27 February 2025
EMA/CHMP/117341/2025
Human Medicines Division

Assessment report for paediatric studies submitted according to Article 46 of the Regulation (EC) No 1901/2006

Enspryng

Satralizumab

Procedure no: EMEA/H/C/004788/P46/001

Note

Assessment report as adopted by the CHMP with all information of a commercially confidential nature deleted.

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Table of contents

1. Introduction 3

2. Scientific discussion 3

2.1. Clinical aspects 3

2.1.1. Introduction 3

2.1.2. Clinical study 3

2.1.3. Discussion on clinical aspects 7

3. CHMP overall conclusion and recommendation 7

1. Introduction

On 2024-11-27, the MAH submitted a completed PASS category 3 study including 1 paediatric patient for Enspryng, in accordance with Article 46 of Regulation (EC) No1901/2006, as amended.

These data are also submitted as part of the post-authorisation measure(s) because WN42349 is a category 3 PASS study.

A short critical expert overview has also been provided.

2. Scientific discussion

2.1. Clinical aspects

2.1.1. Introduction

The MAH submitted the final report for:

- Study WN42349: A Multicenter, Single Arm, Open Label Study to Evaluate the Long-Term Safety and Efficacy of Satralizumab in Patients with Neuromyelitis Optica Spectrum Disorder

2.1.2. Clinical study

Study WN42349: A Multicenter, Single Arm, Open Label Study to Evaluate the Long-Term Safety and Efficacy of Satralizumab in Patients with Neuromyelitis Optica Spectrum Disorder

Description

Following the completion of their double-blind period in Study BN40898 and Study BN40900, patients who had received satralizumab treatment in the open-label extension period of these studies could be enrolled in Study WN42349. In this study, patients were offered treatment with open-label satralizumab for up to 3 years to characterize the long-term safety and efficacy of satralizumab.

The treatment period ended 3 years after the date the first patient enrolled in the study.

Methods

Study participants

The majority of patients were white (n = 95 [57.2%]) and female (n = 142 [85.5%]). The median age when patients received their first dose of satralizumab was 44.5 (range: 13 to 73 years). Eight patients (4.8%) were ≤ 18 years old at the time of first treatment with satralizumab. At baseline, mean annualized relapse rate was 1.18 (SD: 0.55) and mean EDSS was 3.80 (SD: 1.57). About two-thirds of the patients tested positive for anti-AQP4 antibody at screening.

Treatments

All patients received satralizumab 120 mg administered by SC injection Q4W.

Objective(s)

The primary safety objective for this study was to evaluate the long-term safety of satralizumab in patients with NMOSD.

The efficacy objective for this study was to evaluate long-term efficacy of satralizumab.

Outcomes/endpoints

Safety

- Incidence and severity of adverse events (AE), adverse events of special interest (AESI), serious AEs (SAE), and selected AEs.
- Vital signs (temperature, blood pressure, and pulse rate), clinical laboratory tests (hematology, chemistry, and urinalysis), 12-lead electrocardiograms (ECG), and suicidality (Columbia-Suicide Severity Rating Scale [C-SSRS]).

Efficacy

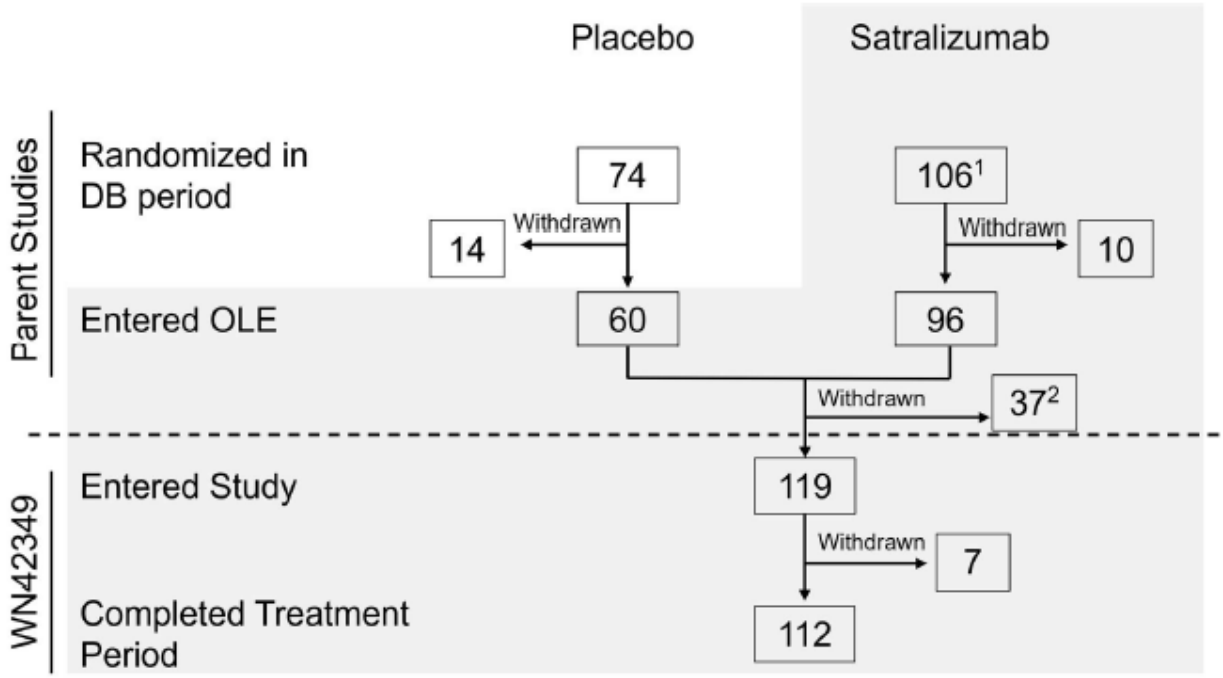
- Time to first relapse (TFR) and proportion of patients who were relapse-free
- Annualised relapse rate (ARR)
- Change in Expanded Disability Status Scale (EDSS) score
- Time to EDSS worsening and proportion of patients without EDSS worsening
- Change in visual acuity

