LCA

Dr Edouard-Jules LAFORGUE

Les attentes pour l’épreuve

L’épreuve de LCA

- 10 minutes de présentation
- 5 minutes d’échanges avec le jury

- Objectif : montrer que vous avez **compris l’article** et que vous êtes capable d’en **faire une lecture critique** → ces points forts et ses points faibles

- Evaluation sur **le fond** (compréhension) **et la forme** (restitution)

- Support visuel
  - Venir avec + sécurité (clé USB +++ et stockage mail)
  - Attention compatibilité des formats (mac/PC)
  - *… chaque année, des étudiants sont sanctionnés sur ces points*

La présentation orale

- **S’entraîner !**

- La répétition permet de voire si l’on respecte le temps
  - Trop court ou trop long = points en moins

  … chaque année, des étudiants sont sanctionnés sur ces points
  - Il ne s’agit pas d’une course, dire ce qu’il faut (ni trop, ni pas assez)

- La répétition permet de répartir les informations et évite les redondance

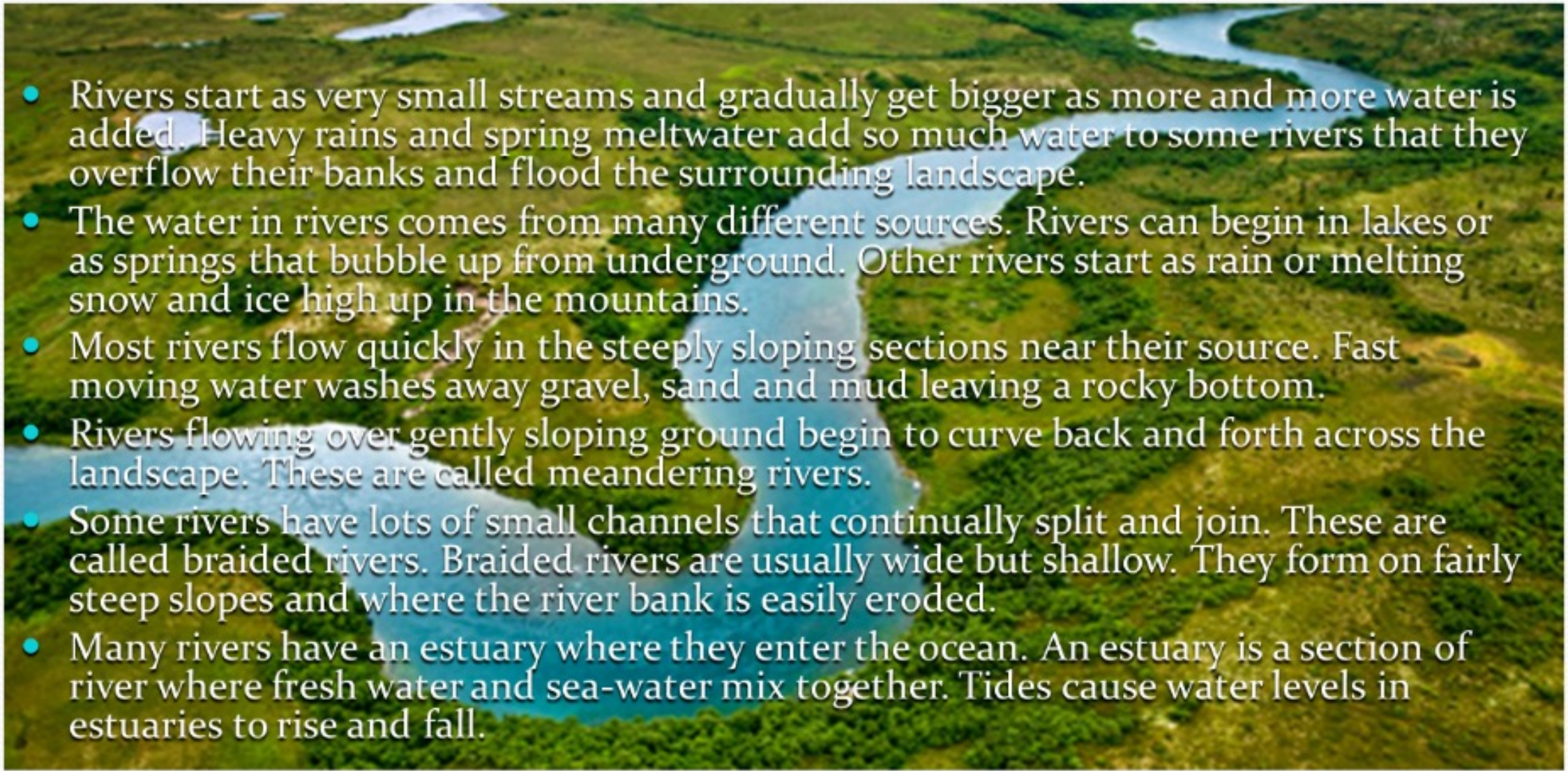
- La répétition permet de connaître son texte et de ne pas lire ses notes

Le support

- Informatif pour l'auditeur = **informations essentielles**
  - Pas de phrase, sinon l'auditeur lit … et ne vous écoute plus
  - Figures et illustrations si pertinentes
  - En LCA, ne pas hésiter à reprendre celles de l'article pour les résultats

- Un **plan de rappel pour l'orateur**
  - Ce n'est pas un prompteur
  - En revanche **l'occasion de se démarquer**

How Rivers Are Formed



- Rivers start as very small streams and gradually get bigger as more and more water is added. Heavy rains and spring meltwater add so much water to some rivers that they overflow their banks and flood the surrounding landscape.
- The water in rivers comes from many different sources. Rivers can begin in lakes or as springs that bubble up from underground. Other rivers start as rain or melting snow and ice high up in the mountains.
- Most rivers flow quickly in the steeply sloping sections near their source. Fast moving water washes away gravel, sand and mud leaving a rocky bottom.
- Rivers flowing over gently sloping ground begin to curve back and forth across the landscape. These are called meandering rivers.
- Some rivers have lots of small channels that continually split and join. These are called braided rivers. Braided rivers are usually wide but shallow. They form on fairly steep slopes and where the river bank is easily eroded.
- Many rivers have an estuary where they enter the ocean. An estuary is a section of river where fresh water and sea-water mix together. Tides cause water levels in estuaries to rise and fall.

