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SBI Pharmaceuticals Co., Ltd
Saitama Medical University

Publication of Confirmatory Clinical Trial Results of 5-ALA Hydrochloride and Sodium Ferrous Citrate for Patients with Mitochondrial Disease

SBI Pharmaceuticals Co., Ltd., (Head office: Minato-ku, Tokyo; Representative Director & President: Yoshitaka Kitao, hereinafter "SBI Pharma"), a subsidiary of SBI Holdings, Inc., engaged in the research and development of pharmaceuticals and medical devices regarding 5-aminolevulinic acid (5-ALA)[*1], and Saitama Medical University (Iruma-gun, Saitama; President: Tsutomu Takeuchi) hereby announces the publication of **the results of investigator-initiated confirmatory clinical trial (SPED-ALA-003) on the efficacy and safety of SPP-004 (5-ALA hydrochloride (5-ALA HCl) and sodium ferrous citrate (SFC))[*2] for patients with mitochondrial disease**, where investigational drug and research funding were provided by SBI Pharma, in the international scientific journal *PLOS One*.

This confirmatory trial was conducted by Professor Akira Otake (currently Visiting Professor and Professor Emeritus) of the Department of Pediatrics at Saitama Medical University in collaboration with Lecturer Yuichi Abe (currently Director of the Department of Neurology at the National Center for Child Health and Development) and Professor Kei Murayama (currently Professor at the Juntendo University Center for Intractable Diseases Research) of Chiba Children's Hospital. SBI Pharma provided the investigational drug and research funds for the study.

Journal	*PLOS One*
Title	A phase III double-blind, placebo-controlled, randomized withdrawal trial of 5-aminolevulinic acid hydrochloride with sodium ferrous citrate for efficacy and safety in patients diagnosed as Leigh syndrome
Authors	Akira Ohtake (Professor Emeritus, Department of Pediatrics, Saitama Medical University Hospital) et al
URL	https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0332283

■Summary

A Phase III[*3] double-blind, placebo-controlled, randomized withdrawal trial was conducted to confirm the efficacy and safety of SPP-004 (5-ALA HCl + SFC) in patients with Leigh syndrome[*4], one of the major types of mitochondrial disease.

Of 54 patients who received SPP-004 for 24 weeks, 28 patients who showed improvement in either cranial nervous symptoms or myopathy symptoms, as defined by the transition criteria, advanced to the 48-week double-blind phase and were randomized 1:1 to either the SPP-004 or placebo groups. The primary endpoint of “discontinuation rate due to insufficient efficacy” was not statistically significant. However, the rate was 15.4% in the SPP-004 group as compared to 50.0% in the placebo group, indicating that a higher proportion of cases in the SPP-004 group maintained efficacy. As to the secondary endpoint of “the time to discontinuation due to insufficient efficacy”, the SPP 004 group exhibited a significantly longer time to discontinuation compared with the placebo group (p=0.0486, log-rank test). There was no notable difference in adverse events between the two groups and all reported adverse drug reactions were of mild severity.

Considering the progressive and severe symptoms of mitochondrial disease, safety of SPP-004 and its effectiveness on the progression of the cranial nervous symptoms and myopathy symptoms of mitochondrial disease were suggested.

*1 5-aminolevulinic acid: An amino acid produced in mitochondria. It is an important substance that serves as a functional molecule related to energy production in the form of heme and cytochromes, and its production is known to decrease with age. 5-aminolevulinic acid is contained in food such as shochu lees, red wine, and Asian ginseng. It is also known as a material forming chloroplasts in plants.

*2 SPP-004 (5-ALA HCl and SFC) is an investigational formulation and is not approved as a drug. This new release is an introduction to the research publication. It does not recommend the use of unapproved drugs.

*3 Phase III trials are important trials that finally confirm the efficacy and safety of a drug in a large number of patients. Clinical trials have three phases. Phase I trials confirm safety in healthy people. Phase II trials examine the efficacy and side effects in a small number of patients and have already been published. (Life (Basel). 2025 Jul 23;15(8):1168.) The results of Phase III trials provide the data necessary for drug approval.

*4 Leigh syndrome is one of the major types of mitochondrial disease (a classification of various diseases based on symptoms). It is a chronic, progressive, intractable disease caused by impaired mitochondrial energy production due to a genetic abnormality, leading to delayed and progressive regression of psychomotor development. At present, there are no fundamental medications or treatments available, and the prognosis is particularly poor when the disease develops in infancy, so the development of a therapeutic drug is urgently needed.

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