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# Efficacy and Safety of Efgartigimod PH20 Subcutaneous in Adult Patients With Pemphigus Vulgaris (PV) or Pemphigus Foliaceus (PF): ADDRESS, a Global Phase 3 Clinical Trial in Progress

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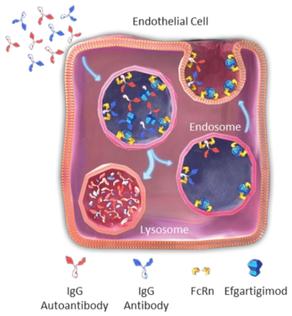
## BACKGROUND

### EFGARTIGIMOD: IgG1 Fc Fragment With ABDEG™ Mutations[1,2]




- Efgartigimod is a human immunoglobulin (Ig)G1 Fc fragment engineered for increased affinity for the neonatal Fc receptor (FcRn)
- Blocks FcRn, outcompeting endogenous IgG binding, preventing recycling of IgG and thereby decreasing serum IgG concentration
- FcRn blockade also leads to rapid decrease in circulating autoantibodies that may effectively treat IgG-mediated autoimmune diseases
- Efgartigimod is an investigational drug proposed for the treatment of IgG-mediated autoimmune disease

### PEMPHIGUS: an IgG-Mediated Autoimmune Disease[3-5]

- Pemphigus vulgaris (PV) and pemphigus foliaceus (PF) belong to a heterogenous group of autoimmune blistering diseases and are clinically characterised by mucosal erosions (PV) and cutaneous blisters (PV and PF)
- PV is characterised by the presence of pathogenic IgG autoantibodies targeting desmoglein 3 (Dsg-3) and, in 50% of the cases, also against desmoglein 1 (Dsg-1)
- PF is attributed to the presence of IgG autoantibodies solely directed against Dsg-1
- Pemphigus is potentially life-threatening, primarily due to secondary infections

### EFGARTIGIMOD WAS WELL TOLERATED AND DEMONSTRATED FAST ONSET OF EFFECT IN PHASE 2 TRIAL[6]

- In an open-label phase 2 adaptive trial (NCT03334058), efgartigimod demonstrated a favourable safety and tolerability profile, consistent with previous studies
- Reductions in serum IgG, including anti-Dsg autoantibodies, were observed along with improved pemphigus disease area index (PDAI) scores
- Efgartigimod, as monotherapy and combined with prednisone, demonstrated a rapid onset of action with disease control (DC) in 90% (28/31) of patients with a median time of 17 days
- Fourteen of 22 (64%) patients on efgartigimod treatment with prednisone 0.1–0.5 mg/kg/d achieved complete remission (CR; efgartigimod doses: 10 mg/kg: median 36 days, range 13–93; 25 mg/kg: 92 days, range 41–287)
- These results support the further evaluation of efgartigimod as a therapy for pemphigus

## PHASE 3 ADDRESS KEY ELIGIBILITY CRITERIA

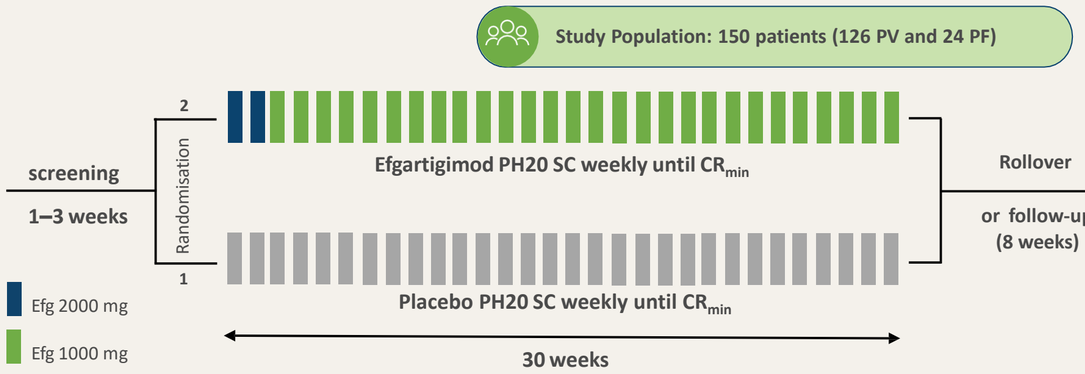
**Inclusion criteria**
- Clinical diagnosis of PV or PF confirmed by histology, positive direct immunofluorescence (IF), and positive indirect IF or enzyme-linked immunosorbent assay
- Moderate to severe pemphigus (PDAI ≥15) at baseline
- Participants are either newly diagnosed or experiencing flare of disease having a maximum of 4 years since disease onset

