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Motor and non motor effects of clinically available infusion therapies in Parkinson's disease

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Disclosures

Advisory boards

Stada, AbbVie (Poland)

Grants (investigator initiated)

GKC, Altoida

Honoraria

AbbVie, AbbVie (Poland), Bial, Britannia, GKC, Stada

The Parkinson's Disease Educational Course for Device-aided therapy options -**Industry Professionals**

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Intestinal gel

Levodopa/carbidopa intestinal gel (LCIG)

Continuous administration of levodopa/carbidopa by infusion into the jejunum



Levodopa/carbidopa/ entacapone intestinal gel (LECIGON)

Continuous administration of levodopa/carbidopa/entacapone gel by infusion into the jejunum



Subcutaneous

Subcutaneous apomorphine infusion

Does not require surgery; reversible.



Abbvie Foslevodopa/Foscarbidopa subcutaneous infusion



Neurosurgery

Deep brain stimulation (DBS)

Requires stereotactic brain surgery





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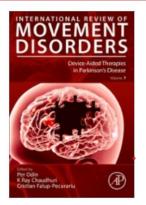


Subcutaneous foslevodopa/ foscarbidopa: A novel 24 h delivery option for levodopa

Karolina Poplawska-Domaszewicza, and K. Ray Chaudhurib, and K. Ray C

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^bParkinson's Foundation Centre of Excellence, King's College Hospital, London, United Kingdom
^cBasic and Clinical Neuroscience Department, The Maurice Wohl Clinical Neuroscience Institute, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, United Kingdom

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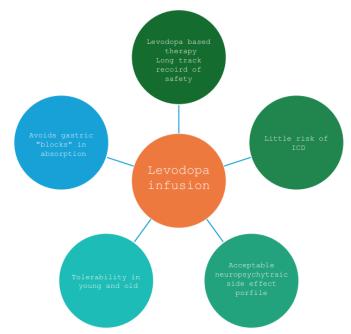
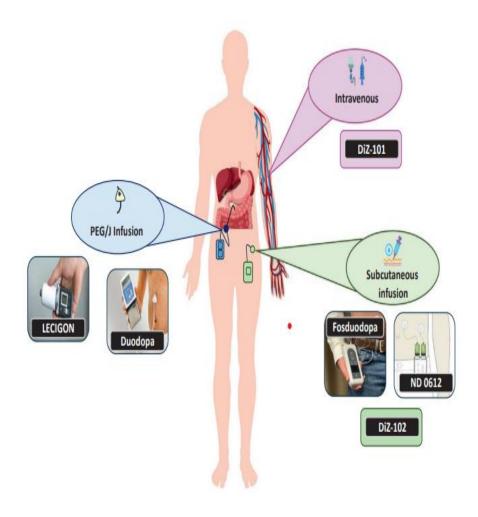


Fig. 1 Potential advantages of levodopa infusion in Parkinson's disease. ICD, impulse control disorder.



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Oral levodopa is introduced into clinical practice, becoming the gold standard for Parkinson's treatment¹

Levodopa infusions story





Continuous delivery of Duodopa® via infusion pump is approved for advanced Parkinson's³





The innovation The innovation and launch of Produodopa®5 of LECIGON®

1970 2000

2010

2020 2024



The unmet need for those with advanced Parkinson's²



The need for a minimally invasive, levodopa-based infusion treatment remains⁴



The launch of Produodopa^{®6}

LCIG, levodopa/carbidopa intestinal gel.

1. Abbott A. Nature. 2010;466:S6-7; 2. Koller WC and Tse W. Neurology. 2004;13;62:S1-8; 3. EMA. EU/3/01/035: Orphan designation for the treatment of advanced idiopathic Parkinson's disease with severe motor fluctuations. Available at: https://www.ema.europa.eu/en/medicines/human/orphan-designations/eu301035. Accessed: April 2024; 4. Antonini A. J Mov Disord. 2009;2:4-9; 5. Rosebraugh M, et al. Ann Neurol. 2021;90:52-61; 6. NICE. First NICE-recommended treatment for Parkinson's set to benefit hundreds. Available at: https://www.nice.org.uk/news/article/first-nice-recommended-treatment-for-parkinson-s-set-to-benefit-hundreds. Accessed: April 2024.

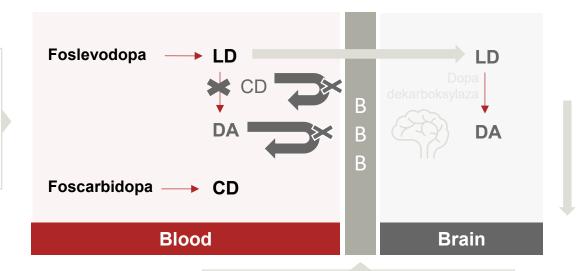
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FOSLEVODOPA/FOSCARBIDOPA

Foslevodopa and foscarbidopa (20:1) convert in vivo into levodopa and carbidopa



LD may improve:

Motor fluctuationsON time in patients responding to LD

CD does not cross the bloodbrain barrier and inhibits peripheral decarboxylation of LD to DA

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24-hour continuous subcutaneous infusion of foslevodopa/foscarbidopa



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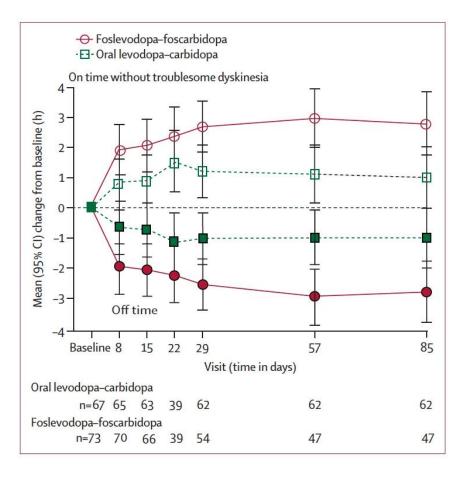
Pivotal Licensing Study

Safety and efficacy of continuous subcutaneous foslevodopa-foscarbidopa in patients with advanced Parkinson's disease: a randomised, double-blind, active-controlled, phase 3 trial

Michael J Soileau, Jason Aldred, Kumar Budur, Nahome Fisseha, Victor SC Fung, Anna Jeong, Thomas E Kimber, Kevin Klos, Irene Litvan, Daniel O'Neill, Weining Z Robieson, Meredith A Spindler, David G Standaert, Saritha Talapala, Eleni Okeanis Vaou, Hui Zheng, Maurizio F Facheris, Robert A Hauser

- A 12-week randomised, double-blind, double-dummy, activecontrolled study
- > 65 academic and community study centres in the USA and Australia.

Interpretation Foslevodopa-foscarbidopa improved motor fluctuations, with benefits in both on time without troublesome dyskinesia and off time. Foslevodopa-foscarbidopa has a favourable benefit-risk profile and represents a potential non-surgical alternative for patients with advanced Parkinson's disease.



Lancet Neurology 2022

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Neurol Ther (2023) 12:1937–1958
https://doi.org/10.1007/s40120-023-00533-1

ORIGINAL RESEARCH

Continuous Subcutaneous Foslevodopa/Foscarbidopa
in Parkinson's Disease: Safety and Efficacy Results
From a 12-Month, Single-Arm, Open-Label, Phase 3
Study

Jason Aldred : Eric Freire-Alvarez : Alexander V. Amelin : Angelo Antonini : Angelo

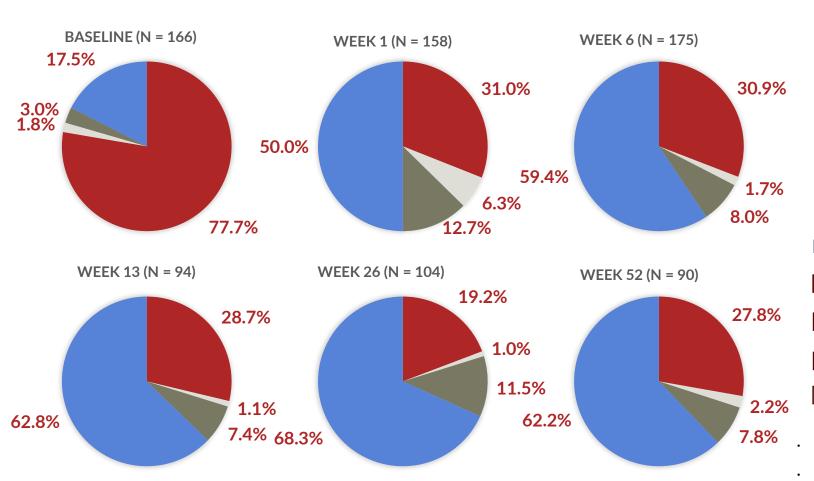
- ➤ 52-week, phase 3, open-label, single-arm, multicenter study to assess the safety, tolerability, and efficacy of foslevodopa/foscarbidopa administered as a 24-hour/day CSCI in patients with aPD
- ➤ 60 sites across 13 countries (Australia, Belgium, Canada, Denmark, Germany, Italy, Japan, Netherlands, Russia, Spain, Sweden, United Kingdom, and United States)
- > patient enrollment- June 2019- August 2021

Conclusion: Foslevodopa/foscarbidopa has the potential to provide a safe and efficacious, individualized, 24-hour/day, nonsurgical alternative for patients with PD.

