Previous research has demonstrated that emotional neglect and emotional abuse are associated with fatigue in patients with MS (Pust et al. Front Psychiatry 2020; 11:811). While the role of emotion dysregulation as a mediator between adverse childhood experiences and long-term effects of childhood trauma has been studied, this relationship has not been previously examined in patients with MS.
Objectives: This study aims to investigate the association between adverse childhood experiences and fatigue and to examine the mediating effect of emotion dysregulation in patients with MS.
Methods: Patients with MS followed in the Neurology Outpatient Clinic at Marmara University, who were evaluated during their clinical examination to be cognitively competent and without any physical disabilities that would prevent them from completing the forms, were included in the study. Adverse childhood experiences were assessed using the expanded version of the Childhood Trauma Questionnaire (CTQ-33), emotion dysregulation was measured by the 16-item Difficulties in Emotion Regulation Scale (DERS-16) and fatigue was evaluated using the Fatigue Severity Scale. The impact of CTQ subscale scores on fatigue and the mediating role of emotion dysregulation were analyzed using SPSS with Process Macro v4.2.
Results: A total of 119 patients completed the survey, with a mean age of 37.45 years, and 71.4% of the participants were women. Emotional abuse and emotional neglect were associated with fatigue in patients with MS. The effect of emotional abuse on fatigue was mediated by emotion dysregulation, with the total effect being 0.81 (95% CI [0.04, 1.58]), the direct effect -0.12 (95% CI [-0.86, 0.63]), and the indirect effect 0.93 (95% CI [0.50, 1.55]). Similarly, the relationship between emotional neglect and fatigue was also mediated by emotion dysregulation, with the total effect being 0.66 (95% CI [0.10, 1.22]), the direct effect -0.05 (95% CI [-0.60, 0.49]), and the indirect effect 0.71 (95% CI [0.39, 1.10]). These results indicate that emotion dysregulation fully mediates the effects of both emotional abuse and emotional neglect on fatigue in patients with MS.
Conclusions: Our findings indicate that the link between fatigue severity and emotional neglect or abuse in MS patients is fully mediated by difficulties in emotion regulation. Consequently, it is suggested that interventions aimed at enhancing emotion regulation strategies may potentially mitigate the effects of adverse childhood experiences on MS-related fatigue. Further research, especially focused on intervention strategies, is needed in this area.

Disclosure of Interest: None Declared

Depressive Disorders

EPP647

Unlocking Potential: The Re-emerging Role of Thyroid Hormone Therapy in Treatment-Resistant Depression

M. Cameira[1]*, P. Abreu[1], M. Pereira[1], M. Soares[1], I. Vidó[1] and I. Lopes[2]
[1]Hospital Júlio de Matos - ULS São José, Lisboa and [2]Hospital do Barreiro - ULS Arco Ribeirinho, Barreiro, Portugal
*Corresponding author.
doi: 10.1192/j.eurpsy.2025.855

Introduction: Treatment-resistant depression (TRD) poses a significant challenge in clinical psychiatry, affecting a substantial proportion of patients who do not respond adequately to standard antidepressant therapies. Recent studies have rekindled interest in thyroid hormone therapy as a potential augmentation strategy for enhancing treatment outcomes in both unipolar and bipolar depression. Thyroid hormones, particularly levothyroxine (LT4) and triiodothyronine (LT3), have been shown to influence mood regulation through their interactions with neurotransmitter systems, thereby offering a promising avenue for improving depressive symptoms in TRD patients.
Objectives: This study explores the potential of thyroid hormones, specifically levothyroxine (LT4) and triiodothyronine (LT3), to enhance treatment outcomes for patients who have not adequately responded to standard antidepressant therapies. It also synthesizes recent findings on the safety profile of thyroid hormone therapy and examines potential gender differences in treatment response.
Methods: A comprehensive review of the literature was conducted, focusing on studies published in the ten years that examined the role of thyroid hormones in TRD. Databases such as PubMed were searched for randomized controlled trials, meta-analyses, and observational studies that assessed the effects of LT3 and LT4 on depressive symptoms and treatment outcomes.
Results: The literature review shows that adjunctive triiodothyronine (T3) significantly enhances treatment response in treatment-resistant depression. A randomized trial found that 53% of patients on T3 had a ≥50% improvement in depression scores after three weeks, compared to 19% for those on levothyroxine (LT4). While LT4 may benefit chronic cases, T3 is generally preferred for its superior efficacy. Thyroid hormone therapy also benefits bipolar depression, especially in rapid cycling patients. Functional imaging studies indicate that supraphysiologic LT4 can improve symptoms by modulating anterior limbic network activity. Some evidence suggests women may respond better than men. Overall, thyroid hormone therapy is well tolerated, with low incidences of adverse effects like tremor, anxiety, and palpitations. However, long-term efficacy remains mixed, with some studies showing no significant differences compared to placebo, and the safety of high-dose therapy is uncertain, highlighting the need for further research.
Conclusions: Thyroid hormone therapy, particularly LT3 and LT4, is a promising augmentation strategy for treatment-resistant unipolar and bipolar depression. While LT3 is noted for its rapid response, further research is needed to clarify its long-term safety and optimal dosing. These findings highlight the importance of considering thyroid therapy for patients who do not achieve satisfactory outcomes with conventional antidepressants.

