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Subthalamic nucleus deep brain stimulation with a multiple independent constant current-controlled device in Parkinson's disease (INTREPID): a multicentre, double-blind, randomised, sham-controlled study

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PUBLISHED	STUDY TYPE	DEVICE
Lancet Neurology	**Multi-center, prospective, double-blind, randomized (3:1) controlled trial with sham control**	**Vercise™ Deep Brain Stimulation System**

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Vitek JL, Jain R, Chen L, et al. Subthalamic nucleus deep brain stimulation with a multiple independent constant current-controlled device in Parkinson's disease (INTREPID): a multicentre, double-blind, randomised, sham-controlled study. Lancet Neurol. 2020;19(6):491-501. doi:10.1016/S1474-4422(20)30108-3

BACKGROUND

The INTREPID Study assessed improvement in motor function and quality of life in PD patients following bilateral subthalamic nucleus (STN) DBS using the Vercise™ Deep Brain Stimulation System with multiple independent current sources that allows for selective activation of individual contacts on the DBS lead there by permitting a defined distribution of applied current.

METHODS

Study Design:

- Multi-center, prospective, double-blind, Randomized (3:1) with sham control

Principal Investigators:

- Dr. Philip Starr (University of California, San Francisco)
- Dr. Jerrold Vitek (University of Minnesota)

Primary Endpoint:

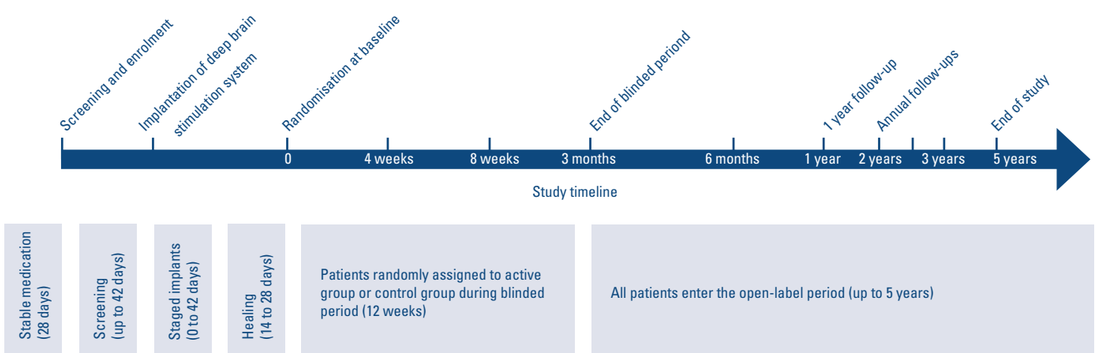
- Mean difference between active and control groups in ON time w/o troublesome dyskinesia, with no increase in antiparkinsonian medications (LED), from post-implant baseline to 12 weeks post-randomization

Sites & Subjects:

- N = 160 randomized subjects
- 23 Sites

Sites & Subjects:

- Up to 5 years post-randomization



BASELINE DEMOGRAPHICS AND CLINICAL CHARACTERISTICS

CLINICAL CHARACTERISTICS/ DEMOGRAPHICS AT SCREENING	
Age (years) - Mean (SD) n	59.9 (7.95) 160
Gender – Male (n %)	72.5% (116/160)
PARKINSON'S DISEASE RELATED SYMPTOMS	
UPDRS III Scores (meds OFF) – Mean (SD) n	43.4 (9.60) 153
UPDRS III Scores (meds ON) – Mean (SD) n	18.5 (8.26) 157
Disease Duration (years) - Mean (SD) n	10.1 (3.61) 160
PD diary: OFF time ON time with troublesome dyskinesias ON time without dyskinesias ON time with non-troublesome dyskinesias Asleep	 6.91 ± 2.99 hours 4.35 ± 2.63 hours 4.65 ± 2.67 hours 3.65 ± 1.90 hours 7.20 ± 1.47 hours

KEY INCLUSION/EXCLUSION CRITERIA:

Key Inclusion Criteria

- Diagnosis of bilateral idiopathic PD with ≥ 5 years of motor symptoms.
- Modified H&Y≥ 2; UPDRS-III score of ≥ 30 (meds off); at least 33% improvement in UPDRS III following meds
- Greater than or equal to 6 hours of poor motor function (OFF time plus ON time with troublesome dyskinesias) per day as assessed by PD diary
- An appropriate candidate for surgical procedures required for bilateral STN DBS

