Supplementary Materials

ECT Procedures

TABLE S1. Seizure Threshold Titration Schedule: Somatics Thymatron System IV

Step	Energy (%)	Program	Charge (mC)	Current (A)	Duration (s)	Frequency (Hz)	Pulse Width (ms)
Step 1	5	LOW 0.25	24.8	0.89	5.6	10	0.25
Step 2	10	LOW 0.25	49.7	0.89	5.6	20	0.25
Step 3	15	LOW 0.25	74.6	0.89	5.6	30	0.25
Step 4	20	LOW 0.25	99.4	0.89	7.4	30	0.25
Step 5	40	LOW 0.25	199.1	0.89	7.5	60	0.25

TABLE S2. Seizure Threshold Titration Schedule: MECTA spECTrum

Step	Parameter Set	Charge (mC)	Current (A)	Duration (s)	Frequency (Hz)	Pulse Width (ms)
Step 1	0.3 ms	24	0.8	2.5	20	0.3
Step 2	0.3 ms	48	0.8	5	20	0.3
Step 3	0.3 ms	72	0.8	7.5	20	0.3
Step 4	0.3 ms	100.8	0.8	7	30	0.3
Step 5	0.3 ms	192	0.8	8	50	0.3

ECT Timing and Session Procedures: Right unilateral (RUL) ECT was given with a Thymatron System IV device or MECTA SPECTRUM device. At baseline, 172 of 240 patients (71.7%) were treated with Thymatron; 68 (28.3%) with Mecta.

Seizure threshold (ST) was determined at the first treatment using the dose titration schedule described in Table S1 above. Dose at subsequent treatments was at 6 times ST. Three of 240 patients (1.3%) had a seizure threshold above possible "6x seizure threshold" but were kept in the study (listed as protocol violations) and were treated below their actual "6x seizure threshold" value.

A generalized seizure ≥ 15 s tonic-clonic motor activity was required for adequacy. Following an abortive or inadequate seizure, restimulation in the same session took place at a stimulus intensity 25% above the level that resulted in the abortive seizure, after a minimum 45 seconds to allow for dissipation of the refractory period following seizure elicitation. If seizure duration still remained below the motor (15 sec) duration cutoff, then the seizure was accepted for that particular treatment.

Blood pressure, pulse, ECG, and pulse oximetry were monitored prior to anesthetic induction and continuously during the procedure. Standardized anesthesia procedures included glycopyrrolate 0.2 mg IV only at the dose titration session, induction with methohexital (~1 mg/kg), muscle relaxation with succinylcholine (~0.75 mg/kg), and ventilation with 100% oxygen throughout. Glycopyrrolate was optional at other treatment sessions, as per clinical discretion. Seizure expression was monitored via left fronto-mastoid EEG, and EMG of the cuffed right foot to record motor manifestations.

Total stimulus charge and seizure duration: At baseline, the mean (±standard deviation) total stimulus charge charge was 30.5 mC ± 14.3; at last ECT, the mean charge was 276.6 mC ± 162.4. Mean motor seizure duration (determined by clinician) over all treatments was 29.2 sec ± 11.3; mean EEG seizure duration (determined by clinician) over all treatments was 48.7 sec ± 18.2.

Mid-Course Re-Titration During Phase 1: 32 of 126 patients (25.4%) who had 6 or more treatments had an increase in charge after treatment 6 and 25 out of 71 (35.2%) had an increase after treatment 9.

Missed Seizures: If no seizure was induced at a suprathreshold treatment session, the dosage was increased by 25% and the patient was restimulated. If the seizure was missed because of an increase in seizure threshold, the dosage used to obtain a seizure in this session was considered the new threshold, and the subsequent treatment was administered using a dosage at 6x the new threshold, or at maximal stimulator output in the case that 6x seizure threshold was higher than maximal stimulator output.