L’organisation

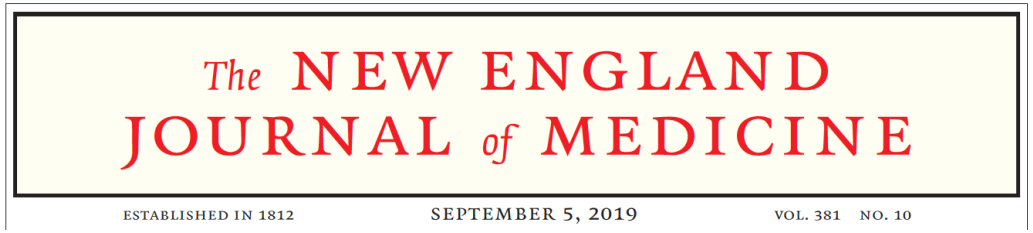
- 10 minutes = 10 diapos
  - 1 dia = 1 min (environ)
- Reprendre la structuration de l’article
- Répartir des diapos par parties
  - *Titre*
  - I : 1 à 2
  - M : 2 à 3
  - R : 2 à 3
  - D : 2 à 3
  - (Conclusion : 1)
  - *Fermeture*
- Conseil d’arriver à la fin de la méthodologie avant la 5ème minute

L’organisation : titre et introduction

- Titre : journal avec Impact Factor

  IF = nb de citations 2 années précédentes / nb articles parus ces 2 années

- Introduction : 1 à 2 diapos
  - Contexte scientifique
  - Place de l’étude dans le contexte
  - A la fin de l’introduction : question de l’article



Impact Factor = 90

➢ *Il est vraisemblable que cet article soit a priori de bonne qualité et amène des données solides et pertinentes.*

L'organisation : titre et introduction

Modèle de l'entonnoir

Contexte général

Problème avec solution possible

Question

A Quick Take is available at NEJM.org

ANTIDEPRESSANTS THAT PRIMARILY enhance monoaminergic neurotransmission involving serotonin or norepinephrine are used in the treatment of major depressive disorder, and their clinical effects are generally evident in 4 to 8 weeks.[1-5] One hypothesis for the mechanism of depression implicates deficits in γ-aminobutyric acid (GABA) and downstream alterations in monoaminergic neurotransmission.[4] This hypothesis is supported by evidence that reduced GABA levels have been observed in plasma, cerebrospinal fluid,[5-7] and cortical brain tissues[8-11] of patients with depression. In addition, reduced expression of GABA-synthesizing enzymes in the brain tissue of persons who have died by suicide,[12,13] a reduced number of GABAergic interneurons in the brain tissue of patients with depression,[14] and reduced mRNA for GABA type A ($GABA_A$) α4 and δ subunits (which encode extrasynaptic $GABA_A$ receptors) in the brain tissue of persons with depression who have died by suicide[15] have been observed.

Neurosteroids, which are synthesized from cholesterol in the brain, are potent modulators of GABA and glutamate.[16] Despite their steroid structure, their target activity and pharmacologic characteristics are distinct from those of glucocorticoids and differ in both genomic and nongenomic effects.[17,18] Preclinical studies have shown that the naturally occurring neurosteroid allopregnanolone is a positive allosteric modulator of synaptic and extrasynaptic $GABA_A$ receptors that affects both phasic and tonic inhibition of neurons.[16,19] In rodents, allopregnanolone is synthesized locally in the brain in response to acute stressors.[19-21] With experimental chronic stress, however, levels of allopregnanolone in the brain decrease, and behavioral changes normalize after treatments that increase allopregnanolone levels.[19,22,23]

Reduced levels of allopregnanolone in the cerebrospinal fluid normalize after successful treatment of depression with antidepressants.[24] Placebo-controlled trials in patients with postpartum depression have shown efficacy of a 60-hour infusion of brexanolone, an intravenous formulation of allopregnanolone, which supports the hypothesis of GABAergic dysfunction in that form of depression.[25,26]

SAGE-217 — an oral, synthetic neurosteroid and positive allosteric modulator of $GABA_A$ receptors — has shown anticonvulsant, anxiolytic, and sedative properties in studies of seizure in rodent models.[27-29] A functional assay measuring both agonistic and antagonistic effects of SAGE-217 has indicated no activity on a panel of 22 nuclear hormone receptors.[30]

Studies of single ascending and multiple ascending doses in healthy volunteers have shown that SAGE-217 has a plasma half-life of 16 to 23 hours, which is compatible with once-daily dosing; sedation is the most common adverse event.[31,32] We previously conducted an open-label, uncontrolled pilot trial of SAGE-217 involving patients with major depressive disorder who were treated for 14 days. The results suggested that SAGE-217, like intravenous brexanolone (with which it shares a similar molecular pharmacology profile), may be associated with a rapid onset of action.[33] Here we report the results of a randomized, double-blind, placebo-controlled trial of SAGE-217 in patients with major depressive disorder. The protocol of the current trial (which also contains the protocol of the open-label pilot trial) and the statistical analysis plan are available with the full text of this article at NEJM.org. The results of the pilot trial are provided in the Supplementary Appendix, available at NEJM.org. The pilot trial and the current placebo-controlled trial recruited different patients.

METHODS

TRIAL DESIGN AND OVERSIGHT

This phase 2 trial was conducted at eight sites in the United States from April 2017 through October 2017. A list of sites and principal investigators is provided in the Supplementary Appendix. Approval was obtained from the institutional review board at each site, and written informed consent was obtained from each patient. Sage Therapeutics designed the trial, provided the SAGE-217 and placebo, collected and analyzed the data, and paid for professional writing assistance. The qualification process for end-point raters and administration of assessments were overseen by Bracket Global (Wayne, PA) (details are provided in the Supplementary Appendix). Confidentiality agreements exist between the authors and Sage Therapeutics. All the authors vouch for the accuracy and completeness of the data and analyses, the fidelity of the trial to the protocol, and the completeness of reporting of adverse events.

T1. Les ATD classiques (IRS/Na) mettent 4 à 8 semaines à agir. Le GABA a une implication dans la physiopathologie de l'EDM.

T2. On a des données sur l'effet des neurostéroïdes sur l'activité GABA.

T3. Le SAGE-217 (neurostéroïde) est-il efficace chez les patients présentant un EDM ?

L’organisation : méthodologie

- Objectif
- Type d’étude
- Critère de jugement principal (+++) ← potentiellement à critiquer en discussion si inadapté (dur / mou)
- CJ secondaires (ne donneront que des tendances)

- Participants ← reflète la population de destination ?
- Design ← adapté ?
- Effectifs ← dépend de risque alpha, puissance, différence à mettre en évidence, écart-type
- Analyse statistique ← adaptée ?

L’organisation : résultats

- Nombre de sujets – flow chart ? Comparabilité des groupes
- Résultat du CJP +++
- Résultats des CJS

- Préférentiellement sous forme graphique
- Significatif ou non
- A ce stade que les résultats

« Il y une réduction significative en faveur du traitement A versus le traitement B sur le score… »

L’organisation : discussion

- **Interprétation des résultats**
  « Le traitement A est significativement plus efficace que le traitement B »

- **Validité interne**
  - Forces de l’article :
    - Les auteurs n’oublieront jamais de les souligner !
  - Faiblesses de l’article :
    - Biais évoqués par les auteurs…
    - … et ceux repérés par vos soins
    - confusion / sélection / suivi / évaluation

- **Cohérence externe :** comparaison littérature existante – compatible avec les connaissances actuelle
- Taille d’effet -> **pertinence clinique ? et extrapolabilité**

L’organisation : conclusion

- **Conclusion**
  - Grand message
  - Perspectives : et la suite ? Essai de phase II → phase III ? / Phase III → AMM ?, etc.

