12 Months Sustained Remission from Depression using Personalized Continuation Therapy with SAINT®

Katy H Stimpson[1], TJ Ford[1], Adi Maron-Katz[1], Michael Feyder[1], Danielle D DeSouza[2], David Carreon[2], Eleanor J Cole[1], Brandon S Bentzley[1]

[1]Magnus Medical, Inc., Burlingame, CA
[2]Acacia Research Center, Acacia Clinics, Sunnyvale, CA

Objective

Evaluate an optimized SAINT continuation treatment paradigm for treatment resistant depression (TRD) patients who initially remitted with SAINT with the goal of maintaining remission.

Synopsis

Throughout 12 months of personalized continuation therapy (PCT) as indicated by a proprietary algorithm, the average MADRS score was 7.07 (SD = 7.1), indicating sustained remission over the monitored period.

Background

TRD is a chronic lifelong relapsing-remitting disease. One of the challenging issues for treating TRD is the long-term efficacy of pharmacological and non-pharmacological treatments[1]. TRD is associated with disproportionate healthcare costs and unemployment, suggesting potentially large economic and societal gains with effective management, beyond its effects on quality of life and wellbeing[2].

SAINT has been demonstrated to be a safe, effective and rapid-acting treatment for TRD in both open label and randomized, controlled settings; however, there is currently no established continuation treatment paradigm for maintaining remission following the initial treatment course[3–5].

Methods

This study was conducted at Acacia Clinics in Sunnyvale, CA from February 2022 to December 2023. Participants were enrolled into this trial of PCT with SAINT if they met the following criteria.

Inclusion:
- Ages 18-80
- Primary MDD diagnosis
- Currently experiencing non-psychotic major depressive episode
- ≥1 failed adequate medication trial in current episode

Exclusion:
- Contraindications to TMS
  - History of seizure disorder
  - Neurological disorders
- Contraindications to fMRI
- Pregnancy, planned pregnancy, or breastfeeding
- Physician discretion

Prior to treatment, all participants underwent structural and functional MRI for individualized left DLPFC target generation.

The SAINT protocol was administered according to previously published parameters. All participants were treated using the MagVenture MagPro XP system (MagVenture A/S, Denmark) with a MagVenture Cool-B65 coil. A Localite neuronavigation system (Localite GmbH Sankt Augustin, Germany) was used to locate and position the functional connectivity MRI generated target for each participant. Stimulation was delivered at a minimum of 90% resting motor threshold, adjusted for cortical depth. Each treatment day consisted of a total of 1800 iTBS pulses delivered over 10 sessions with an intersession interval of 50 minutes. The acute treatment course consisted of 5 consecutive days of SAINT.

Additional courses of SAINT were offered when participants were flagged by a proprietary algorithm that they were trending toward a relapse into a new depressive episode.

Participants were contacted, a MADRS was administered to confirm an increase in depressive symptoms and participants were scheduled for treatment with SAINT. SAINT offered as PCT was identical to the initial treatment parameters with the exception that participants were treated for a minimum of 1 day and up to 5 days (full day increments), until remission occurred as measured by the MADRS.

The primary outcome measure, the clinician rated MADRS with a recall period of 7 days, was administered by a third party assessor at baseline, 5 days post acute treatment and every 2 weeks for the 12 month follow-up period.

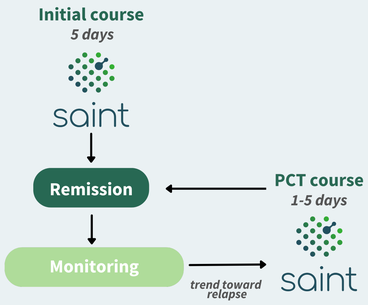

Figure 1

The diagram above describes the Personalized Continuation Therapy schema.

Results

Twenty-one participants with a mean baseline MADRS score of 28.6 (SD = 7.3) were enrolled in the study, entered remission the week following treatment with SAINT and adhered to the protocol. All 21 participants who received PCT as indicated by the proprietary algorithm returned to a state of remission.