Abortive or Inadequate Seizures: If the motor seizure was less than 15 seconds (including the entire duration of the stimulus), the seizure was considered 'abortive' or 'inadequate.' Following an abortive or inadequate seizure, restimulation in the same session took place at stimulus intensity 25% above the level that resulted in the abortive seizure, after a minimum 45 seconds to allow for dissipation of the refractory period following seizure elicitation. If seizure duration still remained below the motor (15 sec) duration cutoffs, then the seizure was accepted for that particular treatment.

HAM-D Training Procedures

The Hamilton Rating Scale for Depression (Ham-D) has been used to assess depression severity for over 50 years (Hamilton 1960, 1967). Multiple versions of the scale now exist and improved inter-rater reliability has been shown with the addition of structured and semi-structured interviews (Miller, Bishop, Norman, & Maddever, 1985; Moberg et al., 2001; Potts, Daniels, Burnam, & Wells, 1990; Williams et al., 2008). The HAM-D has been shown to be a valid and reliable measure in the assessment of geriatric depression (Yesavage et al., 1982). The PRIDE study used a 24-item version of the HAM-D that includes a semi-structured interview for each item, as well as descriptions for rating anchors. In addition, detailed guidelines were developed by the PRIDE team to standardize administration and scoring procedures across sites and raters. Following initial training and review of study guidelines, raters independently scored training tapes developed by the Clinical Coordinating Center (CCC). Raters were certified only after scoring within specified criteria (deviation not greater than one point per item and three points of the total score) on three tapes in comparison to the study "consensus criteria" established by consensus between the CCC Principal Investigator (PI) and the Project Coordinator (PC). Ongoing consistency was achieved through rater review of additional training tapes, posted on the PRIDE study data management system web site (WebDCU). If a rater's scores were not within the consensus criteria, the Project Coordinator scheduled a call with the rater to review guidelines and discuss the rationale for item ratings. The patterns of rater scores were evaluated for evidence of rater drift over time, and measures of inter-rater reliability (IRR)

were required by the Manual of Operating Procedures (MOP) to exceed 0.8. The minimum IRR for PRIDE was 0.88. If indicated, corrective feedback (additional training sessions) was implemented by the CCC via in-person visits or videoconferences. Rating procedures were also reviewed at annual investigator meetings in special half-day rater training sessions and on bimonthly teleconferences conducted by the Project Coordinator and Study Neuropsychologist and attended by Raters and site Study Coordinators.

References

Miller, I. W., Bishop, S., Norman, W. H., & Maddever, H. (1985). The Modified Hamilton Rating Scale for Depression: reliability and validity. *Psychiatry Res, 14*(2), 131-142.