- A la fin de ce processus : possibilité de donner brièvement son avis, contextualisation supplémentaire

Clinical Trial > Nat Med. 2021 Jun;27(6):1025-1033. doi: 10.1038/s41591-021-01336-3. Epub 2021 May 10.

MDMA-assisted therapy for severe PTSD: a randomized, double-blind, placebo-controlled phase 3 study

Comment in

Putting the MD back into MDMA.
Nutt DJ, de Wit H.
Nat Med. 2021 Jun;27(6):950-951. doi: 10.1038/s41591-021-01385-8.
PMID: 34031606 No abstract available.

Psychotherapy-supported MDMA treatment for PTSD.
Krystal JH, Kelmendi B, Petrakis IL.
Cell Rep Med. 2021 Aug 17;2(8):100378. doi: 10.1016/j.xcrm.2021.100378. eCollection 2021 Aug 17.
PMID: 34467253 **Free PMC article.**

Reply to: Caution at psychiatry's psychedelic frontier and Challenges with benchmarking of MDMA-assisted psychotherapy.
Mitchell J, Coker A, Yazar-Klosinski B.
Nat Med. 2021 Oct;27(10):1691-1692. doi: 10.1038/s41591-021-01526-z. Epub 2021 Oct 11.
PMID: 34635856 No abstract available.

Challenges with benchmarking of MDMA-assisted psychotherapy.
Halvorsen JØ, Naudet F, Cristea IA.
Nat Med. 2021 Oct;27(10):1689-1690. doi: 10.1038/s41591-021-01525-0. Epub 2021 Oct 11.
PMID: 34635857 No abstract available.

Le niveau de preuve

Gradation HAS

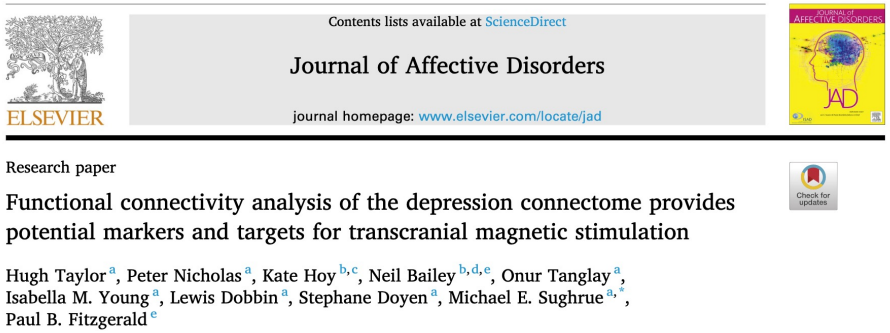
Tableau 2. Grade des recommandations

Grade des recommandations	Niveau de preuve scientifique fourni par la littérature
A Preuve scientifique établie	Niveau 1 - essais comparatifs randomisés de forte puissance ; - méta-analyse d'essais comparatifs randomisés ; - analyse de décision fondée sur des études bien menées.
B Présomption scientifique	Niveau 2 - essais comparatifs randomisés de faible puissance ; - études comparatives non randomisées bien menées ; - études de cohortes.
C Faible niveau de preuve scientifique	Niveau 3 - études cas-témoins.
	Niveau 4 - études comparatives comportant des biais importants ; - études rétrospectives ; - séries de cas ; - études épidémiologiques descriptives (transversale, longitudinale).

Le *worst-of* de la LCA

Introduction

- L'introduction pose le contexte en amenant des références
- Faut-il qu'elles soient appropriées…



Contents lists available at ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

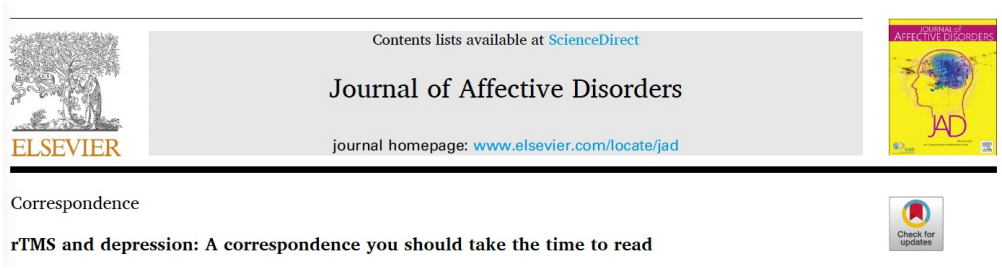
Research paper

Functional connectivity analysis of the depression connectome provides potential markers and targets for transcranial magnetic stimulation

Hugh Taylor[a], Peter Nicholas[a], Kate Hoy[b,c], Neil Bailey[b,d,e], Onur Tanglay[a], Isabella M. Young[a], Lewis Dobbin[a], Stephane Doyen[a], Michael E. Sughrue[a,*], Paul B. Fitzgerald[e]

1. Introduction

Repetitive transcranial magnetic stimulation (rTMS) is recognized as an effective intervention for patients with major depressive disorder (MDD), particularly for patients resistant to first-line treatments (Amad and Fovet, 2022). While a substantial body of evidence supports the superiority of rTMS treatment applied to the left dorsolateral prefrontal cortex (DLPFC) compared to sham treatment, only 30–60 % of patients with treatment resistant MDD show a clinically meaningful response, with an estimated 10–60 % reduction in overall symptom burden (Ma



Contents lists available at ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Correspondence

rTMS and depression: A correspondence you should take the time to read

responder status (Taylor et al., 2023). As part of their rationale, Taylor and colleagues quoted a viewpoint written by two of us (Amad and Fovet, 2022) as supporting the claim that "rTMS is recognised as an effective intervention for patients with major depressive disorder (MDD), particularly for patients resistant to first-line treatments". Ironically, our article says exactly the opposite.

Introduction

- L’introduction pose le contexte en amenant des références
- Faut-il qu’elles soient appropriées…

... The data characteristics are used to complete the modeling of the unknown environment. Currently, there are many mainstream solutions for laser SLAM, such as Grid Mapping, Karto SLAM and Lidar odometry and mapping (LOAM), SegMap algorithm, etc. [3]. The characteristic of laser SLAM is high precision, but its high cost hinders the popularization and application of laser SLAM, and its accuracy will be greatly affected in extreme weather, for instance, heavy rain and snow. ...

