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An open-label study of patients with primary sclerosing cholangitis (PSC) treated with norucholic acid tablets

Submission date 12/11/2024	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol
Registration date 27/01/2025	**Overall study status** Ongoing	[_] Statistical analysis plan [_] Results
Last Edited 07/01/2026	**Condition category** Digestive System	[_] Individual participant data [X] Record updated in last year

Plain English summary of protocol

Background and study aims
During the development of norucholic acid (NCA) over 700 patients have been treated with this new medication so far. This study, called NUT-022/PSC is a kind of follow-up study for the NUC-5 /PSC study; it offers continuous NCA treatment to patients from the NUC-5/PSC study. Another goal of the current study is to gather more information about the safety and efficacy of NCA treatment for PSC patients over a longer time period. This is an open-label, single-arm study. Open-label means that the label of the study medication is not hidden, and that participants know which treatment they get. Single-arm means that all participants receive the same treatment.

Who can participate?
To be able to take part, patients must have participated in the previous NUC-5/PSC study.

What does the study involve?
If patients are eligible, they will be asked if they would like to enrol in the NUT-022/PSC study. They will receive the medication NCA at a dose of 1500 mg per day, taken as three tablets (containing 500 mg NCA each), instead of the 6 capsules (250mg) in NUC-5/PSC study. This should make it easier and more comfortable for them to take the medication. Earlier studies showed that the capsules and the tablets both work in the body in the same way. The patient will come to regular interim visits every 3 months. The final visit will take place at the end of the treatment phase or at the time of participant's withdrawal. Participants will have a total of 8 visits over a period of up to 72 weeks. Diagnostic procedures and examinations done in this study are mostly routine or non-invasive procedures. However, taking blood samples may cause discomfort or even clotting of the vein or nerve injury in rare cases. The total amount of blood withdrawn per visit is about 30 ml. Imaging (like ultrasound) is a non-invasive procedure. The trial will take place at 6 sites in UK which previously participated in the NUC-5/PSC study. Around 125 patients are expected to join globally and 20 expected in UK

What are the possible benefits and risks of participating?
Benefits:

There is no direct health benefit. The patient’s health condition may not improve or may even worsen while participating in this study.
The results of this study should help to develop and provide better treatment for patients with PSC in the future.
Another benefit is to further scientific knowledge; participation in this study will help scientists to gain further knowledge of the efficacy and safety of 1500 mg NCA per day when given over a longer period of time.
Risks:
The medication can trigger side-effects or allergic reactions, patients have been informed about this in the patient information and consent form and that the study doctor should be informed about the side effects for clinical management.
Diagnostic procedures (like the ultrasounds for abdomen and Liver stiffness) and examinations done in this clinical study are mostly routine or non-invasive procedures.
The Blood samples - might cause discomfort, bruising, or, unusually, clotting of the vein at the site where the needle is inserted or venous inflammation (thrombophlebitis) or nerve injury.

Where is the study run from?
Dr Falk Pharma GmbH (Germany)

When is the study starting and how long is it expected to run for?
November 2024 to September 2027

Who is funding the study?
Dr Falk Pharma GmbH (Germany)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Clinical Trials Information System (CTIS)
2024-514292-18

Integrated Research Application System (IRAS)
1011119

Protocol serial number
NUT-022/PSC

Study information

Scientific Title
An open-label study of patients with primary sclerosing cholangitis (PSC) treated with norucholic acid tablets

Study objectives
Primary objective:
To evaluate safety and tolerability of norucholic acid (NCA) film-coated tablets in the treatment of Primary Sclerosing Cholangitis (PSC).

