Clinical Trial Protocol
Iranian Registry of Clinical Trials

22 Nov 2026

Evaluation of Hydroxychloroquine Added to Standard Immunosuppression in High risk Membranous Nephropathy

Protocol summary

Study aim
To evaluate the efficacy of adding hydroxychloroquine to standard immunosuppressive therapy in high-risk patients with primary membranous nephropathy, with the aim of improving therapeutic outcomes and reducing disease-related complications.

Design
A Phase 3, randomized, parallel-group, double-blind, controlled clinical trial involving 50 patients. The Excel `rand` function was used for randomization.

Settings and conduct
Double-blind (study participants and assessors). This randomized clinical trial is being conducted at Imam Reza and Ghaem hospitals in Mashhad. Patients are evaluated at baseline and six months after the start of treatment for proteinuria, serum albumin levels, blood pressure, and anti-PLA2R antibody levels and Scr

Participants/Inclusion and exclusion criteria
Study inclusion criteria: - Age between 18 and 75 years - Diagnosis of Primary Membranous Nephropathy via kidney biopsy. - Persistent high-level proteinuria accompanied by hypoalbuminemia (exceeding 3.5 g/day) that persists after 6 months of maintenance therapy (ACEI or ARB). -Proteinuria exceeding 8 g that persists after 3 months of maintenance therapy. -Positive PLA2R antibody levels (>150) or a rising titer (increase of >25%) during maintenance therapy, reaching a level of 150. - EGFR >30 mL/min. Study exclusion criteria: - History of hypersensitivity to hydroxychloroquine. - Severe liver or heart disease. - Pregnancy or breastfeeding. -EGFR of less than 30 mL/min.

Intervention groups
Intervention group: Standard immunosuppressive therapy (such as cyclophosphamide or rituximab) plus hydroxychloroquine at a dose of 200–400 mg/day for 6 months. Control group: Standard immunosuppressive therapy alone (without hydroxychloroquine).

Main outcome variables
The proteinuria of less than 300 mg in a 24-hour urine sample

General information

Reason for update

Acronym

IRCT registration information
IRCT registration number: **IRCT20261005071301N1**
Registration date: **2026-11-05, 1405/08/14**
Registration timing: **prospective**

Last update: **2026-11-05, 1405/08/14**
Update count: **0**

Registration date
2026-11-05, 1405/08/14

Registrant information

Name
Farimah Amini

Name of organization / entity

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Iran (Islamic Republic of)

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Recruitment status
Not yet recruiting

Funding source

Expected recruitment start date
2026-12-11, 1405/09/20

Expected recruitment end date
2027-06-10, 1406/03/20

Actual recruitment start date
empty

Actual recruitment end date
empty

Trial completion date

empty

Scientific title
Evaluation of Hydroxychloroquine Added to Standard Immunosuppression in High risk Membranous Nephropathy

Public title
Evaluation of The effect of Hydroxychloroquine on reducing proteinuria in High risk Membranous nephropathy patients

Purpose
Treatment

Inclusion/Exclusion criteria

Inclusion criteria:
Age greater than 18 and less than 75 Confirmed diagnosis of primary membranous nephropathy by a nephrologist via kidney biopsy Persistent proteinuria level above 3.5 grams accompanied by hypoalbuminemia that continues after 6 months of treatment with an ACE inhibitors or ARB Proteinuria above 8 grams that persists after 3 months of supportive treatment Phospholipase A2 receptor antibody level above 150, or an increasing titer of more than 25% during supportive treatment that has reached a level of 150 or above Relatively stable kidney function with GFR above 30

Exclusion criteria:
History of hypersensitivity to Hydroxychloroquine Severe liver or heart disease Pregnancy or breastfeeding Chronic Kidney failure with GFR less than 30 ml/min Irregular medication non-adherence

Age
From **18 years** old to **75 years** old

Gender
Both

Phase
3

Groups that have been masked

- Participant
- Care provider
- Investigator
- Outcome assessor

Sample size
Target sample size: **50**

Randomization (investigator's opinion)
Randomized

Randomization description
Patients with a definite diagnosis by a nephrologist who have been included in the study and, based on randomization, are confirmed to be assigned to two groups: intervention and control, based on the combination of block 2 and 4 and 16 blocks of size 2 will be considered. The concealment method (in a closed opaque packet)will be used.

Blinding (investigator's opinion)
Double blinded

Blinding description
To maintain blinding, both groups are given two types of drugs. The intervention group is given hydroxychloroquine and standard treatment, and the control group is given standard drug and placebo. The placebo drug is completely similar in shape, color, and packaging to hydroxychloroquine. The allocation of groups is done by random code, and the patient and the treatment provider are unaware of the content of the codes. The person assigning the codes, the data analyst, the person responsible for drug preparation, and the safety and data monitoring committee are considered informed persons. Blinding (The subjects under study, the assessors, including the tor and the outcome assessor are blinded).

Placebo
Used

Assignment
Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee
Ethics committee of Mashhad University of Medical Sciences

Street address
1st Floor, Faculty of Medicine, Mashhad University of Medical Sciences, Azadi Square, Mashhad

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Razavi Khorasan

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9178833895

Approval date
2026-08-25, 1405/06/03

Ethics committee reference number
IR.MUMS.MEDICAL.REC.1405.236

Health conditions studied

1

Description of health condition studied
Primary Membranous Nephropathy

ICD-10 code

ICD-10 code description
Membranous nephro

Primary outcomes

1

Description
The treatment response is defined as proteinuria of less than 300 mg in a 24-hour urine sample, with measurements taken at two-month intervals

Timepoint

Measurement of proteinuria at baseline and then every two months up to 6 months

Method of measurement

24-hour urine collection

Secondary outcomes

empty

Intervention groups

1

Description

Intervention group: Standard immunosuppressive therapy comprising the Ponticelli regimen (methylprednisolone plus cyclophosphamide) or rituximab, combined with hydroxychloroquine (200–400 mg/day).

Category

Treatment - Drugs

2

Description

Control group: Standard immunosuppressive treatment only (without hydroxychloroquine)

Category

Treatment - Drugs

Recruitment centers

1

Recruitment center

Name of recruitment center

Imam Reza hospital

Full name of responsible person

Farimah Amini

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2

Recruitment center

Name of recruitment center

Ghaem hospital

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Sponsors / Funding sources

1

Sponsor

Name of organization / entity

Mashhad University of Medical Sciences

Full name of responsible person

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Grant name

Grant code / Reference number

Is the source of funding the same sponsor organization/entity?

Yes

Title of funding source

Mashhad University of Medical Sciences

Proportion provided by this source

100

Public or private sector

Public

Domestic or foreign origin

Domestic

Category of foreign source of funding

empty

Country of origin

Type of organization providing the funding

Academic

Person responsible for general inquiries

Contact

Name of organization / entity

Mashhad University of Medical Sciences

Full name of responsible person

Farimah Amini

Position

Nephrology subspecialty fellow

Latest degree
Subspecialist
Other areas of specialty/work
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Sharing plan

Deidentified Individual Participant Data Set (IPD)
Undecided - It is not yet known if there will be a plan to make this available
Study Protocol
Undecided - It is not yet known if there will be a plan to make this available
Statistical Analysis Plan
Undecided - It is not yet known if there will be a plan to make this available
Informed Consent Form
Undecided - It is not yet known if there will be a plan to make this available
Clinical Study Report
Undecided - It is not yet known if there will be a plan to make this available
Analytic Code
Undecided - It is not yet known if there will be a plan to make this available
Data Dictionary
Undecided - It is not yet known if there will be a plan to make this available