Disclosure of Interest: None Declared

EPP648

Silexan reduces functional impairment in patients with a major depressive episode

H.-P. Volz[1], S. Klement[2], E. Seifritz[3] and S. Kasper[4]*
[1]Medical Advisor, Würzburg; [2]Dr. Willmar Schwabe GmbH & Co. KG, Karlsruhe, Germany; [3]Psychiatric Hospital, Zürich, Switzerland and [4]Medical University of Vienna, Vienna, Austria
*Corresponding author.
doi: 10.1192/j.eurpsy.2025.856

Introduction: In a multi-centre, double-blind, randomised, placebo- and reference-controlled clinical Phase III trial in patients with a mild to moderate major depressive episode, Silexan, a special essential oil from *Lavandula angustifolia,* demonstrated a clinically meaningful and statistically significant antidepressant effect (Kasper *et al.* Eur Arch Psychiatry Clin Neurosci 2024; Apr 1, Epub ahead of print). Patients with depression often experience functional impairment, i.e. in their ability to perform activities of daily

living, in their capacity to form and maintain interpersonal relationships, and in their work productivity.
Objectives: We present data from the trial to assess the impact of the symptoms of the depressive episode on the patient`s functional abilities in daily living.
Methods: Adult patients (≥18 years) suffering from a major depressive episode of mild to moderate severity according to ICD-10 were included. Further inclusion criterion was a total score of 19 – 34 points in the Montgomery-Åsberg-Depression Rating Scale (MADRS). Randomised patients took 80 mg Silexan, 50 mg Sertraline, or placebo once daily over 8 weeks. Functional impairment was assessed using the change of the Sheehan Disability Scale (SDS total score) between baseline and week 8, changes of each SDS single item "work" (item 1), "social life/leisure activities" (item 2), and "family life/home responsibilities" (item 3), as well as the number of lost (DL) and underproductive days (DU). The scientific questions if the active treatment groups are superior to placebo in improving functional impairment was investigated as secondary objectives, which were analysed descriptively using an analysis of covariance model with factors for treatment and centre and the baseline value as covariate.
Results: The full analysis set consisted of 498 patients. The changes of the SDS total score differed by 2.40 ($p<0.001$) points (adjusted mean difference) in favour of Silexan compared to placebo and by 0.82 ($p=0.267$) points in favour of Sertraline compared to placebo. The mean differences between Silexan and placebo were 0.98 points for item 1, 0.65 for item 2, and 0.78 for item 3 ($p<0.05$, each). Compared to placebo, both DL ($p=0.055$) and DU ($p=0.011$) occurred less frequently with Silexan. In the primary efficacy endpoint of the trial, the change of the MADRS total score, Silexan was significantly superior to placebo ($p<0.01$).
Conclusions: With Silexan treatment, patients with a major depressive episode coped better with work, social life, or family responsibilities and had fewer lost or underproductive days.

Disclosure of Interest: H.-P. Volz Consultant of: Lundbeck, Pfizer, Schwabe (Spitzner), Bayer, Janssen, neuraxpharm, AstraZeneca, S. Klement Employee of: Dr. Willmar Schwabe GmbH & Co. KG, E. Seifritz Grant / Research support from: Swiss National Science Foundation and University of Zürich, Consultant of: Lundbeck, Schwabe, Janssen, Otsuka, Mepha Pharma, Otsuka Pharma, Recordati, OM Pharma, Takeda, Sunovion Pharma and Angelini, S. Kasper Consultant of: Angelini, Biogen, Boehringer, Esai, Janssen, IQVIA, Mylan, Recordati, Rovi, Sage and Schwabe, Speakers bureau of: Angelini, Aspen Farmaceutica S.A., Biogen, Janssen, Recordati, Schwabe, Servier, Sothema, and Sun Pharma

