Motor and Non-Motor Outcomes of Bemdaneprocel in People With Parkinson's Disease: Results up to 24 Months From a Phase 1 Study

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Introduction

- Current standard treatments for Parkinson's disease (PD) motor symptoms do not address the loss of dopaminergic neurons, an underlying cause of the disease; moreover, they do not specifically address, and may even worsen, some non-motor symptoms[1,2]
- Bemdaneprocel is an investigational therapy comprising dopaminergic neuron progenitors derived from human embryonic stem cells[3-5]
  - Preclinical studies in rodents support safety and proof-of-concept for bemdaneprocel[3,4]
- exPDite, a Phase 1 multicenter, multisite, open-label, nonrandomized study (NCT04802733), met the primary objective of safety and tolerability through 12 months post transplantation and supported the feasibility of stereotactic transplantation[6]

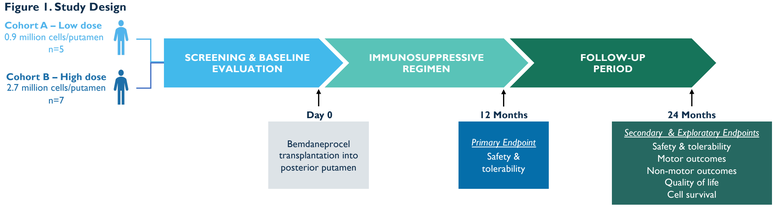
Objective

- To continue evaluating the effects of bemdaneprocel on motor, non-motor, and quality of life outcomes up to 24 months post transplantation, 12 months post discontinuation of immunosuppression, in participants with PD

Methods

- Participants with PD, with motor symptoms inadequately controlled by standard treatments, and who were ≥50 to ≤78 years of age in Canada or ≥60 to ≤78 years of age in the United States were eligible to enroll in the study
  - Eligible participants had a diagnosis of idiopathic PD (based on modified UK Parkinson's Disease Society Brain Bank criteria) with ≥3 to ≤20 years since PD diagnosis, levodopa response (defined as ≥30% improvement on Movement Disorders Society-Unified Parkinson's Disease Rating Scale [MDS-UPDRS] Part III), and a Hoehn and Yahr score of 0–3 in ON state (Canada only), or 0–2 in ON state and 3–4 in OFF state (US only)

Figure 1. Study Design



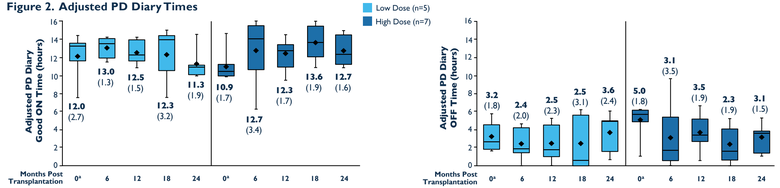
- A total of 12 participants enrolled sequentially
  - The first 5 participants were assigned to the low-dose group (0.9 million cells/putamen); the last 7 were assigned to the high-dose group (2.7 million cells/putamen)
- Bemdaneprocel was administered stereotactically into the posterior putamen bilaterally through a single burr hole on each side in a single session
  - A cannula was used to deliver a total of 9 cell deposits along 3 tracks per hemisphere
- Immunosuppression was initiated during transplantation and continued for 1 year post transplantation
  - **Basiliximab** (20 mg, IV) was administered intraoperatively and on postoperative day 4
  - **Methylprednisolone** (500 mg, IV) was initiated on day 0, tapered to **prednisone** (5 mg, PO), and continued at 5 mg QD for 1 year
  - **Tacrolimus** (PO, BID) was initiated on postoperative day 1 and adjusted to a target trough blood level of 4–7 ng/mL for 1 year
- Secondary motor outcomes included adjusted PD diary good ON time and MDS-UPDRS Part III OFF
- Exploratory motor and non-motor outcomes included MDS-UPDRS Part II, MDS-UPDRS Part III ON, adjusted PD diary OFF time, 39-item Parkinson's Disease Questionnaire (PDQ-39), PD Non-motor Symptom Scale (PD NMSS), and the Neuropsychiatric Inventory Questionnaire (NPI-Q)
- Data are reported as observed scores at baseline and 6, 12, 18, and 24 months post transplantation

