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Results from Phase III SAkuraSky Study for Chugai's Satralizumab in Neuromyelitis Optica Spectrum Disorder Published in The New England Journal of Medicine Online

- Satralizumab added to baseline immunosuppressant therapy significantly reduced risk of relapse in patients with neuromyelitis optica spectrum disorder (NMOSD).
- Satralizumab added to baseline therapy showed a well-tolerated safety profile.
- SAkuraSky study is a global phase III clinical study for NMOSD patients including aquaporin-4 antibodies (AQP4-IgG) seropositive and seronegative patients

TOKYO, November 29, 2019 -- Chugai Pharmaceutical Co., Ltd. (TOKYO: 4519) announced that the results of the SAkuraSky Study (NCT02028884), a global phase III clinical study of satralizumab (development code: SA237) were published on November 27 in the online version of The New England Journal of Medicine (NEJM). Satralizumab is an anti-IL6 receptor humanized recycling antibody under development for the treatment of neuromyelitis optica spectrum disorder (NMOSD). The phase III study examined the efficacy and safety of satralizumab added to baseline therapy in patients with NMOSD.
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"Relapses of NMOSD may lead to accumulation of disabilities and can be life-threatening. These data further reinforce the importance of IL-6 signal inhibition in treating NMOSD," said Dr. Yasushi Ito, Chugai's Executive Vice President, Co-Head of Project & Lifecycle Management Unit. "The SAkuraSky study is the first clinical study to demonstrate the efficacy and safety of an investigational medicine for NMOSD regardless of AQP4-IgG expression."

In SAkuraSky Study, only eight of 41 patients (20%) treated with satralizumab in combination with baseline immunosuppressant therapy experienced a protocol-defined relapse (PDR) compared to 18 of 42 patients (43%) treated with placebo in combination with baseline therapy (HR=0.38, 95% CI: 0.16-0.88; p=0.02 [stratified log-rank test]) in the overall population, representative of NMOSD patients (including anti-AQP4-IgG antibody seropositive and seronegative patients). Importantly, 89%, 78% and 74% of patients on satralizumab in combination with baseline therapy were relapse-free at weeks 48, 96 and 144 compared to 66%, 59% and 49% with placebo in combination with baseline therapy. The proportion of serious adverse events was similar between the satralizumab and placebo treatment groups.

SAkuraSky Study (NCT02028884)

Summary:

A phase III multicenter, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of satralizumab added to baseline treatment in patients with NMOSD

<Primary Endpoint>

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Time to first protocol-defined relapse adjudicated by an independent review committee in the double-blind period

Study Design:

- 83 male and female patients aged from 13-73 years were randomized.
- Patients were randomized to satralizumab or placebo in a 1:1 ratio. Satralizumab (120 mg) or placebo added to baseline treatment (azathioprine, mycophenolate mofetil and/or corticosteroids*) was subcutaneously administered at Week 0, 2, and 4. The subsequent treatment was continued at 4-week intervals.
- The double-blind treatment period ended when the total number of PDR had reached 26. After experiencing a PDR or completion of the study, patients in both groups were offered treatment with satralizumab in an open-label extension period.
- Patients with AQP4-IgG seropositive or seronegative neuromyelitis optica (NMO)** and those with AQP4-IgG seropositive NMOSD were enrolled.

  *Approved indication for Mycophenolate mofetil in Japan is treatment of refractory rejection after kidney transplant (If the patient cannot be treated with existing drugs because of a lack of response, adverse reactions, or another reason and refractory rejection has been diagnosed), suppression of rejection after the organ transplants (kidney, heart, liver, lung, or pancreas transplants), and lupus nephritis. For other drugs, please refer to the latest package insert of each drug.

  **NMO defined in 2006

Main Results:

- In a prespecified primary analysis, only eight of 41 patients (20%) treated with satralizumab in combination with baseline immunosuppressant therapy experienced a protocol-defined relapse (PDR) compared to 18 of 42 patients (43%) treated with placebo in combination with baseline therapy (HR=0.38, 95% CI: 0.16-0.88; p=0.02 [stratified log-rank test]) in the overall population, representative of NMOSD patients (including anti-AQP4-IgG antibody seropositive and seronegative patients). Satralizumab also showed stable results in a post hoc analyses using multiple imputation for censored data.
- 89%, 78% and 74% of patients on satralizumab in combination with baseline therapy were relapse-free at weeks 48, 96 and 144 compared to 66% and 59% and 49% with placebo in combination with baseline therapy.
- In a prespecified AQP4-IgG seropositive subgroup analysis for time to relapse, three of 27 patients (11%) treated with satralizumab experienced a PDR compared to 12 of 28 patients (43%) treated with placebo (HR=0.21, 95% CI: 0.06-0.75). In the AQP4-IgG seronegative subgroup analysis, five of 14 patients (36%) treated with satralizumab experienced a PDR compared to six of 14 patients (43%) receiving placebo (HR= 0.66, 95% CI: 0.20-2.24).
- The proportion of serious adverse events was similar between the satralizumab and placebo treatment groups. A lower rate of infections (including serious infections) was observed in patients treated with satralizumab compared with the placebo group. The most common adverse events in the satralizumab group were upper respiratory tract infection, nasopharyngitis (common cold) and headache.

About neuromyelitis optica spectrum disorder (NMOSD)

NMOSD is an autoimmune disease of the central nervous system characterized by inflammatory lesions in the optic nerves and spinal cord, and cause continual and significant decrease in quality of life due to permanent neurologic disorders Patients with NMOSD frequently experience a relapsing disease course with repeated attacks leading to accumulating neurological damage and disability. Symptoms may include visual impairment, motor disability, and loss of quality of life. In some cases, attacks of NMOSD result in death. Aquaporin-4 antibodies (AQP4-IgG), pathogenic antibodies, are detected in at least two-thirds of NMOSD patients. AQP4-IgG is known to target and damage a specific central nervous cell type called astrocytes, resulting in inflammatory lesions of the optic nerve(s), spinal cord and brain [1-4]. The inflammatory cytokine IL-6 is now emerging as an important factor in NMOSD pathogenesis [5-9].

Diagnostic criteria introduced in 2006 for NMO were characterized by inflammation of the optic nerve (optic neuritis) and the spinal cord (myelitis). These were revised in 2007 with the definition of NMOSD, proposed for diseases with either optic neuritis or myelitis. In 2015, the definition of NMOSD further revised to include a broader spectrum of disease. The diagnostic term NMOSD is now widely used [10].

About satralizumab

Satralizumab, created by Chugai, is an anti-IL-6 receptor recycling antibody. The drug is expected to suppress relapse of NMOSD by inhibiting IL-6 signal transduction which is deeply related to the pathology. In two global phase III clinical studies in NMO and NMOSD patients, the primary endpoint was achieved with satralizumab either as an add-on therapy to baseline immunosuppressant treatment (NCT02028884) or as monotherapy (NCT02073279). These studies represent one of the largest clinical trial programs undertaken for this rare disease. Satralizumab is designated as an orphan drug for the treatment of NMO and NMOSD in Japan, and for the treatment of the same disease group in Europe and the U.S. In addition, it has been granted Breakthrough Therapy Designation by the U.S. Food and Drug Administration in December 2018. The application was accepted for review by EMA and FDA, and filed to MHLW in 2019.

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