

Press release
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Results of a Phase II Clinical Trial

Metformin Improves Motor Skills in Patients with Steinert Myotonic Dystrophy, the Most Common Adult Neuromuscular Disease

Inserm researchers at I-STEM – the Institute for Stem Cell Therapy and Exploration of Monogenic Diseases – report encouraging results with metformin, a known diabetes drug, for the symptomatic treatment of Steinert myotonic dystrophy. A phase II trial conducted in 40 patients at Henri-Mondor Hospital AP-HP has shown that, after 48 weeks of treatment at the highest dose, patients treated with metformin (versus placebo) gain in motor skills and recover a more stable gait. The results of this trial, which received 1.5 million euros in funding from AFM-Téléthon, are published today in *Brain*.

Steinert myotonic dystrophy (DM1) is the most common form of muscular dystrophy in adults. Of genetic origin, its prevalence is estimated at 1/8,000, or about 7 to 8,000 patients in France. It affects the muscles, which weaken (dystrophy) and have difficulty to relax after contraction (myotonia) which disrupts the movements (unstable walking for example). It also affects other organs (heart and respiratory system, digestive system, endocrine system and nervous system). To date, this muscular dystrophy does not benefit from any curative treatment.

The findings published in *Brain* are the result of research conducted for several years at I-STEM. Indeed, thanks to the development of cellular models from pluripotent stem cells, in 2011 Cécile Martinat's team identified new mechanisms at the origin of Steinert myotonic dystrophy ([Cell Stem Cell - March 31, 2011](#)). In 2015, Sandrine Baghdoyan, a research engineer at I-STEM, succeeded in correcting certain splice defects in embryonic stem cells and myoblasts from people with DM1 using metformin, a well-known diabetes drug identified as effective in this new indication thanks to high-throughput screening ([Mol. Therapy - Nov 3, 2015](#)).

Encouraged by these results, I-STEM launched a phase II, single-center, double-blind, randomized controlled clinical trial in 40 patients, in collaboration with teams from Henri Mondor Hospital AP-HP, that of Dr. Guillaume Bassez of the Ile-de-France Reference Center for Neuromuscular Diseases, and that of the Clinical Investigation Center coordinated by Prof. Philippe Le Corvoisier. In this placebo-controlled study, metformin was administered three times daily, orally, with a 4-week increase in dose (up to 3 g/day), followed by 48 weeks at the highest dose. **The evaluation of treatment efficacy was based on the "6-minute walk" test. At the end of the study, after one year of treatment, patients who received metformin gained an average walking distance of about 33 meters on their initial performance whereas the group receiving placebo remained stable (average gain of 3 meters).** This motricity, analyzed in depth using the *Locometryx* tool developed by Jean-Yves Hogrel's Hogrel's Laboratory of Physiology and Neuromuscular Evaluation at the Institute of Myology at the Pitié-Salpêtrière Hospital AP-HP, is closely linked to the fact that metformin improves the overall posture of patients who, in fact, go from walking in an unstable "broad-based" manner before treatment, to a straight, faster and therefore more efficient gait".

These results demonstrate, for the first time, the efficacy of a pharmacological treatment on motor function in Steinert myotonic dystrophy and, to our knowledge, the therapeutic efficacy of a molecule identified on the basis of the modeling of a pathology with pluripotent stem cells.

Publication: [Improved mobility with Metformin in patients with myotonic dystrophy type 1: a randomized controlled trial](#)

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About I-Stem

Created in 2005 by AFM-Téléthon and Inserm, I-Stem is an international reference research and development center dedicated to the development of innovative treatments using pluripotent stem cells (ES and iPS) for rare diseases of genetic origin. With its 67 members of staff, its objective is to use these cells as tools to understand genetic diseases or as "drugs" in cell-therapy or high-throughput-screening programs. Three clinical trials are currently in preparation.

About AFM-Téléthon - www.afm-telethon.fr

AFM-Téléthon is an association of patients and their relatives committed to fighting disease. Thanks to the donations to the Telethon (89.2 million euro in 2017), it has become a major biomedical research player in rare diseases in France and throughout the world. It currently supports clinical trials in genetic diseases affecting the eyes, blood, brain, immune system and muscles. With its laboratories, it is also a singular association with the capacity to design, produce and test its own innovative treatments. **Families can contact us at +33 (0)800 35 36 37 (toll-free from a French landline)**

About Inserm

Created in 1964, the French National Institute of Health and Medical research (Inserm) is a public science and technology institute, jointly supervised by the Ministry of National Education, Higher Education and Research and the Ministry of Social Affairs and Health. Inserm is the only French public organization dedicated to biological and medical research, and human health with around 15,000 researchers, engineers, technicians, practitioner-researchers, post-doctoral researchers and some 300 laboratories. The mission of its scientists is to study all diseases, from the most common to the most rare. Inserm is a founder member of Aviesan*, the French National Alliance for Life Sciences and Health created in 2009.

** Other founding members of Aviesan: CEA, CNRS, CHRU, CPU, INRA, INRIA, Inserm, Institut Pasteur, IRD*

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About AP-HP:

AP-HP is a world-renowned university hospital authority with a European dimension. Its 39 hospitals receive 10 million patients every year for consultations, emergency treatment, scheduled admissions and in-home health care. It provides a round-the-clock public health service for all, which for AP-HP is a matter of both duty and pride. With its 100,000 members of staff – doctors, researchers, allied medical staff, administrative staff and other employees, AP-HP is the leading employer in Ile-de-France. <http://www.aphp.fr>

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