

Treating ALS by blocking the CXCR4/CXCL12 signaling with AMD3100 (Ramot)

code: 10-2014-765

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BACKGROUND

AMD3100 is an FDA approved bicyclam molecule (Plerixafor) that specifically and reversibly blocks SDF-1 binding to CXCR4. AMD3100 has been shown to rapidly mobilize hematopoietic stem and progenitor cells (HSPCs) from the bone marrow (BM) into the blood of mice, non-human primates and humans.

Amyotrophic Lateral Sclerosis (ALS), commonly known as Lou Gehrig's disease, is a progressive neuromuscular disease. ALS is characterized by a progressive degeneration of motor nerve cells in the brain (upper motor neurons) and spinal cord (lower motor neurons). When the motor neurons can no longer send impulses to the muscles, the muscles begin to waste away (atrophy), causing increased muscle weakness.

Astrocytic cells are considered to have a primary role in the pathological process of ALS, and are substantial contributors to motor neuron death. Astroglial abnormalities, such as changes in the release and uptake of astrocytic glutamate preface clinical symptoms of the disease (Vargas et al 2010).

Chemokine receptors, including the G-protein-coupled receptor CXCR4, are expressed widely in neurons and glial cell. The ligand of CXCR4, the chemokine stromal-derived factor 1 (SDF-1), also known as CXCL12, evokes glutamate release and thereby modulates neuronal function or apoptosis. (Allen et al. 2001).

TECHNOLOGY

In this project, a novel formulation of AMD3100 (including Lactate and Zink) was used for the inhibition of the CXCR4/CXCL12 signaling in an ALS mouse model, was shown to result in beneficial effect for ALS symptoms such as improvement of motor function, blood-spinal cord-barrier (BSCB) integrity restoration, increase in remyelination markers and reduce in inflammation.

In addition, the combination therapy demonstrated additional beneficial effect compared to AMD3100 alone.

APPLICATIONS

- A novel patent protected combination therapeutic ALS drug.

ADVANTAGES

- Fairly short regulatory path as AMD3100 is an FDA approved drug.
- AMD3100 can be used in other diseases where:
 - o Remyelination is critical like in MS disease.
 - o CXCR4 has a significant role.
- Synergistic effects of Zink and Lactate with AMD3100
- Strong IP on the use of AMD3100 in ALS and the combination with Zink and Lactate

PATENTS

Method for treating amyotrophic lateral sclerosis by inhibition of cxcr4/cxcl12 signaling - WO2015031722 A1 -National phase in USA and EU

Combined therapies against neurodegenerative diseases based on inhibition of CXCL12 binding to CXCR4 - provisional application filed

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