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Chugai's Anti-IL-8 Recycling Antibody AMY109, Improves Inflammation and Fibrosis in Endometriosis in an Industry-Government-Academia Non-Clinical Study Published in Science Translational Medicine

- The results of a nonclinical study of the anti-IL-8 recycling antibody AMY109 was published in a U.S. scientific journal, Science Translational Medicine
- This nonclinical study is a joint research between Chugai, Jichi Medical University Saitama Medical Center, and Tsukuba Primate Research Center, National Institutes of Biomedical Innovation, Health and Nutrition (hereafter "NIBIOHN")
- The research seeks to understand the pathology of endometriosis, which affects 1 in 10 women in their 20s to 40s and causes pain and infertility[1]
- Currently, the standard of care for endometriosis is symptomatic treatment with hormone-related preparations and analgesics. The results of this nonclinical study suggested that the anti-IL-8 antibody AMY109 could be a novel therapeutic agent based on the pathology of endometriosis

TOKYO, February 24, 2023 -- Chugai Pharmaceutical Co., Ltd. (TOKYO: 4519), Jichi Medical University Saitama Medical Center (Saitama city) and Tsukuba Primate Research Center, NIBIOHN (Tsukuba city) announced that AMY109, an anti-IL-8 recycling antibody® under development for the treatment of endometriosis, has been published in the U.S. scientific journal, Science Translational Medicine on February 22, 2023 (local time), with results from nonclinical studies in monkeys showing improvement in inflammation and fibrosis in endometriosis. These nonclinical studies were presented as a joint research study by Chugai, Jichi Medical University Saitama Medical Center, and Tsukuba Primate Research Center, NIBIOHN at the 44th annual meeting of the Japan Society of Endometriosis on January 21, 2023, in Kochi city.

"Endometriosis is a disease that causes inflammation and fibrosis, severe menstrual cramps, chronic pelvic pain, and infertility, and may change patients' lives. In addition, endometriosis is a disease with high unmet medical needs for which there are currently no fundamental drugs for treatment, and symptomatic treatment is the standard of care. This collaboration confirmed that the inflammatory cytokine IL-8 is involved in the development of inflammation and fibrosis in endometriosis and that treatment with anti-IL-8 antibodies leads to improvement in the pathology of endometriosis. I'm delighted to have this achievement recognized by Science Translational Medicine. We will continue to advance the development

of AMY109, an anti-IL-8 antibody, as a new therapeutic agent for endometriosis, for which innovative new drugs are desired," said Dr. Osamu Okuda, Chugai's President and CEO.

"Endometriosis research has evolved from clinical research to animal model experiments such as rats and nonclinical studies in monkeys, which have menstruation and develop endometriosis like humans. Like laparoscopic surgery in humans, pathological research focuses on reproducing noninvasive clinical procedures, such as detailed observation of findings by video monitoring and collection of lesions. Furthermore, we developed and evaluated new antibody drugs using advanced technologies in the fields of genes, immunity, and pathology. We have aimed to elucidate the pathological mechanism of endometriosis and develop drugs useful for clinical use while maintaining hormone levels. I believe assembling experts from industry, government, and academia and long-term joint research led to this achievement. We are committed to continuing research to contribute to the well-being of women with endometriosis and their families," said Prof. Ryo Konno, MD, PhD, Department of Obstetrics and Gynecology, Jichi Medical University Saitama Medical Center.

"In cynomolgus monkeys, some animals spontaneously develop endometriosis, but the severity of symptoms varies, making it difficult to produce reliable results only from spontaneous animals. In this nonclinical study, cynomolgus monkeys were successfully produced as a model of endometriosis. Furthermore, it was possible to perform experiments in a population with a homogenous degree of symptoms, suggesting the establishment of a reliable evaluation system and the usefulness of the anti-IL-8 antibody AMY109. We hope this study will help as many of those who have endometriosis," said Dr. Tadashi Sankai, D.V.M., Ph.D, Tsukuba Primate Research Center, NIBIOHN.

"A long-acting anti-IL-8 antibody improves inflammation and fibrosis in endometriosis"
http://www.science.org/doi/10.1126/scitranslmed.abq5858

<Study overview>

- When conventional anti-IL-8 antibody (hWS-4) was administered to monkeys with spontaneous endometriosis, shrinkage of lesions and improvement of adhesions were observed. Therefore, an improved AMY109 antibody with a recycling function was prepared, and a monkey model in which endometriosis was surgically induced was constructed and evaluated
- 17 monkeys with endometriosis were assigned to 3 groups: vehicle group, AMY109 low-dose (2 mg/kg, s.c.) group, and AMY109 high-dose (10 mg/kg, i.v.) group, and received the treatment every 4 weeks for 6 times
- The laparoscopic observation was performed before and after administration, and the modified monkey score of the revised American Society for Reproductive Medicine score (r-ASRM score), was used to assess the clinical severity of symptoms in the field of endometriosis in humans was compared. The collected nodular lesion volume was evaluated, and pathological analysis was performed more objectively and quantitatively

<Study Results>

- While the monkey r-ASRM score increased (worsened) in the vehicle group compared to pre-treatment, both the AMY109 low and high-dose groups showed suppression (improvement)

- Nodular lesion volume increased in the vehicle group compared with baseline, while it decreased in both the AMY109 low and high-dose groups
- Pathological fibrosis was not changed in the vehicle group, but was attenuated in the AMY109 low and high-dose groups

About Endometriosis[1,2]

Affecting one out of 10 women in their 20s to 40s, endometriosis is the repeated proliferation and shedding of endometrial tissue outside the uterus, accompanied by dysmenorrhea (pain with menstruation) and chronic lower abdominal pain. It is also a cause of infertility. The disease can interfere with daily life, including absences from work or school, as sufferers find it difficult to do more than lie still when symptoms are severe. The standard treatment is care with hormone-related drugs, and if the pain cannot be controlled with the drugs, the only treatment is the surgical removal of the endometriotic tissue. Unfortunately, many patients experience recurrences within several years after surgery, making this a disease with a high level of unmet medical needs. Endometriosis is caused by inflammation and fibrosis. One of the cytokines, IL-8, is thought to be associated with the progression of endometriosis.

About AMY109

AMY109 is an antibody that binds to IL-8, an inflammatory cytokine, and was created by Chugai. It is developed to apply Chugai's unique recycling antibody technology. With its anti-inflammatory action, AMY109 is expected to offer new value to patients through its mechanism different from that of hormone-related therapy, the standard therapy for endometriosis.

About recycling antibody

Recycling antibody is one of Chugai's proprietary antibody engineering technologies. It is designed to repeatedly bind a single antibody to an antigen, allowing it to work longer in the body. The recycling antibody technology is also applied to Enspryng® [Anti-IL-6 receptor recycling antibody, prevention of relapses of NMOSD (including NMO)].

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[Reference]

1. ESHRE guideline: management of women with endometriosis. Dunselman GA, et al. Hum Reprod. 2014.
2. A long-acting anti-IL-8 antibody improves inflammation and fibrosis in endometriosis. Nishimoto-Kakiuchi A et al. Science Translational Medicine. 2023. http://www.science.org/doi/10.1126/scitranslmed.abq5858 (Accessed Feb 2023)

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