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Keio University School of Medicine  
K Pharma, Inc.

## Ropinirole hydrochloride may attenuate the disease progression of ALS

**In a new clinical trial (ROPALS trial), researchers from Keio University have found a novel drug to be safe and effective for treating amyotrophic lateral sclerosis**

*Tokyo, Japan* – Amyotrophic lateral sclerosis (ALS) is a deadly neurodegenerative disease with no known treatment. In a new randomized clinical Phase I/IIa trial, researchers from Keio University treated ALS patients with ropinirole, a drug often used to treat Parkinson’s disease. After a period of 1 year, they found the drug to be safe and, most importantly, to have a significant effect in functional and survival outcomes, slowing the progression of the disease.

### 1. Research Background

ALS, also known as Lou Gehrig’s disease, is a rare neurological disease that affects the neurons responsible for voluntary movements, such as walking and talking. Perhaps the most notable individual with ALS was Stephen Hawking. As the disease progresses over time, patients lose control over their voluntary muscles; in turn, these muscles weaken, start to twitch, and eventually atrophy. Patients typically begin using wheelchairs soon after their symptoms first appear and may succumb to the disease within a few years. With no treatment options currently available, there is a dire need for new therapeutics to treat and slow the progression of the disease.

“ALS patients suffer greatly from a lack of effective treatments, so this is a critical field of research,” says senior author of the study Prof. Hideyuki Okano. “Recently, cellular disease-in-a-dish models have shown that the drug ropinirole may have beneficial effects in ALS (Fujimori et al. *Nat Med* 2018; Okano et al. *Trends Pharmacol Sci* 2020). (See Fig. 1) In this study, we wanted to build on those findings and test the safety and efficacy of ropinirole in ALS patients (Morimoto et al. *Regen Ther* 2019).”

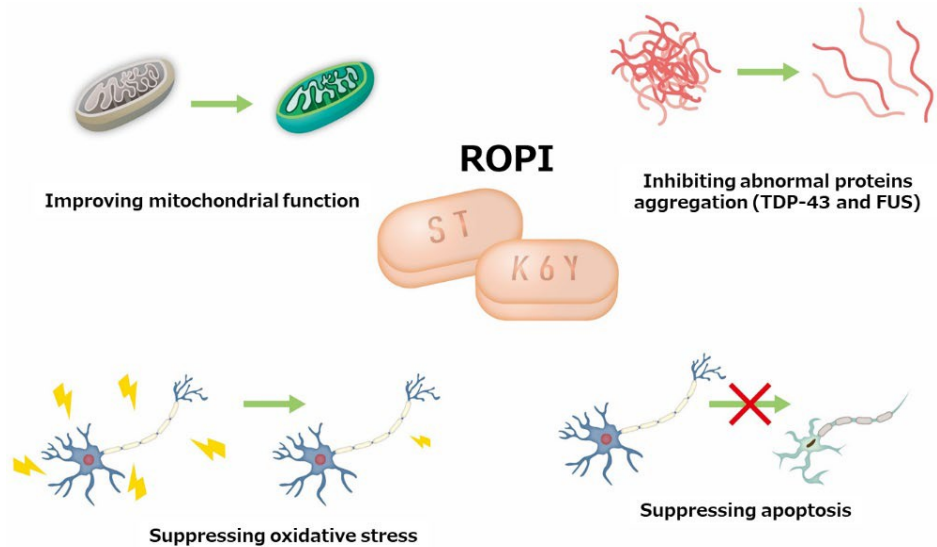


Fig. 1: Possible mechanism of action (MOA) of Ropinirole (ROPI) in ALS.

## **2. Research Significance and Future Development**

To achieve their goal, the researchers designed a Phase I/IIa randomized clinical trial and recruited 20 patients with ALS. Of these patients, 13 received ropinirole hydrochloride, and 7 received a placebo for a total of 48 weeks. While the primary goal of the study was to assess the safety and tolerability of the drug, the researchers also evaluated to what extent ropinirole could show beneficial effects on the functioning and survival of patients with ALS.

The researchers found ropinirole to be well tolerated by the ALS patients overall. Adverse effects associated with ropinirole were mostly known side effects and included complaints related to the gastrointestinal tract and nervous system. To assess the functioning of patients, the researchers applied several objective scoring systems. By comparing the scores of both groups, the researchers found that patients receiving ropinirole had less functional decline and were physically more active. (See Fig. 2) Finally, the researchers evaluated disease progression and survival between both groups and found that patients receiving ropinirole again fared better than patients receiving the placebo. (Median survival: 50.3 weeks vs. 22.4 weeks) Importantly, patients in the ropinirole group took more than twice the time to reach their first disease progression event, which included death, disability, and respiratory failure. This suggests that ropinirole could slow down the progression of the disease.