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Distribution of first morning state on awakening (assessed by 24-hour PD diary)



Daily 'Off' time', h	5.9 (2.2) ^f
Daily 'On' time without dyskinesiac, h	6.5 (3.4) ^f
Daily "On" time with non-troublesome dyskinesia ^e , h	2.6 (2.6) ^f
Daily 'On' time with troublesome dyskinesia ^c , h	1.0 (1.7) ^f
Daily "On" time without troublesome dyskinesia ^c , h	9.1 (2.5)

First morning non-sleep symptom:

"Off" time

"On" time without dyskinesia

"On" time with troublesome dyskinesia

"On" time with non-troublesome dyskinesia

- Permission granted from Neurology and Therapy to re-use images from Aldred J, et al. Neurol Ther 2023.
- Aldred J, et al. Neurol Ther 2023; doi: https://doi.org/10.1007/s40120-023-00533-1.

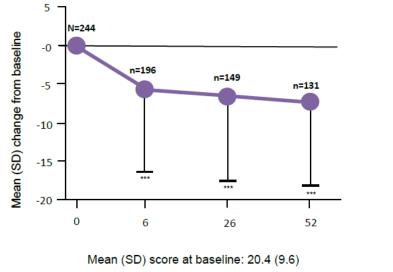
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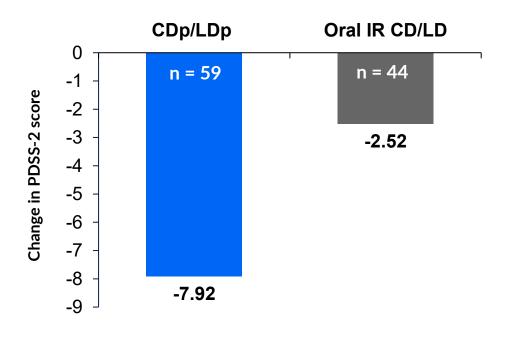


Conclusions: Improved sleep with foslevodopa/foscarbidopa was associated with improved QoL and "Off" time.

Fig: Sleep quality report using PDSS 2 scale in 244 subjects on Foslevodopa/foscarbidopa (Chaudhuri et al 2024).



PDSS-2 total score: Change from baseline to week 12



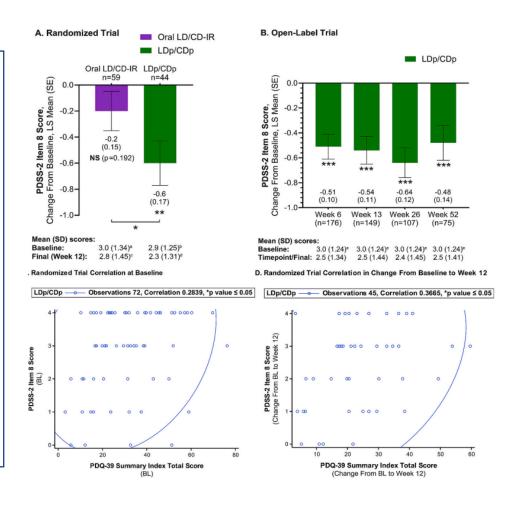
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- Significant improvement in nocturia symptoms with foslevodopa/foscarbidopa compared to oral levodopa at week 12 (p < 0.01)
- In the open label study, there were significant reductions in nocturia scores at weeks 6, 13, 26, and 52 compared to baseline (p < 0.001 for all comparisons)

 Bladder function in PD may involve dopamine D1 receptor activity, and the D1 effect of foslevodopa/foscarbidopa combined with sustained overnight stimulation may be the underlying mechanism, warranting further investigation.



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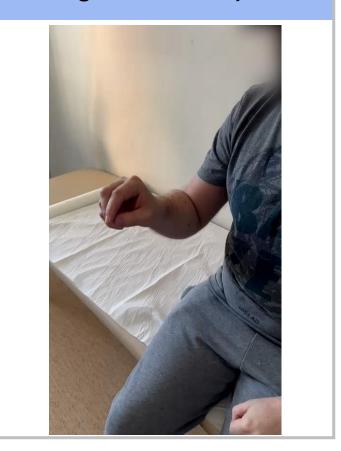


Case study 1: Right-sided bradykinesia and dystonic gait

Age: 39 years Male

Diagnosed with EOPD with dystonia in 2016

Severe right-sided bradykinesia



Right-sided dystonic gait during best "On" state



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Decision on further treatment





Post LDp/CDp after a few



Improvement in writing



Post LDp/CDp after 1 month



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After 3 months





- Courtesy of Prof. R. Chaudhuri and Dr. K. Popławska-Domaszewicz.
- The patient provided consent for the use of these videos within this presentation.

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After 1 year





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The special burden of EOPD and need for specific care



Recognition and characterising non-motor profile in early onset Parkin disease (EOPD)

Karolina Poplawska-Domaszewicz a,b,** , Mubasher A. Qamar b,c , Cristian Falup Pecurari K Ray Chaudhuri b,c,*

High NMS burden High risk of ICD Higher genetic cases

Gene	Association described	Level of evidence
DRD2	Higher risk of ICD in Western population and Asian	+++
GRIN2B	Higher risk of ICD in Western population and Asian	++
DRD1	Higher risk of ICD	++
PRKAG2	Higher risk of ICD	+
MEFV	Higher risk of ICD	+
PRKCE	Higher risk of ICD	+
OPRK1	Higher risk of ICD	+
HTR2A	Higher risk of ICD	+
DDC	Higher risk of ICD	+
DRD3	Higher risk of ICD in Western population and Asian	+
DBH, ACE, BDNF	Higher risk of ICD in Russian population has been described	+
GBA and LRRK2	Higher risk described in PPMI analysis and an observational study	++
Parkin	specific patterns of ICD such as: compulsive shopping, binge eating, and punding/hobbyism	+
PINK1	specific patterns of ICD such as: hypersexuality, compulsive shopping and binge eating	++

Specific genetic mutation	Clinical association
SNCA	Cognitive decline
ATP13A2 (Kufor- Rakeb Syndrome)	Rapid cognitive decline, dementia, and optic atrophy
PRKN	Specific pattern of ICD: compulsive shopping, binge eating, punding, increased hobbyism, and sleep benefit
PINK1	Specific pattern of ICD: hypersexuality, compulsive shopping, and binge eating
GRIN2B, DRD1 and DRD2	Strong links with ICD. Racial variations noted
LRRK2 GBA1 (pathogenic mutations)	Increased rates of ICD
GBA1 (pathogenic mutations)	Cognitive decline, RBD, and dysautonomia
PLA2G6 (PLAN)	Rapid cognitive decline and optic atrophy
DJ-1 PINK1	Association with pain in PD. PINK1 lower back pain described in EOPD
DRD2 rs2283265 polymorphism	Association with pain in EOPD
	mutation SNCA ATP13A2 (Kufor-Rakeb Syndrome) PRKN PINK1 GRIN2B, DRD1 and DRD2 LRRK2 GBA1 (pathogenic mutations) GBA1 (pathogenic mutations) PLA2G6 (PLAN) DJ-1 PINK1 DRD2 rs2283265

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Progress

Fosldopa and gait

Age: 59 years
Male
Self-employed
businessman

Diagnosed with PD in 2007



Post initiation



2-week follow-up



After 2 months

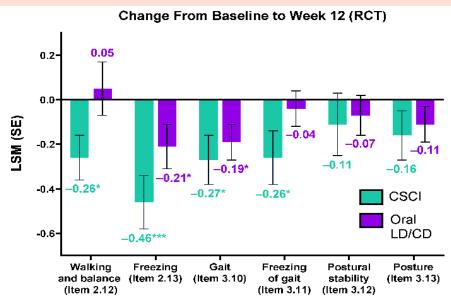


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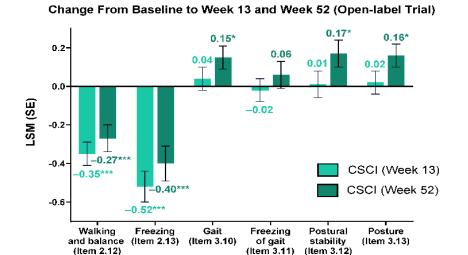


Effect of continuous subcutaneous LDp/CDp treatment on falls, posture, and freezing of gait

Post hoc analysis of single items from LDp/CDp registration trials



- Patients in the LDp/CDp arm achieved significant improvements from baseline to Week 12 in walking and balance, freezing, gait, and freezing of gait
- There were no significant between-arm differences in changes from baseline in postural stability or posture at Week 12.



