Levodopa-carbidopa intestinal gel: overview of efficacy and selection criteria

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School for Advanced Therapies for Movement Disorders
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International Parkinson and Movement Disorder Society European Section

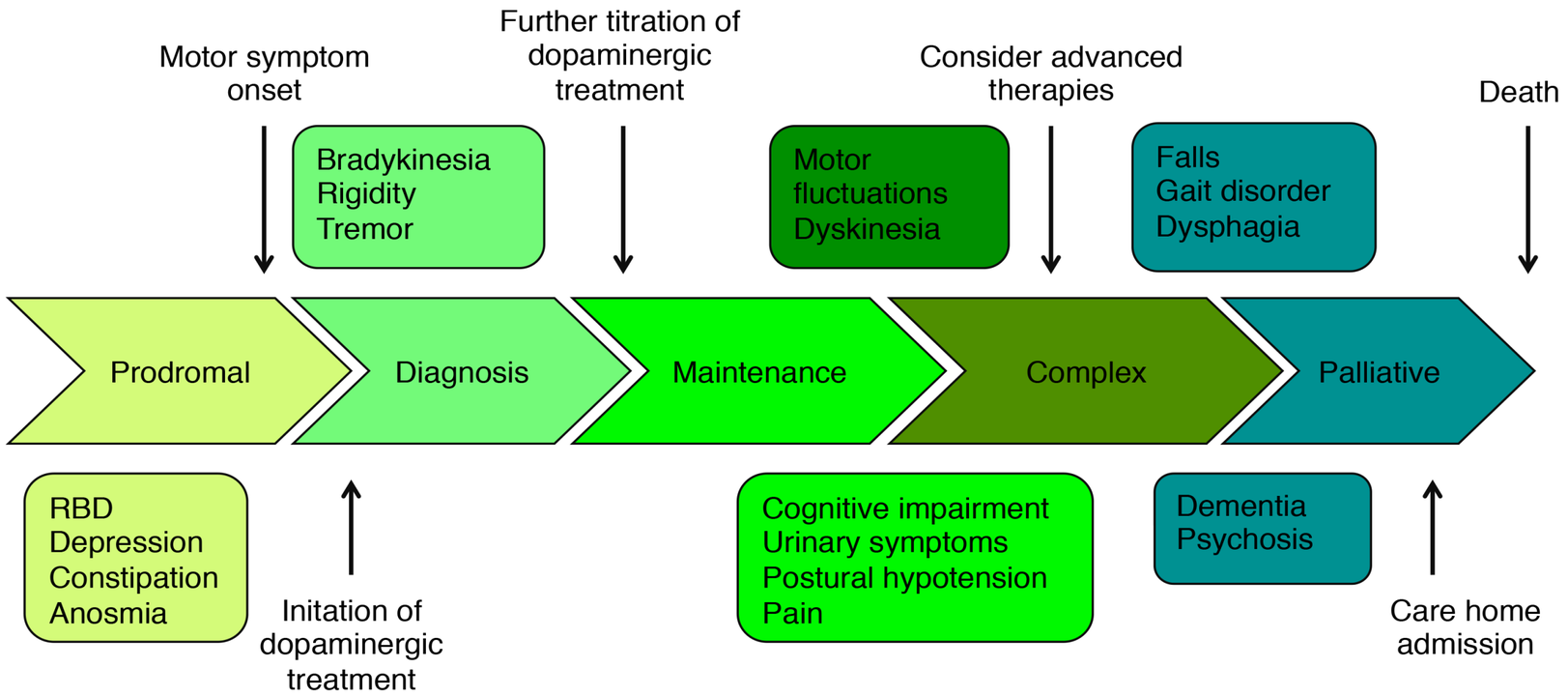
Disclosures for past 24 months

- Grant funding
  - Parkinson's UK, Multiple System Atrophy Trust
- Speaker honoraria
  - Bial, Britannia Pharmaceuticals, Abbvie, Ipsen
- Travel to international meeting
  - Bial
- Trustee and Chair of Scientific Advisory Panel, Multiple System Atrophy Trust
- Deputy chair of ABN Movement Disorders Advisory Group
- International Parkinson and Movement Disorder Society, Evidence-based medicine committee member

Objectives

- Review rationale for levodopa-carbidopa intestinal gel therapies
- Evidence base for LCIG treatment
- Complications and monitoring of therapy
- Selection criteria for LCIG
- New developments

Complex Parkinson's disease



Kobylecki C. *Clin Med* 2020;20:393-398.