Over the 12 months of PCT with SAINT, 19/21 participants required additional SAINT treatment to maintain remission. A mean of 14.9 (SD=13.69) treatment days of SAINT per participant were administered to maintain remission with 95% CI [9.6, 21.0].

A total of 135 treatment courses were administered over the 12-month period. On average, participants required 2.3 days (SD = 1.42) of SAINT per PCT course with 95% CI [1.8, 2.9]. The number of treatment days required for courses of PCT ranged from 1 to 5 days, with 36.3% of courses consisting of 1 day, 32.6% 2 days, 9.6% 3 days, 5.9% 4 days and 15.6% 5 days.

Over the 12 month period in which PCT with SAINT was administered, the percentage of time in which all 21 participants were in remission was an average of 85.7% (SD=19.7) and in response for an average of 95.3% (SD=9.4) as measured by biweekly MADRS scores.

Average PCT MADRS is 7.07

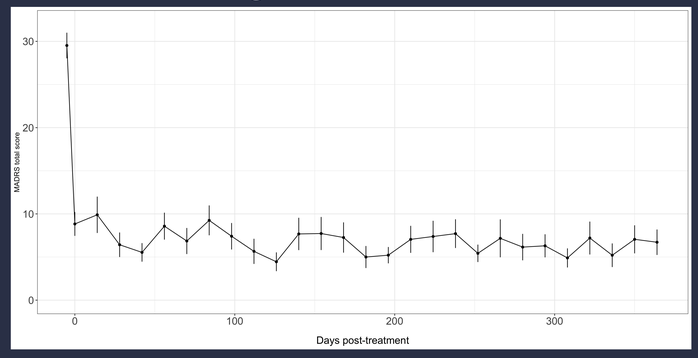

Figure 2

Graph above illustrates the average clinician-rated MADRS score over 12 months while participants received Personalized Continuation Therapy with SAINT. Participants' average MADRS score over the 12 months was 7.07 (SD: 7.1). Error bars show standard error. n=21 subjects

85% of time in remission during PCT

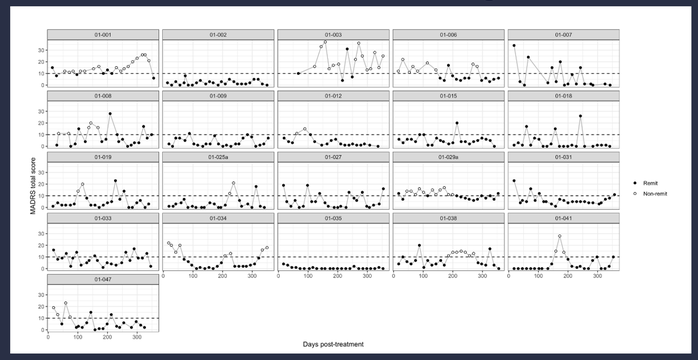

Figure 3

Graph above illustrates the percent of time spent in remission per individual participant. Time not in remission defined as two consecutive follow-up MADRS scores > 10. Black circles indicate MADRS scores in remission. White circles indicate MADRS scores not in remission. Dashed line indicates remission criteria (MADRS ≤ 10). n=21 subjects

95% of time in response during PCT

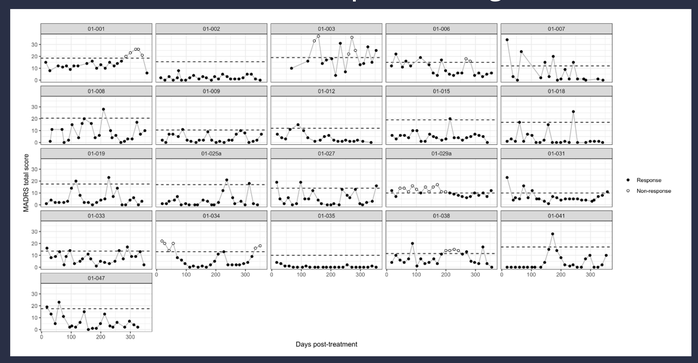

Figure 4

Graph above illustrates the percent of time spent in response per individual participant. Time not in response defined as two consecutive follow-up MADRS scores > 50% of a subject's baseline MADRS total score. Black circles indicate MADRS scores in response. White circles indicate MADRS scores not in response. Dashed line indicates response criteria (MADRS score ≤ 50% of a subject's baseline MADRS score). n=21 subjects

