The effect of FP-025, a MMP-12 inhibitor, on allergen induced airway responses, airway inflammation and aspects of airway remodeling in subjects with mild eosinophilic House Dust Mite (HDM)-allergic asthma

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To determine the effect of FP-025 vs placebo on the allergen (HDM)-induced late asthmatic response expressed as FEV1 AUC3-8h in subjects with clinically stable, mild allergic asthma and blood eosinophilia.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Respiratory disorders NEC
Study type	Interventional

Summary

ID

NL-OMON55388

Source
ToetsingOnline

Brief title
160509 Foresee

Condition

- Respiratory disorders NEC

Synonym
Asthma, COPD

Research involving

Human

Sponsors and support

Primary sponsor: Foresee Pharmaceuticals Co., Ltd
Source(s) of monetary or material Support: Foresee Pharmaceuticals Co.;Ltd

Intervention

Keyword: Asthma, MMP-12 inhibitor

Outcome measures

Primary outcome

Spirometry:

• Area under the time-FEV1 response curve from 3 to 8 hours post-allergen (FEV1 AUC3-8h)

Secondary outcome

- Pharmacodynamic endpoints include the effect of study treatments on allergen (HDM)-induced changes in:

LAR expressed as max% fall in FEV1 from post-diluent baseline;

Early asthmatic response (EAR) expressed as FEV1 AUC0-3h;

EAR expressed as max% fall in FEV1 from post-diluent baseline;

Joint HDM-induced airway response expressed as AUC0-8h;

Airway hyperresponsiveness expressed as PC20FEV1(Meth) or PC20FEV1(Hist) (Day 10-Day 12);

Small airway parameters following HDM-challenge (i.e. R5, R20, R5-R20, AX, X5, Fres);

Fractionated nitric oxide (FeNO);

Blood eosinophils.

- Potential treatment effect (FP-025 versus placebo) on baseline parameters

(i.e. Day 1 versus Day 10), including:

Blood eosinophils;

PC20FEV1(Meth) or PC20FEV1(Hist);

FeNO.

- Safety parameters include physical examination, clinical signs/symptoms

reporting (MedDRA), (S)AEs, vital signs, lung function measurements, overall

asthma symptoms, ECG and clinical safety laboratory outcomes (blood/urine).

- Pharmacokinetic parameters of FP-025 in blood (plasma) include Cmax, tmax,

and AUC0-tau

Study description

Background summary

FP-025 is a novel non-hydroxamate small molecule selective inhibitor of Matrix Metalloproteinase 12 (MMP-12). It has 90-fold selectivity over the next closest family member (MMP-2) and 2-3 orders of magnitude selectivity over the seven other MMP family members (MMP-1, MMP-3, MMP-7, MMP-8, MMP-9, MMP-13, and MMP-14). MMP-12 has been shown to play an important role in several aspects of chronic inflammatory airway diseases like asthma and COPD, including airway inflammation, airway hyperresponsiveness, (small) airways remodeling and disease severity [2-8]. In addition, FP-025 attenuated allergic inflammation and improved lung function in two murine models of allergic inflammation (OVA and HDM models) and even showed normalization of lung histology in the HDM model.

Study objective

To determine the effect of FP-025 vs placebo on the allergen (HDM)-induced late asthmatic response expressed as FEV1 AUC3-8h in subjects with clinically

stable, mild allergic asthma and blood eosinophilia.

Study design

This is a randomized, placebo-controlled, double-blind, 2-way cross-over, 2-centre study in male and female subjects with stable, mild HDM-allergic asthma.

Intervention

Subjects will receive 400 mg FP-025 (8x 50 mg capsules, BID) and matching placebo (8 capsules, BID) from Day 1 (evening = first dose) to Day 12 (morning = last dose); a total of 22 doses per study period.