Reference: Slam Practice: A Review of the Literature

Mobile robot navigation based on Deep Reinforcement Learning: A brief review

Article November 2023 · 37 Reads

Journal of Physics Conference Series

Hongyi Li

View Download

SYSTEMATIC REVIEW | DECEMBER 04 2020

Slam Practice: A Review of the Literature Free

Subject Area: Pharmacology , Psychiatry and Psychology , Public Health

Benoit Schreck ; Caroline Victorri-Vigneau; Marylène Guerlais; Edouard Laforgue; Marie Grall-Bronnec

Eur Addict Res (2021) 27 (3): 161–178.

https://doi.org/10.1159/000511897 Article history

Split-Screen Views Download Share Tools

Abstract

Background: Slamming has been developing since 2011 as a new international phenomenon, mostly among men who have sex with men (MSM). It consists of intravenous drug injection before or during planned sexual activity to sustain, enhance, disinhibit, or facilitate the experience. We aimed to synthesize the available published evidence through a systematic literature review in order to precisely describe this phenomenon and to better characterize the population engaging in this practice and its specific motives. ***Methods:*** A systematic review of

Méthodologie

- Enonciation claire du design
- Garantit la reproductibilité des résultats
- Tout ce qui apparaît dans les résultats doit être énoncé dans la méthodologie

Original article

Comparison of vortioxetine versus venlafaxine XR in adults in Asia with major depressive disorder: a randomized, double-blind study

Abstract

Objective:
This randomized, double-blind 8 week study compared the efficacy and tolerability of fixed-dose treatment with vortioxetine (10 mg/day) and venlafaxine extended release (XR) (150 mg/day) in major depressive disorder (MDD) patients.

Patients and methods

Study design

This randomized, double-blind, multinational, fixed dose of vortioxetine versus an active comparator (venlafaxine XR) study included 443 randomized patients recruited from 31 psychiatric in- and outpatient specialist settings in four countries (China, South Korea, Taiwan and Thailand) from April 2012 to October 2013. The study was conducted in accordance with the principles of Good Clinical Practice[8] and the Declaration of Helsinki[9]. Local

Power and sample size calculations

Power calculations showed that with a power of ≥80% and an expected withdrawal rate of 20% a total of 410 patients should be randomized to demonstrate non-inferiority of vortioxetine to venlafaxine XR, using a 5% level of significance and a standard *t*-test from an ANCOVA. This was based on a non-inferiority comparison of the treatment groups in MADRS total score using a two-sided 95% confidence interval against a margin of +2.5 points[7], a standard deviation of 9.0 and an expected true mean difference of 0 points between treatments.

- Méthode de non-infériorité énoncée très tard
- Modification du protocole en cours d'étude / après les résultats ?

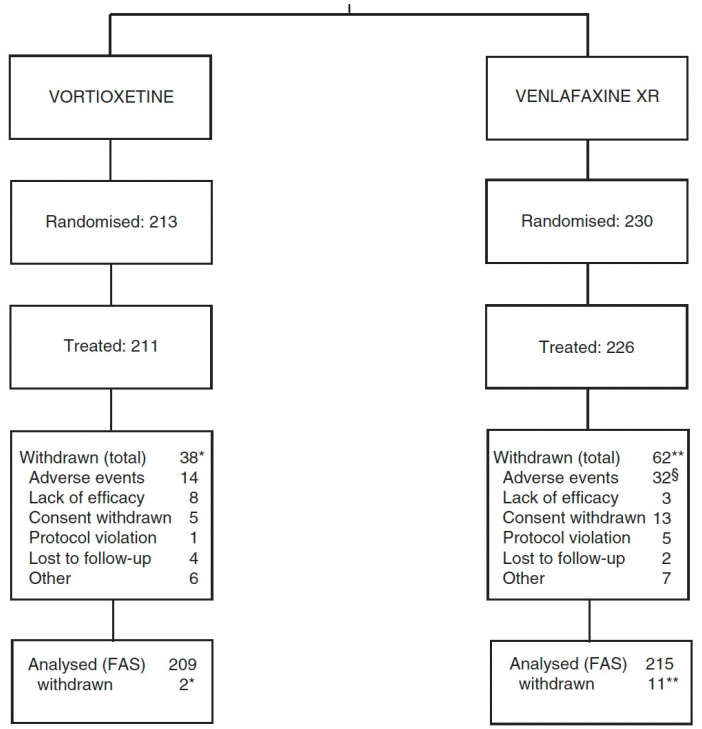
Méthodologie

- Garantit la reproductibilité des résultats
- Enonciation claire du design
- Tout ce qui apparaît dans les résultats doit être énoncé dans la méthodologie

Original article

Comparison of vortioxetine versus venlafaxine XR in adults in Asia with major depressive disorder: a randomized, double-blind study

Following a screening period of up to 7 days, eligible patients were randomized (1:1) to vortioxetine (10 mg/day) or venlafaxine XR (150 mg/day) for 8 weeks of double-blind treatment. Patients in the venlafaxine XR group received 75 mg/day for the first 4 days of treatment in accordance with the recommendations provided in the Summary of Product Characteristics for venlafaxine XR[10].



*including 2 and **11 patients withdrawn from the FAS due to no valid post-baseline MADRS assessment
§including 1 patient withdrawn after the last dose of venlafaxine XR

Episodes dépressifs majeurs

La posologie initiale recommandée de venlafaxine à libération prolongée est de 75 mg en une prise quotidienne. Les patients ne répondant pas à la posologie initiale de 75 mg/jour peuvent bénéficier d'une augmentation de posologie jusqu'à une posologie maximale de 375 mg/jour. Les augmentations posologiques peuvent être effectuées par paliers de 2

- Schémas posologiques non comparables

Méthodologie

Nalmefene in alcohol-dependent patients with a high drinking risk: Randomized controlled trial

Hisatsugu Miyata, MD, PhD,[1] Masayoshi Takahashi, PhD,[2] Yoshiyuki Murai, MSc,[2] Kana Tsuneyoshi, BE,[3] Takako Hayashi, BSc,[4*] Didier Meulien, MD, MSc,[5] Per Sørensen, MSc[6] and Susumu Higuchi, MD, PhD[7]

Aims: Reducing alcohol consumption is one treatment approach for alcohol-dependent patients. This study compared nalmefene 20 mg and 10 mg with placebo, combined with psychosocial support, in alcohol-dependent Japanese patients with a high or very high drinking risk level (DRL).

Methods: This was a multicenter, randomized, double-blind, phase 3 study conducted in alcohol-dependent patients with a high or very high DRL. Patients were randomized to 24 weeks of treatment with as-needed nalmefene 20 mg, 10 mg, or placebo with psychosocial support. The primary endpoint was change in heavy drinking days (HDD) from baseline to week 12. A key secondary endpoint was the change in total alcohol consumption (TAC) from baseline to week 12.