- Significant improvements were observed from baseline in walking and balance and freezing at Weeks 13 and 52
- Gait, postural stability, and posture worsened vs baseline at Week 52
- *P<0.05; ***P<0.001 vs baseline.
- CSCI, continuous subcutaneous infusion; LD/CD, levodopa/carbidopa; LDp/CDp, foslevodopa/foscarbidopa; LSM, least squares mean; SE, standard error 28
- Odin P. et al. FAN 2023

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Improvement of Troublesome Dyskinesia in People With Parkinson's Disease Treated With Foslevodopa/Foscarbidopa

Morten Blaabjerg, Tsao-Wei Liang, S Elizabeth Zauber, Lars Bergmann, Resmi Gupta, Linda Harmer, Megha Shah, Filip Bergquist Bergmann, Resmi Gupta, Linda Harmer,

Department of Neurology, Odense University Hospital, Odense, Denmark: "Department of Neurology, Thomas Jeffercor University, Philedelphin, Pennsylvania, United States: "Department of Neurology, Indiana University, School of Medicine, Indianapolis, Indiana, United States: "AbbVie Inc., North Chicago, Illinois, United States: "Department of Pharmacology, Indianapolis, Indiana, United States: "AbbVie Inc., North Chicago, Illinois, United States: "Department of Pharmacology, Indianapolis, Indiana, United States: "AbbVie Inc., North Chicago, Illinois, United States: "Department of Pharmacology, The Chicago of Chic

OBJECTIVE

To evaluate the effect of LDp/CDp on troublesome dyskinesia (TSD) in people with PD, stratified by baseline duration of TSD

CONCLUSIONS

Continuous delivery of LDp/CDp treatment for 52-weeks was associated with significant improvements in time spent with TSD in those who experienced clinically-relevant levels of TSD at baseline⁸

The majority of patients who experienced TSD at baseline reported no TSD after 52 weeks with continuous delivery of LDp/CDp

This exploratory data suggests that continuous delivery with precise dosing of LDp/CDp may lead to shorter TSD duration and reduced impact on daily function for people with PD who experience TSD

For additional information or to obtain a PDF of this poster

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QR code expiration: June 2, 2025
To submit a medical question, please



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References

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SAFETY PROFILE

LDp/CDp was generally well tolerated in patients with aPD



M15-741 study¹

TEAE preferred terms, n¹ (%)	All subjects N = 244
Infusion site erythema	127 (52.0)
Infusion site nodule	70 (28.7)
Infusion site cellulitis	56 (23.0)
Infusion site edema	47 (19.3)
Hallucination	42 (17.2)
Fall	41 (16.8)
Infusion site pain	38 (15.6)
Infusion site reaction	30 (12.3)
Anxiety	29 (11.9)
Infusion site abscess	27 (11.1)
Dizziness	25 (10.2)



M15-736 study²

TEAE, n ² (%)	Oral IR LD/CD N = 67	LDp/CDp N = 74
Infusion site erythema	1 (1)	20 (27)
Infusion site pain	1 (1)	19 (26)
Infusion site cellulitis	0	14 (19)
Infusion site edema	0	9 (12)
Dyskinesia	4 (6)	8 (11)
Fall	12 (18)	6 (8)
Infusion site bruising	2 (3)	6 (8)
Infusion site hemorrhage	0	6 (8)
Infusion site nodule	0	6 (8)
"On" and "Off" phenomenon	0	6 (8)
Hallucination	1 (1)	5 (7)
Balance disorder	0	4 (5)
Constipation	0	4 (5)
Hallucination, visual	0	4 (5)
Infusion site induration	0	4 (5)
Infusion site infection	0	4 (5)
Infusion site pruritus	0	4 (5)
Peripheral swelling	0	4 (5)



- The most common AEs of special interest were related to the infusion site^{1,2}
- Majority of infusion site AEs were non-serious and mild-to-moderate in severity¹

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Sustained Long-Term Safety and Tolerability of Foslevodopa/ Foscarbidopa in Parkinson's Disease: 96-Week Primary Treatment Period Results from an Ongoing Open-Label Extension Study

Filip Bergquist, 1.2 Jason Aldred, 3 Erik H. Danielsen, 4 Camille Carroll, 5 Cheney Matthews, 6

Jia Jia, 6 Megha Shah, 6 Amy Spiegel, 6 Victor SC Fung 7.8

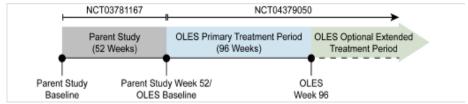
¹Department of Pharmacology, Institute of Neuroscience and Physiology, University of Gothenburg, Gothenburg, Sweden;

*Selkirk Neurology & Inland Northwest Research, Spokane, WA, USA, Department of Neurology, Aurhus University, Aarhus, Denmark;
*Newcastle University, Translational and Clinical Research Institute, Newcastle, UN;
*Spokane, Newcastle University, Translational and Clinical Research Institute, Newcastle, UN;
*Spokane, NewCastle University, Translational and Clinical Research Institute, Newcastle, UN;
*Spokane, NewCastle, University, Translational and Clinical Research Institute, Newcastle, UN;
*Spokane, NewCastle, School, Spokane, New South Wales, Australia, *Department of Neurology, Westmead Hospital, Spokane, New South Wales, Australia, *Topical University New South Wales, *Topical University New South Wales, *Topical University New South Wal

OBJECTIVE

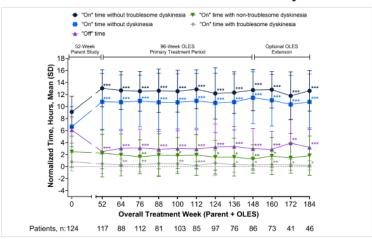
Evaluate the long-term safety, tolerability, and efficacy of foslevodopa/ foscarbidopa (LDp/CDp) in people with advanced Parkinson's disease (PD) treated through week 96 of an open-label extension study (OLES)

Study Design



 The OLES consists of a 96-week primary treatment period and optional extended treatment period that is open-ended and ongoing

Improvements in "Off" and "On" Time Were Sustained from the Parent Study

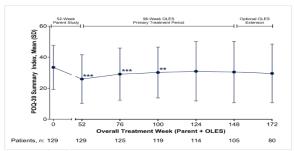


OLES, Open-label extension study. Treatment weeks are defined relative to breatment initiation in the parent study. Week 52 corresponds to the OLES baseline, and week 148 corresponds to the end of the primary treatment period. Patient in at each time point corresponds to the number of patients in the OLES with valid PD daray recording days, p-values indicate companisons to parent study baseline values for patients in the OLES. "p < 0.05, "p < 0.05."

"p < 0.01, "p < 0.01", "p < 0.01".

 Improvements in "Off" time and "On" time without dyskinesia were sustained throughout the OLES, up to 184 weeks of total treatment

Improvements in PDQ-39 Summary Index Were Maintained through 100 Total Weeks of Treatment



OLES, Open-label extension study.

Treatment weeks are defined relative to treatment initiation in the parent study. Week 52 corresponds to the OLES baseline, and week 146 or responds to the end of the primary treatment period. Planet in at each time point corresponds to the number of patients in the OLES with vial PDQ-33 accessments at each vialt. "p = 0.05, "p = 0.01, ""p = 0.001; indicate comparisons to parent study baseline values for patients in the PQ-33 accessments at each vialt." p = 0.05, "p = 0.01, ""p = 0.001; indicate comparisons to parent study baseline values for patients in the OLES with vialt p = 0.05, "p = 0.01, ""p = 0.001; indicate comparisons to parent study baseline values for patients in the OLES with vialt p = 0.05, "p = 0.01, ""p = 0.01; indicate comparisons to the number of patients in the OLES with vialt p = 0.05, "p = 0.01; indicate comparisons to the number of patients in the OLES with vialt p = 0.05, "p = 0.01; indicate comparisons to the number of patients in the OLES with vialt p = 0.01; indicate comparisons to the oles with vialt p = 0.01; indicate comparisons to the number of patients in the OLES with vialt p = 0.01; indicate comparisons to the oles with vialt p = 0.01; indicate comparisons to the oles with vialt p = 0.01; indicate comparisons to the oles with vialt p = 0.01; indicate comparisons to the oles with vialt p = 0.01; indicate comparisons to the oles with vialt p = 0.01; indicate comparisons to the oles with vialt p = 0.01; indicate comparisons to the oles with vialt p = 0.01; indicate comparisons to the oles with vialt p = 0.01; indicate comparisons to the oles with vialt p = 0.01; indicate comparisons to the oles with vialt p = 0.01; indicate comparisons to the oles with vialt p = 0.01; indicate comparisons to the oles with vialt p = 0.01; indicate comparisons to the oles with vialt p = 0.01; indicate comparisons to the oles with vialt p = 0.01; indicate comparisons to the oles with vialt p = 0.01; indicate comparisons to the oles with vialt p = 0.01; indicate compa

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Poster 006

Sustained Long-Term Safety and Tolerability of Foslevodopa/ Foscarbidopa in Parkinson's Disease: 96-Week Primary Treatment Period Results from an Ongoing Open-Label Extension Study

Filip Bergquist, 1,2 Jason Aldred, 3 Erik H. Danielsen, 4 Camille Carroll, 5 Cheney Matthews, 8

Jia Jia, 6 Megha Shah, 6 Amy Spiegel, 6 Victor SC Fung7,8

[†]Department of Pharmacology, Institute of Neuroscience and Physiology, University of Gothenburg, Gothenburg, Sweden;

