Esketamine nasal spray shows higher remission and response rates over 32 weeks of treatment compared with quetiapine extended-release in patients with treatment resistant depression: Results from ESCAPE-TRD, a randomised, phase IIIb clinical trial

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Conclusions: Childhood trauma is linked with anger in adulthood, most strongly for trait anger and borderline personality traits. It is of clinical importance to explore childhood traumatic experience and start trauma-focused interventions when appropriate.

Disclosure of Interest: None Declared

O0066

ESKALE study, a French real-world study describing TRD patients with Esketamine nasal spray: final analysis

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Introduction: Treatment resistant depression (TRD) affects a substantial proportion of patients with depression and carries a large unmet need. Esketamine nasal spray (NS), in combination with a selective serotonin reuptake inhibitor (SSRI) or serotonin norepinephrine reuptake inhibitor (SNRI), has been shown to reduce depressive symptoms and risk of relapse, in patients with TRD (Popova, V., et al. 2019. Am J Psychiatry; Daly, E.J., et al. 2019. JAMA Psychiatry). Esketamine NS has been authorised by European Medicines Agency as treatment for resistant depression since December 2019. ESKALE, is the first French observational study to describe TRD patients treated with Esketamine NS under real-world settings and to provide data on this innovative solution for patients.

Objectives: To describe patients with TRD at Esketamine NS initiation and during the following 12-month period in real-world clinical practice.

Methods: ESKALE is a French, observational, multicentre, retrospective study of adult patients with moderate to severe TRD defined as a non-response to ≥ 2 oral antidepressant. Each patient was included in one of the 3 cohorts according to Esketamine NS start date: Temporary Authorisation for Use (ATUc) cohort, post-ATU cohort or post-launch period cohort. Data were collected from medical records of patients treated with Esketamine NS between 10-29-2019 and 06-14-2022. Primary objective is to describe patients' profile and Esketamine NS conditions of use at esketamine initiation and during the 12-month period after esketamine initiation in real-world clinical practice (either patient had stop or not the treatment). Secondary objectives are to describe Esketamine NS management, safety profile and patient pathway.

Results: Two standard descriptive statistical interim analysis were conducted and published in several conferences (Samalin L, et al. Presented at EPA Hybrid congress June 2022. P.2482; Samalin L, et al. Presented at ECNP Vienna, October 2022. P.0122). This final analysis describes the data collected from medical records of patients included in the study from 04-08-2020 to 06-30-2021. 157 patients were included from 26 French centers, the majority (>65%) of patients were females. Average age was 49 years old with 27 patients > 65 years old. Duration of the current depressive episode was up to 2,5 years (mean) with an average of more than three episode in the patient's entire life (mean). At esketamine initiation, 3 patients out of 4 were clinically perceived to have severe depression with a MADRS score of 32.0 (median). Patients had mainly depression with anxious distress specifier. Esketamine NS dose at initiation was mainly 56mg.

Conclusions: Eskale is the first French cohort study generating real-world evidence on treatment resistant depression patients treated with Esketamine nasal spray. Results of the final analysis confirmed the 2 interim analysis results already published.

Disclosure of Interest: None Declared

O0067

Esketamine nasal spray shows higher remission and response rates over 32 weeks of treatment compared with quetiapine extended-release in patients with treatment resistant depression: Results from ESCAPE-TRD, a randomised, phase IIIb clinical trial

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Introduction: Treatment resistant depression (TRD) is estimated to affect 10–30% of patients with major depressive disorder (Al-Harbi *et al.* Patient Prefer Adherence 2012; 6 369–88). Esketamine nasal spray (NS), in combination with a selective serotonin reuptake inhibitor (SSRI) or serotonin norepinephrine reuptake inhibitor (SNRI), increases remission and response rates in patients with TRD compared with placebo plus SSRI/SNRI (Popova *et al.* Am J Psychiatry 2019; 176 428–38). ESCAPE-TRD (NCT04338321) is the first randomised clinical trial to compare esketamine NS to quetiapine extended-release (XR), an antipsychotic augmentation therapy for patients with TRD.

