A Study to Evaluate the Safety, Tolerability, and Effects on NSAID-Induced Small Bowel Pathology of K-196 in Healthy Volunteers.

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Primary:1. To characterize the safety and tolerability of multiple oral doses of K-196 alone and in combination with naproxen/omeprazole in healthy subjects.Secondary:1. To assess the effects of K-196 compared to placebo on the proportion of...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal inflammatory conditions
Study type	Interventional

Summary

ID

NL-OMON51579

Source
ToetsingOnline

Brief title
CS0394

Condition

- Gastrointestinal inflammatory conditions

Synonym
Inflammatory bowel disease (IBD)

Research involving
Human

Sponsors and support

Primary sponsor: Kallyope, Inc.

Source(s) of monetary or material Support: Kallyope;Inc.

Intervention

Keyword: safety, tolerability

Outcome measures

Primary outcome

To characterize the safety and tolerability of multiple oral doses of K-196

alone and in combination with naproxen/omeprazole in healthy subjects.

Secondary outcome

Small bowel mucosal breaks; PK

Study description

Background summary

Treatment of Crohn*s disease (CD) and ulcerative colitis (UC) is based on the disease severity and aimed at alleviating symptoms, improving quality of life, and inducing disease remission. Currently available treatments target the intestinal inflammation associated with disease, typically with general anti-inflammatory medications, including corticosteroids and aminosalicylates, followed by immunomodulatory therapies. Despite significant treatment options, IBD remains an area of critical unmet need with less than 50% of patients with moderate-severe disease attaining long-term clinical remission. In vitro, K-196 was shown to protect against low calcium-induced disassembly of intercellular junctions resulting in reduced permeability of test probes across cellular monolayers. In a dextransodium sulfate (DSS) chemical injury colitis model, K-196 prevented DSS-induced intestinal permeability, body weight loss, rectal bleeding, and diarrhea. K-196 treatment reduced levels of fecal lipocalin, an abundant neutrophil protein shed into stool that is used as a marker of inflammation and barrier integrity. In a DSS recovery paradigm where K-196 dosing was initiated only after the onset of colitis, K-196 treatment resulted in less body weight loss, bleeding, and diarrhea vs. vehicle. Additionally, in a 5-fluoruracil-induced injury model, K-196 prevented the development of diarrhea, reduced body weight loss, and reduced fecal lipocalin levels. Altogether these data suggest that K-196 can modulate barrier function by altering permeability of intercellular junctions and by protecting the

viability of epithelial cells against cytotoxic stressors.

Study objective

Primary:
1. To characterize the safety and tolerability of multiple oral doses of K-196 alone and in combination with naproxen/omeprazole in healthy subjects.

Secondary:
1. To assess the effects of K-196 compared to placebo on the proportion of subjects with 1 or more small bowel mucosal breaks detected by video capsule endoscopy (VCE) following naproxen/omeprazole.
2. To assess the effects of K-196 compared to placebo on the mean number of small bowel mucosal breaks detected by VCE following naproxen/omeprazole.
3. To characterize the pharmacokinetics on K-196 on Day 14 in healthy subjects (AUC0-8h, Cmax, Ctrough).

Study design

This is a 14-day, randomized, double blind (Sponsor open), placebo-controlled, parallel-group trial.
K-196 or placebo will be administered in a double-blind manner.
Naproxen/omeprazole will be open-label.

Intervention

K-196 capsules or matching placebo, naproxen, omeprazole.

Study burden and risks

Since the study is being executed in healthy volunteers, there are no anticipated benefits of the IMP. Please see the overall benefitrisk in the CSP for further information.

Contacts

Public
Kallyope, Inc.

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New York NY 10016
US
Scientific
Kallyope, Inc.

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US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Understand the trial procedures and agree to participate by providing written informed consent.
2. Be willing and able to comply with all trial procedures and restrictions.
3. Be healthy between 18 to 59 years of age, inclusive, at the Screening Visit.
4. Have a Body Mass Index (BMI) >=18.0 and <30.0 (kg/m2) at the Screening Visit.
5. Be a nonsmoker who has not used tobacco or nicotine-containing products (e.g., nicotine patch) for at least 3 months before administration of the initial dose of trial drug and agrees to abstain from smoking tobacco or the use of nicotine-containing products while on study.
6. Be judged to be in good health by the Investigator, based on clinical evaluations including laboratory safety tests, medical history, physical examination, 12-lead ECG, and vital sign measurements performed at the Screening Visit and before administration of the initial dose of trial drug.

Exclusion criteria

1. Has participated in another investigational study within the following time period: 30 days, 5 half-lives or twice the duration of the biological effect of the investigational product (whichever is longer or based on local regulations) prior to the Screening Visit. The window will be derived from the date of the last study procedure and/or AE related to the study procedure in the previous study to the Screening Visit of the current study.
2. Is an employee or immediate family member (e.g., spouse, parent, child, sibling) of the Sponsor or study site.

3. Has a history of significant multiple and/or severe allergies (e.g., food, drug, latex allergy) or has had an anaphylactic reaction or significant intolerance to prescription or nonprescription drugs or food.
4. Has a known hypersensitivity or contraindication to any component of K-196, related compounds or its excipients.
5. Has known hypersensitivity to naproxen or any components of the drug product
6. Has history of asthma, urticaria or other allergic-type reactions after taking naproxen or other NSAIDs.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	31-05-2023
Enrollment:	70
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Klean-Prep
Generic name:	Klean-Prep
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Lactulose
Generic name:	Lactulose

Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Nap.
Generic name:	Nap.
Product type:	Medicine
Brand name:	Naproxen
Generic name:	Naproxen
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Omeprazole
Generic name:	Omeprazole
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	22-12-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-01-2023
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-01-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2022-003522-42-NL
CCMO	NL83065.056.22