[†]Department of Neurology, Sahigrenska University Hospital, Gothenburg, Sweden;

[†]Seikirk Neurology & Inland Northwest Research, Spokane, WA, USA, [†]Department of Neurology, Aarhus University, Aarhus, Denmark;

[†]Newcastle University, Translational and Clinical Research Institute, Newcastle, UK; [†]AbbVie Inc., North Chicago, II., USA;

Sydney Medical School, Sydney, New South Wales, Australia; [†]Department of Neurology, Westmead Hospital, Sydney, New South Wales,

OBJECTIVE

Evaluate the long-term safety, tolerability, and efficacy of foslevodopa/ foscarbidopa (LDp/CDp) in people with advanced Parkinson's disease (PD) treated through week 96 of an open-label extension study (OLES)

Adverse Events During the OLES

	Total, n (%), N=129
Any AE	119 (92.2)
Any AE considered associated with LDp/CDp	96 (74.4)
Any serious AE	48 (37.2)
Any severe AE	42 (32.6)
Any AE leading to discontinuation of LDp/CDp	17 (13.2)
Any AE leading to death	7 (5.4)
Most common AEs (≥15% of patients)	
Fall	42 (32.6)
Infusion site erythema	29 (22.5)
Infusion site cellulitis	24 (18.6)
Hallucination	22 (17.1)

AE, adverse event; LDp/CDp, foslevodopa/foscarbidopa.

AEs were evaluated in from OLES baseline until the data cutoff in the safety analysis set, defined as any patients who received any LOp/CDp in this period. All AEs are treatment-emergent and do not imply relationship to study drug unless indicated.

- Overall, 92.2% of patients experienced ≥1 AE in the OLES
- AEs were the primary reason for discontinuation in n=13 (10.1%) patients
- The LDp/CDp safety profile was generally similar to that reported in the parent study¹ but showed notable shifts
- Falls were more frequent in the OLES than in the parent study (32.6% vs 16.8%¹)
- The OLES had lower rates for infusion-site erythema (22.5% vs 52.0%¹) and cellulitis (18.6% vs 23.0%¹)
- Hallucinations were similar in frequency in both studies. In the OLES, majority were mild (n/N=8/22) or moderate (n/N=12/22)

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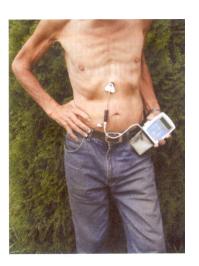


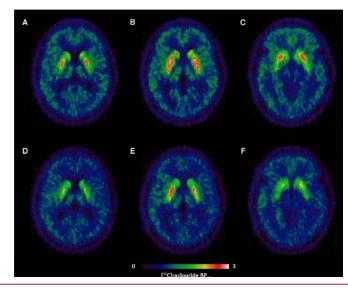


Levodopa/carbiodopa intestinal gel

Duodopa infusion provides stable striatal dopamine levels

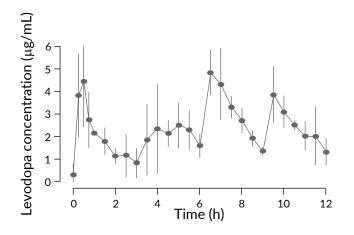
Levodopa-Carbidopa Intestinal Gel (LCIG)

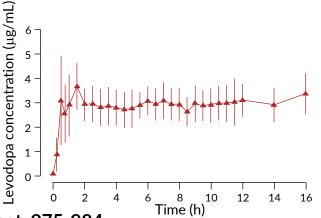




Decreases in [11C]raclopride binding potential before (A-C) and after (D-F) LCIG infusions (PET).

Plasma concentrations of levodopa with oral tablets vs LCIG²





1. Politis M, et al. (2017) Mov Disord, 235-240; 2. Othman AA, et al. (2015) Clin Pharmacokinet, 975-984.

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Adv Ther (2021) 38:2854–2890 https://doi.org/10.1007/s12325-021-01747-1

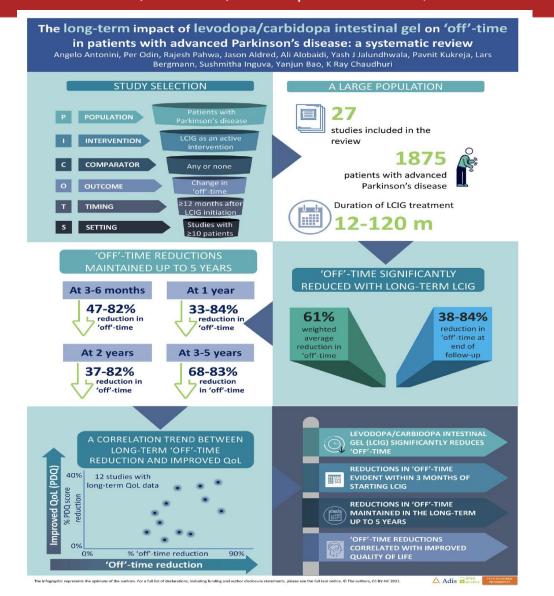


REVIEW

The Long-Term Impact of Levodopa/Carbidopa Intestinal Gel on 'Off'-time in Patients with Advanced Parkinson's Disease: A Systematic Review

Angelo Antonini · Per Odin · Rajesh Pahwa · Jason Aldred · Ali Alobaidi · Yash J. Jalundhwala · Pavnit Kukreja · Lars Bergmann · Sushmitha Inguva · Yanjun Bao · K. Ray Chaudhuri

Continuous dopaminergic stimulation provided by LCIG reduces OFF time and improves other motor complications that are not well controlled with oral levodopa. These improvements are sustained for more than 12 months and up to 5 years.



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Clinical Research

Levodopa Carbidopa Intestinal Gel in Advanced Parkinson's Disease: DUOGLOBE Final 3-Year Results

K. Ray Chaudhuri^{a,*}, Norbert Kovács^b, Francesco E. Pontieri^{c,d}, Jason Aldred^e, Paul Bourgeois^f, Thomas L. Davis^g, Esther Cubo^h, Marieta Anca-Herschkovitschⁱ, Robert Iansek^j, Mustafa S. Siddiqui^k, Mihaela Simu^l, Lars Bergmann^m, Mayra Ballina^m, Pavnit Kukreja^m, Omar Ladhani^m, Jia Jia^m and David G. Standaertⁿ

- global multicenter, single arm, non-interventional, postmarketing, observational study
- ➤ 55 sites across 10 countries (Australia, Belgium, Hungary, Israel, Italy, Romania, Slovenia, Spain, United Kingdom, and the United States)
- > 195 patients

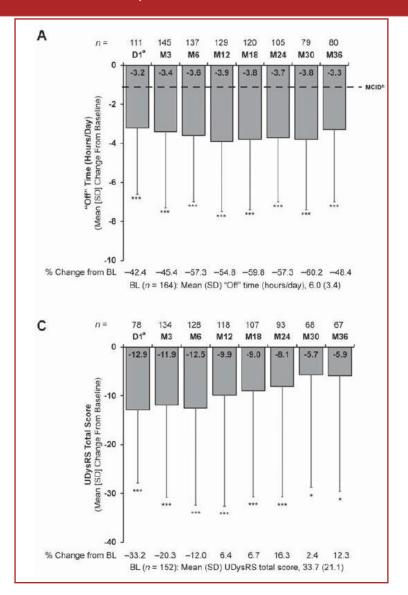
Characteristic	Total
	N = 195
Sex, n (%)	
Male	120 (61.5)
Female	75 (38.5)
Age (y); mean \pm SD	70.2 ± 8.2
<65 y, n (%)	44 (22.6)
65–75 y, n (%)	95 (48.7)
>75 y, n (%)	56 (28.7)
BMI; mean \pm SD BMI, kg/m ²	25.9 ± 4.1^{a}
PD duration, y: mean ± SD	11.2 ± 4.8
<10 y, n (%)	94 (48.5)
$\geq 10 \text{ y, } n (\%)$	100 (51.5)
Time to LCIG initiation, y; mean \pm SD from:	
PD symptoms	12.2 ± 5.0
Start of motor fluctuations	5.6 ± 4.7

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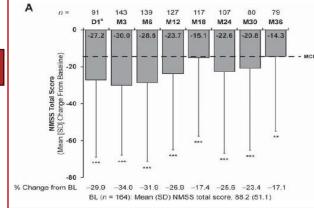


Off period

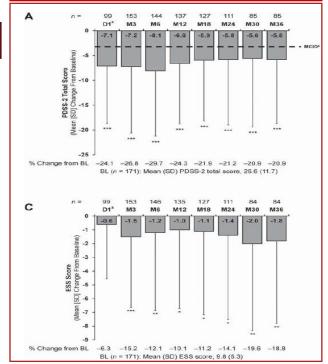
Dyskinesia



NMSS



PDSS



Chaudhuri et al. JPD 2023

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Range of potential MIC

Movement Disorders Vol. 24, No. 10, 2009, pp. 1468–1474 © 2009 Movement Disorder Society

