A Phase 2/3, Randomized, Double-Blinded, Placebo-Controlled, Parallel-Group Study to Investigate the Efficacy and Safety of Efgartigimod PH20 SC in Adult Participants With Bullous Pemphigoid

Published: 26-04-2022
Last updated: 14-09-2024

This study has been transitioned to CTIS with ID 2023-508645-40-00 check the CTIS register for the current data. Parts A and B:To evaluate the efficacy of efgartigimod PH20 SC on achieving sustained remission in the treatment of participants with...

Ethical review	Approved WMO
Status	Pending
Health condition type	Autoimmune disorders
Study type	Interventional

Summary

ID

NL-OMON53428

Source
ToetsingOnline

Brief title
A phase 2/3 study in adults with bullous pemphigoid (BALLAD)

Condition

- Autoimmune disorders
- Skin and subcutaneous tissue disorders NEC

Synonym
Bullous Pemphigoid, Lever's Pemphigoid

Research involving
Human

Sponsors and support

Primary sponsor: PPD
Source(s) of monetary or material Support: argenx BV

Intervention

Keyword: Bullous Pemphigoid, Efgartigimod, Phase 2/3, Skin Disease

Outcome measures

Primary outcome

Parts A and B:

Proportion of participants who are in complete remission (CR) while receiving efgartigimod PH20 SC or placebo and have been off oral corticosteroid (OCS) therapy for >=8 weeks at week 36

Secondary outcome

Part B only:

1. Cumulative dose of OCS from baseline to week 36

2. Proportion of participants who achieve an Investigator Global Assessment of Bullous Pemphigoid (IGA BP) score of 0 while receiving efgartigimod PH20 SC or placebo and have been off OCS therapy for >=8 weeks at week 36

3. Proportion of participants who achieve control of disease activity (CDA) while receiving efgartigimod PH20 SC or placebo and remain free of relapse through week 36

4. Proportion of participants who are in CR while receiving efgartigimod PH20 SC or placebo and have been receiving minimal OCS therapy for >=8 weeks at week 36. (Minimal OCS therapy is defined as <=0.1 mg/kg/day of prednisone [or an

equivalent dose of another OCS].)

5. Changes from baseline in the 24 hour average itch score from the Itch

Numerical Rating Scale (NRS)

Study description

Background summary

Bullous Pemphigoid (BP) is a chronic autoimmune blistering disease (AIBD) of the elderly that is caused by IgG and IgE autoantibody activity against BP180 and BP230 (hemidesmosomal proteins of the dermal-epidermal junction). This autoantibody activity triggers a variety of immune responses in the skin that ultimately lead to blistering and pruritus.
Efgartigimod, a neonatal Fc receptor (FcRn) antagonist, blocks FcRn mediated recycling of IgG, thereby reducing total IgG serum levels, including IgG autoantibodies. Efgartigimod PH20 SC (efgartigimod coformulated with recombinant human hyaluronidase PH20 [rHuPH20]) represents a rational therapeutic approach to autoimmune diseases mediated by IgG autoantibodies, including BP.
This double-blinded, placebo-controlled study will determine whether sustained remission is attainable with once-weekly administration of efgartigimod PH20 SC while tapering oral corticosteroid (OCS) therapy within a 36-week treatment period.

Study objective

This study has been transitioned to CTIS with ID 2023-508645-40-00 check the CTIS register for the current data.