Results: At week 12, 234, 206, and 154 patients who received placebo, nalmefene 20 mg, and 10 mg were included in the primary endpoint analysis. Compared with placebo,

Cochrane Database of Systematic Reviews | Review - Intervention

Managed alcohol as a harm reduction intervention for alcohol addiction in populations at high risk for substance abuse

Wendy Muckle, Jamie Muckle, Vivian Welch, Peter Tugwell Authors' declarations of interest

Version published: 12 December 2012 Version history

https://doi.org/10.1002/14651858.CD006747.pub2

Authors' conclusions

The lack of evidence does not allow for a conclusion regarding the efficacy of MAP on their own, or as compared to brief intervention, moderate drinking, no intervention or 12-step variants. It is the review authors' opinion that it is likely to be the

- Critère non validé
- Contre placebo alors que des traitement de référence existent

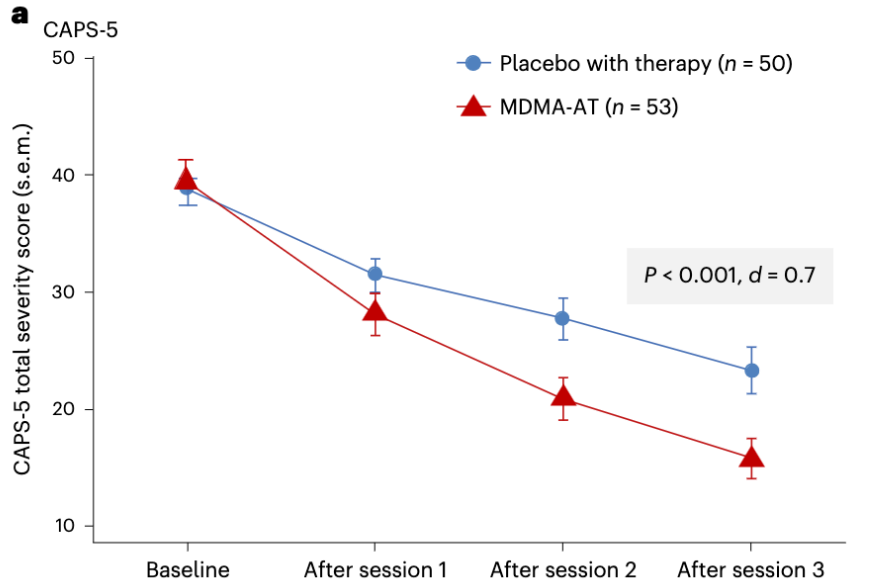
Méthodologie

nature medicine

Article

https://doi.org/10.1038/s41591-023-02565-4

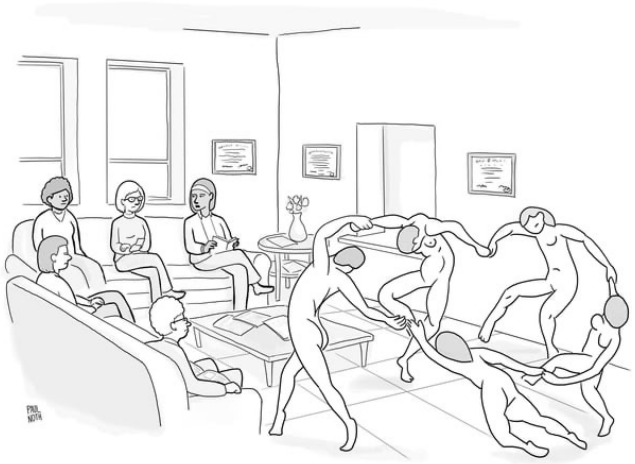
MDMA-assisted therapy for moderate to severe PTSD: a randomized, placebo-controlled phase 3 trial



Exploratory outcomes

In the MDMA-AT group, 45 of 52 (86.5%) participants were responders with a clinically meaningful improvement at 18 weeks after baseline, defined as a ≥10-point reduction in CAPS-5 total severity score, versus 29 of 42 (69.0%) in the placebo with therapy group (Fig. 3). By study end, 37 of 52 (71.2%) participants in the MDMA-AT group no longer met DSM-5 criteria for PTSD versus 20 of 42 (47.6%) participants in the placebo with therapy group. Furthermore, 24 of 52 (46.2%) participants in the MDMA-AT group and nine of 42 (21.4%) participants in the placebo with therapy group met remission criteria (Fig. 3). The net number of participants needed to treat for each responder analysis group was as follows: responder, six; non-responder, six; loss of diagnosis, four; remission, four.

A blinding survey conducted at study termination showed that 33 of 44 (75.0%) participants in the placebo with therapy group were certain or thought they received placebo, whereas nine of 44 (20.5%) participants inaccurately thought that they received MDMA, and two of 44 (4.5%) participants could not tell. In the MDMA-AT group, 49 of 52 (94.2%) participants were certain or thought that they received MDMA; one of 52 (1.9%) participants inaccurately thought that they received



"So I'm guessing we're in the placebo group."

- Placebo non adapté
- Perte de l'insu

Méthodologie

Esketamine Nasal Spray versus Psychoactive Comparator for Rapid Reduction of Depressive Symptoms in Adolescents with Major Depressive Disorder at Imminent Suicide Risk

Colette Kosik-Gonzalez, MA[1]*, Dong Jing Fu, MD, PhD[1], Li (Nancy) Chen, PhD[1], Rosanne Lane, MAS[1], Wayne C. Drevets, MD[2], Carla M. Canuso, MD[1]

Janssen Research and Development, LLC, [1]Titusville, NJ, [2]San Diego, CA

Table 2: CDRS-R: Change From Baseline to 24 Hours Post-First Dose

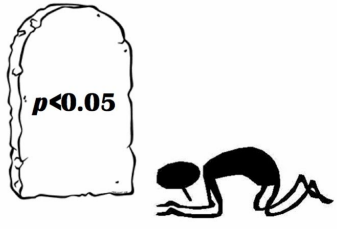
	Oral Midazolam + SOC	Esketamine 28 mg + SOC	Esketamine 56 mg + SOC	Esketamine 84 mg + SOC	Esketamine 56 + 84 mg
Baseline					
N	63	28	31	23	54
Mean (SD)	76.1 (10.65)	77.6 (8.08)	76.4 (9.08)	75.3 (11.78)	75.9 (10.23)
Change from Baseline to 24 hours post-first dose					
N	63	28	31	23	54
Mean (SD)	-26.2 (16.72)	-29.6 (18.15)	-31.8 (12.92)	-30.3 (17.48)	-31.2 (14.90)
ANCOVA analysis[a]					
Diff. of LS means[b] (SE)		-2.4 (3.35)	-5.9 (3.23)	-5.7 (3.65)	-5.8 (2.74)
95% CI on difference		-9.08, 4.19	-12.25, 0.53	-12.91, 1.55	-11.19, -0.35
2-sided p-value			0.072	0.123	0.037

CDRS-R = Children's Depression Rating Scale-Revised; CI = confidence interval, LS = least squares, SD = standard deviation, SE = standard error; SOC = standard-of-care

a. Based on analysis of covariance (ANCOVA) model with treatment (midazolam, esketamine 28 mg, 56 mg, and 84 mg) and analysis center as factors and baseline value as a covariate.

b. Esketamine + SOC minus psychoactive comparator + SOC.

Notes: CDRS-R total score ranges from 17 to 113; a higher score indicates a more severe condition. Negative change in score indicates improvement. Negative difference favors esketamine.