> Intrajejunal Levodopa Infusion in Parkinson's Disease: A Pilot Multicenter Study of Effects on Nonmotor Symptoms and Quality of Life

Holger Honig, MD, ¹ Angelo Antonini, MD, ² Pablo Martinez-Martin, MD, ³ Ian Forgacs, FRCP, ⁴ Guy C. Faye, FRCP, ⁴ Thomas Fox, MD, ¹ Karen Fox, MD, ¹ Francesca Mancini, MD, ² Margherita Canesi, MD, ² Per Odin, MD, PhD, ¹ and K. Ray Chaudhuri, MD, FRCP, DSc ^{4*}

TABLE 2. Importance of the change induced by duodenal levodopa/carbidopa treatment

	Patients worsened	Patients stable	Patients improved	Effect		Base	eline	10% of maximum	Mean difference
	(%)	(%)	(%)	size	SRM	½ SD	1/4 SD	possible score	in score
UPDRS 3-Motor examination	13.6	18.2	68.2	0.54	0.79	7.0	3.5	10.8	-7.54^{a}
UPDRS 4-Complications	0	0	100	2.03	1.76	1.5	0.7	2.3	-5.91
UPDRS-Dyskinesia score ^b	0	13.6	86.4	1.61	1.50	1.3	0.6	1.6	-3.77
PD Sleep Scale ^c	0	0	100	2.16	1.51	6.6	3.3	15.0	28.51
PDQ-8	9.1	13.6	77.3	1.28	1.09	9.2	4.6	10.0	-23.4
NMSS-Total score	4.5	0	95.5	0.89	1.23	28.2	14.1	36.0	-50.55
Cardiovascular	0	40.9	59.1	0.67	0.81	1.8	0.9	2.4	-2.41
Sleep/Fatigue	0	13.6	86.4	0.72	1.02	7.9	3.9	4.8	-11.32
Mood/Cognition	18.2	22.7	59.1	0.49	0.58	7.6	3.8	7.2	-7.50^{a}
Perception/Hallucinations	9.1	63.6	27.3	0.30	0.44	2.6	1.3	3.6	-1.54^{a}
Attention/Memory	0	54.5	45.5	0.40	0.67	4.0	2.0	3.6	-3.27^{a}
Gastrointestinal	4.5	27.3	68.2	0.67	0.89	4.6	2.3	3.6	-6.23
Urinary	9.1	22.7	68.2	0.62	0.81	5.3	2.7	3.6	-6.64
Sexual	13.6	40.9	45.5	0.48	0.50	4.1	2.0	2.4	-3.91^{a}
Miscellaneous	9.1	13.6	77.3	0.97	1.02	4.0	2.0	4.8	-7.73

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LCIG





LCIG, levodopa/carbidopa intestinal gel. Courtesy of Prof. R. Chaudhuri and Dr. K. Popławska-Domaszewicz. The patient provided consent for the use of these videos within this presentation.

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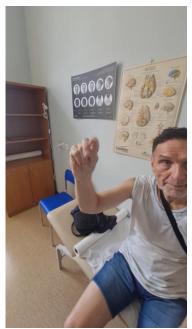


PD-FOG

Before Duodopa



Duodopa therapy



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Study reference	Participants	Study design	Treatment	Main findings	FOG subtype
Levodo	pa-carbidopa inte	estinal gel (LCIG)			
[60]	65 advanced PD	Observational, retrospective, a review of medical records	Mean duration of LCIG therapy was 3.7 years	FOG improved (FOG present only in 22% of patients at 1 year follow-up compared to 46% at baseline).	Unknown
[61]	91 advanced PD	Observational, retrospective, a review of medical records	Mean time of follow up of 18 \pm 8.4 months	Gait disorders (freezing, festination, postural instability) improved in 61.4% of patients (three point scale).	Unknown
[62]	32 advanced PD with FOG	Observational, retrospective, a review of medical records	Mean duration of LCIG therapy was 2.59 ± 1.12 years	FOG that present in OFF condition and improved but did not disappear completely in ON condition can be further improved by LCIG (UPDRS freezing score).	31 patients with responsive FOG and one with resistant- FOG
[63]	177 advanced PD, in which 122 patients with FOG	Observational, retrospective, multi-center, cross-sectional, uncontrolled	Mean duration of LCIG therapy was 34.7 months, 80.8% of patients ≥12 months	FOG improved in 76.2% of patients (subjective assessment by clinicians).	Unknown
[64]	28 PD	Prospective, open label, uncontrolled	17/28 patients reached the 24- month follow-up	FOG improved (FOGQ)	Unknown
[65]	25 PD	Prospective, open label, uncontrolled	20 patients continued on treatment to 6 months.	FOG improved (FOGQ)	Unknown
[66]	5 PD with FOG	Prospective, open label, uncontrolled	24 h LCIG therapy, 6 months	360° turn time reduced, FOG improved (FOGQ) and fall frequency reduced	Resistant
[56]	7 PD with FOG	Prospective, open label controlled, unrandomized	Evaluations were performed in "On" state (60–90 min after taking	FOG improved on LCIG (FOGQ and UPDRS freezing score)	Resistant
			the morning oral levodopa or LCIG).	Gao et al. Translational Neu	

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Journal of Parkinson's Disease 13 (2023) 769–783 DOI 10.3233/JPD-225105 IOS Press

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Clinical Research

Levodopa Carbidopa Intestinal Gel in Advanced Parkinson's Disease: DUOGLOBE Final 3-Year Results

K. Ray Chaudhuri^{a,*}, Norbert Kovács^b, Francesco E. Pontieri^{c,d}, Jason Aldred^e, Paul Bourgeois^f, Thomas L. Davis^g, Esther Cubo^h, Marieta Anca-Herschkovitschⁱ, Robert Iansek^j, Mustafa S. Siddiqui^k, Mihaela Simu^l, Lars Bergmann^m, Mayra Ballina^m, Pavnit Kukreja^m, Omar Ladhani^m, Jia Jia^m and David G. Standaertⁿ

SAFETY PROFILE

Deaths Deaths considered possibly related to LCIG ^a $ \begin{array}{c} \text{Datients (30.2\%)} \\ 34 \text{ (17.4)} \\ 1 \text{ (0.5)} \\ \hline \\ \text{Common} \\ \text{SAEs (≥ 4} \\ \text{patients)} \\ \text{SAEs} \\ (reasonable of the constant of th$	Parameters		n (% of N = 195)
Any SAE leading to drug withdrawal Any severe AE 69 (35.4) Patients remaining on LCIG despite study discontinuation 32 of 106 discontinuation patients (30.2% $34 (17.4)$ Deaths considered possibly related to LCIGa 1 (0.5) Common SAEs (≥ 4 emergent patients) SAEs (reasonable possibility) MedDRA v23.1 Preferred Term $n (\% \text{ of } N=195)$ $N=195)$ Fall $8 (4.1)$ $2 (1.0)$ PD $8 (4.1)$ $3 (1.5)$ Urinary tract infection $7 (3.6)$ $1 (0.5)$	Any SAE	107 (54.9)	
Any severe AE Patients remaining on LCIG despite study discontinuation 32 of 106 discontinuation patients (30.2% $34 (17.4)$ Deaths considered possibly related to LCIG ^a 34 (17.4) $1 (0.5)$ Hip fracture $1 (0.5)$ $1 (0.5)$ $1 (0.5)$ $1 (0.5)$ Hip fracture	Any SAE with reasonable possibility of car	usal relationship to LCIG	31 (15.9)
Patients remaining on LCIG despite study discontinuation 32 of 106 discontinuation patients (30.2% 34 (17.4) $\begin{array}{c} \text{Deaths} \\ \text{Deaths considered possibly related to LCIG}^{\text{a}} \\ \end{array} \begin{array}{c} \text{Common} \\ \text{SAEs} (\geq 4 \\ \text{patients}) \\ \end{array} \begin{array}{c} \text{SAEs} \\ \text{(reasonable possibility} \\ \text{MedDRA v23.1 Preferred Term} \\ \end{array} \begin{array}{c} n \ (\% \ \text{of} \\ N = 195) \\ \end{array} \begin{array}{c} N = 195) \\ \text{Fall} \\ \text{PD} \\ \text{PD} \\ \text{Urinary tract infection} \\ \text{Hip fracture} \\ \end{array} \begin{array}{c} 8 \ (4.1) \\ \text{Common} \\ \text{SAEs} \\ \text{(reasonable possibility} \\ \end{array}$	Any SAE leading to drug withdrawal		53 (27.2)
Deaths Deaths considered possibly related to LCIGa $ \begin{array}{c} \text{Deaths} \\ \text{Deaths considered possibly related to LCIGa} \\ \\ \text{Common} \\ \text{SAEs} (\geq 4 \\ \text{patients}) \\ \text{SAEs} \\ \text{(reasonable possibility)} \\ \hline \text{MedDRA v23.1 Preferred Term} \\ \text{MedDRA v23.1 Preferred Term} \\ \\ \text{Fall} \\ \text{PD} \\ \text{PD} \\ \text{SAEs} \\ \text{(reasonable possibility)} \\ \hline \text{Fall} \\ \text{SAEs} \\ \text{(reasonable possibility)} \\ \text{N=195} \\ \\ \text{Fall} \\ \text{SAEs} \\ \text{(reasonable possibility)} \\ \text{N=195} \\ \text{N=195} \\ \text{N=195} \\ \text{Deaths considered possibly related to LCIGa} \\ \text{SAEs} \\ \text{(reasonable possibility)} \\ \text{N=195} \\ \text{N=195} \\ \text{N=195} \\ \text{N=195} \\ \text{N=195} \\ \text{Deaths considered possibly related to LCIGa} \\ \text{N=105} \\ \text$	Any severe AE		69 (35.4)
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Patients remaining on LCIG despite study dis	continuation	32 of 106 discontinued
Deaths considered possibly related to LCIG ^a Common Treatment-SAEs (≥ 4 emergent patients) MedDRA v23.1 Preferred Term $N = 195$ Fall $N = 195$ $N = 195$ Fall $N = 195$ $N = 195$ $N = 195$ Fall $N = 195$ Fall $N = 195$ Fall $N = 195$			patients (30.2%)
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Deaths		34 (17.4)
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Deaths considered possibly related to LCIGa		1 (0.5)
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$			
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$		Common	Treatment-
		SAEs (≥4	emergent
		patients)	SAEs
MedDRA v23.1 Preferred Term n (% of $N=195$) n (% of $N=195$) Fall 8 (4.1) 2 (1.0) PD 8 (4.1) 3 (1.5) Urinary tract infection 7 (3.6) 1 (0.5) Hip fracture 6 (3.1) 0			(reasonable
			possibility)
Fall 8 (4.1) 2 (1.0) PD 8 (4.1) 3 (1.5) Urinary tract infection 7 (3.6) 1 (0.5) Hip fracture 6 (3.1) 0	MedDRA v23.1 Preferred Term	n (% of	n (% of
PD 8 (4.1) 3 (1.5) Urinary tract infection 7 (3.6) 1 (0.5) Hip fracture 6 (3.1) 0		N = 195)	N = 195)
Urinary tract infection 7 (3.6) 1 (0.5) Hip fracture 6 (3.1)	Fall	8 (4.1)	2 (1.0)
Hip fracture $6 (3.1)$	PD	8 (4.1)	3 (1.5)
1	Urinary tract infection	7 (3.6)	1 (0.5)
Pneumonia 6 (3.1) 0	Hip fracture	6 (3.1)	0
	Pneumonia	6 (3.1)	0
Abdominal pain 6 (3.1) 4 (2.1)	Abdominal pain	6 (3.1)	4(2.1)
Device dislocation 5 (2.6) 2 (1.0)	Device dislocation	2 (1.0)	
Femoral neck fracture 4 (2.1) 0	Femoral neck fracture	0	
Hyponatremia 4 (2.1) 1 (0.5)		4 (2.1)	1 (0.5)
Sepsis 4 (2.1) 0	Sepsis	4 (2.1)	0

