VANTAGE Trial: Three Year Outcomes of a Prospective, Multi-center Trial Evaluating Deep Brain Stimulation With a New Multiple-source, Constant-current Rechargeable System in Parkinson's Disease

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CNS 2016 ANNUAL MEETING San Diego CALIFORNIA SEPTEMBER 24-28, 2016

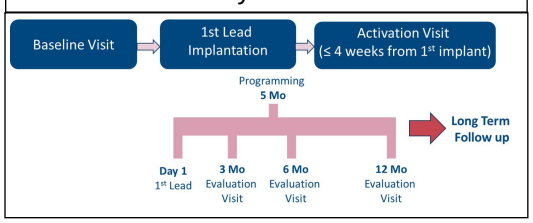
Introduction

Deep Brain stimulation (DBS) of the subthalamic nucleus (STN) is an established therapeutic option for patients with advanced Parkinson's disease (PD), supported by several randomized controlled trials. A device that enables fractionalisation of current using a multiple-source mode of delivery can permit the application of a well-defined, shaped electrical field. Thus, we postulated that a multiple-source, constant-current device (CE marked) that permits well-defined distribution of current would lead to motor improvement in patients with Parkinson's disease. In this report, we present the three year, long-term follow up results of patients in the VANTAGE clinical cohort that employed multiple independent current control (MICC) DBS in the management of symptoms of Parkinson's disease.

Methods

Study Design	Prospective, Multicenter, Non-Randomized, Open-Label
Study Device	Vercise (Boston Scientific, Valencia, CA, USA)
No. of Subjects/Sites	N = 40 implanted subjects from 6 European Centers
Primary Endpoint	Change in UPDRS III scores stim ON/meds OFF at 6 mos. compared with pre-operative scores (Baseline meds OFF).
Assessment Follow-Up	Weeks 12, 21, 26 and Year 1, 2, and 3 post lead placement
Study Assessments during Long Term Follow up	• Levodopa Equivalent Dose (LED) • Global Impression of Change (CGI) – Clinician and Subject • Parkinson's Disease Questionnaire (PDQ-39) • Modified Schwab and England (SE)

Subjects implanted bilaterally with a multiple source, current-controlled DBS system



Key Inclusion Criteria

- Diagnosis of bilateral idiopathic PD = 5 years
- Modified Hoehn and Yahr in the OFF state = 2
- UPDRS III = 30 off meds that improved by = 33% with medications
- Appropriate surgical candidate for DBS

Key Exclusion Criteria

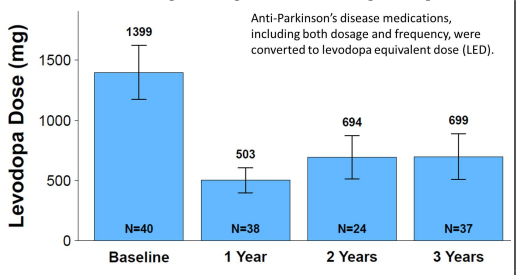
- Any intracranial abnormality or medical condition that would contraindicate DBS surgery.
- Any finding in neuropsychological screening assessments that would contraindicate DBS surgery, including dementia.

Results

Baseline Characterisitics

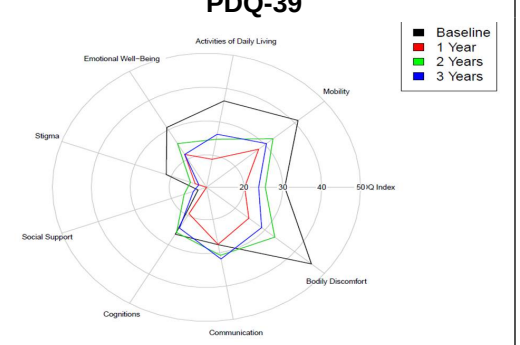
Age (years) - Mean (SD)	60.2 (7.82)
Gender - n (%)	
Male	27 (67.5%)
Parkinson's Disease Related Symptoms	
Disease Duration (years) - Mean (SD)	11.7 (4.57)
H&Y scale Meds OFF - Mean (SD)	2.69 (0.71)
UPDRS III Meds OFF - Mean (SD)	37.4 (8.90)
UPDRS III Meds ON - Mean (SD)	14.0 (8.21)
Total UPDRS Meds ON - Mean (SD)	30.3 (12.74)
Duration of OFF time in motor diary (hours) - Mean (SD)	5.4 (3.13)
Neuropsyhometric Testing	
BDI-II Meds ON - Mean (SD)	9.4 (6.57)
Mattis Dementia Rating Scale (DRS-2) Meds ON - Mean (SD)	140.1 (3.55)

Levodopa Equivalents (LED)



