CNS 2018 ANNUAL MEETING
HOUSTON, TEXAS
OCTOBER 6-10, 2018

INTREPID: A Prospective, Double Blinded, Multicenter Randomized Controlled Trial Evaluating Deep Brain Stimulation with a New Multiple Source, Constant Current Rechargeable System in Parkinson's Disease

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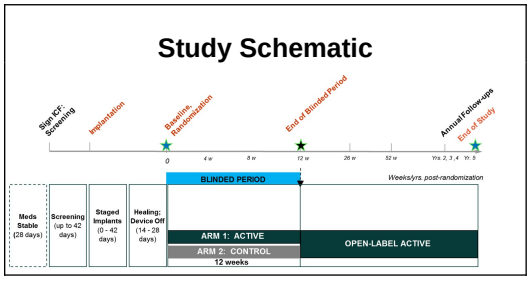
Introduction

Deep Brain Stimulation (DBS) is an effective treatment for motor signs and fluctuations associated with Parkinson's disease (PD). Although DBS efficacy has been substantiated by several randomized controlled trials (RCTs), the degree of improvement varies significantly. The INTREPID Study assessed improvement in motor function and quality of life in PD patients following bilateral subthalamic nucleus (STN) DBS using a new device with multiple independent current sources that allows for selective activation of individual contacts on the DBS lead thereby permitting a defined distribution of applied current.

Methods

Study Design	Multi-center, prospective, double-blind, randomized (3:1) with sham control
Study Device	Vercise DBS System (Boston Scientific, Valencia, CA, USA)
Subjects	160 randomized subjects
Primary Endpoint	Difference in the mean change from baseline to 12 weeks post randomization between the treatment and control groups in the mean number of waking hours per day with good symptom control and no troublesome dyskinesia as measured on the PD diary, with no increase in anti-parkinsonian medications

Study Schematic



Key Inclusion Criteria

- Diagnosis: bilateral idiopathic PD, = 5 yrs motor symptoms)
- Modified H&Y= 2; UPDRS-III score of = 30 (meds off)
- = 6 hours of poor motor function per day (PD diary)
- = 33% imp.in UPDRS-III scores following meds
- DRS-2 (Dementia Rating Scale -2): =130 & BDI-II: <17
- An appropriate candidate required for bilateral STN DBS

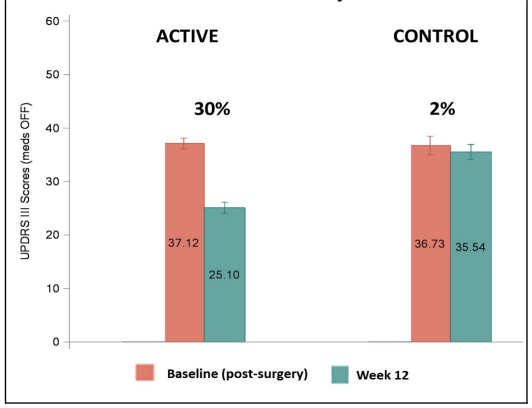
Key Exclusion Criteria

- Intracranial abnormality/condition that contraindicates DBS
- Have any significant psychiatric condition likely to comprimise subject's ability to comply with study protocol
- History of suicide attempt or current active suicidal

Results

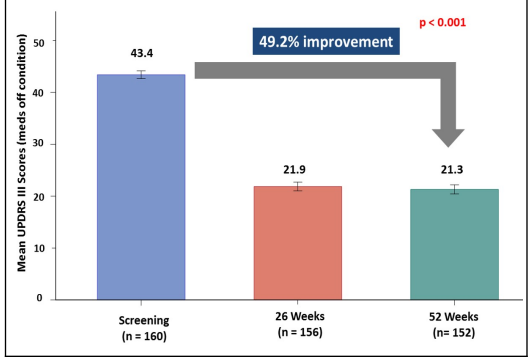
Clinical Characteristics / Demographics at Screening	
Age (years) - Mean (SD) n	59.9 (7.95) 160
Gender – Male (n %)	72.5% (116/160)
UPDRS III (meds OFF) – Mean (SD) n	43.4 (9.60) 153
UPDRS III (meds ON) – Mean (SD) n	18.5 (8.26) 157
Disease Duration (years) - Mean (SD) n	10.1 (3.61) 160