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RESEARCH ARTICLE

CLINICAL PRACTICE

Levodopa-Entacapone-Carbidopa Intrajejunal Infusion in Advanced Parkinson's Disease - Interim Analysis of the ELEGANCE Study

Daniel Weiss, MD,^{1,*} Wolfgang H. Jost, MD,² József Attila Szász, MD,³ Zvezdan Pirtošek, MD,⁴ Ivan Milanov, MD,⁵ Volker Tomantschger, MD,⁶ Norbert Kovács, MD,⁷ Harry Staines, PhD, CSTAT,⁸ Bharat Amlani, MPharm,⁹ Niall Smith, BSc,⁹ and Teus van Laar, MD,¹⁰

Conclusions: Routine use of LECIG for up to 12 months provided sustained control of motor symptoms, and was well tolerated with a positive impact on QoL and high patient satisfaction.









Lecigon infusion shows strong effect on all aspects of sleep dysfunction in PD

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EXPERT REVIEW OF MIGICAL DEVICES

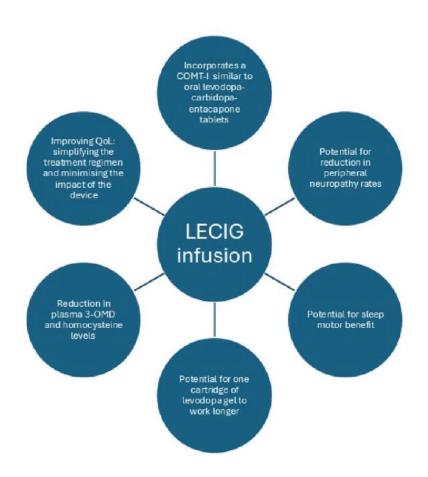
Expert Review of Medical Devices

The device-aided intrajejunal delivery of levodopaentacapone-carbidopa intestinal gel the treatment of Parkinson's disease: overview of efficacy and safety

Karolina Popławska-Domaszewicz, Vinod Metta, Per Odin & K Ray Chaudhuri

Published online: 08 May 2025.





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Apomorphine is the only dopamine agonist with equivalent efficacy to levodopa



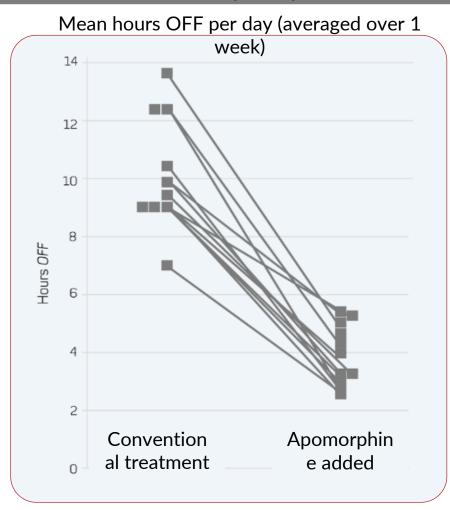
- Broad spectrum dopamine agonist activating all dopamine D1-like (D1, D5) and D2-like (D2, D3, D4) receptors with a rapid and reliable effect¹
- Supported by clinical evidence and experience of efficacy and safety over 30 years¹
- Despite advances in therapy apomorphine remains the only dopamine agonist with equivalent efficacy to levodopa²
- Subcutaneous apomorphine infusion provide continuous dopaminergic stimulation via continuous drug delivery ³
- Jenner P, Katzenschlager R. Parkinsonism Relat Disord. 2016;33 Suppl 1:S13-21
- 2. Stibe CM, et al. Lancet. 1988;1(8582):403-6.
- 3. APO-go® POD 5 mg/ml solution for infusion in cartridge. Summary of Product Characteristics. 2022.

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Apomorphine equipotent to levodopa International Parkinson and

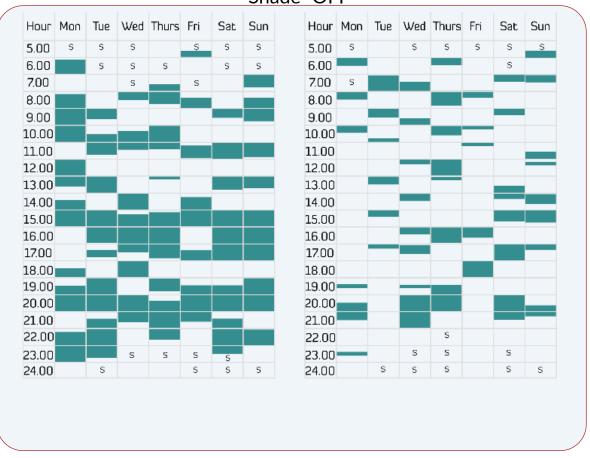


Subcutaneous apomorphine effective for the management of ON-OFF oscillations in 19 PD patients



Diary recording OFF periods before and after apomorphine.

Shade=OFF



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APOMORPHINE

 intermittent apomorphine injection (penject) continuous subcutaneous apomorphine infusion (pump)







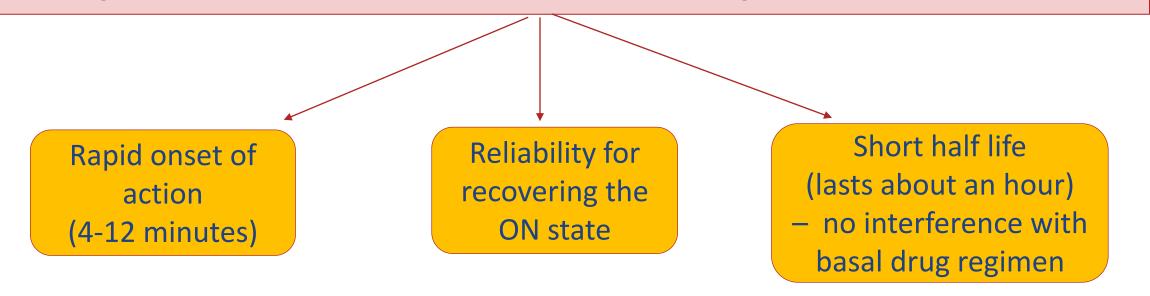
Trenkwalder, Chaudhuri et al. Expert Consensus Group report on the use of apomorphine in the treatment of Parkinson's disease e Clinical practice recommendations. Parkinsonism and Related Disorders, 2015.