PD medications remain stable up to 3 years post lead placement

PDQ-39

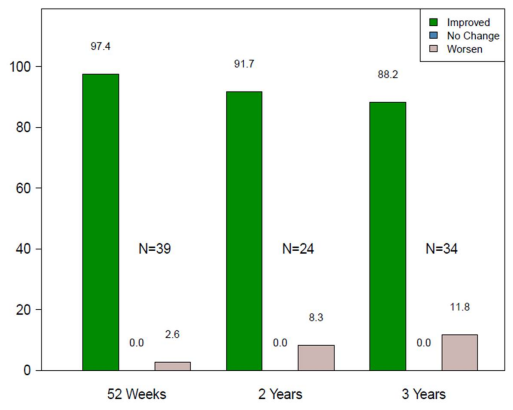


PDQ-39 demonstrates continued improvement in quality of life

At 3 years post-lead placement:

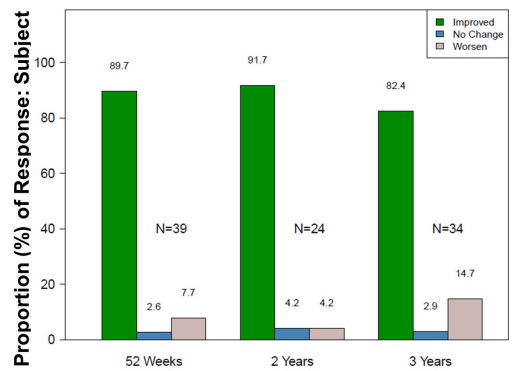
- Bodily Discomfort and ADL show significance
- Mobility, Emotional well-being show continued improvement
- Cognition is same as at Baseline as expected following DBS

Global Impression of Change – Clinician



CGI Scores (based on clinician) may be impacted by change in site personnel over the course of the study

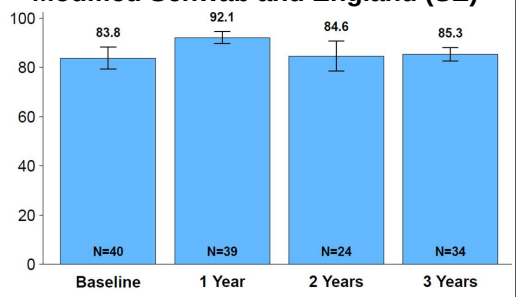
Global Impression of Change – Subject



CGI Scores (based on subject) may be impacted by length of recall (Baseline to 3 yrs. following lead placement)

Caution: Investigational Device. Limited by Federal (or US) law to investigational use only. Not available for sale.
Results from different clinical investigations are not directly comparable. Information provided for educational purposes only.

Modified Schwab and England (SE)



SE Scores tend to remain stable up to 3 yrs. post lead placement

Summary of Adverse Events

Serious Adverse Event (SAE)	All		Related to Device		Related to Procedure	
	n	n of subjects with event (%)	n	n of subjects with event (%)	n	n of subjects with event (%)
Infections and infestations	9	7 (17.5%)	2	1 (2.5%)	1	1 (2.5%)
Localised Infection	1	1 (2.5%)	1	1 (2.5%)	0	0 (0.0%)
Staphy. Infection	1	1 (2.5%	1	1 (2.5%)	0	0 (0.0%)
Implant Site Infection	1	1 (2.5%)	0	0 (2.5%)	1	1 (2.5%)
Injury and Procedural Complications	7	3(7.5%)	0	0(0.0%)	1	1(2.5%)
Device Migration	1	1 (2.5%)	0	0(0.0%)	1	1(2.5%)
General disorders	1	1(2.5%)	1	1(2.5%)	1	1(2.5%)
Implant site pain	1	1(2.5%)	1	1(2.5%)	1	1(2.5%)
Nervous System Disorders	3	2(5.0%)	0	0(0.0%)	0	0(0.0%)
Musculoskeletal and connective Disorders	3	2(5.0%)	0	0(0.0%)	0	0(0.0%)
Respiratory / Thoracic Disorders	2	2(5.0%)	0	0(0.0%)	1	1(2.5%)
Respiratory Depression	1	1(2.5%)	0	0(0.0%)	1	1(2.5%)
TOTAL	35	16(40.0%)	3	2(5.0%)	4	2(5.0%)

Conclusions

- The results of the VANTAGE study demonstrated highly significant improved motor function ($p < 0.0001$), as assessed by UPDRS III meds off at 6 months post first lead implant as compared with Baseline meds off – successfully meeting the study primary endpoint (Timmermann et al., 2015).
- At Year 3 post lead implantation, medication usage, quality of life outcomes including PDQ-39 and Schwab England Scale remain stable.
- A total of 147 adverse events were reported in 37 patients during the entire study. Of these, 35 events were considered as Serious Adverse Events (3 events related to device and 4 events related to procedure).