Results

Participant flow

Of the 180 patients enrolled in the parent studies, 119 were subsequently enrolled in Study WN42349. Of them, 7 prematurely withdrew from treatment. Of the 180 enrolled patients, 9 adolescent patients participated in the parent study BN40898. Eight of them enrolled into Study WN42349; at the time of enrolment, 7 were adults and 1 was adolescent.

Figure 1. Patient Disposition from Parent Studies to Study WN42349



DB = double-blind; OLE = open label extension.
1 One patient was enrolled directly into the OLE period of the parent study and is included in the satralizumab treatment arm of the intent-to-treat population.
2 Two patients were reported as discontinued from the parent study OLE on the day they enrolled into Study WN42349.

Study dates:

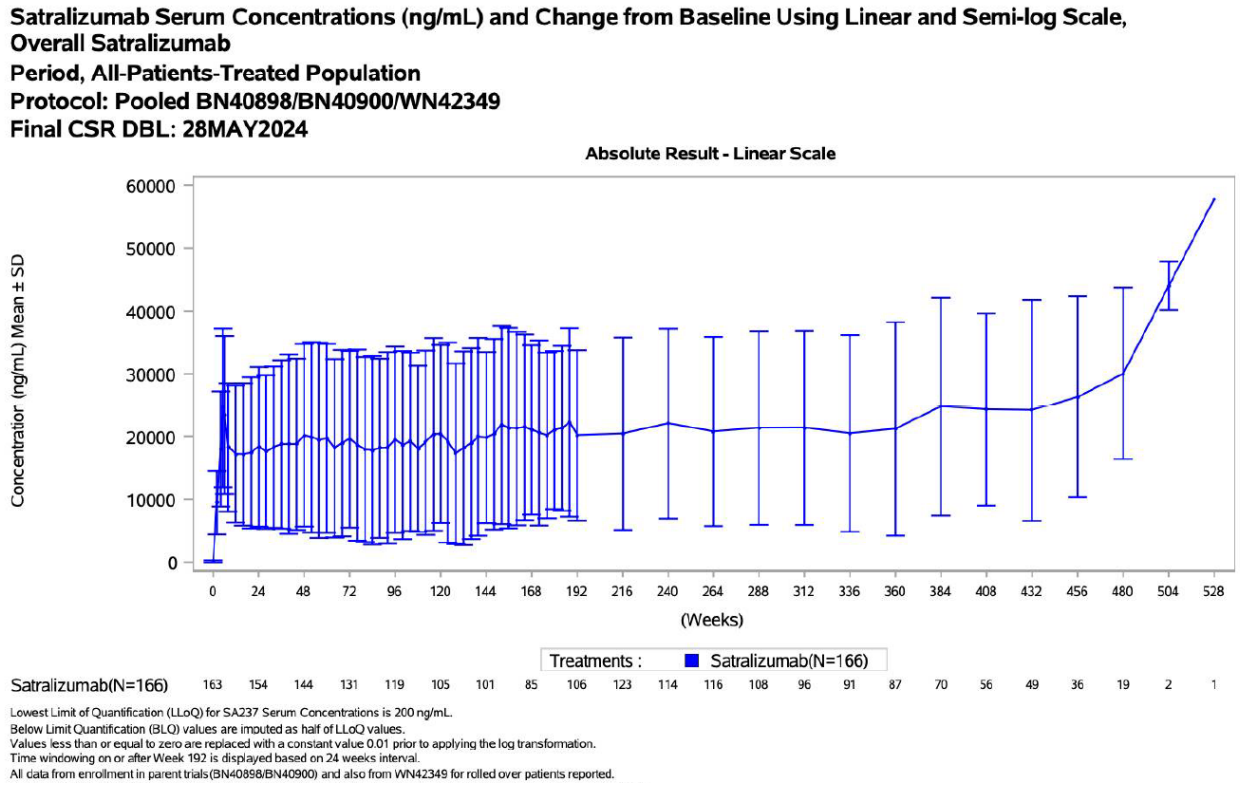
First patient enrolled: 2 March 2021

Last patient last visit: 28 May 2024

Pharmacokinetics

Based on graphical analysis, satralizumab serum concentrations remained stable throughout the Study WN42349 treatment period and were consistent with those observed in previous Studies BN40898 and BN40900 Phase III studies. Overall satralizumab serum concentrations were maintained during the parent Phase III studies and roll-over study throughout the overall satralizumab treatment period (Figure 2).