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So why APOMORPHINE PEN?

Fills gaps in the control of motor functioning with usual medication



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intermittent apomorphine injection (penject)

- "Rescue therapy" for motor and non-motor "off" periods inadequately controlled by oral/transdermal treatments
- patients with unpredictable and predictable 'off' periods
- off symptoms that may improve include: off-related dystonia, freezing, non-motor symptoms, including pain, early morning 'off' states (early morning dystonia, akinesia, nonmotor fluctuations)
- when absorption of oral levodopa is impaired or the patient has gastric emptying problems (gastroparesis) to treat delayed "on"



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Apomorphine Injection: Other actions Apomorphine can have tremorolytic action





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Apomorhine can be useful for dystonic pain



Thanks Courtesy Prof Chaudhuri/Dr V Metta

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continuous subcutaneous apomorphine infusion (pump)

- "off" periods not adequately controlled by oral treatment
- when rescue doses of apomorphine injection are effective but too frequent (for example, more than 4-6 times per day)
- dyskinesias limit further therapy optimalization
- simplify complex PD dosing regimens to improve convenience





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Apomorphine subcutaneous infusion in patients with Parkinson's disease with persistent motor fluctuations (TOLEDO): a multicentre, double-blind, randomised, placebo-controlled trial Lancet Neurol 2018; 17: 749-59

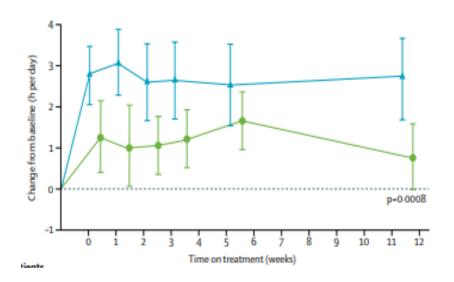
Regina Katzenschlager, Werner Poewe, Olivier Rascol, Claudia Trenkwalder, Günther Deuschl, K Ray Chaudhuri, Tove Henriksen, Teus van Laar, Kevin Spivey, Senthil Vel, Harry Staines, Andrew Lees

a significant decrease in off-time hours per day in the 12 week of treatment

62% of patients in the apomorphine arm experienced more than two hours of reduction of off time from baseline compared to 29% for placebo ¹7

Time on treatment (weeks)

the on-time troublesome dyskinesia free period was higher in the apomorphine group (2.77 ± 3.26 hours) as compared to the placebo group (0.80 ± 2.93 hours)



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TOLEDO 52-week OLP results: key efficacy outcomes confirmed those of the DBP

Methods:

All patients completing the 12-week DBP

The primary objective →evaluation of long-term safety of APO.

Results:

84 patients entered the OLP (40 previously on APO, 44 on placebo) and 59 patients (70.2%) completed the study.

Reduction in daily OFF time and improvement in ON time without troublesome dyskinesia were sustained for up to 64 weeks.

Mean (±SD) daily levodopa-equivalent dose decreased from DBP baseline to week 64 by 543 mg (±674) and levodopa dose by 273 mg (±515).

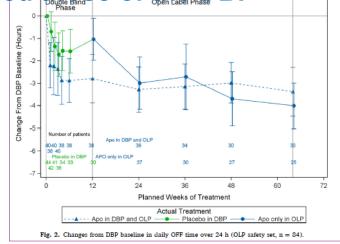
Conclusions:

The safety and efficacy of APO infusion were demonstrated with long-term use for persistent motor fluctuations, allowing substantial reductions in oral PD medication.

Katzenschlager R, et al. Parkinsonism Rel Dis. 2021;83:79-85.

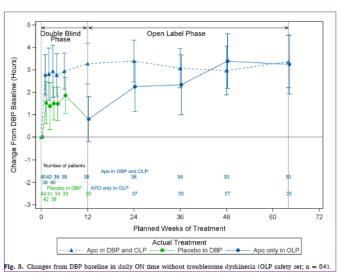
Pooled data for week 64 (n=55)

Mean (±SD) change from DBP baseline in daily OFF time -3.66 (2.72) hours



Pooled data for week 64 (n=55)

Mean (±SD) change from DBP baseline in daily ON time without troublesome dyskinesia 3.31 (3.12) hours



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Research article

Continuous, subcutaneous apomorphine infusion for Parkinson disease motor fluctuations: Results from the phase 3, long-term, open-label United States InfusON study

Journal of Parkinson's Disease

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| DOI: 10.1177/1877718X241310727
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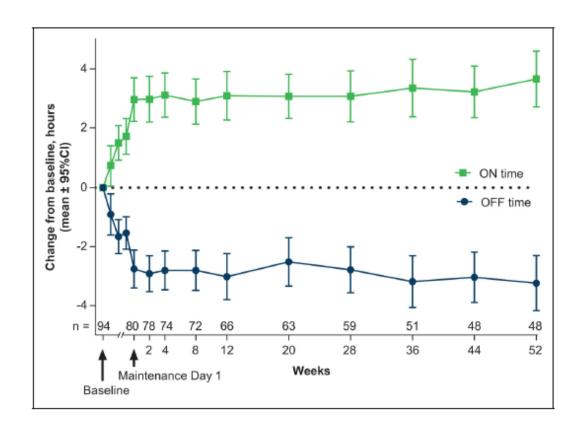
InfusON: A US-based post-hoc analysis of open-label, long-term outpatient use of apomorphine infusion

- Phase III study: confirmed long-term (1 year) safety profile and tolerability¹
- Aligned with the results of the TOLEDO study^{2,3}

1. Isaacson SH, et al. J Parkinsons Dis. 2025;15(2):361-373.

- 2. Katzenschlager R, et al. Lancet Neurol. 2018;17(9):749-59.
- 3. Katzenschlager R, et al. Parkinsonism Relat Disord. 2021;83:79-85.

Mean changes from baseline in daily OFF time (blue) and daily ON time without troublesome dyskinesia (green)



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Journal of Parkinson's Disease 1 (2011) 197–203 DOI 10.3233/JPD-2011-11037 197

Chronic Subcutaneous Infusion Therapy with Apomorphine in Advanced Parkinson's Disease Compared to Conventional Therapy: A Real Life Study of Non Motor Effect

Pablo Martinez-Martin^a, Prashanth Reddy^f, Angelo Antonini^b, Tove Henriksen^c, Regina Katzenschlager^d, Per Odin^e, Antonia Todorova^f, Yogini Naidu^g, Susanne Tluk^g, Chandni Chandiramani^f, Anne Martin^f and Kallol Ray Chaudhuri^{f,g,*}

Changes following apomorphine infusion in motor and QOL indices

	Control			Apomorphine			
	Baseline (SD)	Follow-Up (SD)	р	Baseline (SD)	Follow-Up (SD)	р	
UPDRS–Motor Examination	20.06 (9.68)	19.35 (12.80)	0.69	36.94 (11.42)	15.35 (8.21)	0.0003	
UPDRS- Complications	7.93 (5.43)	7.00 (4.46)	0.48	10.00 (6.43)	3.53 (3.52)	0.0003	
PDQ-8	35.84 (23.10)	44.85 (17.57)	0.02	55.70 (19.80)	32.35 (21.54)	0.001	

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Table 1
Changes following Apomorphine infusion and continuing conventional therapy (comparator) in motor, non-motor, and quality of life dimensions

	Control			Apomorphine			
	Baseline	Follow-up	p	Baseline	Follow-up	p	
UPDRS-Motor exam	20.06 (9.68)	19.35 (12.80)	0.69	36.94 (11.42)	15.35 (8.21)	0.0003	
UPDRS-Complications	7.93 (5.43)	7.00 (4.46)	0.48	10.00 (6.43)	3.53 (3.52)	0.0003	
NMSS-Cardiovascular	1.29 (2.97)	1.18 (2.90)	0.45	4.65 (5.63)	2.76 (3.51)	0.03	
Sleep	12.29 (9.58)	12.06 (9.32)	0.90	22.06 (11.47)	10.71 (9.63)	0.0003	
Mood/apathy	8.35 (10.33)	8.06 (8.78)	0.79	22.76 (19.85)	11.29 (13.04)	0.0005	
Perceptual	2.23 (5.03)	2.59 (6.26)	0.90	4.59 (6.92)	1.88 (3.35)	0.04	
Attention	6.00 (8.40)	7.18 (7.76)	0.16	12.82 (9.62)	8.71 (7.75)	0.006	
Gastrointestinal	5.94 (5.97)	7.12 (6.49)	0.24	7.35 (7.35)	4.41 (5.11)	0.002	
Urinary	4.29 (3.57)	6.23 (4.26)	0.06	10.70 (8.93)	5.71 (6.72)	0.001	
Sexual	3.12 (6.58)	3.29 (6.12)	0.97	2.53 (5.96)	2.00 (3.94)	0.42	
Miscellany	4.12 (5.67)	4.29 (5.55)	0.61	18.47 (14.54)	9.47 (9.70)	0.0003	
NMSS-Total score	47.65 (43.40)	52.00 (37.65)	0.22	105.94 (65.43)	56.94 (45.39)	0.0003	
PDQ-8	35.84 (23.10)	44.85 (17.57)	0.02	55.70 (19.80)	32.35 (21.54)	0.001	

Benjamini-Hochberg correction: p < 0.027; UPDRS: Unified Parkinson's Disease Rating Scale; NMSS: Non-Motor Symptoms Scale; PDQ-8: Parkinson's Disease Questionnaire-8 items.