Study burden and risks

The dosage levels of the study drug are based on a previous clinical trial conducted by the sponsor. The risk to health at the chosen dose is limited, but the patients may experience any of the side effects in the ICF or symptoms that have not been reported before. Volunteers health is closely monitored during the study to minimize these risks. If the volunteers experience side effects, the investigator will treat them where necessary. If new information is available on the safety of the study medication, the volunteers are informed as soon as possible. The blood collection procedure is not dangerous.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Females or males, between 18 and 55 years of age at Screening, inclusive, on the day of signing the Informed Consent Form (ICF).
2. Apart from a clinically stable asthma and HDM-allergy, subjects should be generally healthy with no history of a clinically relevant medical condition that in the opinion of the investigator might interfere with successful study conduct and no clinically relevant abnormalities on medical history, physical exam, vital signs, laboratory parameters or ECG at Screening.
3. Subject has a BMI >= 18.0 kg/m2 and <= 32.0 kg/m2 (and weighs >=50 kg).
4. Subjects have been diagnosed with asthma cf GINA guidelines.
5. Subjects should have established allergy for HDM (serum HDM-specific IgE or positive SPT at Screening or documented within 1 year pre-screening).
6. No severe exacerbation of asthma within past 1 year requiring hospital admission and/or treatment with oral corticosteroids; no (never) intensive care admissions for asthma or intubation).
7. FEV1 should be >=70% of predicted on Screening Day 2.
8. On Screening Day 2, PC20FEV1(Meth) should be <16 mg/mL if methacholine chloride is used (or adjusted by a factor of 1.2 if methacholine bromide is used). If histamine is used, PC20FEV1(Hist) should be <16 mg/mL.
9. Baseline blood eosinophils should be >=150 cells/µL at Screening or documented within 3 months before Screening Day 1.
10. Subjects should have a documented airway late response to inhaled HDM on Screening Day 3.
11. Subjects of childbearing potential must be willing to use adequate contraception (double-barrier) or must refrain from intercourse.
12. Female subjects of non-childbearing potential must have had >= 12 months of spontaneous amenorrhea (with follicle-stimulating hormone [FSH] >= 30 mIU/mL). Surgically sterile women are defined as those who have had a hysterectomy, bilateral ovariectomy (for *benign* reasons), or bilateral tubal ligation.
13. All female subjects should have a negative pregnancy test at Screening and on Day -1.
14. Negative alcohol breath test on Screening Day 1 and Day -1.
15. Negative cotinine test on Screening Day 1 and Day -1.

16. Negative urine drug screen for recreational and other drugs on Screening Day 1 and Day -1.
17. Subjects are non-smokers. A non-smoker is defined as an individual who has abstained from smoking for at least 1 year prior to Screening Day 1. Number of years smoked x number of packs per day should be <5 pack years.
18. Subject should be willing and able to perform the lung function tests and other study-related procedures and comply with study protocol requirements.
19. Subject should provide a signed and dated informed consent.

Exclusion criteria

1. Subject has any active and/or chronic (physical or mental) condition requiring maintenance (pharmaco)therapy or which otherwise precludes subject from safe or adequate study participation (ineligibility will be assessed by the PI).
2. Subject has a history of cancer (exception: localized basalioma or cervix carcinoma in situ).
3. Subject had any major (nasal) surgery in the 6 months before Screening Day 1.
4. Subject is pregnant or lactating.
5. Subject is using immunotherapy that according to the PI may interfere with the study (e.g. in case of immunotherapy with HDM or when subject is in the updosing phase of any immunotherapy).
6. Subject regularly used alcohol (intake of >21 units/wk for males and >14 units/wk for females) and/or recreational drugs within the last 6 months prior to screening.
7. Subject had any respiratory (viral) infections (e.g. common cold) within 3 weeks of Screening Day 1 or on Day -1.
8. Subject is using maintenance asthma therapy or long-acting bronchodilators or any other anti-asthma or anti-allergic medications (as detailed in the protocol) other than infrequent use of SABA prn only.
9. Subject is using prohibited medications as detailed in the protocol.
10. Multi-sensitized symptomatic subjects with seasonal (pollen) allergies should be included outside of the relevant allergen season and/or should not be in frequent contact with the relevant allergen during the study.
11. Subject has any known allergic response for the medications used or known severe allergic reactions or anaphylaxis (to food/medications/insect venoms).
12. Subject participated in medical studies in the past 3 months (non-biologicals) or in the past 6 months (biologicals).
13. Subject is anticipated not to comply with study medication or other aspects of the study (at the discretion of the investigator).

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	22-05-2018
Enrollment:	32
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Placebo
Generic name:	Placebo

Ethics review

Approved WMO Date:	22-03-2018
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-05-2018
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-08-2018

Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-08-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	27-08-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-11-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-05-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	03-06-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	16-09-2021
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	EUCTR2017-005164-17-NL
CCMO	NL64799.056.18

Study results

Results posted: 29-01-2024

Summary results
Trial ended prematurely

First publication
07-12-2023