Online intervention to reduce depressive symptoms in multiple sclerosis: an international multicenter randomized controlled phase III trial


Introduction: Major depressive disorder (MDD) is one of the most common comorbidities in multiple sclerosis (MS) and is associated with lower quality of life, faster disease progression, higher morbidity and risk for earlier all-cause mortality. However, despite its clinical relevance, treatment options for MS-associated depression remain limited.

Objectives and aims: To evaluate the effectiveness and safety of a computerized depression management program in MS.

Methods: We conducted a three arm, parallel group, randomized, controlled phase III trial of an MS-specific, internet-based, cognitive behavioral therapy (iCBT) program to reduce depressive symptoms. Patients with neurologist confirmed diagnosis of MS and self-reported depressive symptoms were randomized 1:1:1 (no stratification, no blocking) to one of two versions of iCBT (stand alone or therapist-guided) alongside treatment as usual (TAU) or a control condition, in which participants received TAU and were offered access to the iCBT program after 6 months. The predefined primary endpoint was severity of depressive symptoms as measured by the Beck Depression Inventory – II (BDI-II) at week 12 after randomization.

Results: Between June 1, 2017 and November 30, 2020, n=279 participants were enrolled. Drop-out rate at week 12 was 17.9%. Both versions of the iCBT program significantly reduced depressive symptoms at week 12 compared to the control group (BDI-II between group mean difference vs control: stand alone iCBT 6.32 points [95% CI: 3.37; 9.27]; p < .0001; guided iCBT: 5.80 points [95% CI: 2.71; 8.88]; p < .0001). No occurrence of suicidality, the predefined safety measure, was observed during the trial. Clinically relevant worsening of depressive symptoms was observed in n=3 participants in the control group, n=1 in stand alone iCBT and none in guided iCBT.

Conclusions: This trial provides confirmatory evidence for safety and effectiveness of an MS-specific iCBT tool to reduce depressive symptoms in MS.

Disclosure: This trial provides confirmatory evidence for safety and effectiveness of an MS-specific iCBT tool to reduce depressive symptoms in MS. SMG reports honoraria from Hexal and Celgene and research grants from Biogen. TF reports personnel fees for consultancies (including data monitoring committees and advisory boards) from Bayer, BMS, CSL Behring, Enanta, Fresenius Kabi, Galapagos, Johnson & Johnson, LivaNova, Minoryx, Novartis, Roche and Vifor. BM is an employee of GAIA Group, developer, owner and distributor of digital health interventions including Deprexis and the MS-specific iCBT Amiria. RMM: nothing to disclose. JH: nothing to disclose. SA: nothing to disclose. JBS: nothing to disclose. AL: nothing to disclose. LI: nothing to disclose. KR: nothing to disclose. DS: nothing to disclose. HP: nothing to disclose. SGL: nothing to disclose. JSC: nothing to disclose. JHue: nothing to disclose. CAFR: nothing to disclose. MC: nothing to disclose. EG: nothing to disclose. SL: nothing to disclose. JP: nothing to disclose. GP: nothing to disclose. CR: nothing to disclose. SSZ: nothing to disclose. AMK: nothing to disclose. IKP has received honoraria for speaking at scientific meetings, serving at scientific advisory boards and consulting activities from Adamas Pharma, Almirall, Bayer Pharma, BMS, Biogen, Celgene, Desitin, Janssen, Merck, Novartis, Roche, Sanofi-Genzyme and Teva. She has received research support from the German MS Society, Celgene, Novartis, Roche, and Teva. FP reports honoraria from Alexion, Bayer, Biogen, Merck Serono, Sanofi Genzyme, Novartis, Viela Bio, Roche, UCB, Mitsubishi Tanabe and Celgene and research grants from Biogen, Genzyme, Merck, Serono, Novartis, Bayer, Roche, Parexel and Almirall. NLS receives research grants from Biogen, National MS Center, PCORI, NIH JB: nothing to disclose. PAA: nothing to disclose. CH received research grants from Merck, Novartis, Roche.