POS1049

Safety, Tolerability, and Efficacy of Empasiprubart in Adults With Dermatomyositis (EMPACIFIC): A Phase 2, Randomized, Double-Blinded, Placebo-Controlled, Multicenter Study

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BACKGROUND

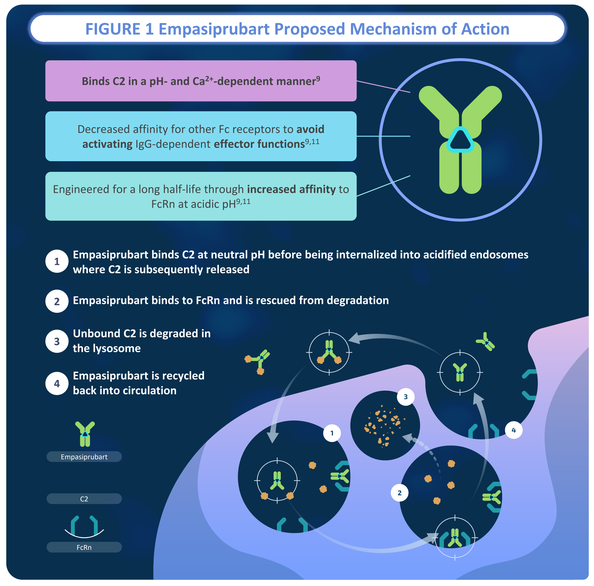
Dermatomyositis (DM)

- DM is a systemic, idiopathic, inflammatory myopathy characterized by muscle inflammation that causes progressive, symmetrical, proximal skeletal muscle weakness and is associated with characteristic skin manifestations[1,2]
- Its complex pathogenesis is incompletely understood, but histological findings suggest that DM may, at least in part, be complement mediated[3–7]
- IVIg, the only approved treatment for DM, has a high treatment burden and is associated with an increased risk of thromboembolic events[8]

Empasiprubart Binds C2 and Blocks Activation of the Classical and Lectin Complement Pathways

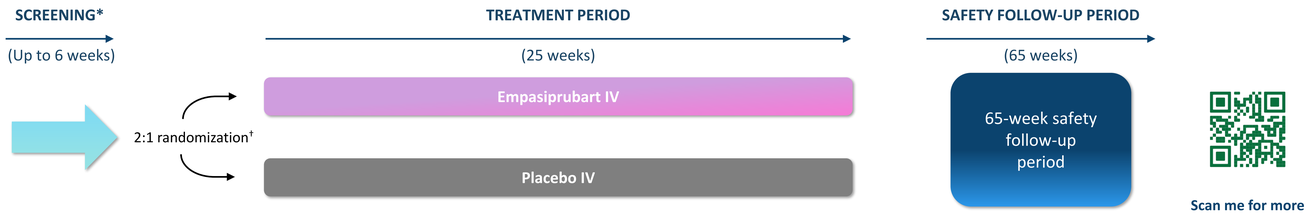
- Empasiprubart is a first-in-class, humanized, monoclonal antibody that specifically binds to C2[10] (**Figure 1**)
- Empasiprubart is being investigated in several autoimmune and neuromuscular conditions, including multifocal motor neuropathy and chronic inflammatory demyelinating polyradiculoneuropathy[11]
- Upstream complement inhibition by empasiprubart can not only reduce the tissue damage mediated by deposition of complement complexes, but also broadly target complement-mediated inflammatory effects

FIGURE 1 Empasiprubart Proposed Mechanism of Action



STUDY DESIGN

FIGURE 2 EMPACIFIC: A Phase 2, Randomized, Double-Blinded, Placebo-Controlled, Multicenter Study to Evaluate the Safety, Tolerability, and Efficacy of Empasiprubart in Adults With DM (NCT06284954)



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*The screening period aims to enroll 42 participants and may be extended to accommodate the participant's vaccination schedule by 14 days to a total of 56 days. †An estimated 27 participants will be randomized.

KEY ELIGIBILITY CRITERIA

Inclusion

- At least 18 years of age
- Clinical diagnosis of DM/JDM (diagnosis date of JDM ≤5 years before screening)
- Active muscle disease at screening and before first study drug administration*
- Has at least mild skin disease at screening and before first study drug administration
- On stable background treatment
- Received required immunizations†

Exclusion

- Known autoimmune disease or any medical condition that would interfere with accurate assessment of clinical symptoms of DM
- History of malignancy unless considered cured by adequate treatment with no evidence of recurrence for ≥3 years before first study drug administration
- Clinically significant, insufficiently resolved active infection
- Known complement component deficiency as assessed by investigator
- Inflammatory or noninflammatory myopathies other than DM; glucocorticoid-induced myopathy

*Defined as an MMT8 score ≤142 and at least 1 of the following: **A.** CK, ALD, LDH, AST, or ALT ≥2 times the upper limit of normal at screening **B.** Electromyography (fibrillation potentials specific for active muscle inflammation) ≤18 weeks before baseline; **C.** An MRI depicting active muscle inflammation: edema on T2 sequences ≤18 weeks before baseline; **D.** Muscle biopsy demonstrating signs of active inflammation ≤18 weeks before baseline. †First meningococcal, pneumococcal, and the single *Haemophilus influenzae* type B vaccine ≥14 days before first study drug administration.

STUDY ENDPOINTS

1 Primary Endpoint: Safety

- Incidence and severity of AEs
- IMP discontinuation rate due to AEs
- Physical and laboratory safety assessments

2 Secondary Endpoint: Efficacy*

- Mean TIS at Weeks 13 and 25, as assessed by the 2016 ACR/EULAR criteria[12] using 6 CSMs (PhGA, PGA, MMT8, HAQ-DI, Muscle enzymes, EGA as assessed by the MDAAT)

3 Exploratory Endpoints*

- Proportion of patients reaching TIS improvement
- Efficacy in achieving clinical response in outcome measures including muscle strength, damage, and endurance; disease and skin disease activity; pain, fatigue, and physical function; QoL
- PK, PD, and immunogenicity of empasiprubart
- Impact of empasiprubart on complement activation

*Measured at weeks 13 and 25.

KEY TAKEAWAYS

DM is a systemic, idiopathic, inflammatory myopathy that may be complement mediated

Empasiprubart is a first-in-class, humanized, monoclonal antibody that binds to C2, blocking downstream activation of both the classical and lectin complement pathways

By blocking upstream complement activity, empasiprubart may reduce tissue inflammation in patients with DM

The EMPACIFIC phase 2 study will evaluate the safety, tolerability, clinical efficacy, PK, PD, and immunogenicity of empasiprubart in adults with DM

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ABBREVIATIONS

ACR, American College of Rheumatology; AE, adverse event; ALD, aldolase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CK, creatine kinase; CSM, core set measure; EGA, Extramuscular Global Assessment; EULAR, European Alliance of Associations for Rheumatology; Fc, fragment crystallizable; FcRn, neonatal Fc receptor; HAQ-DI, Health Assessment Questionnaire Disability Index; IgG, immunoglobulin G; IMP, investigational medicinal product; IV, intravenous(ly); IVIg, intravenous immunoglobulin; JDM, juvenile dermatomyositis; LDH, lactate dehydrogenase; MDAAT, Myositis Disease Activity Assessment Tool; MMT8, Manual Muscle Testing 8; PD, pharmacodynamics; PGA, Patient Global Assessment of Disease Activity; PhGA, Physician Global Assessment of Disease Activity; PK, pharmacokinetics; TIS, Total Improvement Score.

DISCLOSURES AND ACKNOWLEDGMENTS

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