Safety and Tolerability of Bemdaneprocel in People With Parkinson's Disease: Results up to 24 Months From a Phase 1 Study

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Introduction

- Bemdaneprocel is an investigational therapy comprising dopaminergic neuron progenitors derived from human embryonic stem cells currently being developed for people with Parkinson's disease (PD)[1-3]
  - Preclinical studies in rodents support safety and proof-of-concept for bemdaneprocel[1,2]
  - Bemdaneprocel is stereotactically administered in a single surgical session under general anesthesia and requires immunosuppression for 12 months post transplantation
- 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[4]
  - Understanding the long-term safety and tolerability of bemdaneprocel is necessary for further clinical development

Objective

- To continue evaluating the safety and tolerability of bemdaneprocel through 24 months post transplantation, 12 months post discontinuation of immunosuppression, in participants with PD

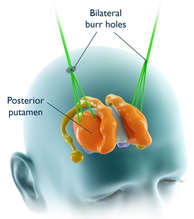
Methods

- 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
- Unified Dyskinesia Rating Scale (UDysRS) observed scores and anti-Parkinson's disease medication use (calculated as levodopa equivalent daily doses) were summarized at baseline and 6, 12, 18, and 24 months post transplantation
- Cranial magnetic resonance images (MRI) were taken at baseline, 6, 12, 18, and 24 months post transplantation; representative images are shown

Figure 2. Surgical Procedure



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)
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)

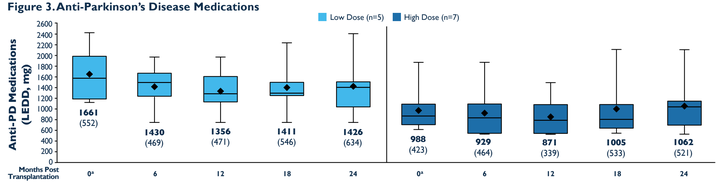
Table 2. Summary of TEAEs and SAEs Through 24 Months Post Transplantation

	Low Dose (n=5)	High Dose (n=7)	Total (N=12)
Participants reporting, n (%) [number of events]			
TEAEs by maximum CTCAE grade[a]	5 (100) [43]	7 (100) [46]	12 (100) [89]
Mild	1 (20.0) [29]	3 (42.9) [37]	4 (33.3) [66]
Moderate	3 (60.0) [13]	3 (42.9) [8]	6 (50.0) [21]
Severe	1 (20.0) [1]	1 (14.3) [1]	2 (16.7) [2]
TEAEs[b]			
Related to cannula	1 (20.0) [1]	0	1 (8.3) [1]
Related to surgery	0	3 (42.9) [3]	3 (25.0) [3]
Related to immunosuppressive drugs	3 (60.0) [16]	5 (71.4) [12]	8 (66.7) [28]
Related to disease	3 (60.0) [10]	3 (42.9) [5]	6 (50.0) [15]
TESAEs[b]	1 (20.0) [1][c]	2 (28.6) [2][d]	3 (25.0) [3]
Related to surgery	0	1 (14.3) [1]	1 (8.3) [1]
Deaths	0	0	0
Study discontinuations	0	0	0

[a]There were no life-threatening TEAEs, or deaths related to adverse event. [b]There were no TEAEs or TESAEs related to syringe, transplanted cells, [18]F-DOPA scan, or MRI. [c]One SAE of COVID-19. [d]One SAE of gastrointestinal hemorrhage and 1 SAE of seizure. CTCAE, Common Terminology Criteria for Adverse Events; [18]F-DOPA, [18]F-fluorodopa; MRI, magnetic resonance imaging; SAE, serious adverse event; TEAE, treatment-emergent adverse event; TESAE, treatment-emergent serious adverse event.

