INNOVATION PARTNERSHIPS
UNIVERSITY OF MICHIGAN

Tofacitinib for Treatment of Amyotrophic Lateral Sclerosis

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Category
Therapeutics and Vaccines
Life Sciences

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OVERVIEW

Use of tofacitinib to delay progression and reduce severity of amyotrophic lateral sclerosis (ALS)

- Causes inhibition of the janus kinase (JAK) pathway to downregulate natural killer (NK) cell activity
- Has been shown to diminish symptoms of ALS, and may be administered with existing therapies

MODALITY

Pill/ tablet; oral administration

INDICATION

Treatment of Amyotrophic Lateral Sclerosis (ALS)

PUBLICATIONS

- "Tofacitinib extends survival in a mouse model of ALS through NK cell-independent mechanisms"
- "Tofacitinib Suppresses Natural Killer Cells In Vitro and In Vivo: Implications for Amyotrophic Lateral Sclerosis"

INTELLECTUAL PROPERTY

- US10660895 "Methods for treating amyotrophic lateral sclerosis"
- US11452724 "Methods for treating amyotrophic lateral sclerosis"
- EP3837011 "Methods for treating amyotrophic lateral sclerosis"
- JP7505780 "Treatment of amyotrophic lateral sclerosis"

BACKGROUND

Amyotrophic lateral sclerosis (ALS) is an adult-onset disorder characterized by motor neuron degeneration that presents initially with dysarthria, dysphagia, and diffuse muscle weakness. Disease progression causes muscle atrophy, spasticity, paralysis, and death from respiratory failure commonly occurs around 3-5 years after diagnosis. Treatment options for ALS are limited, though the immune system of affected patients plays a role in disease progression and serves as a potential route for therapeutic interventions. Whereas immune cells are thought to contribute to disease progression, an active immune system can also play a protective role in this setting as evidenced by acceleration of ALS following global immune suppression. So a need exists to determine the most beneficial methods to either augment or deplete specific immune cell populations in ALS patients in the hopes of altering the disease course and slowing its progression.

INNOVATION

Researchers have determined that tofacitinib, an inhibitor of the janus kinase (JAK) pathway, impacts the increased natural killer (NK) cell numbers and activation which occur during ALS, providing a potential means for treating the disease. NK cells function in the immune system to combat cancerous cells or infectious agents, while normal cells are protected from NK cell-mediated toxicity via expression of the major histocompatibility complex class I (MHC I). However, since motor neurons in ALS patients lack MHC I expression, the destructive effects of NK cells inappropriately manifest on nerve cells. The inhibition of the JAK pathway by tofacitinib prevents the immune system from skewing toward the destructive behaviors associated with upregulation and increased activity of NK cells. Tofacitinib is also associated with upregulation of CD4 T cells that are thought to protect against neuron damage in ALS patients. The use of tofacitinib has correlated with reduction or amelioration of ALS symptoms in mouse models, and it may be given concurrently with existing ALS treatments.