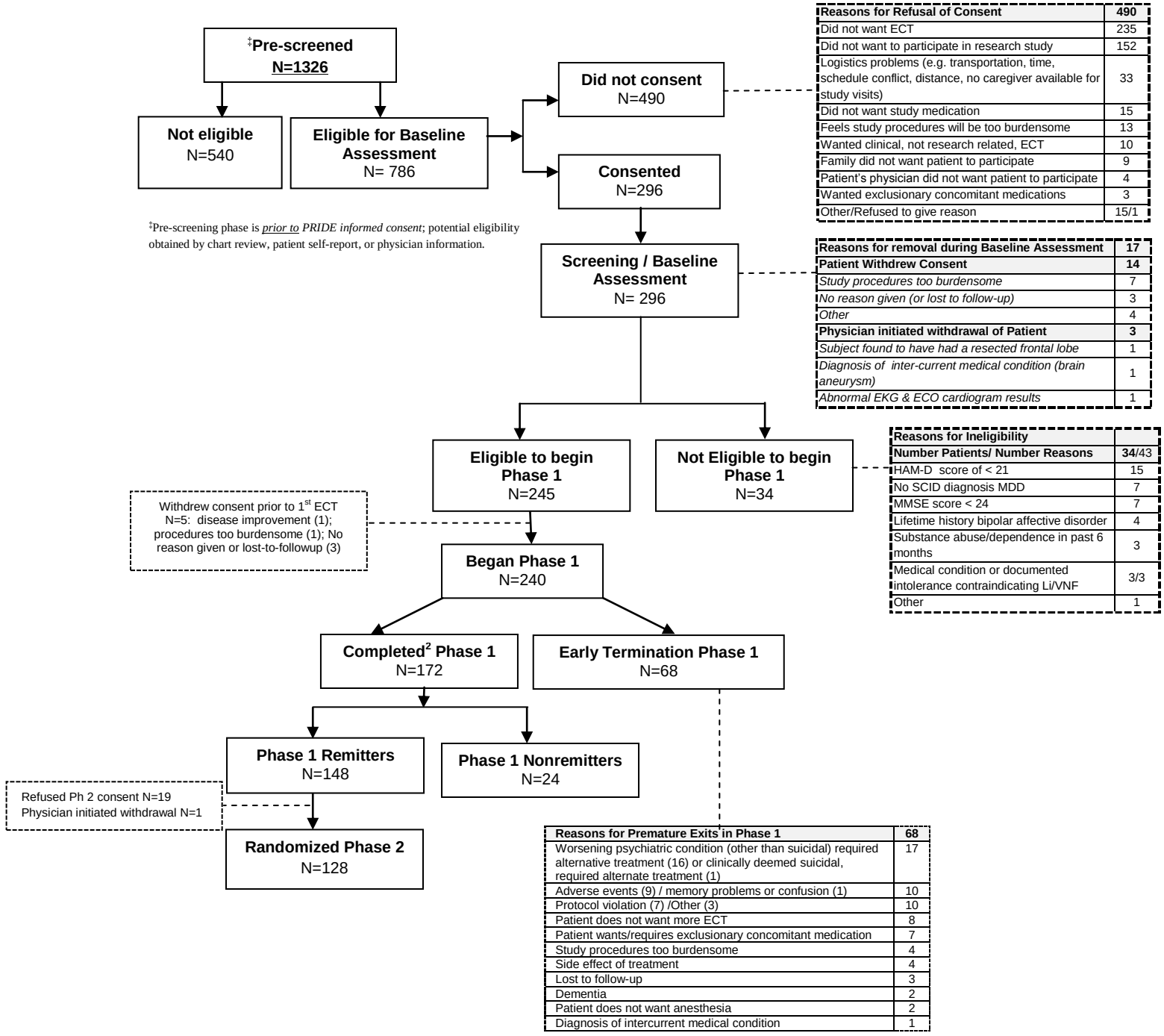
Moberg, P. J., Lazarus, L. W., Mesholam, R. I., Bilker, W., Chuy, I. L., Neyman, I., & Markvart, V. (2001). Comparison of the standard and structured interview guide for the Hamilton Depression Rating Scale in depressed geriatric inpatients. Am J Geriatr Psychiatry, 9(1), 35-40.

Potts, M. K., Daniels, M., Burnam, M. A., & Wells, K. B. (1990). A structured interview version of the Hamilton Depression Rating Scale: evidence of reliability and versatility of administration. *J Psychiatr Res, 24*(4), 335-350.

Williams, J. B., Kobak, K. A., Bech, P., Engelhardt, N., Evans, K., Lipsitz, J., . . . Kalali, A. (2008). The GRID-HAMD: standardization of the Hamilton Depression Rating Scale. *Int Clin Psychopharmacol, 23*(3), 120-129. doi: 10.1097/YIC.0b013e3282f948f5

Yesavage, J. A., Brink, T. L., Rose, T. L., Lum, O., Huang, V., Adey, M., & Leirer, V. O. (1982). Development and validation of a geriatric depression screening scale: a preliminary report. *J Psychiatr Res, 17*(1), 37-49.