No tachyphylaxis observed over 12 months

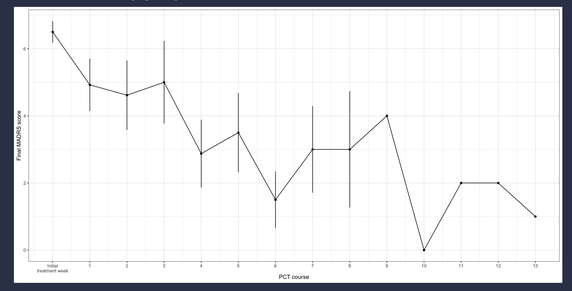

Figure 5

Graph above illustrates the average MADRS score following each course of PCT. Error bars represent +/- SE. n=13 subjects

68.9% of PCT courses ≤ 2 days

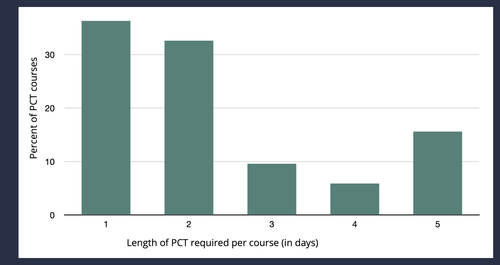

Figure 6

Graph above illustrates the distribution of PCT course lengths across all participants. On average, participants required 2.3 days (SD = 1.42) of SAINT per PCT course with 95% CI [1.8, 2.9]. n=21 subjects

Discussion

This study demonstrates that following an initial remission with an acute course of SAINT, continuation therapy given in response to a trend toward relapse is effective at maintaining participants in a non-depressed state over a 12 month period.

Two-thirds of PCT courses administered during this trial required only 1-2 days of treatment per course to sustain participants in a state of remission.

Further, no tachyphylaxis was observed with MADRS scores remaining consistently below MADRS scores recorded following the initial treatment course, suggesting that the fMRI-generated target is durable for at least 12 months of treatment. This also suggests that there are not diminishing responses to SAINT longitudinally.

To the best of our knowledge, this is the first study published showing feasibility of monitoring and effectively maintaining patients in remission from depression following a successful course of rTMS.

Importantly, PCT with SAINT was found to be a safe approach with no adverse cognitive or other serious adverse effects.

References

1. McIntyre RS, Alsuwaidan M, Baune BT, et al. Treatment□resistant depression: definition, prevalence, detection, management, and investigational interventions. World Psychiatry. 2023;22(3):394-412. doi:10.1002/wps.21120
2. Zhdanava M, Pilon D, Ghelerter I, et al. The Prevalence and National Burden of Treatment-Resistant Depression and Major Depressive Disorder in the United States. J Clin Psychiatry. 2021;82(2). doi:10.4088/JCP.20m13699
3. Williams NR, Sudheimer KD, Bentzley BS, et al. High-dose spaced theta-burst TMS as a rapid-acting antidepressant in highly refractory depression. Brain J Neurol. 2018;141(3):e18. doi:10.1093/brain/awx379
4. Cole EJ, Stimpson KH, Bentzley BS, et al. Stanford Accelerated Intelligent Neuromodulation Therapy for Treatment-Resistant Depression. Am J Psychiatry. 2020;177(8):716-726. doi:10.1176/appi.ajp.2019.19070720
5. Cole EJ, Phillips AL, Bentzley BS, et al. Stanford Neuromodulation Therapy (SNT): A Double-Blind Randomized Controlled Trial. Am J Psychiatry. 2022;179(2):132-141. doi:10.1176/appi.ajp.2021.20101429

Acknowledgements

Thank you greatly to all who were involved in this study. Specific acknowledgements for their contributions go to Nathan Meng MD, Erica Nakano, Vivian Hoang, Peter Sedaros, and Clive Veerapal.