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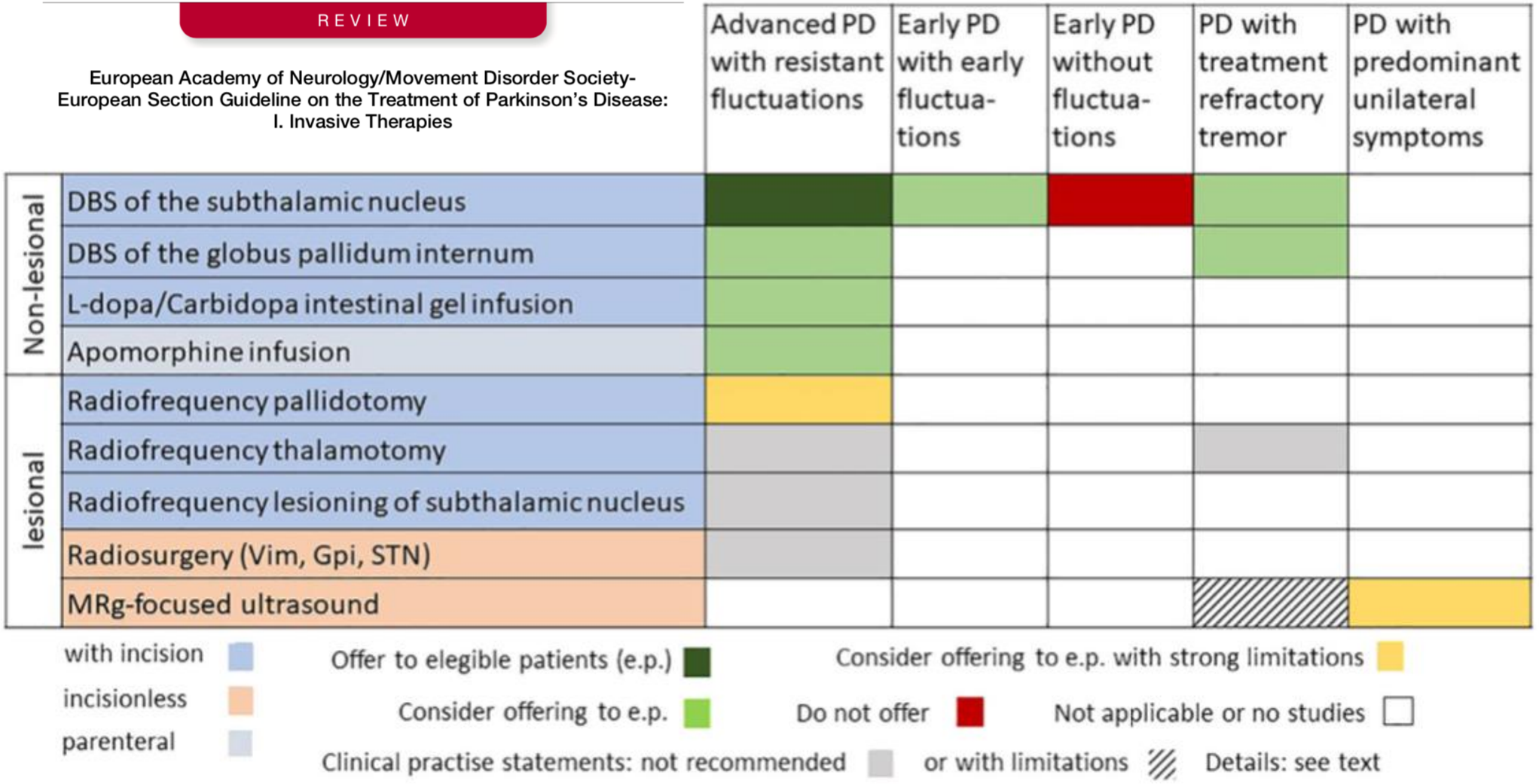
REVIEW