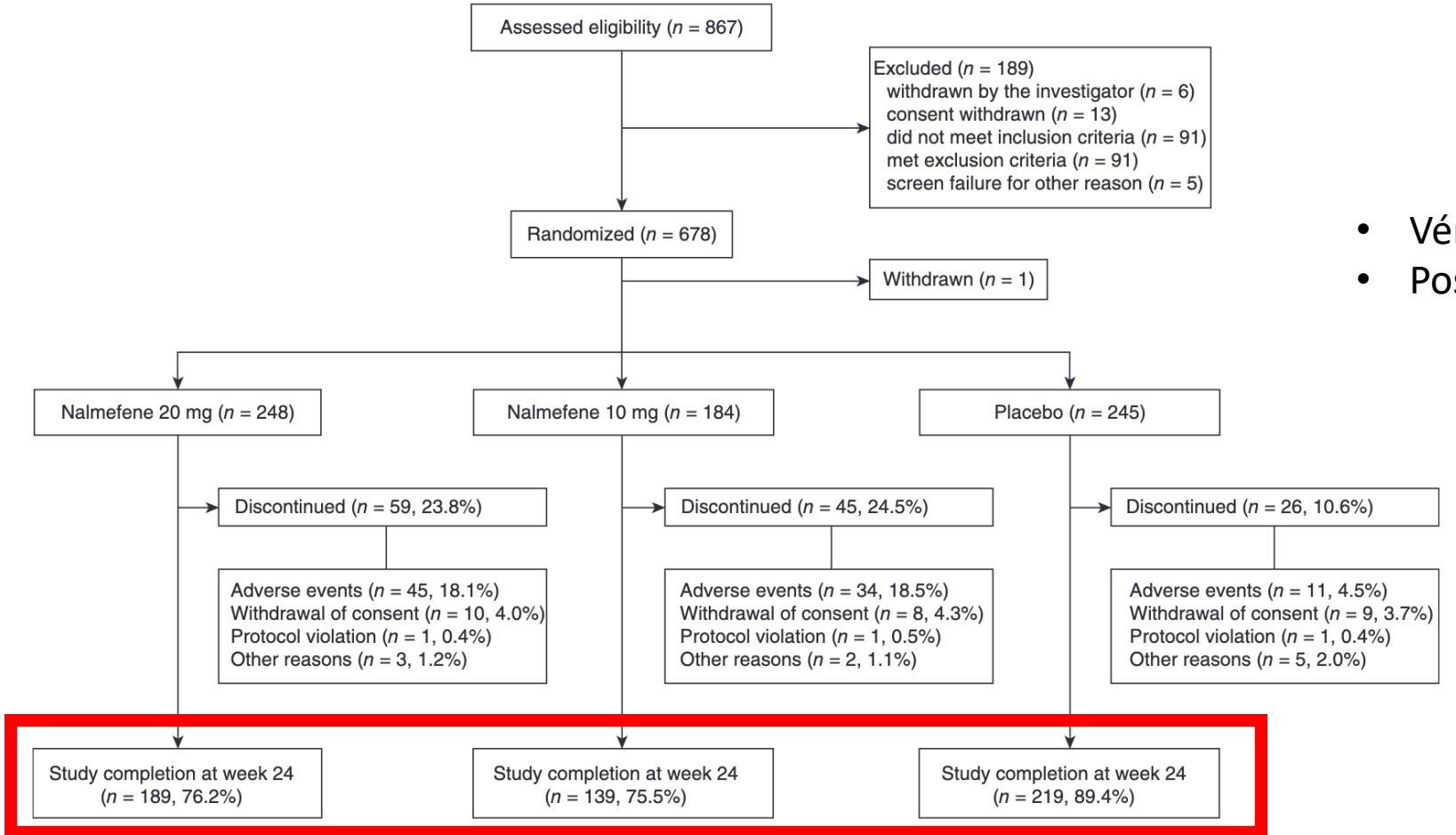


- Multiplier les tests pour qu'un résultat soit significatif

Résultats

Nalmefene in alcohol-dependent patients with a high drinking risk: Randomized controlled trial

Hisatsugu Miyata, MD, PhD,[1] Masayoshi Takahashi, PhD,[2] Yoshiyuki Murai, MSc,[2] Kana Tsuneyoshi, BE,[3] Takako Hayashi, BSc,[4]* Didier Meulien, MD, MSc,[5] Per Sørensen, MSc[6] and Susumu Higuchi, MD, PhD[7]



- Vérifier la comparabilité des groupes
- Possible biais d'attrition

Résultats

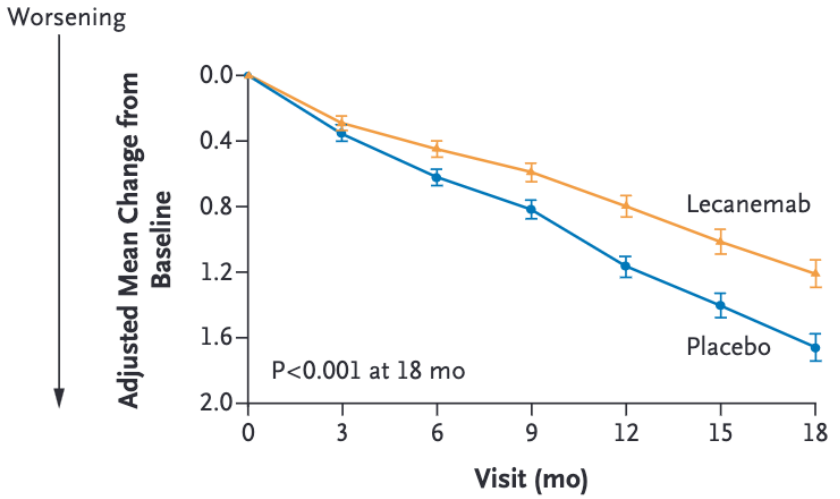
- Choix de la représentation graphique

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 5, 2023 VOL. 388 NO. 1

Lecanemab in Early Alzheimer's Disease

C.H. van Dyck, C.J. Swanson, P. Aisen, R.J. Bateman, C. Chen, M. Gee, M. Kanekiyo, D. Li, L. Reyderman, S. Cohen, L. Froelich, S. Katayama, M. Sabbagh, B. Vellas, D. Watson, S. Dhadda, M. Irizarry, L.D. Kramer, and T. Iwatsubo