Results

Table 1. Participant Demographics and Baseline Characteristics

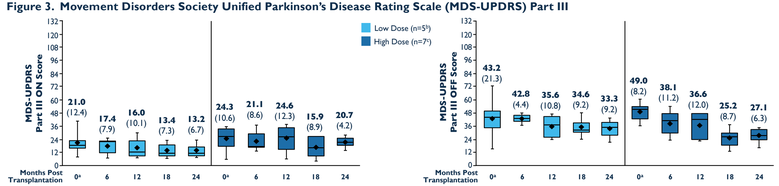
	Low Dose (n=5)	High Dose (n=7)	Total (N=12)
Age, years			
Mean (standard deviation)	66.8 (6.8)	66.7 (4.8)	66.8 (5.4)
Sex, n (%)			
Male	4 (80.0)	5 (71.4)	9 (75.0)
Female	1 (20.0)	2 (28.6)	3 (25.0)
Race, n (%)			
Asian	0	1 (14.3)	1 (8.3)
White	3 (60.0)	5 (71.4)	8 (66.7)
Other	1 (20.0)	1 (14.3)	2 (16.7)
Multiple	1 (20.0)	0	1 (8.3)
Time since Parkinson's disease diagnosis, years			
Mean (standard deviation)	11.0 (3.7)	7.8 (2.2)	9.1 (3.2)
Hoehn and Yahr Stage (OFF state), n (%)			
2	1 (20.0)	0	1 (8.3)
3	4 (80.0)	7 (100.0)	11 (91.7)
Hoehn and Yahr Stage (ON state), n (%)			
2	5 (100.0)	7 (100.0)	12 (100.0)

Figure 2. Adjusted PD Diary Times



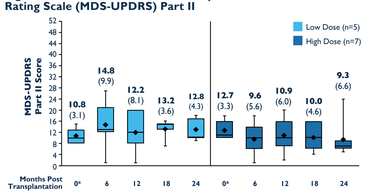
Horizontal lines, median; diamonds, mean; boxes, quartiles 1 and 3; whiskers, extreme values. Annotations on graphs are **mean** (standard deviation). Good ON time is the sum of ON time without dyskinesia and ON time with non-troublesome dyskinesia. PD diary time[7] is adjusted for 16-hour waking days. *The baseline value (0 months post transplantation) is defined as the last recorded value before the first dose of immunosuppressive drugs or cell transplant surgery. PD, Parkinson's disease.

Figure 3. Movement Disorders Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part III



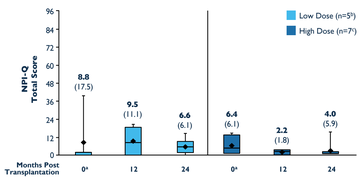
Horizontal lines, median; diamonds, mean; boxes, quartiles 1 and 3; whiskers, extreme values. Annotations on graphs are **mean** (standard deviation). MDS-UPDRS Part III contains 18 items with a subscore range of 0–132 points; higher scores indicate more severe motor symptoms.[8] *The baseline value (0 months post transplantation) is defined as the last recorded value before the first dose of immunosuppressive drugs or cell transplant surgery. [5]Except for Part III OFF at 18 months post transplantation, where n=6. [7]Except for Part III OFF at 24 months post transplantation, where n=4.

Figure 4. Movement Disorders Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part II



Horizontal lines, median; diamonds, mean; boxes, quartiles 1 and 3; whiskers, extreme values. Annotations on graphs are **mean** (standard deviation). MDS-UPDRS Part II contains 13 items with a subscore range of 0–52 points; higher scores indicate more severe motor symptoms.[8] *The baseline value (0 months post transplantation) is defined as the last recorded value before the first dose of immunosuppressive drugs or cell transplant surgery. MDS-UPDRS, Movement Disorders Society-Unified Parkinson's Disease Rating Scale.

Figure 5. Neuropsychiatric Inventory Questionnaire (NPI-Q)



Horizontal lines, median; diamonds, mean; boxes, quartiles 1 and 3; whiskers, extreme values. Annotations on graphs are **mean** (standard deviation). Total score range: 0–96 (lower scores indicate improvement).[9] *The baseline value (0 months post transplantation) is defined as the last recorded value before the first dose of immunosuppressive drugs or cell transplant surgery. [9]Except at 12 months post transplantation, where n=4. [1]Except at 12 and 24 months post transplantation, where n=6. NPI-Q was administered at baseline and 12 and 24 months post transplantation. NPI-Q, Neuropsychiatric Inventory Questionnaire.