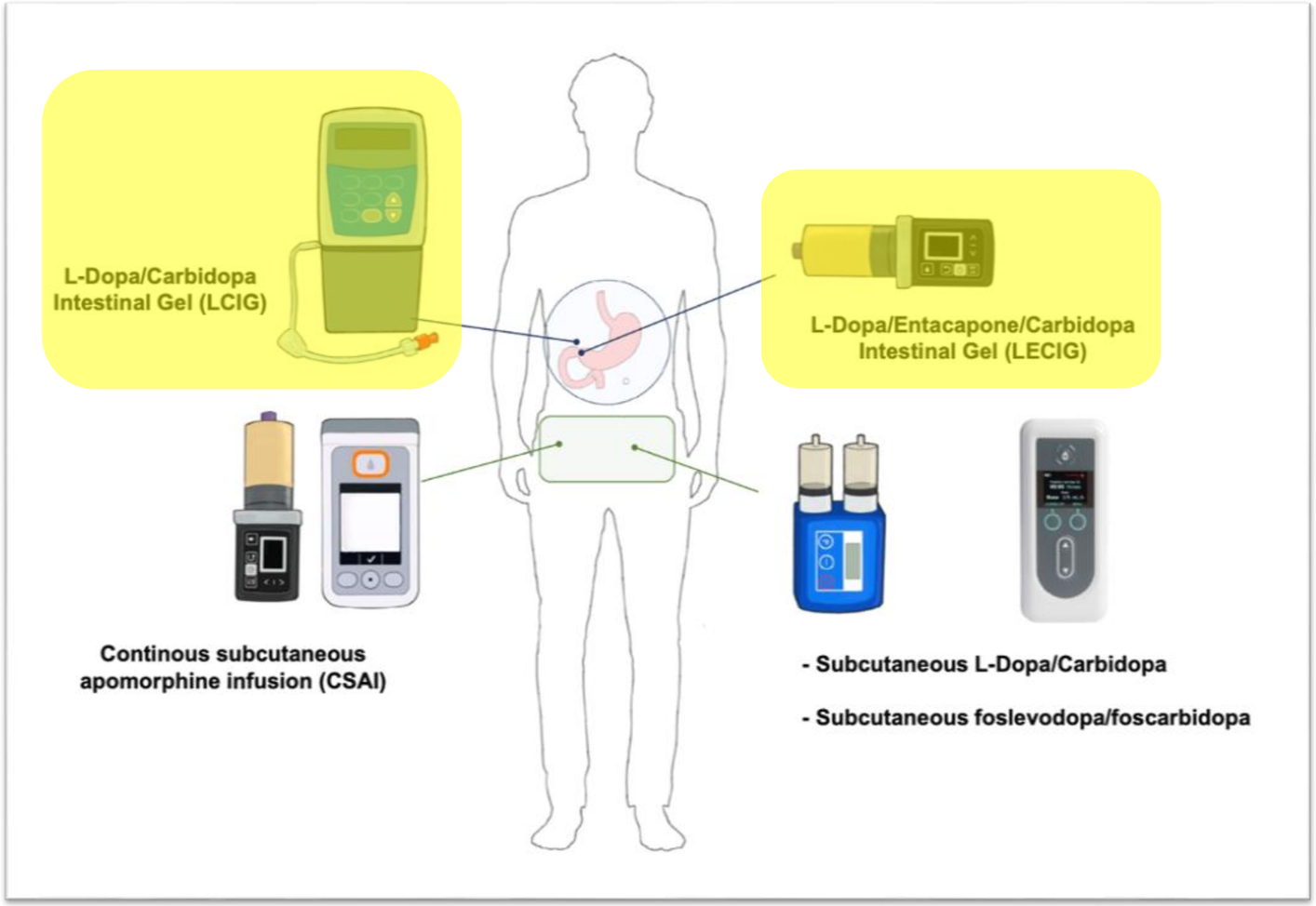
European Academy of Neurology/Movement Disorder Society-European Section Guideline on the Treatment of Parkinson's Disease: I. Invasive Therapies