**Exclusion criteria**
- Any other non-PV/non-PF autoimmune blistering disease (e.g., paraneoplastic pemphigus, drug-induced pemphigus, pemphigus vegetans, and pemphigus erythematosus)
- History of refractory disease (failure to respond to first-line and second-line therapies)
- Use of rituximab/anti-CD20 biosimilars within 6 months prior to baseline
- Systemic pemphigus therapy other than oral corticosteroids. Conventional immunosuppressants (e.g., azathioprine, cyclophosphamide, methotrexate, mycophenolate mofetil) and dapsone must be discontinued before baseline
- Contraindication to oral corticosteroids

## Phase 3 ADDRESS (ARGX-113-1904) Trial Design

address pemphigus study

Efgartigimod Multicentre, Randomised, Double-Blind, Placebo-Controlled Trial in Pemphigus (Vulgaris and Foliaceus)




**Efgartigimod co-formulated with hyaluronidase PH20 for convenient SC administration in <2 min**
HCP-supported administration at home
Self-administration in open-label extension

**ARGX-113-1905 open-label extension**
address+ pemphigus study
Remission off therapy
Duration of remission
Flare and retreatment

**Rollover conditions**
At end of study (week 30) upon flare after $CR_{min}$, treatment failure (absence of DC*, non-controlled flare, prednisone-related SAE)

### Concomitant corticosteroid treatment

- Prednisone (or equivalent) starting dose **0.5 mg/kg/day**
- **Increase** dose with disease progression or delayed DC (up to 1.5 mg/kg/day for 3 weeks*)
- **$CR_{min}$** is the absence of new lesions and complete healing of established lesions while the participant is receiving minimal prednisone therapy of ≤10 mg/day for ≥2 months (8 weeks)
- **Protocol-defined tapering** below 0.5 mg/kg/day from sustained CR (2 weeks) or EoC (4 weeks) until minimal therapy (10 mg/day); when $CR_{min}$ is reached, prednisone can be further tapered upon clinical judgement by the investigator
- Escalate dose in case of flare

CR: complete remission; $CR_{min}$: CR on minimal therapy; DC: disease control; Efg: efgartigimod; EoC: end of consolidation; HCP: health care provider; SAE: serious adverse event; SC: subcutaneous.

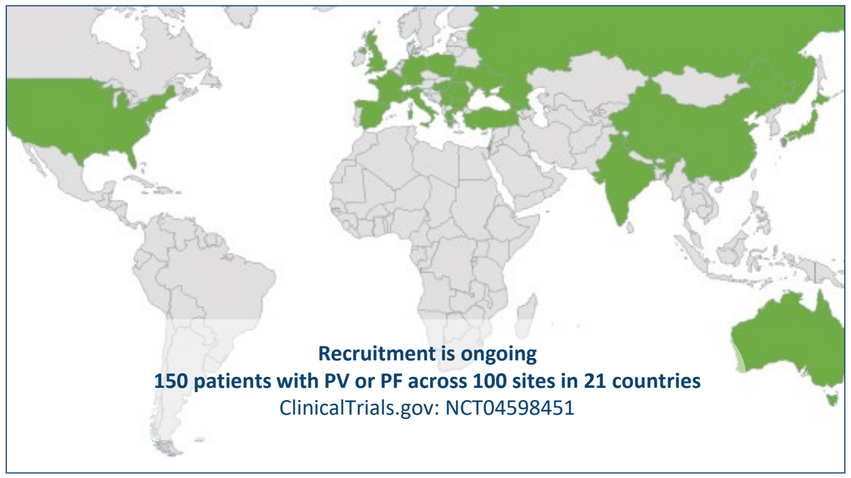
### PHASE 3 ADDRESS CLINICAL TRIAL PRIMARY ENDPOINT

**Proportion of patients with PV who achieve CR on minimal therapy within 30 weeks**

### SECONDARY AND ADDITIONAL ENDPOINTS

- Proportion of patients with PV or PF who achieve CR on minimal therapy within 30 weeks
- Cumulative prednisone dose
- Time to DC*
- Time to CR†
- Rate of treatment failure
- Rate of treatment flare
- PDAI at each visit
- Safety
- Health-related quality of life: EQ-5D-5L and ABQOL
- Glucocorticoid Toxicity Index
- Pharmacokinetics and pharmacodynamics
- Immunogenicity

*DC = no new lesions, established lesions starting to heal.
†CR = absence of new lesions and established lesions completely healed except for post-inflammatory hyperpigmentation or erythema from resolving lesions.



**Recruitment is ongoing**
**150 patients with PV or PF across 100 sites in 21 countries**
ClinicalTrials.gov: NCT04598451

## We gratefully acknowledge the clinicians, patient organizations, and scientists who have collaborated on the design of this trial

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