Introduction: We report the results of a phase 1b/2a, open-label, multiple ascending dose trial of domagrozumab, a myostatin inhibitor, in patients with FKRP-associated limb-girdle muscular dystrophy.

Methods: Nineteen patients were enrolled and assigned to one of three dosing arms (5 mg/kg, 20 mg/kg, or 40 mg/kg every 4 weeks). Following 32 weeks of treatment, participants receiving the lowest dose were switched to the highest dose (40 mg/kg) for an additional 32 weeks. An extension study was also conducted. The primary endpoints were safety and tolerability. Secondary endpoints included muscle strength, timed function testing, pulmonary function, lean body mass, pharmacokinetics, and pharmacodynamics. As an exploratory outcome, muscle fat fractions were derived from whole-body magnetic resonance images.

Results: Serum concentrations of domagrozumab increased in a dose-dependent manner and modest levels of myostatin inhibition were observed in both serum and muscle tissue. The most frequently occurring adverse events were injuries secondary to falls. There were no significant between-group differences in the strength, functional, or imaging outcomes studied.

Discussion: We conclude that although domagrozumab was safe in patients in LGMD2I, there was no clear evidence supporting its efficacy in improving muscle strength or function. This article is protected by copyright. All rights reserved.

Keywords: FKRP; clinical trial; domagrozumab; limb-girdle muscular dystrophy; myostatin inhibition; whole-body MRI.

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