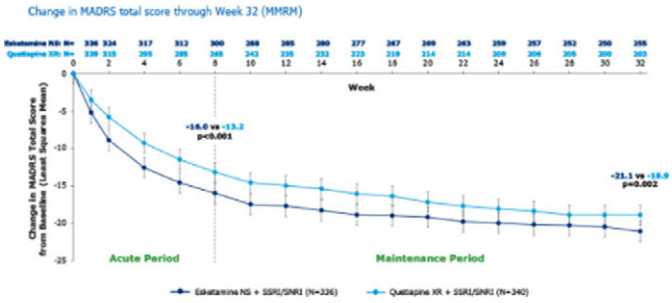
Objectives: To explore the efficacy and safety of esketamine NS compared with quetiapine XR in TRD over 32 weeks (wks).

Methods: In the ESCAPE-TRD phase IIIb open-label, rater-blinded trial, patients were randomised 1:1 to esketamine NS (56/84 mg; twice per wk, weekly or every 2 wks) or quetiapine XR (150–300 mg daily) both in combination with an ongoing SSRI/SNRI. Remission (Montgomery-Åsberg Depression Rating Scale [MADRS] total score of ≤10) and response (≥50% improvement in

MADRS total score from baseline or MADRS≤10) rates were analysed over time using last observation carried forward. MADRS change from baseline was analysed using Mixed Models for Repeated Measures (MMRM). The most common adverse events (AEs) leading to discontinuation are reported for patients who received ≥1 dose of study medication.

Results: At baseline, 336 patients were randomised to esketamine NS and 340 to quetiapine XR. A significantly higher percentage of patients in the esketamine NS group achieved remission (at each visit from Wk6 [p=0.008] onward) and response (at each visit from Day 15 [p<0.001] onward) versus patients treated with quetiapine XR. Esketamine NS significantly improved MADRS score compared to quetiapine XR at each visit from Day 8 onwards, with an average difference over time in the least squares means total MADRS score change from baseline of -2.4 (**Figure**). The most common AEs leading to treatment discontinuation for esketamine NS were dizziness (n=2, 0.6%), dissociation (n=2, 0.6%) and vomiting (n=2, 0.6%), and for quetiapine XR were sedation (n=7, 2.1%), weight increased (n=6, 1.8%) and somnolence (n=5, 1.5%).

Image:



Conclusions: Esketamine NS increased the percentage of patients achieving response and remission and improved MADRS total score over time compared with quetiapine XR. Rates of discontinuation arising from the most common AEs were generally lower with esketamine NS than quetiapine XR.

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O0068

Improvement in Depression Symptoms Measured by Montgomery-Åsberg Depression Rating Scale and Quick Inventory of Depressive Symptomatology-Self Rated Items after Randomised Double-blind COMP360 Psilocybin Therapy for Treatment-resistant Depression

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Introduction: COMP360 is a synthetic, proprietary, purified form of psilocybin in development for treatment-resistant depression (TRD) with FDA Breakthrough Therapy designation. In a recent phase IIb study, COMP360 psilocybin 25mg was superior to 1mg on change from baseline (CFB) to Week 3 on the Montgomery-Åsberg Depression Rating Scale (MADRS) total score (primary efficacy endpoint), when administered alongside psychological support. Quick Inventory of Depressive Symptomatology-Self Rated (QIDS-SR_{16}) total score (exploratory efficacy endpoint) showed similar results.

Objectives: To analyse changes in specific depression symptoms after psilocybin treatment in the aforementioned study, as measured by individual item scores on the MADRS and QIDS-SR_{16} (range 0-6 and 0-3).

Methods: Participants with TRD were randomised to single doses of psilocybin 25mg (n=79), 10mg (n=75), or 1mg (n=79). A remote, blinded rater assessed the MADRS at Baseline, Day 2 (the day post-psilocybin), and Weeks 1, 3, 6, 9, and 12. The QIDS-SR_{16} was self-rated at Baseline, Day 1, Day 2, and Weeks 1, 2, 3, 6, 9, and 12. At each time point, descriptive statistics were calculated for each MADRS and QIDS-SR_{16} individual item score.

Results: At Week 3, MADRS items with the largest differences in mean CFB in the 25mg arm were Inability to Feel, Apparent Sadness, Lassitude, and Reported Sadness. Greater improvement in the 25mg arm was apparent from Day 2 and remained to Week 12 (Lassitude remained to Week 6 only). On the QIDS-SR_{16}, the item with the largest difference in mean CFB at Week 3 in the 25mg arm was in Feeling Sad and remained evident to Week 12 (Table 1).