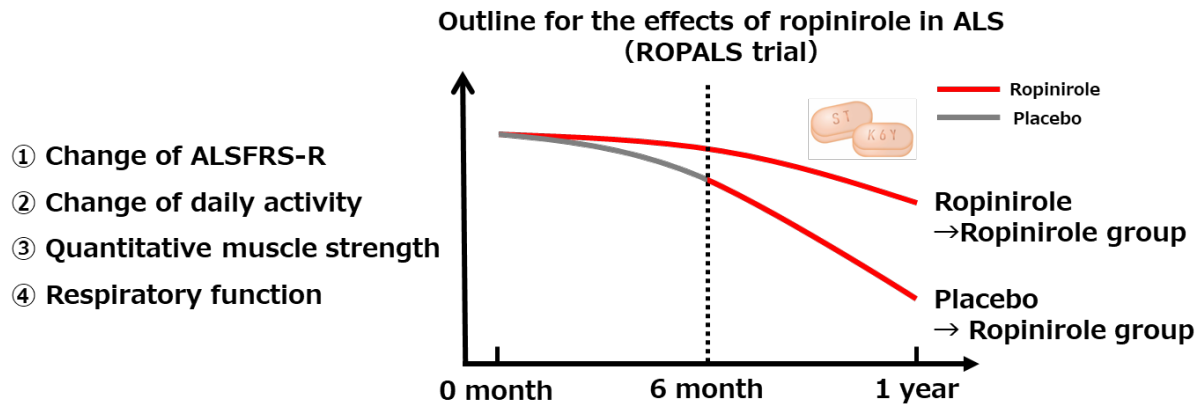


Fig. 2: Outline for the effects of ropinirole in ALS (ROPALS trial).

“These are striking results that show ropinirole had extensive positive effects on both the functioning and survival of the patients and that it might become a novel treatment for ALS,” explain lead authors of the study Dr. Satoru Morimoto and Prof. Shinichi Takahashi. “Our results demonstrate how lab-based cellular models can identify novel drugs, which we can test in subsequent randomized clinical trials, and ultimately show beneficial effects.”

### 3. Notes

The basic research related to ROPALS trial was supported by the National Research and Development Organization (AMED) (The Program for Intractable Diseases Research utilizing Disease-specific iPS cells); “Research on intractable neurological diseases using disease-specific iPS cell technology”, the Translational Research Acceleration Network Program, and the Translational Research Support Center (Keio University).

In addition, in the implementation of this clinical trial was supported by the AMED (Intractable Disease Practical Application Research Project; “Phase 1/2a Study of Ropinirole Hydrochloride Extended-Release Tablets in Patients with Amyotrophic Lateral Sclerosis (ALS)”), K pharma, Inc. (<https://kpharma.co.jp/>) and supplied investigational drugs from GlaxoSmithKline Co., Ltd.

A patent application for "Amyotrophic Lateral Sclerosis Therapeutic Agent and Therapeutic Composition" has already been filed as a patent related to the content of this research.

**[Research Paper]**

English Title : Ropinirole hydrochloride remedy for amyotrophic lateral sclerosis - Protocol for a randomized, double-blind, placebo-controlled, single-center, and open-label continuation phase I/IIa clinical trial (ROPALS trial).

Authors : Satoru Morimoto, Shinichi Takahashi, Komei Fukushima, Hideyuki Saya, Norihiro Suzuki, Masashi Aoki, Hideyuki Okano, Jin Nakahara

English Title : Ropinirole Hydrochloride, a Candidate Drug for ALS Treatment.

Authors : Shinichi Takahashi, Satoru Morimoto, Hideyuki Okano

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The article “Phase 1–2a Trial of Ropinirole hydrochloride for ALS based on iPSC drug discovery” is currently in preparation to be submitted for publication.

**Summary** : Researchers from Keio University evaluated the safety and efficacy of a novel drug for amyotrophic lateral sclerosis (ALS) in a new clinical trial. By comparing ALS patients receiving the candidate drug ropinirole with patients receiving a placebo, they found that ropinirole was safe overall and that it showed the beneficial effects on the functioning and survival of ALS patients. This study demonstrates that ropinirole could be a novel drug for the currently intractable ALS.

**Tweet** : Ropinirole improves functioning and survival of ALS patients

**Primary keyword** : Medicine/Health

**Additional keywords** : Clinical Trials, Death/Dying, Musculature, Neurobiology

\*Please direct any requests or inquiries for coverage to the contact information provided below in advance.

[Inquire regarding this clinical trial]

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\*A color version of this press release is available. Please contact the above address for more information.