Press Release

Nîmes, May 9th 2025

New insights into the treatment of ALS: MIROCALS clinical trial results published in The Lancet

Results of the MIROCALS (Modifying Immune Responses and Outcomes in ALS) clinical trial are published today in The Lancet (*click here*). This is the first study to investigate the effectiveness and safety of low-dose interleukin-2 (IL2LD) for amyotrophic lateral sclerosis (ALS), also known as Motor Neuron Disease (MND).

Key findings and implications for ALS/MND treatment

The trial demonstrated that $IL2_{LD}$ is safe, compared to placebo. Although the primary analysis o did not show a significant benefit for survival, a pre-planned more detailed analysis taking into account the complexity of ALS/MND revealed a statistically significant survival benefit in about 80% of the study participants who had lower levels of a cerebrospinal fluid (CSF) biomarker (phosphorylated neurofilament heavy chain protein – pNFH) indicating the rate of motor neuron damage. In these people, the risk of death at the end of the study was reduced by over 40%.

These findings provide encouraging evidence that modifying the immune system could be a useful strategy for altering ALS/MND progression. While $IL2_{LD}$ is not currently licensed for ALS/MND treatment, the MIROCALS results suggest that $IL2_{LD}$ should now be considered for development as a safe and well tolerated treatment for ALS, adding to the disease-modifying effect of riluzole.

The MIROCALS trial

Between 2017 and 2019 the MIROCALS trial recruited 220 people newly diagnosed with ALS/MND, who were initially treated with riluzole (the standard treatment for ALS/MND) before being randomised to receive either $IL2_{LD}$ or a placebo for 18 months. The trial was double-blind, to prevent participants and investigators knowing which treatment participants were given. During the trial safety was monitored and day-to-day function measured. As ALS/MND is a fatal condition the key (primary) measure of the effect of $IL2_{LD}$ at the end of the trial was survival.

The MIROCALS project sponsored by the University Hospital of Nîmes (France) was coordinated by Dr Gilbert Bensimon, University Hospital of Nîmes, Sorbonne University of Paris and Assistance Publique-Hôpitaux de Paris, France, and Professor P Nigel Leigh, Brighton and Sussex Medical School, Universities of Brighton and Sussex, UK. The MIROCALS Consortium included prestigious research institutions, medical centres and logistical organisations, across the UK, France, Italy, Sweden and Ireland. The Partnership included researchers from the University Hospital of Nîmes, Assistance Publique-Hôpitaux de Paris (AP-HP), Brighton and Sussex Medical School, King's College London, Queen Mary University of London, the University of Sheffield, Humanitas Institute of Milan and the University of Gothenburg, with biobanking expertise from Généthon, and logistical support from WGK

Contacts presse
Michaël VIDEMENT– Directeur de la Communication et des Affaires culturelles
+ 33 6 61 43 28 12 / michael.videment@chu-nimes.fr

Direction de la Communication et des Affaires culturelles
+33 4 66 68 33 04 / direction.communication@chu-nimes.fr

Ltd and ICON plc. The clinical trial involved 7 ALS/MND Centres in the UK (6 in England, 1 in Scotland) and 10 in France.

Funded by awards from the European Commission H2020 programme, The Programme Hospitalier pour la Recherche Clinique (PHRC, French Health Ministry) and a number of UK and French charitable organisations, the trial aimed to explore the potential of interleukin-2 as a treatment for ALS/MND.

Interleukin-2 is a molecule known to regulate the immune system in humans. The drug used in the trial, aldesleukin, is a manufactured Human Interleukin-2 which has been used in high doses in some cancers. Low doses of interleukin-2 ($IL2_{LD}$) have been found to specifically reduce inflammation by increasing the number of white blood cells known as regulatory T cells (Tregs) in the blood.

Dr Gilbert Bensimon, MIROCALS study coordinator and principal investigator, stated: "*ALS/MND is a complex disorder. The encouraging findings of the MIROCALS trial represent a significant step toward designing better trials and expediting the development of urgently needed treatments for ALS/MND. Importantly* $IL2_{LD}$*, was well-tolerated over a long period. Our findings underline the importance of the immune system as a target for treatments aimed at slowing the progression of this devastating condition.*"

Professor Nigel Leigh, Chief Investigator and co-coordinator of the MIROCALS study, and Professor of Neurology at Brighton and Sussex Medical School, added: "*This trial provides very promising evidence that* $IL2_{LD}$ *benefits people with ALS/MND. The data, blood and CSF samples from the people who generously took part in the trial are now being used to advance our understanding of ALS and help the development of new therapies that can further slow disease progression and improve the lives of people living with ALS/MND. We are extremely grateful to The Motor Neurone Disease Association, The MyName'5 Doddie Foundation, MND Scotland, AFM-Téléthon France, and Association pour la Recherche sur la SLA who have contributed to supporting the trial and the ongoing work*."

Future directions

In 2023, ILTOO Pharma was granted the exclusive license of the MIROCALS trial data by the MIROCALS Consortium and has engaged in the process of regulatory approval of IL-2LD for ALS treatment. "*ILTOO Pharma is committed to promoting IL-2LD as a novel therapeutic approach for ALS,*" said Professor José Achache, Chairman of ILTOO Pharma. "*The MIROCALS study represents an important step forward for ILTOO Pharma, which is engaged with regulatory authorities, patient's associations and the scientific community to accelerate the next phases of development towards market approval in ALS*".

About Amyotrophic Lateral Sclerosis (ALS)/Motor Neurone Disease (MND)

ALS affects approximately 45,000 people across Europe simultaneously. It attacks the nerves that control movement (motor neurons) so that the muscles no longer function, but generally spares sensory functions (sight, hearing, and sensation). ALS generally progresses inexorably but at different rates in different people. It can ultimately leave people unable to move, speak, and breathe. About a quarter of people with ALS die within a year of symptom onset, and more than half within two to three years of diagnosis. However, some people with ALS live for 10 years or more. Care involves coordinated input from health and social care professionals, psychological and emotional support, and expert advice and interventions on communication aids, nutrition, and breathing difficulties.

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Although one drug, riluzole, has shown some ability to slightly slow the progression of the disease, there is still no cure. The underlying cause of ALS is not yet understood.

About Nîmes University Hospital

Nîmes University Hospital (CHU) brings together a hospital community of 1,397 doctors and 5,963 non-medical professionals. Its fundamental missions include care, teaching, research, and training. Nîmes University Hospital is a reference establishment in clinical research, innovation, and high-quality care. ***The project was funded by the Personalising health and care du programme Horizon 2020 (H2020-PHC-2014-2015) (€5,980,435) and the National PHRC (€1,122,429).***

More information at www.chu-nimes.fr

MIROCALS
Modifying Immune Response & Outcomes in Amyotrophic Lateral Sclerosis

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