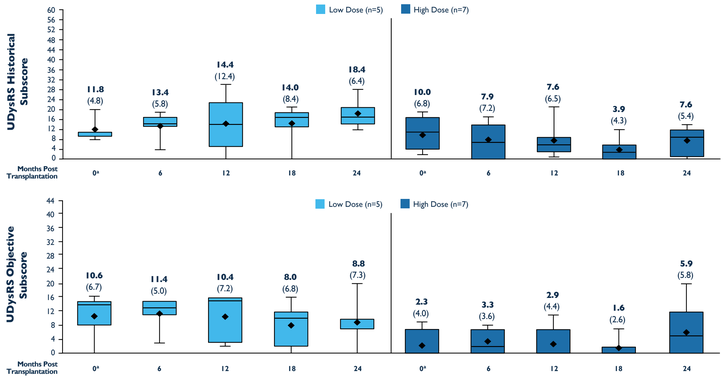
- None of the 3 treatment-emergent serious adverse events were related to transplanted cells or immunosuppression, and there were no graft-induced dyskinesias
- TEAEs in nervous system disorders and infections and infestations System Organ Classes were reported for 8/12 (66.7%) participants each
  - The most frequently reported treatment-emergent adverse events in the nervous system disorders System Organ Class (n=8, 66.7%) were dyskinesia (n=3, 25.0%) and tremor (n=2, 16.7%)
  - The most frequently reported treatment-emergent adverse events in the infections and infestations System Organ Class (n=8, 66.7%) were COVID-19 (n=4, 33.3%) and pneumonia (n=2, 16.7%)

Figure 3. Anti-Parkinson's Disease Medications



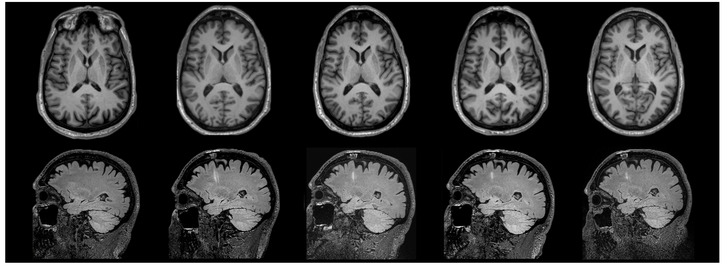
Horizontal lines, median; diamonds, mean; boxes, quartiles 1 and 3; whiskers, extreme values. Annotations on graphs are **mean** (standard deviation). *The baseline value (0 months post transplantation) is defined as the last recorded value before the first dose of immunosuppressive drugs or cell transplant surgery. LEDD, levodopa equivalent daily dose; PD, Parkinson's disease.

Figure 4. Unified Dyskinesia Rating Scale (UDysRS)



Horizontal lines, median; diamonds, mean; boxes, quartiles 1 and 3; whiskers, extreme values. Annotations on graphs are **mean** (standard deviation). The UDysRS Historical subscore is made up of Part I (disability of ON dyskinesia, 11 items) and Part II (disability of OFF dystonia, 4 items). The UDysRS Objective subscore is made up of Part III (Impairment, 7 items) and Part IV (Disability, 4 items). Each item is rated on a scale of 0 (normal) to 4 (severe), with a total possible score of 60 (Historical) and 44 (Objective); higher scores represent more severe symptoms.[3] *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. UDysRS, Unified Dyskinesia Rating Scale.

Figure 5. Representative Magnetic Resonance Images



Conclusions

- Bemdaneprocel was well tolerated and had a favorable safety profile in all 12 participants through 24 months post transplantation, 12 months post discontinuation of immunosuppression
  - No serious adverse events were attributed to transplanted cells or immunosuppression, and there were no graft-induced dyskinesias, deaths, or study discontinuations
- Anti-Parkinson's disease medication use was stable, and there were no intracerebral hemorrhages or mass lesions
- 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. Kim TW, et al. *Cell Stem Cell.* 2021;28(2):343-55.e5. 2. Piao J, et al. *Cell Stem Cell.* 2021;28(2):217-29.e7. 3. Kriks S, et al. *Nature.* 2011;480(7378):547-51. 4. Henchcliffe C, et al. Presented at: International Congress of Parkinson's Disease and Movement Disorders; August 27–31, 2023; Copenhagen, Denmark. 5. Goetz CG, et al. *Mov Disord.* 2008;23(16):2398-403.

Disclosures: W Stemple, N Floro, N Abid, and **A Lampron** are full-time employees of BlueRock Therapeutics, LP. **H Sarva** has done consulting work for BlueRock Therapeutics, Neuroderm, Neurocrine, 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. **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. **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.

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