Table 2. 39-Item Parkinson's Disease Questionnaire (PDQ-39)

	Low Dose (n=5)		High Dose (n=7)	
PDQ−39 Domain, mean (SD)	Baseline	24 months post transplantation	Baseline	24 months post transplantation
Mobility	27.5 (10.9)	26.5 (28.5)	15.4 (13.2)	14.3 (15.7)
Activities of daily living	30.8 (10.0)	31.7 (13.4)	24.4 (19.8)	17.9 (22.8)
Emotional well-being	23.3 (8.6)	21.7 (18.0)	8.9 (11.1)	6.0 (6.7)
Stigma	21.3 (12.2)	10.0 (8.4)	6.3 (8.1)	2.7 (7.1)
Social support	20.0 (9.5)	8.3 (8.3)	4.8 (12.6)	1.2 (3.2)
Cognition	18.8 (15.9)	13.8 (14.3)	15.2 (14.8)	18.8 (24.5)
Communication	23.3 (13.7)	25.0 (22.1)	7.1 (13.1)	8.3 (18.6)
Bodily discomfort	35.0 (26.6)	33.3 (25.7)	39.3 (15.0)	33.3 (18.0)
Summary index	**25.0 (6.3)**	**21.3 (15.1)**	**15.2 (8.4)**	**12.8 (11.1)**

The PDQ-39 contains 8 domains (mobility [10 items], activities of daily living [6 items], emotional well-being [6 items], stigma [4 items], social support [3 items], cognition [4 items], communication [3 items], and bodily discomfort [3 items]). Each item is scored from 0 (never) to 4 (always); domain scores are calculated as a percentage of the maximum score (range of 0–100); the summary index is the arithmetic mean of all domain scores; lower scores indicate increasing quality of life.[10] PDQ-39, 39-item Parkinson's Disease Questionnaire.

Table 3. Parkinson's Disease Non-Motor Symptom Scale (PD NMSS)

	Low Dose (n=5)		High Dose (n=7)	
PD NMSS Domain, mean (SD)	Baseline	24 months post transplantation	Baseline	24 months post transplantation
Cardiovascular including falls	0.8 (0.8)	1.6 (3.1)	0.9 (1.6)	0.4 (1.1)
Sleep/fatigue	4.6 (4.1)	13.2 (6.5)	8.9 (4.4)	8.9 (14.0)
Mood/cognition	2.4 (2.9)	5.4 (7.0)	0.6 (1.0)	2.9 (7.6)
Perceptual problems/hallucinations	0.6 (1.3)	1.2 (1.8)	1.1 (3.0)	1.7 (4.5)
Attention/memory	3.2 (5.0)	5.8 (7.2)	1.7 (2.1)	1.7 (2.2)
Gastrointestinal tract	2.8 (3.5)	1.6 (2.6)	3.6 (4.6)	2.3 (3.4)
Urinary	4.6 (3.1)	8.4 (6.5)	11.7 (7.9)	10.0 (12.2)
Sexual function	1.0 (1.7)	2.2 (4.9)	4.0 (8.9)	3.1 (6.1)
Miscellaneous	4.8 (8.1)	7.4 (7.4)	8.1 (12.8)	4.0 (6.1)
Total score	**24.8 (24.5)**	**46.8 (33.9)**	**40.6 (23.4)**	**35.0 (47.9)**

The PD NMSS consists of 30 items across 9 domains (cardiovascular [2 items], sleep/fatigue [4 items], mood/cognition [6 items], perceptual problems/hallucinations [3 items], attention/memory [3 items], gastrointestinal tract [3 items], urinary [3 items], sexual function [2 items], miscellaneous [4 items]). Each item is scored based on severity (0–3) and frequency (1–4); severity and frequency scores are multiplied and summed to produce domain scores and a total score of 0–360 (lower scores indicate less severe and frequent symptoms).[11] PD NMSS, Parkinson's Disease Non-Motor Symptom Scale; SD, standard deviation.