Deuschl G *et al. Mov Disord* 2022;37(7):1360-1374.

Rationale for Infusion therapies

- Achieve continuous dopaminergic stimulation
- Reduce oral medication burden
- Bypass dysfunctional gastrointestinal tract in PD

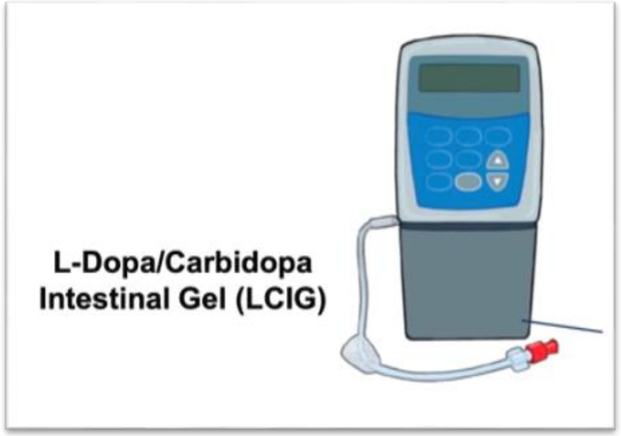


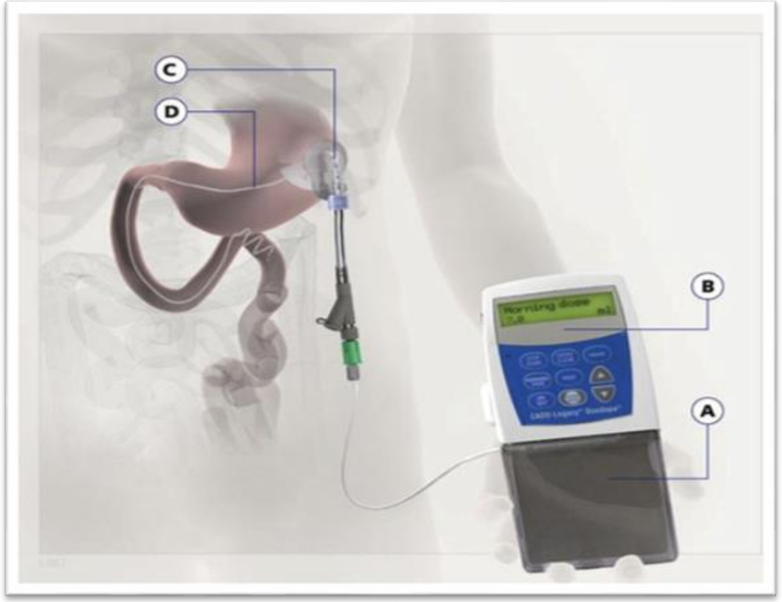
Antonini A *et al. J Neural Transm* 2023;130:1349-1358.

