A randomized, double-blind, double-dummy, active-controlled, multicenter, 2-part Phase II study on replacement of steroids by IFX-1 in active granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA)

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

Summary

ID

NL-OMON55826

Source
ToetsingOnline

Brief title
IFX-1-P2.5 IXchange

Condition

- Vascular disorders NEC

Synonym
Granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA)

Research involving

Human

Sponsors and support

Primary sponsor: InflaRx GmbH
Source(s) of monetary or material Support: Pharmaceutical Industry

Intervention

Keyword: efficacy, IFX-1, polyangiitis, safety

Outcome measures

Primary outcome

The primary efficacy endpoint is the proportion of subjects achieving clinical response defined as reduction in BVASv3 * 50% at Week 16 compared to Baseline (= screening assessment) and no worsening in any body system. Subjects who receive rescue therapy until Week 16 will be considered as not having achieved clinical response.

Secondary outcome

1.Proportion of subjects with clinical response, defined as reduction in BVASv3 * 50% and no worsening in any body system at each measurement time point except Week 16. Subjects who receive rescue therapy will be considered as not having achieved clinical response at each time point later than the first administration of rescue therapy

2.Proportion of subjects with a clinical remission defined as having a BVASv3 = 0 at Week 16

3.Change from baseline (=screening assessment) in BVASv3 total score at Week 16

4.Absolute values and absolute and relative change from Day 1 in the VDI at Week 16

5.Absolute values and absolute and relative change from Day 1 in the PGA at

Week 16

6.Absolute values and absolute and relative change from Day 1 in eGFR in

mL/min/1.73 m^2 at Week 16.

Study description

Background summary

GPA and MPA most commonly occur in older adults, although these diseases have been reported at all ages. The incidence of these conditions in the United States of America is approximately 6,000 new cases per year, and the estimated prevalence is 25,000 to 30,000 cases. The overall incidence rates of AAV in Europe are reported to be in the range of 13 to approximately 20 per million. Although treatment failures and disease relapses decreased due to the improvement of remission-induction regimens during recent years, patients with MPA and GPA treated with conventional regimens have a 9-fold increased mortality risk in the first year attributed to infection, cardiovascular disease, malignancies, vasculitis activity, and renal disease It is proven that current therapies contribute to more than half of this increased risk rather than the underlying disease itself. Most of the side effects are attributed to the high-dose of GCs, which are still part of Standard of Care for MPA and GPA. GCs have long-term side effects such as osteoporosis, Cushing*s syndrome, increased infection risk and risk of diabetes mellitus , and progressive organ damage. Therefore, the replacement of GCs by IFX-1 may improve the short- and long-term safety of treatment of MPA and GPA for the induction of remission.

Study objective

The primary objective is to evaluate the efficacy of IFX-1 treatment as a replacement for glucocorticoids [GC] therapy in subjects with GPA and MPA.

Secondary objectives:

*To assess safety and tolerability of IFX-1
*To compare GC-induced toxicity of standard-dose GC and reduced dose GC with IFX-1 treatment
*To generate data for PK and PD modelling of IFX-1 treatment.

Study design

This is a prospective, randomized, double-blind, double-dummy, active-controlled, multicenter, 2-part Phase II study evaluating the efficacy of IFX-1 treatment in the replacement of GCs in subjects with GPA or MPA

Intervention

Patients should visit the clinics and be willing to receive their study drug comparator an/or placebo according to the dosing schema.
Furthermore their data of Medical history and demographic data will be collected They must undergo physicial and vital signs examinations. An electrocardiogram will be made. Blood and urine will be collected.

Study burden and risks

In a pharmaceutical trial like this one, every risk or side effect cannot be predicted. Each person's reaction to a test drug may be different.
The ability of IFX-1 to treat GPA/MPA in combination with immunosuppressive therapy has not yet been demonstrated. Expected GC-related side effects are fewer. Furthermore, the safety of IFX-1 has been investigated in 3 Phase II studies, conducted in 48 subjects with early septic organ dysfunction treated with IFX-1. Overall, IFX-1 was safe and well tolerated in all these studies, and no additional risks associated with the administration of IFX-1 were observed.
Because IFX-1 is an antibody/protein, a general risk for anaphylactic reactions exists. Subjects who are included in this study are treated with IFX 1 at the study site so that adequate treatment and care is available in case of an anaphylactic reaction. To date, no anaphylactic reactions have been reported after administration of IFX-1 in clinical Phase I and II studies. The hypothesized benefit of treatment with IFX-1, therefore, outweighs the potential risks for the subjects participating in this study.

