The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

FREE PREVIEW

Trial of Psilocybin versus Escitalopram for Depression

Robin Carhart-Harris, Ph.D., Bruna Giribaldi, B.Sc., Rosalind Watts, D.Clin.Psy., Michelle Baker-Jones, B.A., Ashleigh Murphy-Beiner, M.Sc., Roberta Murphy, M.D., Jonny Martell, M.D., Allan Blemings, M.Sc., David Erritzoe, M.D., and David J. Nutt, M.D.et al.

April 15, 2021
N Engl J Med 2021; 384:1402-1411
DOI: 10.1056/NEJMoa2032994

Related Articles

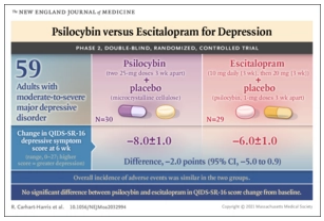
Abstract

BACKGROUND Psilocybin may have antidepressant properties, but direct comparisons between psilocybin and established treatments for depression are lacking.

METHODS In a phase 2, double-blind, randomized, controlled trial involving patients with long-standing, moderate-to-severe major depressive disorder, we compared psilocybin with escitalopram, a selective serotonin-reuptake inhibitor, over a 6-week period. Patients were assigned in a 1:1 ratio to receive two separate doses of 25 mg of psilocybin 3 weeks apart plus 6 weeks of daily placebo (psilocybin group) or two separate doses of 1 mg of psilocybin 3 weeks apart plus 6 weeks of daily oral escitalopram (escitalopram group); all the patients received psychological support. The primary outcome was the change from baseline in the score on the 16-item Quick Inventory of Depressive Symptomatology–Self-Report (QIDS-SR-16; scores range from 0 to 27, with higher scores indicating greater depression) at week 6. There were 16 secondary outcomes, including QIDS-SR-16 response (defined as a reduction in score of >50%) and QIDS-SR-16 remission (defined as a score of ≤5) at week 6.

occurred in 70% of the patients in the psilocybin group and in 48% of those in the escitalopram group, for a between-group difference of 22 percentage points (95% CI, −3 to 48); QIDS-SR-16 remission occurred in 57% and 28%, respectively, for a between-group difference of 28 percentage points (95% CI, 2 to 54). Other secondary outcomes generally favored psilocybin over escitalopram, but the analyses were not corrected for multiple comparisons. The incidence of adverse events was similar in the trial groups.

CONCLUSIONS On the basis of the change in depression scores on the QIDS-SR-16 at week 6, this trial did not show a significant difference in antidepressant effects between psilocybin and escitalopram in a selected group of patients. Secondary outcomes generally favored psilocybin over escitalopram, but the analyses of these outcomes lacked correction for multiple comparisons. Larger and longer trials are required to compare psilocybin with established antidepressants. (Funded by the Alexander Mosley Charitable Trust and Imperial College London's Centre for Psychedelic Research; ClinicalTrials.gov number, NCT03429075.)



VISUAL ABSTRACT

Psilocybin versus Escitalopram for Depression

FREE

Continue reading this article

SELECT AN OPTION BELOW:

Create your account to get 2 free subscriber-only articles each month.

GET FREE ACCESS NOW

SUBSCRIBE FOR FULL ACCESS →

Already have an account?

SIGN IN

Print subscriber?

Funding and Disclosures

Supported by a private donation from the Alexander Mosley Charitable Trust and by the founding partners of Imperial College London's Centre for Psychedelic Research. Infrastructure support was provided by the NIHR Imperial Biomedical Research Centre and the NIHR Imperial Clinical Research Facility.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

Dr. Carhart-Harris reports receiving consulting fees from COMPASS Pathways, Entheon Biomedical, Mydecine, Synthesis Institute, Tryp Therapeutics, and Usona Institute; Dr. Giribaldi, receiving consulting fees from SmallPharma; Dr. Watts, receiving advisory board fees from Usona Institute and being employed by Synthesis Institute; Dr. Baker-Jones, receiving fees for facilitating meetings from Synthesis Institute; Dr. Erritzoe, receiving consulting fees from Field Trip and Mydecine; and Dr. Nutt, receiving consulting fees from Awakn, H. Lundbeck, and Psyched Wellness, advisory board fees from COMPASS Pathways, and lecture fees from Takeda Medical Research Foundation and owning stock in Alcarelle. No other potential conflict of interest relevant to this article was reported.

Dr. Carhart-Harris, Ms. Giribaldi, and Dr. Watts contributed equally to this article.

The views expressed are those of the authors and not necessarily those of the National Health Service, the National Institute for Health Research (NIHR), or the Department of Health and Social Care.

A data sharing statement provided by the authors is available with the full text of this article at NEJM.org.

We thank Ms. Renee Harvey, Dr. Graham Campbell, Dr. Benjamin Waterhouse, Dr. Frederico Magalhães, Mr. James Close, Dr. Leor Roseman, Ms. Hilary Platt, Mr. Gregory Donaldson, and Dr. Chris Timmermann for their voluntary assistant guide roles; Dr. Meg Spriggs and Ms. Laura Kärtner for their support with data collection; Dr. Louise Paterson and Dr. Robin Tyacke for their assistance with randomization, blinding, and drug accountability; Ms. Ghazel Mukhtar for her assistance with administrative tasks; and Dr. Tim Read for his clinical supervision and guidance.

Author Affiliations

From the Centre for Psychedelic Research, Department of Brain Sciences, Faculty of Medicine, Imperial College