Levodopa-carbidopa intestinal gel

- Gel suspension of levodopa/carbidopa (4:1) in water solution of carboxy methylcellulose
- Delivered via PEG-J tube
- Morning loading dose
- Continuous rate
- Boost doses

- Contraindications
  - Abnormal upper GI anatomy
  - Significant dementia or psychosis



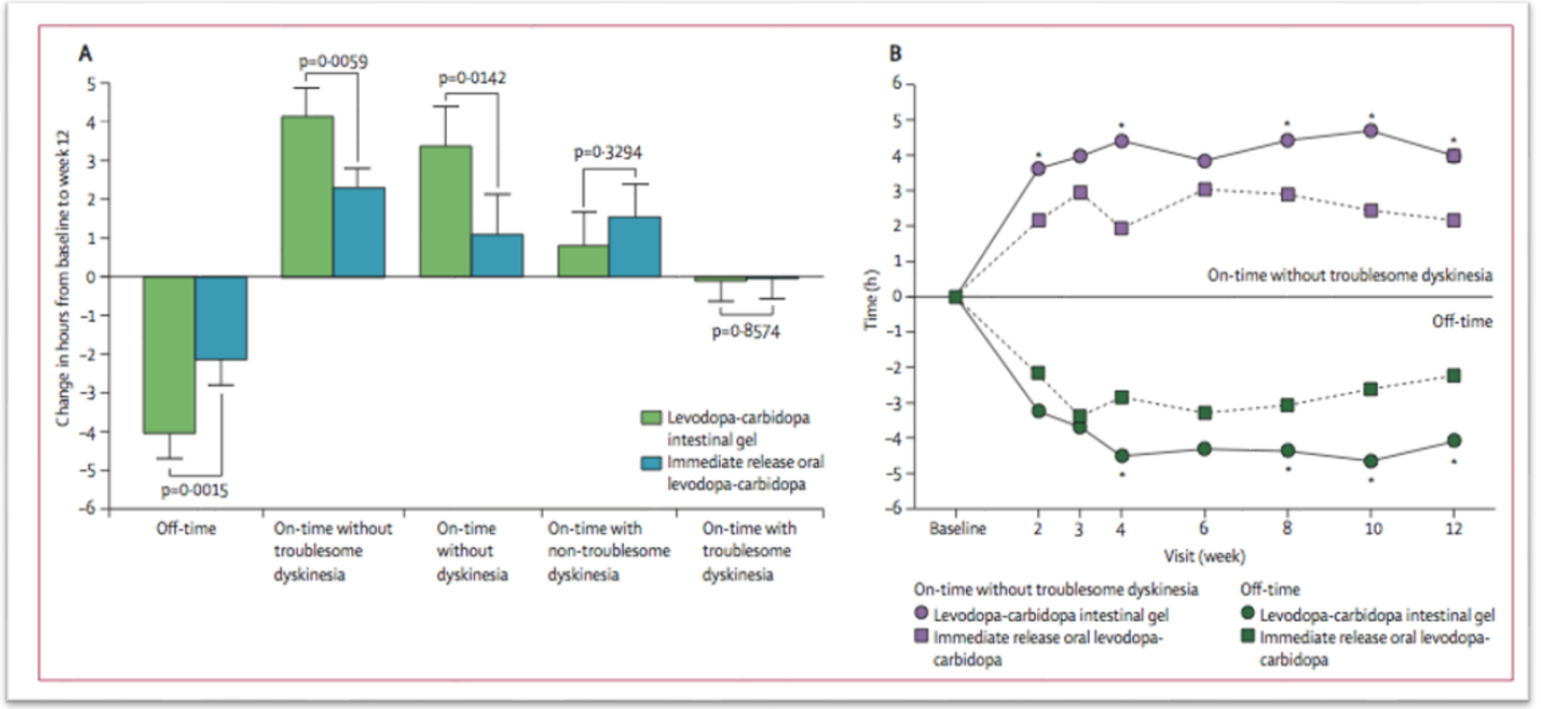


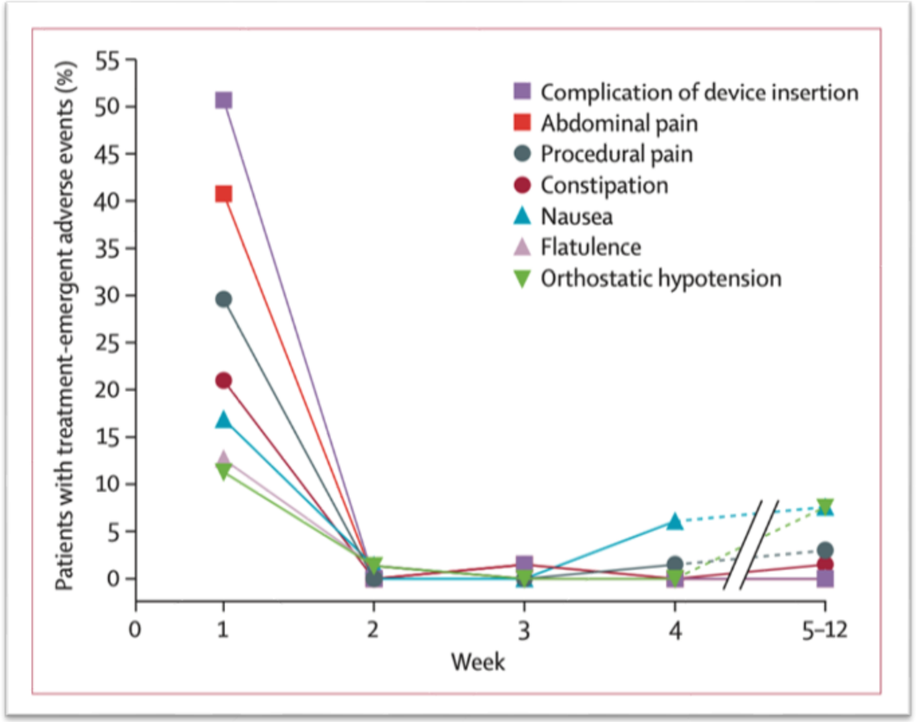
Evidence for LCIG

Randomized controlled trial
LCIG n=35
Levodopa IR n=31

Continuous intrajejunal infusion of levodopa-carbidopa intestinal gel for patients with advanced Parkinson's disease: a randomised, controlled, double-blind, double-dummy study

C Warren Olanow, Karl Kieburtz, Per Odin, Alberto J Espay, David G Standaert, Hubert H Fernandez, Arvydas Vanagunas, Ahmed A Othman, Katherine L Widnell, Weining Z Robieson, Yili Pritchett, Krai Chatamra, Janet Benesh, Robert A Lenz, Angelo Antonini, for the LCIG Horizon Study Group





