and quality of life and symptoms assessed using standardized scales, including the

	EORTC QLQ-C30, FAACT (Functional Assessment of Anorexia/Cachexia Therapy), Hospital Anxiety and Depression Scale (HADS), and Cancer Fatigue Scale (CFS). ● 3. Tumor response and survival measures: objective response rate based on RECIST 1.1 and progression-free survival (PFS). ● 4. Safety assessments: liver function tests and blood lipid levels. ● 5. Exploratory assessments: exploratory metabolic and inflammatory biomarkers, etc.
Safety Evaluation	Safety will be evaluated based on vital signs, physical examinations, laboratory tests (complete blood count, blood chemistry, urinalysis, etc.), 12-lead ECG, and the occurrence of adverse events/serious adverse events. All assessments will be performed according to the Schedule of Assessments. The investigator may increase the frequency or scope of assessments as clinically indicated (e.g., in the event of an AE or SAE).
Sample Size	This study plans to enroll 20 participants with malignant solid tumors and cachexia. Participants are planned to receive MitoQ 20 mg/day (one 10-mg capsule), orally once daily for 12 weeks. The primary endpoint is the preliminary efficacy of MitoQ in patients with cancer cachexia, assessed by comparing improvement in muscle function before and after MitoQ treatment at Weeks 7 and 13 using handgrip strength and the 6-minute walk test. The sample size was calculated based on a superiority test for the primary estimand. This is a single-arm clinical trial, and the primary outcome is handgrip strength after 12 weeks of intervention in patients with cancer, which is a continuous variable. Handgrip strength is used as the primary continuous outcome. The standard deviation and minimal clinically meaningful difference were determined based on baseline handgrip-strength data from previous literature. With a two-sided alpha of 0.05, 80% power, a minimal clinically meaningful difference set at one tenth of the mean

	handgrip strength in the cachexia control group (delta=3.5), and a 10% dropout rate, calculation using the sample-size formula for a single-arm continuous outcome indicated that at least 20 participants with cancer are required. This sample size is expected to provide adequate statistical power to detect a clinically meaningful benefit in handgrip strength following MitoQ intervention.
Statistical Analysis	1) Analysis populations: the intention-to-treat population will serve as the primary analysis set (all randomized participants analyzed according to their originally assigned groups); the per-protocol population will serve as the sensitivity analysis set. 2) Primary endpoint analysis: analysis of covariance will be used, with baseline body weight as a covariate, to compare the change in body weight between the two groups at Week 12. Missing data will be handled using multiple imputation. A fixed-sequence testing strategy will be used for multiplicity adjustment of the primary endpoint to control the Type I error rate. 3) Secondary endpoint analyses: a mixed model for repeated measures will be used for continuous variables, and the chi-square test or Fisher’s exact test will be used for categorical variables. All tests will be two-sided with alpha=0.05. 4) Subgroup analyses: prespecified subgroups include (1) tumor type (pancreatic cancer vs. other); (2) baseline CRP level (>=10 mg/L vs. <10 mg/L); and (3) age (<65 years vs. >=65 years). Interaction tests will be used for subgroup analyses, with P<0.10 considered indicative of an interaction. 5) Interim analysis: one interim analysis is planned when 50% of enrollment has been completed and all relevant participants have completed the Week 12 visit, to assess futility and superiority (reviewed by the DSMB). O’

	Brien-Fleming boundaries will be used to control the Type I error rate. 6) Other: statistical analyses will be performed by an independent statistician under blinded conditions, and the final report will be prepared in accordance with the CONSORT statement. **Safety Analysis** AEs will be coded using the MedDRA dictionary. AEs will be summarized by treatment group according to System Organ Class (SOC) and Preferred Term (PT), including treatment-emergent adverse events (TEAEs), treatment-related adverse events (TRAEs), SAEs, etc. The number of participants and incidence rates will be calculated, and relevant AE listings will be provided. Vital signs, ECG findings, and other clinical laboratory results will be summarized by change from baseline. Abnormal clinical laboratory results will additionally be presented in separate listings. Vital signs, ECG findings, and other clinical laboratory results will be summarized by change from baseline. Abnormal clinical laboratory results will additionally be presented in separate listings.