Secondary objective:
To assess the efficacy of NCA in patients with PSC.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 07/01/2025, East Midlands – Nottingham 2 REC (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 207 1048 154; nottingham2.rec@hra.nhs.uk), ref: 24/EM/0262

Study design
Interventional non randomized

Primary study design
Interventional

Study type(s)
Efficacy, Safety

Health condition(s) or problem(s) studied
Primary sclerosing cholangitis (PSC)

Interventions
This is an open-label, single-arm study. To be able to take part, patients must have participated in the previous NUC-5/PSC study. If patients are eligible, they will be asked if they would like to enrol in the NUT-022/PSC study. They will receive the medication NCA at a dose of 1500 mg per day, taken as three tablets (containing 500 mg NCA each) orally daily. The patient will come to regular interim visits every 3 months. Participants will have a total of 8 visits over a period of up to 72 weeks.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Norucholic acid

Primary outcome(s)
Current primary outcome measure as of 23/05/2025:

Occurrence of adverse events during the 18 months treatment period with NCA, and, in particular,
· how serious and severe they are,
· if they have a causal relationship with the study drug,
· if they have been observed previously under the treatment with NCA, or if they are unexpected (“new”), and
· if they lead to withdrawal of NCA.

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Previous primary outcome measure:

1. Occurrence of Treatment emergent adverse events (TEAEs) is measured using patient records at the time of consent, screening phase, treatment phase, and during 4 weeks after EOT /withdrawal visit
2. Occurrence of Serious TEAEs is measured using patient records at the time of consent, screening phase, treatment phase, and during 4 weeks after EOT/withdrawal visit
3. Occurrence of Severe TEAEs is measured using patient records at the time of consent, screening phase, treatment phase, and during 4 weeks after EOT/withdrawal visit
4. Occurrence of Adverse Drug reactions (ADRs) is measured using patient records at the time of consent, screening phase, treatment phase, and during 4 weeks after EOT/withdrawal visit
5. Occurrence of Unexpected TEAEs is measured using patient records at the time of consent, screening phase, treatment phase, and during 4 weeks after EOT/withdrawal visit

Key secondary outcome(s))
Current secondary outcome measures as of 23/05/2025:

Safety:
Change from the beginning of treatment (“baseline”) to the end of treatment
· in vital signs (e.g. blood pressure, heart rate), and

· in laboratory values (e.g. blood count, blood coagulation, thyroid hormone, kidney function parameters, blood coagulation, urine examination).
Efficacy endpoints include:
· course of liver stiffness from baseline to end of treatment,
· course in alkaline phosphatase (ALP) and other liver enzymes from baseline to end of treatment (ALP is a liver enzyme particularly important for the evaluation of PSC),
· occurrence of relevant strictures of the bile ducts during the treatment period,
· course of pruritus (itchiness),
· course of fatigue (tiredness),
· occurrence of “clinical events” like cancer, transplantation, and cirrhosis-related events.

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Previous secondary outcome measures:

1. (Safety) Changes from baseline in vital signs (blood pressure, heart rate) and body weight – measured at baseline, v 2 to v7
2. (Safety) Changes from baseline in haematology, serum chemistry (other than efficacy variables) and urinalysis -measured at baseline, v 2 to v7
3. (Efficacy) Course of liver stiffness – measured at screening and at v7
4. (Efficacy) s-ALP in categories from baseline to EoT - measured at baseline, v 2 to v7

Completion date
30/09/2027

Eligibility

Key inclusion criteria
Current inclusion criteria as of 23/05/2025:

Male and female patients ≥ 18 years, with PSC, who have participated in the NUC-5/PSC study.

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Previous inclusion criteria:

1. Signed informed consent.
2. Males or females ≥ 18 years.
3. Patient has previously been diagnosed with PSC, has participated in the previous NUC 5/PSC trial and
3.1. has completed the DBE phase with Visit 22, or
3.2. has prematurely terminated the DBE phase after this trial has been started, under the condition that the premature termination was due to lack of efficacy*
*Lack of efficacy as defined in the NUC-5/PSC trial.
4. Women of childbearing potential, i.e. fertile, following menarche and until becoming post-menopausal unless permanently sterile, who are sexually active have to apply a highly effective method of birth control with a low failure rate (i.e., less than 1 % per year) when used constantly and correctly such as combined (estrogen and progestogen containing) hormonal contraception associated with inhibition of ovulation (oral,intravaginal or transdermal), progestogen-only hormonal contraception associated with inhibition of ovulation (oral,injectable or implantable), intrauterine device (IUD), intrauterine hormone-releasing system (IUS),bilateral tubal occlusion,