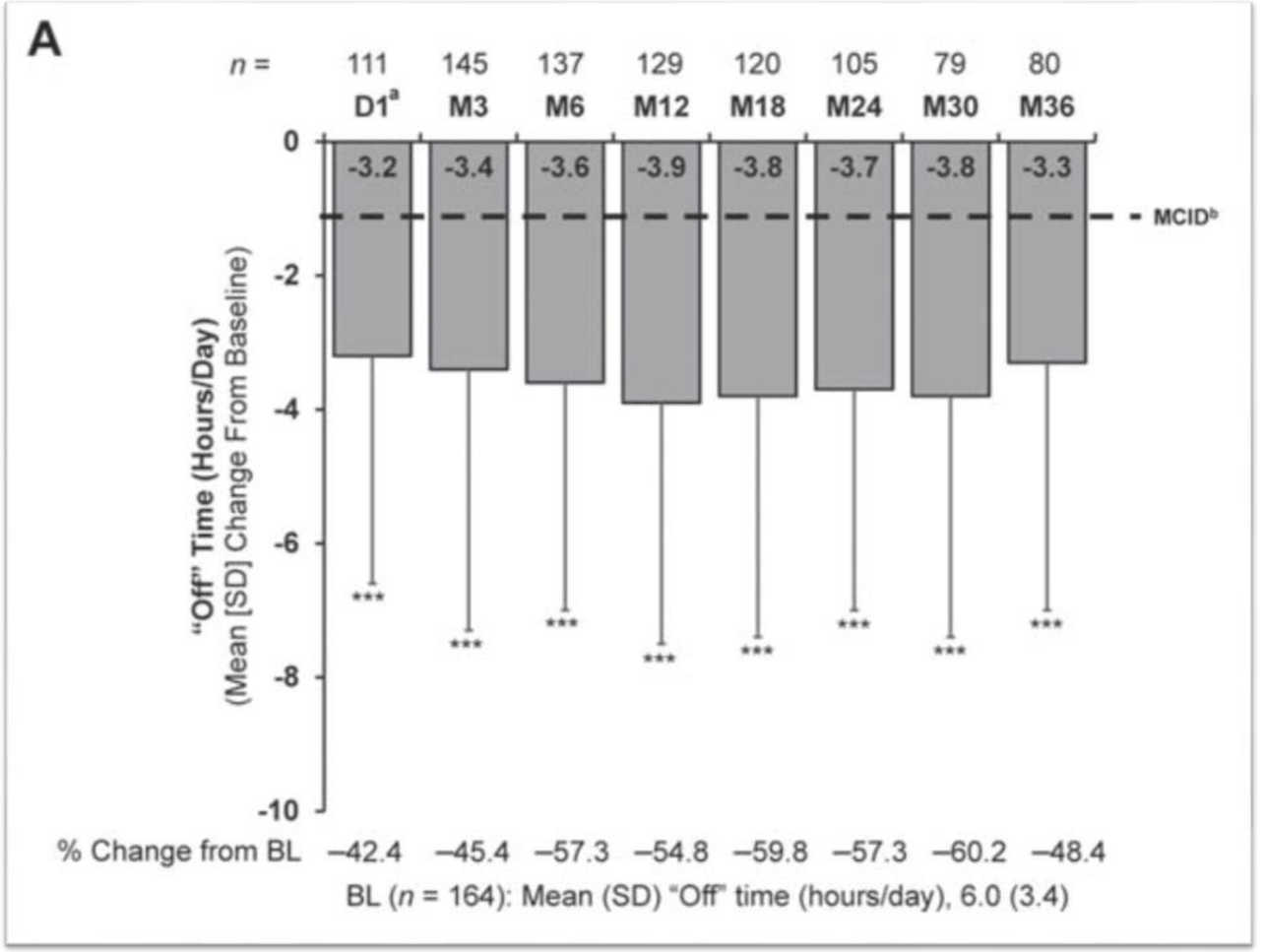
1. Olanow CW *et al. Lancet Neurol* 2014;13:141-49.

	Levodopa-carbidopa intestinal gel (n=35)	Immediate-release oral levodopa-carbidopa (n=31)	Treatment difference (95% CI)	p value
Primary efficacy outcome				
Off-time, h per day	−4·04 (0·65)	−2·14 (0·66)	−1·91 (−3·05 to −0·76)	0·0015
Secondary efficacy outcomes				
On-time without troublesome dyskinesia, h per day*	4·11 (0·75)	2·24 (0·76)	1·86 (0·56 to 3·17)	0·0059
On-time without dyskinesia, h per day†	3·37 (1·04)	1·09 (1·05)	2·28 (0·47 to 4·09)	0·0142
On-time with non-troublesome dyskinesia, h per day†	0·81 (0·86)	1·54 (0·86)	−0·73 (−2·22 to 0·76)	0·3294
On-time with troublesome dyskinesia, h per day†	−0·11 (0·52)	−0·03 (0·52)	−0·08 (−0·98 to 0·82)	0·8574
PDQ-39 summary index	−10·9 (3·3)	−3·9 (3·2)	−7·0 (−12·6 to −1·4)	0·0155
Mean CGI-I score at final assessment‡	2·3 (0·4)	3·0 (0·4)	−0·7 (−1·4 to −0·1)	0·0258
UPDRS part II§	−1·8 (1·3)	1·3 (1·3)	−3·0 (−5·3 to −0·8)	0·0086
UPDRS part III§	−1·5 (2·4)	−2·9 (2·4)	1·4 (−2·8 to 5·6)	0·5020
EQ-5D	0·05 (0·04)	−0·02 (0·04)	0·07 (−0·01 to 0·15)	0·0670
Zarit Burden Interview	−2·8 (3·7)	1·7 (3·3)	−4·5 (−10·7 to 1·7)	0·1501
Levodopa total daily dose, mg	91·7 (96·6)	249·7 (94·9)	−158·0 (−324·5 to 8·5)	0·0625
Overall mean (SD) levodopa rescue dose, mg	139·8 (20·3)	180·6 (21·9)	−40·8 (−100·4 to 18·8)	0·1762

