ADDITIONAL DISCLOSURE DATA FOR SWITZERLAND

Name of Sponsor/Company: Janssen Pharmaceutical K.K.*

* This study was conducted by Janssen Pharmaceutical K.K. in Japan. The term “sponsor” is used to represent Janssen Pharmaceutical K.K.

Date: *03 Jun 2020*

Swiss marketing authorisation data

Swiss Marketing Authorisation number: 67103

Swiss Marketing Authorisation date: 25 February 2020

Name of the preparation: Spravato – 28 mg – nasal spray

Name of active pharmaceutical ingredient: Esketamine (JNJ-54135419-AAC)

Clinical trial data

1. **Clinical trial identification**

Protocol No.: 54135419TRD2005

Title of Study: A Randomized, Double-blind, Multicenter, Placebo-controlled Study to Evaluate the Efficacy, Safety and Tolerability of Fixed Doses of Intranasal Esketamine in Japanese Subjects With Treatment Resistant Depression

Study Name: None

EudraCT Number: None

NCT No.: NCT02918318

2. **Protocol change history**

Protocol and Amendments:

Original Protocol, 20 June 2016

Amendment-1, 20 September 2016– substantial

Amendment-2, 17 March 2017– substantial

Amendment-3, 31 August 2017– substantial

Amendment-4, 30 August 2018– substantial

Amendment-5, 21 December 2018– substantial

3. Clinical trial investigators and study centres

Principal Investigator*:* Takatoshi Mori, MD

Study Centres: Countries and number of sites in each country in which the study was conducted: Japan (58)

4. Medication used

Test Product, Dose and Mode of Administration, Batch No.: Intranasal esketamine was supplied as a clear and colorless solution containing 16.14% weight/volume (w/v) esketamine hydrochloride (equivalent to 14% w/v esketamine base), in a nasal spray pump (device), which delivered 16.14 mg esketamine hydrochloride (14 mg esketamine base) per 100 µL spray. Each individual nasal spray device contained a total of 28 mg (ie, 2 sprays). Intranasal esketamine batch numbers were: 502169, 160663, and 170900.

Reference Therapy, Dose and Mode of Administration, Batch No.: Intranasal placebo was supplied as a clear and colorless solution containing water for injection with a bittering agent (denatonium benzoate [Bitrex®] at a final concentration of 0.001 mg/mL) added to simulate the taste of the intranasal esketamine solution. The placebo solution was provided in matching nasal spray devices; each individual nasal spray device contained 2 sprays. Intranasal placebo batch numbers were: 502264, 160665, and 162284A.

5. Study population

Number of participants – planned: 183

Number of participants – analysed: 202

6. Summary and conclusion

- The fixed dosed intranasal esketamine (28-, 56-, 84-mg) did not demonstrate significant improvement in depressive symptoms as compared to intranasal placebo as an add-on to an continued oral AD confirmed as nonresponse in the OL prospective lead-in phase in Japanese subjects with TRD as measured by the change in the MADRS total score from baseline to the end of the 4-week DB induction phase.
- The results of secondary efficacy endpoints were consistent with the primary endpoint.
- Plasma esketamine concentrations exhibited expected dose-dependent increases across the 28-, 56-, and 84-mg doses. Mean plasma esketamine and noresketamine concentrations were consistent on Days 4 and 25.

- Overall, a higher incidence of TEAEs was observed in all esketamine dose groups compared with the placebo group during the DB induction phase. The incidence of TEAEs of increased BP, TEAEs potentially suggestive of abuse, transient dizziness or vertigo during the DB induction phase were higher in the esketamine dose groups (28-, 56-, and 84-mg) as compared with the placebo group. Most of these TEAEs were mild or moderate in severity. None of the subjects experienced TEAEs of dissociation that required concomitant medications during the DB and OL induction phases. Suicidal ideation and behavior measured by C-SSRS improved in all esketamine groups and placebo group in the DB induction phase. Throughout the study, the percentage of subjects reporting suicidal ideation was similar in all esketamine groups and placebo. Transient elevation of CADSS and BP elevation in a dose-response manner immediately after intranasal administration but spontaneously resolved within a short period. Based on a review of AE, BPRS plus (+), and CADSS data, no cases of treatment emergent psychosis were observed in any subject in either of the intranasal esketamine dose groups during the study. In general, intranasal esketamine doses (28-, 56-, and 84 -mg) evaluated in this study appeared to be safe and tolerated in Japanese subjects with TRD and no new safety concerns were identified.

7. Results reporting

Date of Clinical Trial Report: 22 April 2020

Prepared by: Janssen Pharmaceutical K.K.

Publication(s) Reference(s): None

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