Parts A and B:
To evaluate the efficacy of efgartigimod PH20 SC on achieving sustained remission in the treatment of participants with bullous pemphigoid (BP)

Study design

ARGX-113-2009 is an operationally seamless 2 part, phase 2/3, prospective, global, multicenter, randomized, double blinded, placebo controlled study to investigate the efficacy, safety, tolerability, immunogenicity, participant-reported outcome measures (including those assessing participant QoL), PK, and PD of efgartigimod PH20 SC administered via subcutaneous (SC) injection in adult participants with moderate to severe BP. This study intends to demonstrate that efgartigimod is an effective and safe treatment for BP,

providing participants with control of disease activity (CDA) and eventually remission while reducing their cumulative exposure to OCS.
The study will consist of 2 parts:
• Part A is a phase 2 evaluation that intends to provide proof of concept for the therapeutic activity of efgartigimod PH20 SC in participants with BP.
• Part B is a phase 3 evaluation that intends to confirm the results obtained from part A in a separate, larger group of participants with BP.
An interim analysis will be performed during part A (on data obtained through week 26 for all Part A participants) to assess the primary endpoint and several secondary endpoints, confirm the appropriate sample size for part B of the study, and determine whether the efficacy results observed through week 26 of part A warrant continued study of efgartigimod PH20 SC for the treatment of participants with BP (futility analysis).
Other than differences in main goals, endpoints, and statistical analyses, parts A and B are identical in schedule, structure, assessments, and conduct.

Intervention

Participants with moderate-to- severe BP will be randomly assigned in a 1:1 ratio to 1 of the following study intervention groups:
Efgartigimod*PH20 SC or Placebo*PH20*SC
Efgartigimod PH20 SC or placebo will be administered at a fixed dosage throughout the 36-week treatment period, while the dosage of concurrent OCS therapy will be adjusted according to each participant*s BP disease status throughout the study.

Study burden and risks

The most common side effects reported in completed clinical studies in healthy participants who received efgartigimod were:
• headache
• an abnormal white blood cell count
• chills or feeling cold
• increase in the level of a blood test marker for inflammation (C reactive protein)
• common cold
• injection-site reactions like redness, bruise, and pain
• black and blue marks at the injection site
• diarrhea
• back pain
• pins and needles sensation

Some of these side effects were seen in the groups who received efgartigimod at higher doses than the dose used in this study.
The most common side effects in clinical studies in patients with immune thrombocytopenia (a bleeding disease), myasthenia gravis (a nervous system

disease that causes muscle weakness), immune thrombocytopenia (a bleeding disease), and pemphigus (a skin disease that can cause blisters) who received efgartigimod through an infusion were:
• headache
• common cold
• upper respiratory tract infection
• nausea
• urinary tract infection
• muscle pain
• mouth/throat discomfort
• back pain
• dizziness
• small bleeding under the skin
• black and blue marks
• bruising
• high blood pressure
• diarrhea
• abdominal pain
• vomiting
• flu-like symptoms

Contacts

Public
PPD

Zonneoordlaan 17
Ede 6718 TK
NL
Scientific
PPD

Zonneoordlaan 17
Ede 6718 TK
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Participants are eligible to be included in the study only if all of the following criteria apply:
1. The participant is willing and able to do the following:
a. understand the requirements of the study
b. provide written informed consent (including consent for the use and disclosure of research-related health information)
c. comply with the study protocol procedures (including required study visits).
2. The participant is male or female and has reached the local legal age of consent at the time of signing the informed consent form (ICF).
3. Participants have clinical signs of BP (ie, presence of bullae), with or without the presence of urticarial/eczematous/erythematous plaques or pruritus at the screening and baseline visits. The diagnosis of BP must be confirmed by positive histopathology and DIF before randomization to treatment assignment, and by positive serology (by IIF, CLEIA, or ELISA, according to local practice) at screening (Section 8.1.2).
4. The participant has an IGA BP score of 3 or 4 at screening and baseline.
5. The participant has a Karnofsky performance status of at least 60% at screening.
6. The participant agrees to use contraceptive measures consistent with local regulations. WOCBP must have a negative serum pregnancy test at screening and a negative urine pregnancy test at baseline before receiving IMP.