FIGURE S1. PRIDE Consort Chart - Phase 1[a]



Reasons for Refusal of Consent	490
Did not want ECT	235
Did not want to participate in research study	152
Logistics problems (e.g. transportation, time, schedule conflict, distance, no caregiver available for study visits)	33
Did not want study medication	15
Feels study procedures will be too burdensome	13
Wanted clinical, not research related, ECT	10
Family did not want patient to participate	9
Patient's physician did not want patient to participate	4
Wanted exclusionary concomitant medications	3
Other/Refused to give reason	15/1

Reasons for removal during Baseline Assessment	17
Patient Withdrew Consent	**14**
Study procedures too burdensome	7
No reason given (or lost to follow-up)	3
Other	4
Physician initiated withdrawal of Patient	**3**
Subject found to have had a resected frontal lobe	1
Diagnosis of inter-current medical condition (brain aneurysm)	1
Abnormal EKG & ECO cardiogram results	1

Reasons for Ineligibility	
Number Patients/ Number Reasons	**34**/43
HAM-D score of < 21	15
No SCID diagnosis MDD	7
MMSE score < 24	7
Lifetime history bipolar affective disorder	4
Substance abuse/dependence in past 6 months	3
Medical condition or documented intolerance contraindicating Li/VNF	3/3
Other	1

Reasons for Premature Exits in Phase 1	68
Worsening psychiatric condition (other than suicidal) required alternative treatment (16) or clinically deemed suicidal, required alternate treatment (1)	17
Adverse events (9) / memory problems or confusion (1)	10
Protocol violation (7) /Other (3)	10
Patient does not want more ECT	8
Patient wants/requires exclusionary concomitant medication	7
Study procedures too burdensome	4
Side effect of treatment	4
Lost to follow-up	3
Dementia	2
Patient does not want anesthesia	2
Diagnosis of intercurrent medical condition	1

[a] HAM-D is 24-item Hamilton Rating Scale for Depression; MMSE is Mini Mental State Exam; SCID is Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I)

TABLE S3. Reasons for Ineligibility for the PRIDE Study

Reason	Total
Ineligible (by chart review or physician info)	**540**
Subject has lifetime history of bipolar affective disorder	**129**
Subject has a current diagnosis of dementia	**58**
Patient has a medical condition contraindicating Li or VLF	42
Patient lacks capacity to provide informed consent	**35**
Subject has substance dependence in past 6 months	**30**
Patient has language barriers	**27**
Diagnosis of exclusionary neurological/neurodegenerative/cognitive disorder other than Parkinson's Disease (e.g seizures disorder, cognitive disorder NOS)	**21**
MDD not severe enough and ECT not clinically indicated	**20**
Patient has diagnosis of Parkinson's Disease	**20**
Subject has lifetime history of schizoaffective disorder	**18**
Patient has general medical co-morbidities precluding ECT treatment (hyponatremia, cancer, brain hemorrhage)	**18**
Patient has a documented history of intolerance to Li	**13**
Patient needs treatment before testing can establish eligibility	**13**
Patient has a documented history of intolerance to VLF	**12**
Patient not able to participate in clinic visits (e.g. out of state resident/transportation issues/no caregiver available for outpatient visits, ect.)	**12**
Patient failed to respond to an adequate trial of ECT in the current depressive episode	**11**
Subject has lifetime history of schizophrenia	**7**
Patient requires exclusionary concomitant medications	**7**
Patient wants/needs different type of ECT (e.g. bitemporal placement)	**7**
Subject has a current diagnosis of delirium	**5**
Patient failed to respond to an adequate trial of Li + VLF in the current depressive episode	**2**
Patient is not age 60 years or older	**1**
Subject has lifetime history of intellectual disability	**1**
Other	**31**

Time to Reorientation After ECT

Time to reorientation was measured as a categorical variable in which orientation was evaluated only at fixed intervals (3, 5, 10, 15, and 20 minutes) using five reorientation items: (1) eyes open on command; (2) name; (3) age; (4) date of birth; and (5) day of week. A patient was considered reoriented at the time point at which all five reorientation questions were answered correctly. For those not fully reoriented at 20 minutes, there was no further assessment of time (and data were reported as % reoriented at > 20 minutes).

FIGURE S2. Phase 1 (Visits 1–3) Frequency Distribution of Reorientation Time After Treatment