Conclusions

- Participants who received bemdaneprocel, particularly those in the high-dose cohort, experienced improvement or stability across most secondary and exploratory motor, non-motor, and quality of life outcomes through 24 months post transplantation, 12 months post discontinuation of immunosuppression
- Improvements in self-reported good ON time and OFF times, as well as motor function while off medication, were observed sooner after transplantation and were more pronounced in the high-dose cohort
- All participants have enrolled in a continued-evaluation study (NCT05897957) for ongoing evaluation of safety and efficacy
- These results support the continued development of bemdaneprocel for the treatment of people with Parkinson's disease

References: 1. Debowe I, et al. *Mov Disord.* 2024;39(2):235-48. 2. Khan TS. *Cleve Clin J Med.* 2012;79 Suppl 2:S8-13. 3. Kim TW, et al. *Cell Stem Cell.* 2021;28(2):343-55.e5. 4. Piao J, et al. *Cell Stem Cell.* 2021;28(2):217-29.e7. 5. Kriks S, et al. *Nature.* 2011;480(7378):547-51. 6. Henchcliffe C, et al. Presented at: International Congress of Parkinson's Disease and Movement Disorders; August 27–31, 2023; Copenhagen, Denmark. 7. Hauser RA, et al. *Clin Neuropharmacol.* 2000;23(2):75-81. 8. Goetz CG, et al. MDS-UPDRS. *The MDS-Sponsored Revision of the Unified Parkinson's Disease Rating Scale.* Milwaukee, WI: International Parkinson and Movement Disorder Society; 2008. 9. Cummings JL, Coffey CE. In: Coffey CE, Cummings JL, eds. *The American Psychiatric Press Textbook of Geriatric Neuropsychiatry.* Washington, DC: American Psychiatric Press, Inc.; 1994:4-15. 10. Peto V, et al. *Qual Life Res.* 1995;4(3):241-8. 11. Chaudhuri KR, et al. *Mov Disord.* 2007;22(13):1901-11.

Disclosures: W Stemple, N Abid, and **A Lampron** are full-time employees of BlueRock Therapeutics, LP. **C Henchcliffe** has received honoraria for consulting from AskBio and Certara; stock options for scientific advisory board participation from Axent Biosciences; honoraria for scientific advisory board participation from Bayer AG, Canary Health Technologies, and ProjenX; honoraria for data safety monitoring board meetings from MeiraGTx; research support from BlueRock Therapeutics and Weston Brain Institute; and honoraria for presentations from the American Academy of Neurology, ASGCT, and the Parkinson Study Group. **H Sarva** has done consulting work for BlueRock Therapeutics, Neurocrine, Neuroderm, and Novo Nordisk; and has received clinical trial support from Biogen, BlueRock Therapeutics, Covance, Genentech, Insightec, National Institutes of Health (NIH), Neuroderm, and Prevail Therapeutics. **A Lozano** has nothing to disclose. **A Fasano** has stock ownership in InBrain Pharma; has received payments as consultant and/or speaker from Abbott, AbbVie, Boston Scientific, CereGate, Dompé Farmaceutici, InBrain Neuroelectronics, Iota, Ipsen, Medtronic, Merz, Paladin Labs, Sunovion, Syneos Health, and UCB; has received research support from AbbVie, BlueRock Therapeutics, Boston Scientific, ES, Medtronic, and Praxis; and receives royalties from Springer. **S Kalia** has received consultant and/or speaker honoraria from Abbott, Boston Scientific, Medtronic, and Novo Nordisk. **K Yu** has nothing to disclose. **C Brennan** has nothing to disclose. **V Tabar** is a scientific advisor for BlueRock Therapeutics.

Support and Acknowledgments: This study was supported by BlueRock Therapeutics, LP. The authors thank Marcus Yountz and Ahmed Enayetallah, former employees of BlueRock Therapeutics, for their contributions to this study. Under the direction of the authors, Benjamin M. Hiller, PhD, of Peloton Advantage, LLC, an OPEN Health company, provided medical writing and editorial support for this poster, which was funded by BlueRock Therapeutics, LP. Bemdaneprocel is investigational and has not been approved for treatment by any health authority.

Presented at the 2024 International Congress of Parkinson's Disease and Movement Disorders®; September 27–October 1, 2024; Philadelphia, Pennsylvania, USA