Key Exclusion Criteria

- Any intracranial abnormality or medical condition that contraindicates DBS surgery
- Have any significant psychiatric condition likely to compromise the subject's ability to comply with requirements of the study protocol

RESULTS

PRIMARY ENDPOINT

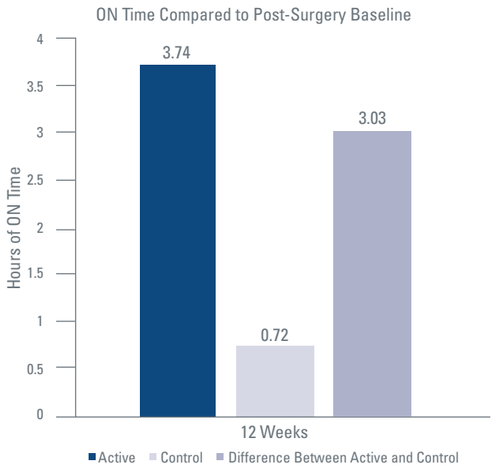
ON Time Without Troublesome Dyskinesias

At the end of the blinded phase (12-weeks):

- A 3.74 ± 4.79 hour improvement in ON time was reported in the active group compared to a 0.72 ± 3.56 hour improvement in the control group compared to post-implant activation

At the end of the blinded phase (12-weeks):

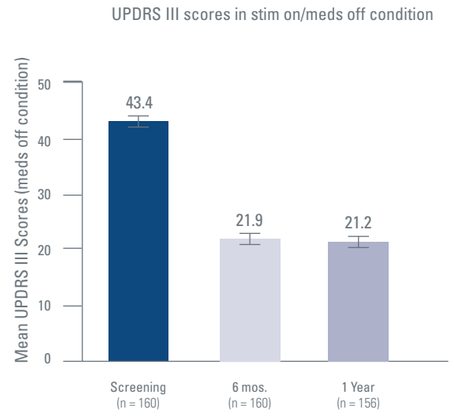
- The difference in mean change from the baseline visit (post-implant) to 3 months post-randomization in increased ON time between the active and control groups was 3.03 ± 4.52 (P < 0.001)



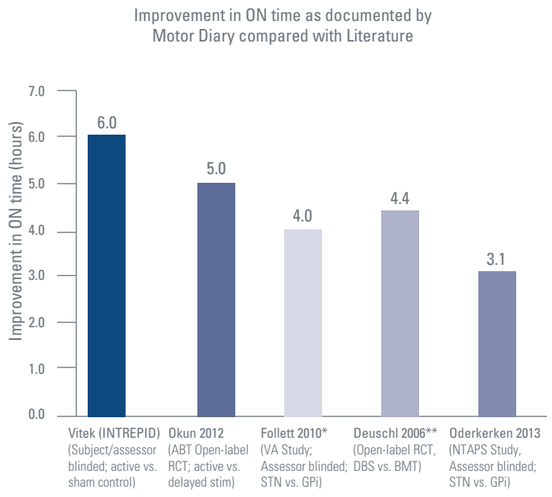
UPDRS III SCORES (STIM ON/MEDS OFF)

51%

Improvement in UPDRS III at 1 year (n = 160)



IMPROVEMENT IN ON TIME AT 1 YEAR



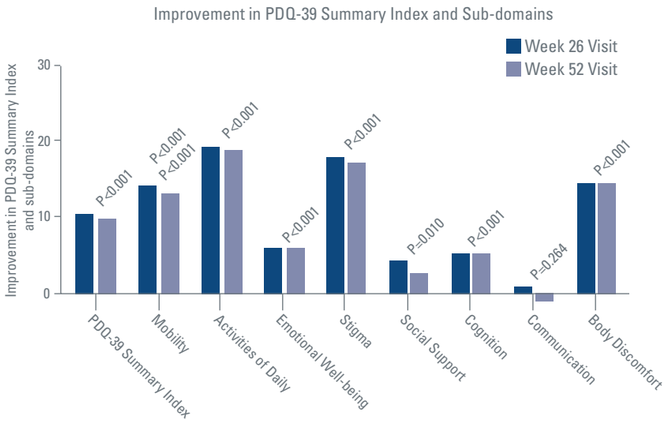
IMPROVEMENT IN ON TIME

6.0 hours

- At 1 year, a 6 ± 3.8 hour increase in ON time without troublesome dyskinesias was reported compared with Screening (P < 0.001)
- Higher improvement than other similar studies in the literature

