Design of a randomized, double-blind, placebo-controlled Phase 2 clinical trial of IMO-8400, a Toll-like receptor antagonist, in patients with dermatomyositis

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BACKGROUND

Dermatomyositis (DM), a severe idiopathic inflammatory myopathy, is characterized by chronic autoimmunity in muscle and skin tissue. Toll-like receptors (TLRs) are key components of the innate immune system involved in the disease pathogenesis. IMO-8400 is a novel oligonucleotide-based antagonist of TLRs 7, 8 and 9 that has demonstrated activity in patients with psoriasis. Here, we describe the rationale for and design of a randomized, double-blind, placebo-controlled Phase 2 clinical trial of IMO-8400 in adult patients with DM.

DESIGN

Development of IMO-8400 for the treatment of rare immune-mediated inflammatory diseases

- IMO-8400 is a synthetic oligonucleotide-based antagonist of TLRs 7, 8 and 9.
- Activity observed in preclinical disease models
- Evidence of TLR antagonist established in human clinical trials in psoriasis
- IMO-8400 generally well tolerated in ≥100 subjects to date at dose levels up to 3.2 mg/kg weekly
  - Phase 1 trial in healthy subjects
  - Phase 1/2 trial in patients with dermatomyositis
  - Phase 1/2 trial in patients with diffuse large B-cell lymphoma

TLR-like receptors (TLRs) are believed to play a critical role in the disease pathogenesis of DM

- ROS (susceptible to oxidative stresses) and NLRP3 inflammasome upregulation
- Pro-inflammasome activity
- Pro-inflammatory cytokines
- Upregulation of proinflammatory and proapoptotic genes
- Alterations in the immune system

Sample size assumptions

- Sample size 36 (12 per treatment arm)
- Standard deviation of 8.5 points
- 1-sided significance level 0.05
- Planned statistical analysis

Additional exploratory clinical endpoints

- Muscle strength and function
- Manual muscle testing (MMT)
- 10-meter walk test
- Timed up and go
- 4-Step Chair
- Patient-reported outcomes
  - SF-36 Health Survey (SF-36)

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