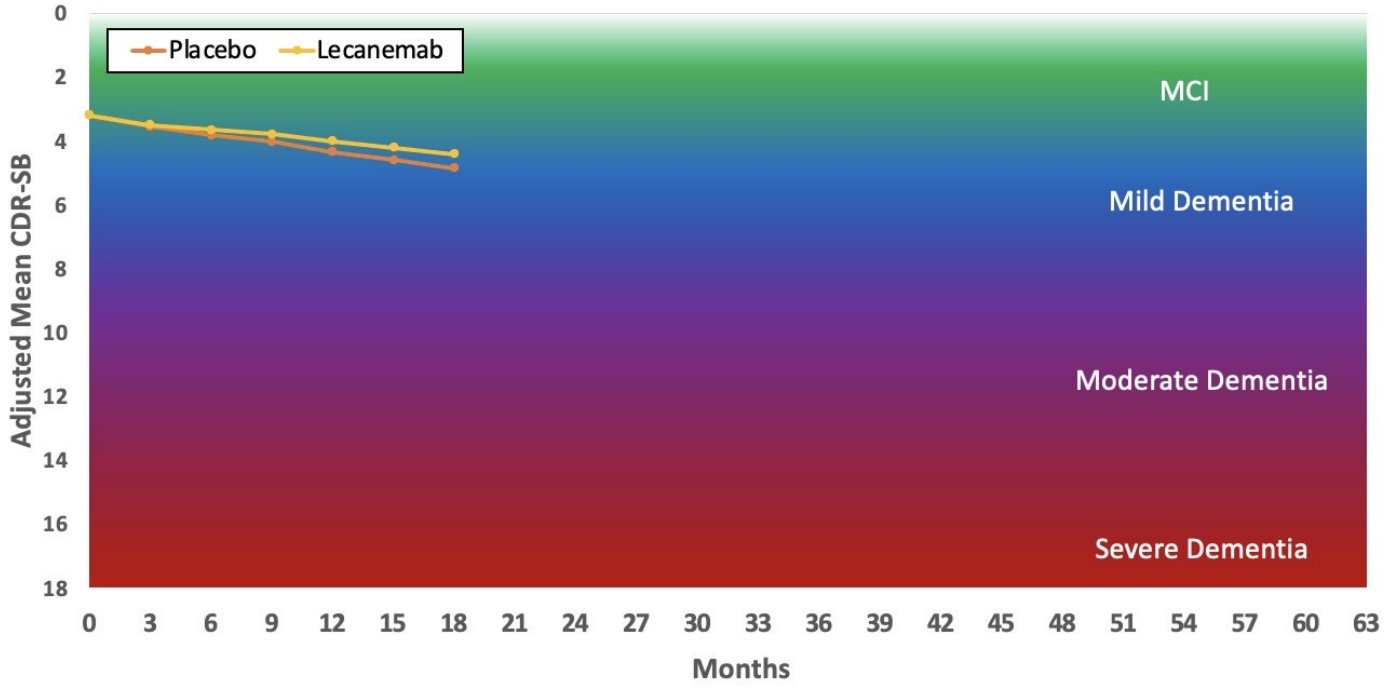
No. of Participants

Lecanemab	859	824	798	779	765	738	714
Placebo	875	849	828	813	779	767	757

METHODS

We conducted an 18-month, multicenter, double-blind, phase 3 trial involving persons 50 to 90 years of age with early Alzheimer's disease (mild cognitive impairment or mild dementia due to Alzheimer's disease) with evidence of amyloid on positron-

Change in Clinical Dementia Rating–Sum of Boxes (CDR-SB) Score



Résultats

Original article

Comparison of vortioxetine versus venlafaxine XR in adults in Asia with major depressive disorder: a randomized, double-blind study

Analysis of the primary efficacy endpoint

The primary analysis tested for non-inferiority of vortioxetine and venlafaxine XR using the change from baseline in MADRS total score at Week 8 based on the FAS.

Table 3. Treatment-emergent adverse events (TEAEs) with an incidence of ≥5% in either treatment group in the 8 week treatment period (APTS).

Preferred Term	Vortioxetine 10 mg *n* (%) (*n* = 211)	Venlafaxine XR 150 mg *n* (%) (*n* = 226)
Patients with TEAEs	125 (59.2)	153 (67.7)
Nausea	51 (24.2)	53 (23.5)
Dizziness	17 (8.1)	29 (12.8)
Headache	17 (8.1)	15 (6.6)
Dry mouth	12 (5.7)	24 (10.6)
Accidental overdose†	10 (4.7)	12 (5.3)
Decreased appetite	10 (4.7)	23 (10.2)*
Constipation	9 (4.3)	18 (8.0)
Insomnia	5 (2.4)	16 (7.1)*

APTS: all-patients-treated set.
†Defined as a dose of study medication that exceeds the dose prescribed.
*$p < 0.05$ (Fisher's exact test).

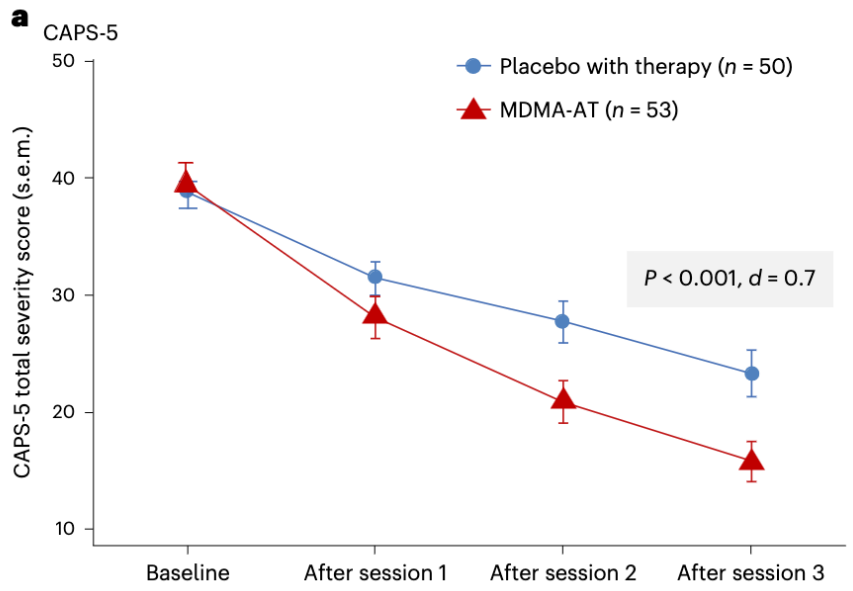
- Analyse statistique décrite uniquement pour le CJP
- N'apparaît que lorsqu'en faveur du traitement étudié

Discussion

nature medicine

Article https://doi.org/10.1038/s41591-023-02565-4

MDMA-assisted therapy for moderate to severe PTSD: a randomized, placebo-controlled phase 3 trial



Exploratory outcomes

In the MDMA-AT group, 45 of 52 (86.5%) participants were responders with a clinically meaningful improvement at 18 weeks after baseline, defined as a ≥10-point reduction in CAPS-5 total severity score, versus 29 of 42 (69.0%) in the placebo with therapy group (Fig. 3). By study end, 37 of 52 (71.2%) participants in the MDMA-AT group no longer met DSM-5 criteria for PTSD versus 20 of 42 (47.6%) participants in the placebo with therapy group. Furthermore, 24 of 52 (46.2%) participants in the MDMA-AT group and nine of 42 (21.4%) participants in the placebo with therapy group met remission criteria (Fig. 3). The net number of participants needed to treat for each responder analysis group was as follows: responder, six; non-responder, six; loss of diagnosis, four; remission, four.