Figure 2. Satralizumab Serum Concentrations Using Linear and Semi-log Scale: Overall Satralizumab Period (All-Patients-Treated Population)



The PK data from this roll-over study showed that satralizumab serum concentrations remained stable and consistent with those observed in the parent Study BN40898 and Study BN40900 Phase III studies. Therefore, population PK analysis of the updated dataset is not expected to provide additional insights into the PK profile of satralizumab in this population and was not performed. Furthermore, given that exposure-efficacy and exposure-safety relationships could not be identified in the Phase III study datasets, repeating these analyses using the dataset including the rollover study data is not expected to provide additional insights. Therefore, the relationship between selected covariates and serum concentrations as well as the relationship between satralizumab serum concentrations or PK parameters and efficacy or safety endpoints were not further explored in this study.

Efficacy results

Time to First Relapse (TFR) (All-Patients Treated Population):

Median TFR was not reached (range: 2–525 [censored] weeks) as of the CCOD. At Week 456 the Protocol Defined Relapse assessed by Investigator (iPDR)-free rate was 67.1% (95% CI: 58.6, 74.3). A Kaplan-Meier plot of time to iPDR during the overall satralizumab period was provided.

When considering use of rescue therapy as an intercurrent event on TFR, median TFR was not reached (range: 0–525 [censored] weeks). At Week 456 the iPDR or rescue therapy-free rate was 53.8% (95% CI: 45.1, 61.7).

In the ITT Population, median TFR for patients originally randomized to placebo was 119.1 weeks (95% CI: 52.4, NE) and median TFR was not reached for patients originally randomized to satralizumab (range: 2–525 [censored] weeks). At Week 456 the iPDR-free rate was 39.8% (95% CI: 27.5, 51.9) for patients originally randomized to placebo and 60.1% (95% CI: 49.5, 69.3) for patients originally randomized to satralizumab. When considering use of rescue therapy as an intercurrent event, TFR (iPDR or rescue therapy) was 60.4 weeks (95% CI: 29.9, 144.3) for patients randomized to placebo and 246.1 weeks (95% CI: 122.9, NE) for patients randomized to satralizumab. At Week 456 the iPDR-free rate was 33.7% (95% CI: 22.2, 45.5) for patients originally randomized to placebo and 44.6% (95% CI: 34.3, 54.3) for patients originally randomized to satralizumab.

At the 8th year of the study period, the event-free rate in the overall population was 67.1% (95% CI: 58.6, 74.3). In the AQP4-IgG seropositive subgroup, the event-free rate was 67.1% (95% CI: 56.4, 75.8).

Use of Acute Relapse/Rescue Therapy (Treated Clinical Relapse):

Overall, 58 (34.9%) patients used rescue therapy during the overall satralizumab period. In the AQP4-IgG seropositive subgroup, 40 (36.0%) used rescue therapy during the overall satralizumab period.

Change in Expanded Disability Status Scale Score:

The mean change in EDSS scores from randomization/first dose of satralizumab to every 24 weeks after the randomization/first dose of satralizumab visit was analyzed. Median time to EDSS worsening was not reached (range: 0–525 [censored] weeks). At Week 456, the EDSS worsening-free rate was 57.0% (95% CI: 46.8, 66.0).

Change in Visual Acuity (Snellen Chart):

Visual acuity was maintained through Week 480 (data truncated after Week 480 because of the low number of patients at risk).

Safety results

The key safety findings are as follows:

- A total of 3037 AEs were reported among the 166 patients treated with satralizumab, with the majority of patients (97.6%) reporting at least one AE during the overall study period.
- The majority of AEs were reported in the SOC Infections and Infestations.
- The majority of AEs were of mild or moderate intensity. None were fatal.
- The most frequent treatment-related AEs were leukopenia and decreased white blood cell count, neutropenia, and IRR.
- The most frequently reported SAEs were in the SOCs Infections and infestations and Injury, poisoning and procedural complications. Overall, 5 patients (3.0%) discontinued treatment due to an SAE.

• The most frequently reported infection AEs were upper respiratory tract infection, urinary tract infection, and nasopharyngitis.

• The most frequently reported serious infection AEs were urinary tract infection and cellulitis.

• All infusion-related reactions (IRRs) were non-serious and the majority were of mild/moderate severity.

2.1.3. Discussion on clinical aspects

The safety profile is unchanged. This longer-term follow up data shows that clinical benefit is maintained over 8 years of treatment. Accordingly, the benefit-risk profile of satralizumab remains favourable for the treatment of NMOSD.

3. CHMP overall conclusion and recommendation

☒ **Fulfilled: No regulatory action required.**