P242

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

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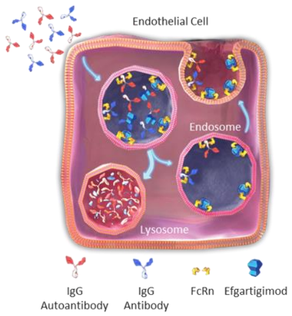
BACKGROUND

EFGARTIGIMOD: IgG1 Fc Fragment With ABDEGTM Mutations[1,2]



- Efgartigimod is a human IgG1 Fc fragment engineered for increased affinity for the neonatal Fc receptor (FcRn)
- Blocks FcRn, outcompeting endogenous immunoglobulin G (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 characterized by mucosal erosions (PV) and cutaneous blisters (PV and PF)
- PV is characterized by the presence of pathogenic IgG autoantibodies targeting desmoglein 3 (Dsg3) and, in 50% of the cases, also against desmoglein 1 (Dsg1)
- PF is attributed to the presence of IgG autoantibodies solely directed against Dsg1
- Pemphigus is potentially life-threatening, primarily due to secondary infections

EFGARTIGIMOD WAS WELL TOLERATED AND DEMONSTRATED FAST ONSET OF EFFECT IN PHASE 2 TRIAL

- In an open-label phase 2 adaptive trial (NCT03334058), efgartigimod demonstrated a favorable safety and tolerability profile, consistent with previous studies
- There was a strong correlation between serum IgG level reduction, autoantibody level reduction, and improvement of the pemphigus disease area index (PDAI) scores and clinical outcomes
- 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%) of patients on efgartigimod treatment with prednisone 0.1–0.5 mg/kg/d achieved complete clinical 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 ELISA
- 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

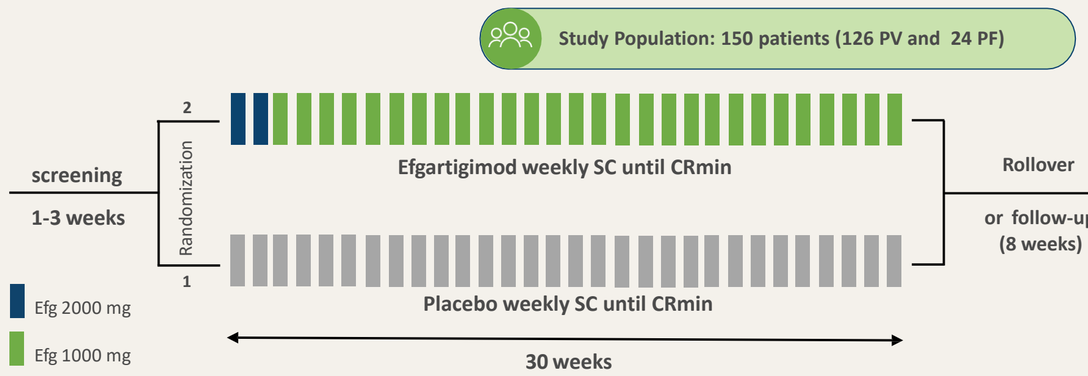
Exclusion criteria

- 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 Multicenter, Randomized, Double-blind, Placebo-controlled Trial in Pemphigus (Vulgaris and Foliaceus)



Efgartigimod co-formulated with hyaluronidase for convenient SC administration in <2min
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 CRmin, 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*)
- **Protocol-defined tapering** below 0.5 mg/kg/day from sustained CR (2 weeks) or EoC (4 weeks) until minimal therapy (10 mg/day)
- Escalate dose in case of flare

CR: complete clinical remission; CRmin: complete clinical remission on minimal therapy; DC: disease control; Efg: efgartigimod; EoC: end of consolidation; HCP: health-care provider; SAE: serious adverse event; SC: subcutaneous.

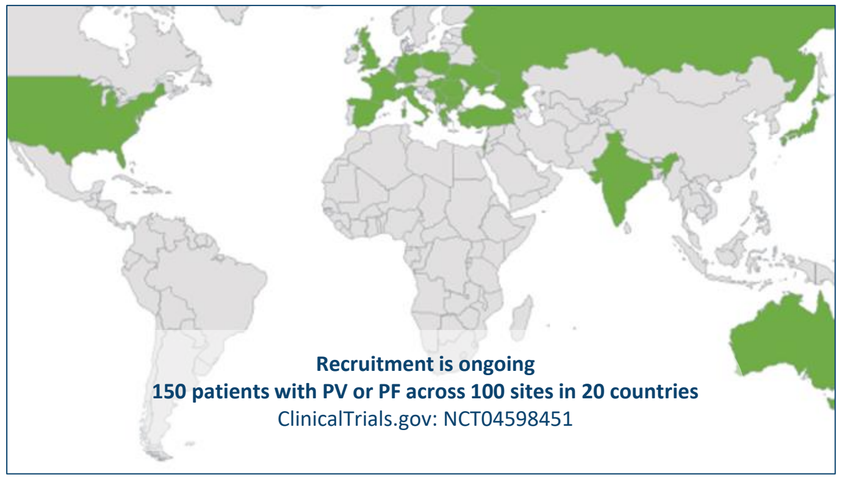
PHASE 3 ADDRESS CLINICAL TRIAL PRIMARY ENDPOINT

Proportion of PV patients who achieve clinical remission on minimal therapy within 30 weeks

SECONDARY AND ADDITIONAL ENDPOINTS

- Proportion of PV and PF patients who achieve clinical remission on minimal therapy within 30 weeks
- Cumulative prednisone dose
- Time to disease control*
- Time to complete clinical remission†
- 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 (GTI)
- Pharmacokinetics and pharmacodynamics
- Immunogenicity

*Disease control = no new lesions, established lesions starting to heal
†Clinical remission = 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 20 countries
ClinicalTrials.gov: NCT04598451

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

DISCLOSURES AND ACKNOWLEDGMENTS

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