A blinding survey conducted at study termination showed that 33 of 44 (75.0%) participants in the placebo with therapy group were certain or thought they received placebo, whereas nine of 44 (20.5%) participants inaccurately thought that they received MDMA, and two of 44 (4.5%) participants could not tell. In the MDMA-AT group, 49 of 52 (94.2%) participants were certain or thought that they received MDMA; one of 52 (1.9%) participants inaccurately thought that they received

(1) the groups did not separate after the first experimental session; (2) placebo with therapy dropouts did not uniformly occur after the first experimental session; and (3) blinding survey data (Supplementary Table 6) showed that not all participants correctly identified the treatment that they received.

- Non prise en compte du biais
- Formulation avantageuse

Discussion

ORIGINAL RESEARCH

Esketamine Nasal Spray for Rapid Reduction of Major Depressive Disorder Symptoms in Patients Who Have Active Suicidal Ideation With Intent: Double-Blind, Randomized Study (ASPIRE I)

Dong-Jing Fu, MD, PhD[a,*]; Dawn F. Ionescu, MD[b]; Xiang Li, PhD[c]; Rosanne Lane, MAS[c]; Pilar Lim, PhD[c]; Gerard Sanacora, MD, PhD[d]; David Hough, MD[a]; Husseini Manji, MD[a]; Wayne C. Drevets, MD[b]; and Carla M. Canuso, MD[a]

Severity of suicidality. At the 24-hour endpoint, patients in both treatment groups experienced improvement in the severity of their suicidality as measured by CGI-SS-r, though there was no statistically significant difference between treatment groups (2-sided $P = .107$). The Hodges-Lehmann estimate of the treatment difference (95% CI) was 0.0 (−1.00 to 0.00).

CONCLUSIONS

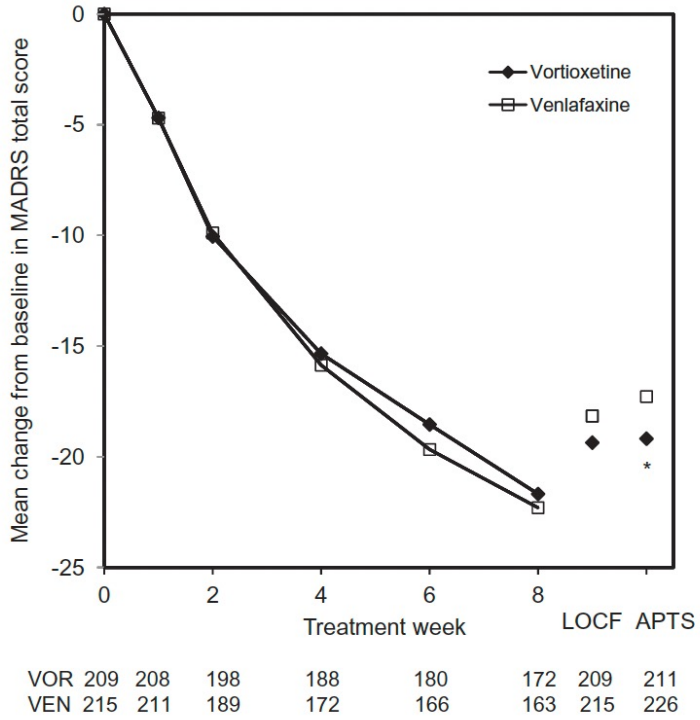
Taken together, our findings suggest esketamine nasal spray may address the unmet need for a rapid-acting antidepressant in patients with MDD and active suicidal ideation with intent, for which there is no approved pharmacologic treatment.

→ Extrapolabilité discutable

Discussion

Original article

Comparison of vortioxetine versus venlafaxine XR in adults in Asia with major depressive disorder: a randomized, double-blind study



Conclusion

In conclusion, vortioxetine in a dose of 10 mg/day was at least as effective as venlafaxine XR 150 mg/day in treating MDD over 8 weeks, with a numerical advantage on the MADRS of 1.2 points. This advantage was statistically significant in the post-hoc analysis of the APTS population, and vortioxetine was better tolerated. The results of this study further support the established efficacy of vortioxetine and also confirm the safety and good tolerability of vortioxetine seen in the pivotal clinical studies.

Spin de conclusion → insiste sur un critère secondaire d'une analyse post-hoc

Conflits d’intérêts

- Doivent êtres déclarés
- Accessibles sur transparence.sante.gouv.fr

• NANTES

Catégorie : Professionnel de santé

Profession : Médecin

Semestre: Sélectionner un semestre | Type de déclaration: Sélectionner un type de décl... | Commune d'exercice: Sélectionner une commune ... | Entreprise: Sélectionner une entreprise

Entreprises	Déclaration	Date	Objet convention / Nature avantage	Montant	Demande de rectification en cours	Détails
JANSSEN-CILAG	avantage	7 novembre 2016	Autre	44€	Non	Détails
JANSSEN-CILAG	avantage	7 novembre 2016	Autre	158€	Non	Détails
GILEAD SCIENCES	avantage	2 mai 2019	Autre	24€	Non	Détails
Laboratoires ETHYPHARM	convention	30 septembre 2019	Contrat de participation à une manifestation	220€	Non	Détails
Laboratoires ETHYPHARM	avantage	7 décembre 2019	Autre	606€	Non	Détails

Conflits d'intérêts

THÉRAPEUTIQUE

Bénéfices de la réduction de la consommation d'alcool : comment le faire avec nalméfène

Benefits in reducing alcohol consumption: How nalmefene can help

P. Bendimerad[a,*], L. Blecha[b]

Conclusion

Au total, trois éléments clés peuvent justifier la mise en avant de la proposition de réduction de la consommation avec le nalméfène. D'abord, les preuves scientifiques montrent un bénéfice en termes de réduction des risques et des dommages liés à la forte consommation d'alcool. Ensuite, les effets concrets et immédiats sur la motivation des patients en leur proposant des stratégies congruentes avec leurs objectifs personnels, ce qui favoriserait une meilleure adhérence aux soins. Enfin, la mise en place d'une approche combinée associant la prise d'une nouvelle molécule, le nalméfène, avant les situations évaluées par le patient comme étant à risque de consommation et un soutien psychosocial (BRENDA) permet d'améliorer les chances de succès.

Déclaration d'intérêts

Les auteurs n'ont pas transmis de déclaration de conflits d'intérêts.

LETTRES À LA RÉDACTION

Qui peut réellement bénéficier du nalméfène ? Ce que nous disent les évaluations indépendantes

Conflits d'intérêts

Bendimerad et Blecha n'ont pas fourni leur déclaration d'intérêt. Cette situation est une atteinte aux pratiques internationales relatives aux conflits d'intérêts et à la législation française. Sur la base de données publiques transparence santé du Gouvernement français (transparence.sante.gouv.fr), on relève pourtant, concernant le Dr Bendimerad, 20 avantages reçus des laboratoires Lundbeck et 18 conventions signées avec ce même laboratoire pour la période allant de janvier 2013 à décembre 2014.

Des questions ?