A Phase 1b/2 study of the anti-myostatin adnectin RG6206 (BMS-986089) in ambulatory boys with Duchenne muscular dystrophy: A 72-week treatment update

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Background:
Pharmacologic inhibition of myostatin, a negative regulator of muscle growth, has been shown to increase skeletal muscle mass in several species, including humans.

Objective:
To assess the safety, tolerability, pharmacokinetics (PK) and pharmacodynamics of the anti-myostatin adnectin RG6206 (BMS-986089) in a Phase 1b/2 study (NCT02515669) in ambulatory boys with Duchenne muscular dystrophy (DMD).

Methods:
Forty-three ambulatory boys with DMD, aged 5–10 years, were randomized to receive weekly subcutaneous injections of RG6206 (4–50 mg) or placebo during a 24-week double-blind phase (treatment: placebo ratio 3:1). All participants then received RG6206 throughout a 48-week open-label phase.

The primary endpoint of this study was safety and tolerability over 24 weeks. Secondary endpoints included the PK of RG6206, frequency and titer of anti-drug antibodies (ADAs), and effect on serum myostatin levels. Exploratory outcomes included timed function tests and dual-energy X-ray absorptiometry imaging of lean body mass (LBM).

Results:
At 24 weeks' treatment, the most common adverse events were mild-to-moderate injection site reactions, which resolved without change to study treatment. No clinically significant changes in laboratory values, vital signs, electrocardiogram parameters or echocardiogram were observed. One patient had a positive ADA titer at a single time point; this was not accompanied by hypersensitivity or injection site reactions. RG6206 treatment resulted in a dose-dependent reduction (77–97%) in free myostatin.

We will report on the effect of treatment on LBM index in boys with DMD who received RG6206 for 72 weeks compared with boys with DMD in the Collaborative Trajectory Analysis Project who had not received any treatment.
Conclusions:
No drug-related safety findings leading to withdrawal from the study were identified. In total, 41 patients from this study are now enrolled in a 228-week open-label extension. A Phase 2/3 RG6206 study is actively recruiting (NCT03039686).

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