vasectomized partner, or sexual abstinence (only accepted as a highly effective contraceptive measure if it is the usual and preferred lifestyle of the patient), throughout the treatment period and for four weeks following the last dose of study treatment. Women of nonchildbearing potential may be included if surgically sterile or postmenopausal for at least 2 years. The investigator is responsible for determining whether the patient has this adequate birth control for study participation.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
99 years

Sex
All

Total final enrolment
0

Key exclusion criteria
Current exclusion criteria as of 23/05/2025:

Patients who discontinued the NUC-5/PSC study due to adverse drug reactions (side effects of the study drug) are not eligible. Other exclusion criteria include chronic alcohol consumption, advanced cirrhosis, liver transplantation, severe infections and other severe diseases

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Previous exclusion criteria:

1. History or presence of chronic alcoholic consumption (daily consumption >30 g in men, >20 g in women)
2. Abnormal renal function at screening
3. Thyroid-stimulating hormone (TSH) >ULN at screening (elevated levels [4.2-10 µU/mL] are acceptable if fT4 ismeasured and within the normal range).
4. Any severe concomitant cardiovascular, renal, endocrine, or psychiatric disorder, which in the opinion of the investigator might have an influence on the patient’s compliance, or any disorder which in the opinion of the investigator may affect the patient’s safety.
5. Any active malignant disease
6. Known intolerance/hypersensitivity to study drug, or drugs of similar chemical structure or pharmacological profile
7. Well-founded doubt about the patient’s cooperation, e.g., because of addiction to alcohol or

drugs.
8. Existing or intended pregnancy or breast-feeding.
9. Participation in another clinical trial (other than the NUC-5/PSC trial) within the last 30 days prior to screening visit, simultaneous participation in another clinical trial, or previous enrolment in this trial and intake of Investigational Medicinal Product (IMP) within this trial
10. Imprisoned persons, persons admitted to nursing homes, persons under legal guardianship, and persons not able to express their consent (e.g. due to mental impairment).
11. Patients who discontinued study participation in NUC-5/PSC due to an AE possibly caused by the study drug.
12. Liver Cirrhosis or any cirrhosis-related symptoms which in the opinion of the investigator may affect the patient's safety.
13. Any known relevant infectious disease (e.g., active tuberculosis, AIDS defining diseases).

Date of first enrolment
31/03/2025

Date of final enrolment
31/03/2026

Locations

Countries of recruitment
United Kingdom

Austria

Belgium

Denmark

France

Germany

Hungary

Netherlands

Norway

Poland

Sweden

Switzerland

Study participating centre
Norfolk and Norwich University Hospital
Colney Lane
Colney

Norwich
England
NR4 7UY

Study participating centre
University Hospitals Birmingham NHS Foundation Trust
Queen Elizabeth Hospital
Mindelsohn Way
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B15 2GW

Study participating centre
Royal Free London NHS Foundation Trust
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Study participating centre
Kings College Hospital
Mapother House
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SE5 8AB

Study participating centre
Freeman Hospital
Freeman Road
High Heaton
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Sponsor information

Organisation
Dr Falk Pharma (Germany)

ROR
https://ror.org/05sh9vm75

Funder(s)

Funder type
Industry

Funder Name
Dr. Falk Pharma

Alternative Name(s)
Falk Pharma, Dr Falk Pharma, Dr Falk Pharma GmbH, Dr. Falk Pharma GmbH, Dr. Falk Pharma UK Ltd

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The data collected will be transferred and stored in a pseudonymised form in the clinical data base that has restricted access to sponsor and its representatives. For analysis purposes, the participants will always be identified by their 5-digit participant number. The data will be stored for at least 25 years after the end or termination of the clinical trial.

IPD sharing plan summary
Stored in non-publicly available repository