EPP649

Top-line Results from ESCAPE-LTE: An Open-Label Extension Study to Assess Long-term Safety of Esketamine Nasal Spray in Treatment Resistant Depression

Y. Godinov[1], D. J. Fu[2], C. von Holt[3], J. Buyze[4], R. Mehta[5], A. Reif[6,7]*, T. Messer[8], I. Bitter[9], R. Frey[10], L. Häggström[11], A. E. Anıl Yağcıoğlu[12], R. Nielsen[13] and W. J. Cubała[14]

[1]Janssen EMEA, Sofia, Bulgaria; [2]Janssen Research & Development LLC, New Jersey, United States; [3]Janssen EMEA, Neuss, Germany; [4]Janssen Pharmaceutica NV, Beerse, Belgium; [5]Janssen Inc., Toronto, Canada; [6]Department of Psychiatry, Psychosomatic Medicine and Psychotherapy, Goethe University Frankfurt, University Hospital, Frankfurt; [7]Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, Theodor-Stern-Kai 7, 60596, Frankfurt am Main; [8]Danuvius Klinik GmbH, Technische Universität München, Pfaffenhofen an der Ilm, Germany; [9]Department of Psychiatry and Psychotherapy, Semmelweis University, Budapest, Hungary; [10]Department of Psychiatry and Psychotherapy, Medical University of Vienna, Vienna, Austria; [11]Affecta Psychiatric Clinic, Halmstad, Sweden; [12]Department of Psychiatry, Hacettepe University Faculty of Medicine, Ankara, Türkiye; [13]Aalborg University Hospital, Aalborg, Denmark and [14]Department of Psychiatry, Faculty of Medicine, Medical University of Gdańsk, Gdańsk, Poland
*Corresponding author.
doi: 10.1192/j.eurpsy.2025.857

Introduction: ESCAPE-LTE was a phase 4, long-term, open-label extension (OLE) study for patients (pts) with treatment resistant depression (TRD) who were continuing esketamine nasal spray (ESK-NS) treatment following ESCAPE-TRD. ESCAPE-TRD was a randomised, phase IIIb trial comparing the efficacy and safety of ESK-NS versus quetiapine extended release (Q-XR), when both were flexibly dosed alongside an ongoing selective serotonin/serotonin-norepinephrine reuptake inhibitor (SSRI/SNRI), in pts with TRD. The study demonstrated that ESK-NS significantly increased the probability of achieving remission at Week 8, and of being relapse-free through Week 32 after remission at Week 8, versus Q-XR (Reif *et al.* NEJM 2023; 389 1298–309).
Objectives: To assess the long-term safety, tolerability and efficacy of ESK-NS alongside an SSRI/SNRI in pts with TRD. Here, the study design of ESCAPE-LTE is described; top-line results will be reported in the poster.
Methods: ESCAPE-LTE was a single-arm, 2-year OLE to ESCAPE-TRD in 14 countries. Pts eligible for ESCAPE-LTE were those who completed ESK-NS treatment in combination with an SSRI/SNRI in ESCAPE-TRD through to the end of the study (Week 32), continued to benefit from the ESK-NS treatment regimen and for whom commercial ESK-NS was not accessible in their country. The starting dose of ESK-NS was based on the pts' dose (28 mg [≥65 years and adults of Japanese ancestry], 56 mg or 84 mg) and frequency (weekly or biweekly) at completion of the maintenance phase (Week 32) of ESCAPE-TRD. Investigators were able to change the dose and frequency within label recommendations during the OLE based on clinical judgment.
The primary objective was to assess the long-term safety and tolerability of ESK-NS. The secondary objective was to assess the long-term efficacy of ESK-NS based on the proportion of pts being relapse-free at Week 104 (or end-of-study).
The primary endpoints were the number of pts who developed treatment-emergent adverse events, and suicidal ideation and behaviour, assessed by the Columbia-Suicide Severity Rating Scale (C-SSRS). Safety assessments also included body weight and vital sign measurements and clinical laboratory tests. The secondary endpoint was no relapse until the end of the prospective observation at Week 104 (or end-of-study); relapse was defined as a worsening of depressive symptoms as indicated by a total Montgomery-Åsberg Depression Rating Scale (MADRS) score of ≥22 at two consecutive assessments; hospitalisation for worsening depression, suicide prevention or attempt; or any other event assessed by the investigator to be indicative of relapse.
Results: 183 pts were enrolled in the ESCAPE-LTE. Top-line study results will be reported in the poster.