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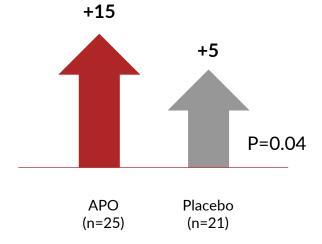
APOMORPHEE is the first randomised, double-blind, placebocontrolled trial to assess safety, tolerability and efficacy of a nighttime only apomorphine infusion

- 46 patients (advanced PD and moderate-severe insomnia) enrolled
- Sleep disturbances were improved according to difference in PDSS
- Acceptable safety profile
- Positive effects observed on motor symptoms on morning awakening

subcutaneous night-time only apomorphine infusion might be useful to manage sleep disturbances in patients with advanced Parkinson's disease and moderate to severe insomnia

APOMORPHEE: night-time only apomorphine study

Mean change in PDSS score (N=46)



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SAFETY PROFILE

OLP safety set (n=84)	n (%)
Patients with at least one AE	83 (98.8)
AEs related to the study medication	77 (91.7)
Serious treatment-related AEs	8 (9.5)
AEs leading to study	14 (16.7)
discontinuation:	4 (4.8)
 Infusion site reactions 	2 (2.4)
 Fatigue 	1 (1.2)
Autoimmune haemolytic	1 (1.2)
anaemia	1 (1.2)
• Delirium	1 (1.2)
 Dementia 	` ,
Disturbance in attention	1 (1.2)
	1 (1.2)
• Lymphoma	1 (1.2)
 Nausea 	` ,
 Panic attack 	1 (1.2)
 Somnolence 	

OLP safety set (n=84)	n (%)
AEs with a local intolerability (skin changes at injection site)	60 (71.4)
Most common AEs (≥10%	
frequency)	46 (54.8)
 Infusion site nodules 	19 (22.6)
 Nausea 	19 (22.6)
 Somnolence 	14 (16.7)
 Dyskinesia 	14 (16.7)
• Fall	13 (15.5)
 Insomnia 	12 (14.3)
 Constipation 	11 (13.1)
 Dizziness 	11 (13.1)
 Infusion site erythema 	9 (10.7)
Headache	_ , , ,

- Safety profile of APO was consistent with extensive clinical experience
- Common treatmentrelated adverse events:
 - Mild or moderate infusion site nodules
 - Somnolence
 - Nausea

AE, adverse event; DBP, double-blind phase; OLP, open-label phase

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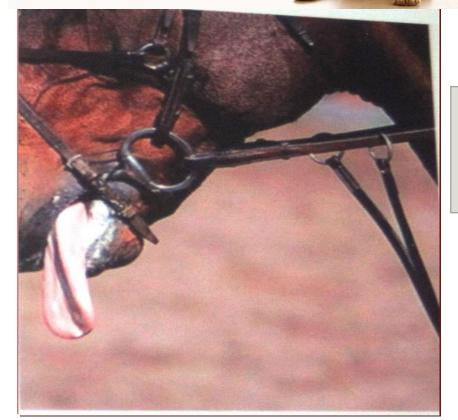


Apomorphine is the emetic of choice in dogs

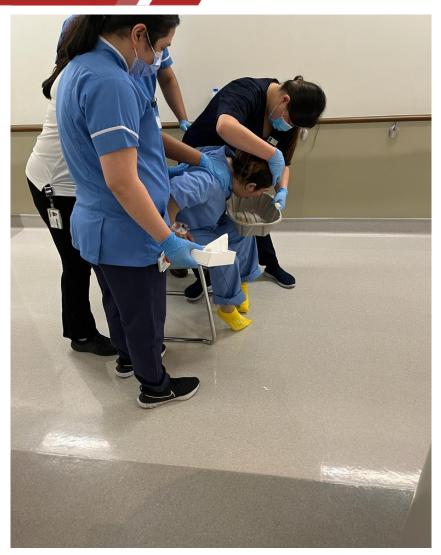


Click for 10 ways to help the medicine go down and important questions to ask your veterinarian.





Preferably use Domperidone 10mg TID



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Review > Expert Opin Drug Deliv. 2025 Aug 1:1-18. doi: 10.1080/17425247.2025.2539962.

Online ahead of print.

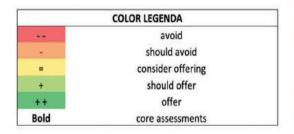
Navigating the therapeutic landscape in advanced Parkinson's disease: a comprehensive review from infusion therapies to stem cells

Carmelo Fogliano ¹, Leonardo Rigon ^{1 2}, K Ray Chaudhuri ^{3 4}, Karolina Popławska-Domaszewicz ^{3 5}, Cristian Falup-Pecurariu ^{6 7}, Iulia Murasan ⁷, Andrea Guerra ¹, Michela Garon ¹, Per Odin ⁸ ⁹, Nobutaka Hattori ¹⁰, Angelo Antonini ¹ ²

DAT selection

Individualized approach based on patient's characteristics and preferences

Patient's characteristics	DBS	SCLI	CSAI	LCIG	LECIG
Younger age (<65 years)	++	+	+	*	*
Dementia		-		=	=
MCI	-	+	=	++	++
Psychosis/hallucination	10.0		7.7	+	+
High-dose levodopa requirement	++	=	4	++	++
ICDs	++	+	+	++	++
DDS and Punding	++	-	2	++	++
Limited caregiving	=	4	:	=	=
Sleep disturbances	+	++	++	+	+
Apathy	=	+	+	=	=
Levodopa-resistant tremor	++			:###	
Entacapone intolerance	++	++	++	++	
Severe orthostatic hypotension	++	+	(E)	+	+
Daytime sleepiness	++	+	-	+	+
Levodopa-resistant dysphagia	=	=	=	++	++
Morning akinesia	++	++	+	+	+
Carry-on device intolerant	++	=	=		=
Genetic data	Based o	n mutatio	n-specific	clinical ph	nenotype



	ABBREVIATIONS
DBS	deep brain stimulation
SCLI	subcutaneous continuous levodopa infusion
CSAI	continuous subcutaneous apomorphine infusion
LCIG	levodopa carbidopa intestinal gel
LECIG	levodopa entacapone carbidopa intestinal gel
ICDs	impulse control behavior disorders
DDS	dopamine dysregulation syndrome
MCI	mild cognitive impairment

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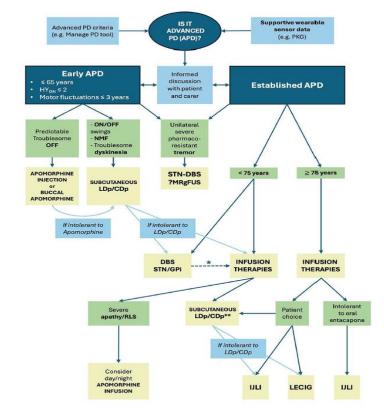
Neurol Ther https://doi.org/10.1007/s40120-024-00635-4

REVIEW

Subcutaneous Levodopa: A New Engine for the Vintage Molecule

Karolina Poplawska-Domaszewicz \cdot Lucia Batzu \cdot Cristian Falup-Pecurariu \cdot K. Ray Chaudhuri

Neurol Ther



^{*} To be considered as subsequent step, if needed.

** Home nursing option to consider for elderly patients.

Fig. 3 Potential algorithm for clinical use of available advanced therapies treatment options. PD Parkinson's disease, APD advanced PD, PKG Personal KinetiGraph, HY Hohen & Yahr, NMF non-motor fluctuations, MRgFUS MRI-guided focused ultrasound, DBS deep brain stimula-

tion, STN subthalamic nucleus, GPi globus pallidus internus, RLS restless legs syndrome, IJLI intrajejunal levodopa infusion, LECIG levodopa—entacapone—carbidopa intestinal gel, \hat{r} indicates possible consideration of the technique if locally available

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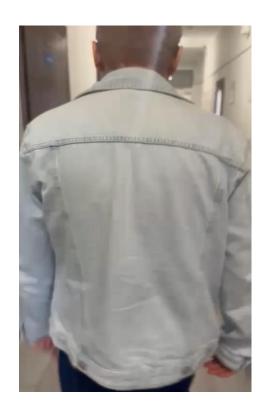


DAT combinations & switches

Before- APO



1 mont after DBS+APO



3 months after DBS+APO



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Case study: Apomorphine → Foslevodopa/Foscarbidopa

Age: 65 years
PD-2009
2019-2024- CSAI
2025-

dopa/foskarbiod Bef

Before

Titration process



After 3 months

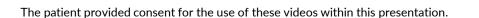
Progress



After 1 year

International Parkinson and





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FUTURE AFRICA







Thank you for your attention











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