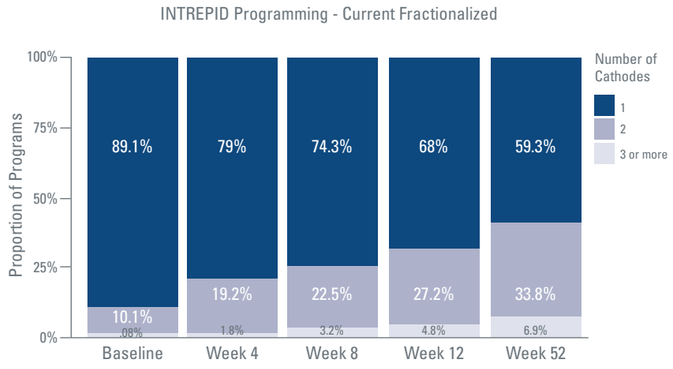
34%

Improvement in Quality of Life at 1 year



41%

of programs used more than a single contact at one year



CONCLUSIONS

- The study successfully met the primary endpoint and several secondary endpoints based on outcomes reported during the 12-week blinded period.[1]
- At 1 year, UPDRS III scores (stim on/meds off) improved 51% and ON time without troublesome dyskinesias (PD-diary) increased 6 ± 3.8 hours compared with screening ($p < 0.001$), respectively.[1]
- Overall Improvement in quality of life, medication reduction and high satisfaction with therapy was maintained
- The overall safety profile of the DBS System was comparable to other published reports

SAFETY PROFILE

Safety Profile is comparable to Literature reports

Surgical complications across all patients who underwent implantation (n = 196) [whether or not they went on to be randomized in the study]

EVENT	NUMBER OF EVENTS (SUBJECTS)	RATE
Infection occurring in first 6 months of surgery associated with partial/total hardware removal (SAE)	7 (7)	7/196 (3.6%)
Symptomatic Perioperative Intracranial Hemorrhage (SAE) occurring during surgery or postsurgical hospitalization	4 (4)	4/196 (2.0%)
Symptomatic Peri Lead Edema (SAE)	6 (6)	6/196 (3.1%)
Return to OR due to electronic malfunction	4 (4)	4/196 (2.0%)
Return to OR due to lead breakage/lead migration	0 (0)	0/196 (0%)
Return to OR due to hardware erosion occurring > 6 mos. after implantation	2 (2)	2/196 (1.0%)

- Deaths: 7 deaths (unrelated to the study-device and/or implant procedure)
- No unanticipated adverse events
- No lead breakage/lead fractures

Rate = Number of subjects with event/total number of implanted subjects*100

1. Vitek JL, Jain R, Chen L, et al. Subthalamic nucleus deep brain stimulation with a multiple independent constant current-controlled device in Parkinson's disease (INTREPID): a multicentre, double-blind, randomised, sham-controlled study. Lancet Neurol. 2020;19(6):491-501. doi:10.1016/S1474-4422(20)30108-3

Results from different clinical investigations are not directly comparable. Information provided for educational purposes only.

Indications for Use: The Vercise™ Deep Brain Stimulation (DBS) Systems are indicated for use in bilateral stimulation of the subthalamic nucleus (STN) as an adjunctive therapy in reducing some of the symptoms of moderate to advanced levodopa-responsive Parkinson's disease (PD) that are not adequately controlled with medication.

Contraindications, warnings, precautions, side effects. The Vercise DBS Systems, or any of its components, are contraindicated for: Diathermy as either a treatment for a medical condition or as part of a surgical procedure, Electroconvulsive Therapy (ECT) and Transcranial Magnetic Stimulation (TMS) as the safety of these therapies in patients implanted with the Vercise DBS Systems have not been established, Magnetic Resonance Imaging (MRI), patients who are unable to operate the system, patients who are poor surgical candidates or who experience unsuccessful test stimulation. Refer to the Instructions for Use provided with the Vercise DBS Systems or BostonScientific.com for potential adverse effects, warnings, and precautions prior to using this product.

Caution: U.S. Federal law restricts this device to sale by or on the order of a physician.

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