GFRAL RECEPTOR INHIBITOR FOR THE TREATMENT OF AMYOTROPHIC LATERAL SCLEROSIS

KEYWORDS

- ❑ AMYOTROPHIC LATERAL SCLEROSIS
- ❑ CACHEXIA
- ❑ SHORT HAIRPIN RNA
- ❑ GDF15
- ❑ GFRAL

AREA

- ❑ PHARMACEUTICAL

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Patent Type
Patent for invention.

Ownership
Sapienza University of Rome 100%

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Industrial & Commercial Reference
Pharmaceutical. Pharmaceutical industries involved in the development and marketing of medicines for hospital use.

Time to Market
TRL 4 – technology validated in lab

Availability
Assignment, exclusive or non-exclusive license, research, development, experimentation, collaboration and start-up

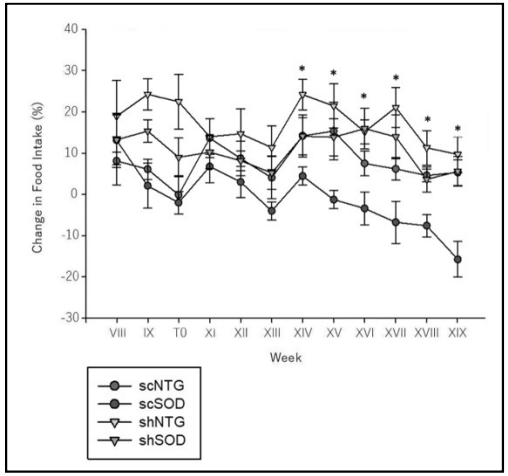

Fig. 1 Representative graph of food intake in hSOD1G93A mice and non-transgenic mice injected with GFRAL AAV silencing shRNA (sh group) or empty vector (sc group) at 10 weeks of age - T0. A significant increase in food intake was reported in subjects receiving GFRAL silencing (sh group), from week XIV to week XIX. Treatment SH VS SC *p<0.05.

Abstract
In amyotrophic lateral sclerosis (ALS), weight loss is an important clinical feature among patients at the time of diagnosis. The invention consists in demonstrating the involvement of Growth differentiation factor15(GDF15) in the metabolic dysregulation that occurs during ALS progression. GDF15, by acting on its receptor GFRAL, causes anorexia and weight loss in several pathologies. It is proposed to administer artificial short hairpin RNA molecules capable of silencing the GFRAL gene, to counteract weight loss by acting on GDF15 signaling, thus improving the symptoms and quality of life of ALS patients.

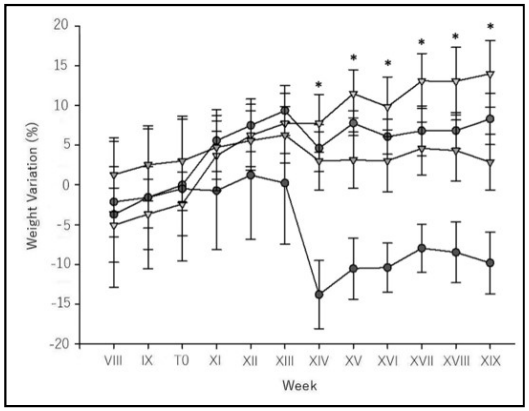

Fig. 2 Representative graph of body weight in hSOD1G93A mice and non-transgenic mice injected with GFRAL AAV silencing shRNA (sh group) or empty vector (sc group) at 10 weeks of age - T0. A significant increase in body weight was reported in subjects receiving GFRAL silencing (sh group), from week XIV to week XIX. Treatment SH VS SC *p<0.05.

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Technical Description

The patent relates to a GFRAL receptor inhibitor for the treatment of amyotrophic lateral sclerosis (ALS), in particular for the treatment of cachexia and/or to reduce weight loss in ALS patients. The inhibitor is a polynucleotide short hairpin RNA (shRNA). An inhibitor is an agent able to decrease or inhibit the expression of the GFRAL receptor gene. This polynucleotide is able to bind, at least partially, the gene coding for GFRAL and inhibiting its expression, or coding for a molecule capable of binding to the GFRAL gene inhibiting its expression.

Technologies & Advantages

With prevalence of 56%-62% in ALS patients, weight loss is defined as an important and independent prognostic factor. In addition, several studies have reported that the progression of the disease is directly proportional with weight loss or with a low body mass index (BMI), at the time of diagnosis. By implementing specific dietary programs, including various high-calorie fat or sugar diets, ALS patients have shown slower disease progression and better quality of life. This observation focused attention on the influence of the ALS patient's metabolic condition on disease progression. The GDF15 cytokine receptor polynucleotide inhibitor, GFRAL, aims to improve weight loss and cachexia in SLA patients.

Applications

1. A GFRAL receptor inhibitor for use in the treatment of amyotrophic lateral sclerosis (ALS).
2. A GFRAL receptor inhibitor for use in the treatment of ALS-associated cachexia and/or to block and/or reduce weight loss and/or to increase appetite in a person with ALS.
3. The inhibitor for use according to claim 1 or 2 in which the inhibitor blocks, prevents and/or decreases the interaction between GFRAL and GDF15, or blocks, silences and/or decreases the expression of the coding gene for the GFRAL receptor.
4. The inhibitor for use in any of the previous applications where ALS is a sporadic form (sSLA) or a familial genetic form (fsla).

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