OBJECTIVE: To evaluate the effects of tirasemtiv on muscle function in a murine model of ALS.

BACKGROUND: Tirasemtiv, a fast skeletal muscle activator that enhances the response to calcium and amplifies the response of muscle to neural input, is being developed as a potential treatment for neuromuscular diseases.

METHODS: Female B6SJL-SOD1 G93A mice were treated with single doses of tirasemtiv at 10 mg/kg or vehicle (100 µl saline) intraperitoneally at two stages of disease: at 90-100 days of age and at 110-115 days of age. Tirasemtiv increased forelimb grip strength, grid hang time, and rotarod performance in B6SJL-SOD1 G93A mice. Tirasemtiv also increased respiratory function. These results indicate that tirasemtiv has the potential to improve muscle function and respiratory in patients suffering from ALS.

RESULTS: Tirasemtiv increased forelimb grip strength, grid hang time, and rotarod performance in B6SJL-SOD1 G93A mice. Tirasemtiv significantly increased respiratory function.

CONCLUSIONS: Tirasemtiv is a fast skeletal muscle activator that enhances the response to calcium and amplifies the response of muscle to neural input. Tirasemtiv increased forelimb grip strength, grid hang time, and rotarod performance in B6SJL-SOD1 G93A mice.


SUMMARY AND CONCLUSIONS: A single dose of tirasemtiv significantly increases submaximal isometric force, as well as forelimb grip strength, grid hang time, and rotarod performance in a transgenic mouse model of ALS, with functional deficits. Diaphragm force and tidal volume are significantly higher in tirasemtiv-treated B6SJL-SOD1 G93A mice. These results support the potential of fast skeletal muscle activators to improve muscle function in neuromuscular diseases.

The FAST SKELETAL MUSCLE TROPONIN ACTIVATOR TIRASEMTIV INCREASES MUSCLE FUNCTION AND PERFORMANCE IN THE B6SJL-SOD1G93A ALS MOUSE MODEL

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INCREASES MUSCLE FUNCTION AND PERFORMANCE IN THE B6SJL-SOD1G93A ALS MOUSE MODEL

B6SJL-SOD1 mice exhibit significant functional deficits prior to tirasemtiv administration

Tirasemtiv increased forelimb grip strength, grid hang time, and rotarod performance in B6SJL-SOD1 G93A mice.

REFERENCES