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. Male or female, * 18 years of age.
2. Written informed consent obtained from subject.
3. Diagnosis of GPA or MPA according to the definitions of the Chapel Hill Consensus Conference (CHCC).
4.History of positive antigen-specific ANCA testing since the time of diagnosis or at screening, or documented evidence of either antiproteinase 3 (anti-PR3) or anti-myeloperoxidase (anti-MPO) (for newly diagnosed subjects a recent positive antigen-specific ANCA testing is mandatory for inclusion)
5. Have * 1 "major" item, or * 3 other items, or * 2 renal items on the Birmingham Vasculitis Activity Score Version 3 (BVASv3).
6. Newly diagnosed or relapsed GPA or MPA that requires treatment with CYC or RTX plus GCs.
7. Estimated glomerular filtration rate (eGFR) * 20 mL/min/1.73 m^2.

Exclusion criteria

Subjects who fulfil any of the following criteria at screening are not eligible to participate in the study:
1.Any other multi-system autoimmune disease as listed in Appendix 18.4.
2.Require mechanical ventilation because of alveolar hemorrhage at screening.
3.Known hypersensitivity to any investigational medicinal product (IMP) (i.e. GC, IFX-1) and/or any excipients.
4.Subject with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption.
5.Have required management of infections, as follows:

a.Chronic infection requiring anti-infective therapy (such as latent tuberculosis, pneumocystis, aspergillosis, cytomegalovirus, herpes simplex virus, herpes zoster and atypical mycobacteria) within 3 months before screening.
b.Use of intravenous antibacterials, antivirals, anti-fungals, or anti parasitic agents within 30 days of screening.
6.Current and/or history (within the previous 5 years) of drug and/or alcohol abuse and/or dependence.
7.Evidence of Hep B, C and/ or HIV infection. Only subjects with documented negative historical results (within 4 weeks before screening) for Hep B, C Virus and HIV or a negative test by Screening can be included into the study.
8.Any of the following abnormal laboratory findings at screening:
a.White blood cells < 3,500/mm3
b.Platelet count < 100,000/mm3
c.Transaminase values (AST and/or ALT) * 2.5 times the upper limit of normal range (ULN)
d.Total bilirubin * 1.5 times ULN
e.Alkaline Phosphatase (ALP) > 3 times ULN
9.Current or history of malignancy, lymphoproliferative, or myeloproliferative disorder except squamous cell or basal cell carcinomas of the skin and cervical carcinoma in situ with curative surgical treatment.
10.Received CYC or RTX within 12 weeks before screening or within 12 weeks before CYC or RTX is started for remission induction within 2 weeks before screening.; If subject is on AZA, MMF or MPS or MTX, these drugs must be discontinued prior to receiving the first dose of CYC or RTX.
11.Received > 3 g cumulative intravenous GCs within 4 weeks before screening (RTX intravenous GC premedication is separate and does not count to the 3 g).
12.a.Received an oral daily dose of a GC of > 10 mg prednisoneequivalent for more than 6 weeks continuously prior to screening.
b.Received an oral daily dose of a GC of > 80 mg prednisone equivalent within 2 weeks before screening.
13.Received a CD20 inhibitor, anti-tumor necrosis factor treatment, abatacept, alemtuzumab, any other experimental or biological therapy, intravenous immunoglobulin or plasma exchange, antithymocyte globulin, or required renal dialysis within 12 weeks before screening.
14.Received a live vaccination within 4 weeks before screening or planned between screening and Week 2774.
15.Either active or latent tuberculosis treatment is ongoing.
16.Pregnant or lactating.
17.Clinically significant abnormal electrocardiogram (ECG) during screening.
18.Female subjects of childbearing potential unwilling or unable to use a highly effective method of contraception (pearl index < 1) during treatment and for at least 3 months after last administration of IFX- 1/Placebo-IFX-1 (or up to 12 months, the timeframes for Standard of Care agents have to be considered as described in the respective Prescribing Information/SPCstimeframes). Contraception methods regarded as highly effective methods and the duration of contraception are further described in Section 7.7.

19.Evidence or suspicion that the subject might not comply with the requirements of the study protocol.
20.The subject is an employee or direct relative of an employee of the sponsor (InflaRx GmbH).
21.The subject is imprisoned or lawfully kept in an institution.
22.The subject has participated in an investigational clinical study during the 12 weeks (or 5 times the half-life of the previous IMP, whichever is longer) before screening, or plans to participate in another investigational clinical study during their participation in this study.
23.Male subjects with female partners of childbearing potential unwilling to use contraception (condoms) during treatment and for at least 3 months after last administration of IFX-1/Placebo-IFX-1.

Study design

Design

Study phase:	2
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):	03-04-2019
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Glucocorticoids (GC)
Generic name:	PREDNISONE
Registration:	Yes - NL intended use

Product type:	Medicine
Brand name:	IFX-1
Generic name:	N/A

Ethics review

Approved WMO Date:	20-12-2018
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-03-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-05-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-07-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-12-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	07-01-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO	

Date:	11-05-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-05-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	03-03-2021
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	EUCTR 2018-000768-2-NL
CCMO	NL67655.056.18