See protocol for the full list of criteria

Exclusion criteria

Participants are excluded from the study if any of the following criteria apply: 1. Other forms of pemphigoid (including but not limited to pemphigoid gestationis, drug induced BP that resolves after culprit-drug withdrawal, anti-p200 pemphigoid, mucous membrane pemphigoid, and cicatricial pemphigoid), or other AIBDs (including but not limited to epidermolysis bullosa acquisita, pemphigus vulgaris, and exfoliative erythroderma) 2. Received unstable dose of treatments known to cause or exacerbate BP (eg, angiotensin converting enzyme inhibitors, penicillamine, furosemide, phenacetin, dipeptidyl peptidase 4 inhibitor) for at least 4 weeks prior to the baseline visit 3. Use of BP

treatments other than OCS, TCS, conventional immunosuppressants (eg, azathioprine, cyclophosphamide, methotrexate, mycophenolate mofetil), or dapsone, including the following: a. sulfasalazine, IVIg, subcutaneous administration of immunoglobulin (SCIg), immunoadsorption or plasma exchange within 8 weeks of the baseline visit b. tetracyclines with or without nicotinamide at doses higher than the recommended daily allowance (RDA)/dietary reference intake (DRI) within 2 weeks of the baseline visit c. any monoclonal antibody (including rituximab or another anti-CD20 biologic) within 6 months of the baseline visit d. complementary therapies*such as traditional Chinese medicines, herbs, or procedures (eg, acupuncture)*within 4 weeks (or 5 half-lives) of the baseline visit, if the investigator determines that such therapies may interfere with the study*s efficacy assessments and/or potentially risk the safety of the participant 4. Known contraindication to OCS therapy 5. Active, chronic or latent infection at screening 6. Positive COVID-19 test result at screening (testing performed if required per local regulations) 7. Any other known autoimmune disease that, in the opinion of the investigator, would interfere with an accurate assessment of clinical symptoms of BP or put the participant at undue risk 8. History of malignancy unless deemed cured by adequate treatment with no evidence of recurrence for >=3 years before the first administration of the IMP. Participants with the following cancers can be included at any time, provided they are adequately treated prior to their participation in the study: a. Basal cell or squamous cell skin cancer b. Carcinoma in situ of the cervix c. Carcinoma in situ of the breast d. Incidental histological finding of prostate cancer (tumor-node metastasis [TNM] stage T1a or T1b) 9. Clinical evidence of other significant serious diseases, have had a recent surgery, or who have any other condition that, in the opinion of the investigator, could confound the results of the study or put the patient at undue risk or prevent participants from complying with protocol requirements. 10. Use of an investigational product within 3 months or 5 half-lives (whichever is longer) before the first dose of IMP 11. Previously participated in a clinical study with efgartigimod or currently participating in another interventional clinical study. 12. Known hypersensitivity to any of the components of the administered treatments 13. Positive serum test at screening for an active infection with any of the following conditions: a. HBV that is indicative of an acute or chronic infection, unless associated with a negative HBsAg or negative HBV DNA test38 b. HCV based on HCV antibody assay unless a negative RNA test is available c. HIV based on test results that are associated with an AIDS-defining condition or a CD4 count <=200 cells/mm3 14. Primary or secondary hypogammaglobulinemia with total IgG serum levels <4 g/L at screening. [Note: Study candidates with total IgG serum levels of 4 6 g/L at screening may be permitted to participate in the study following discussion and agreement between the investigator and the sponsor.] 15. Current or history (ie, within 12 months of screening) of alcohol, drug, or medication abuse assessed by the investigator 16. Pregnant or lactating females and those who intend to become pregnant during the study 17. Live or live-attenuated vaccine received <4 weeks before baseline visit

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-11-2022
Enrollment:	2
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Efgartigimod
Generic name:	Efgartigimod

Ethics review

Approved WMO Date:	26-04-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-07-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek

	(Assen)
Approved WMO Date:	23-08-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-10-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-10-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-11-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-02-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	19-07-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-09-2023
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
EU-CTR	CTIS2023-508645-40-00
EudraCT	EUCTR2021-003087-27-NL
CCMO	NL81014.056.22