Week 12: UPDRSIII Scores (stim on/meds off)



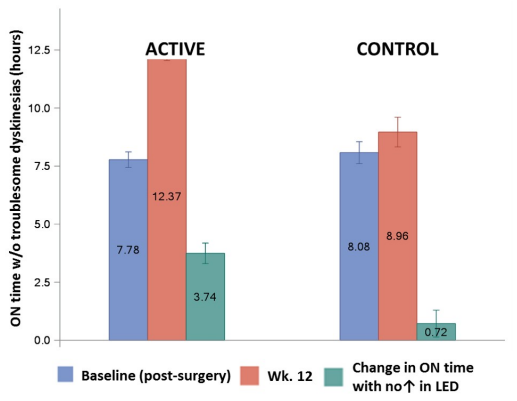
A 30% improvement in UPDRS III scores in active group was reported at Week 12 compared to post-implant Baseline

1 Year: UPDRS III Scores (stim on/meds off)



A 49.2% improvement in UPDRS III scores at 1 year

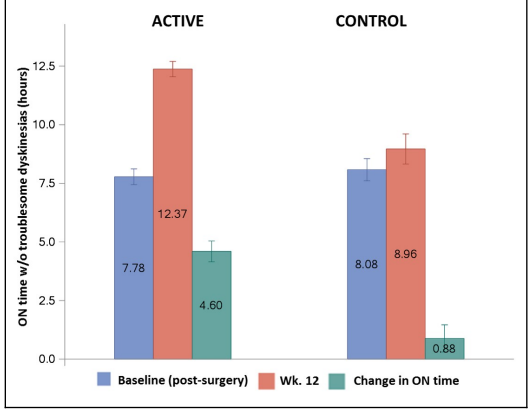
Week 12: Study Primary Endpoint



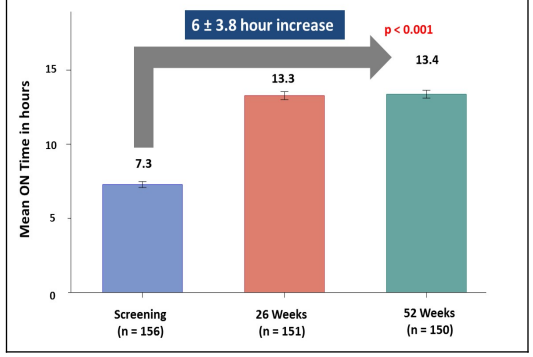
The study successfully met its primary endpoint (p<0.001)

- Mean difference of 3.03 ± 4.52 hrs. (p < 0.001) between active and control groups in ON time w/o troublesome dyskinesia, with no increase in antiparkinsonian medication(LED), from post-implant baseline to 12 weeks post-randomization
- A larger improvement (4.6 vs 3.7 hr.) in ON time was noted when the primary endpoint analysis was repeated without the anti-PD medication rule

Week 12: ON Time without Troublesome Dyskinesias



1 year: ON Time without Troublesome Dyskinesias



A 6 ± 3.8 hour increase in ON time without troublesome dyskinesias was reported at 52 Weeks post randomization compared to Screening.

Safety

- A total of 103 Serious Adverse events were reported in the study as of Dec 2017.
- Three deaths were reported in study (Unrelated to device, procedure or stimulation)
- Infection (8 events) most commonly reported SAE with relationship to device, procedure or stimulation
- No lead breakages/fractures
- No unanticipated adverse events.

Conclusions

- The study successfully met primary endpoint and several secondary endpoints based on outcomes of blinded period (12 weeks)
- A 49.2% improvement (p < 0.001) in UPDRS III scores (stim on/meds off) and a 6 hour improvement in ON time without troublesome dyskinesias (PD-diary) at 1 year compared with screening (p < 0.001)
- 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