Data are the least squares mean change from baseline to week 12 (SE) unless otherwise stated. PDQ=Parkinson Disease Questionnaire. CGI-I=Clinical Global Impression–Improvement. UPDRS=Unified Parkinson's Disease Rating Scale. EQ-5D=EuroQual quality of life-5 Dimensions. *On-time without troublesome dyskinesia equals on-time without dyskinesia plus on-time with non-troublesome dyskinesia. †Measure not part of hierarchical analysis; ‡For CGI-I, 1 is very much improved, 2 is much improved, 3 is minimally improved, 4 is no change, 5 is minimally worse, 6 is much worse, and 7 is very much worse. §UPDRS was completed in the on-state.

Table 2: **Treatment efficacy**

1. Olanow CW *et al. Lancet Neurol* 2014;13:141-49.

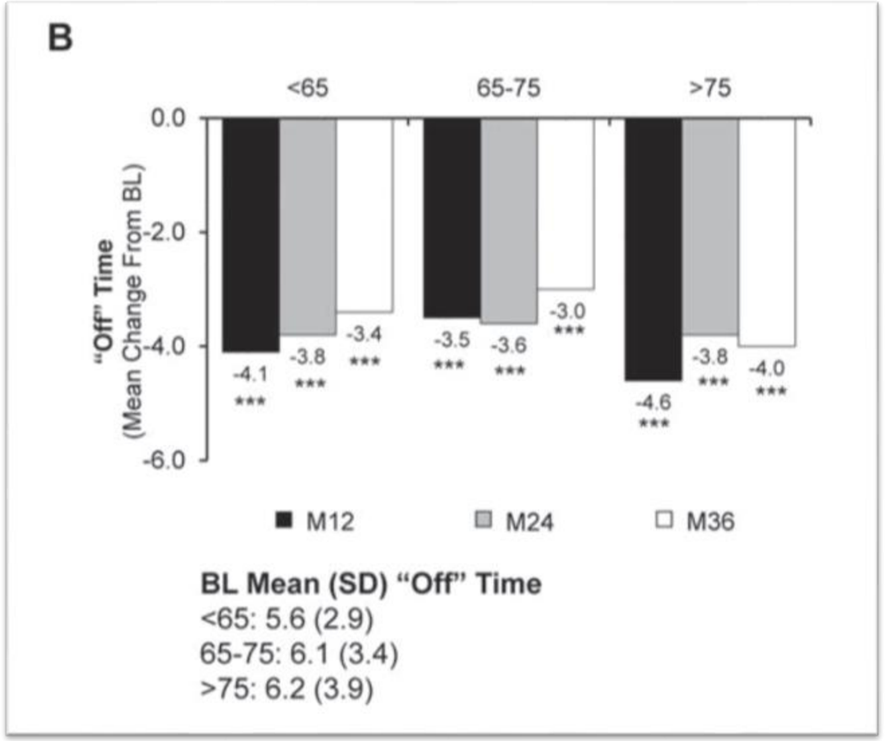


1. Chaudhuri KR *et al. J Parkinsons Dis* 2023;13:769-783.

Open label registry
N=195 (120 male)
Mean age 70.2 (56 >75y)

Clinical Research

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



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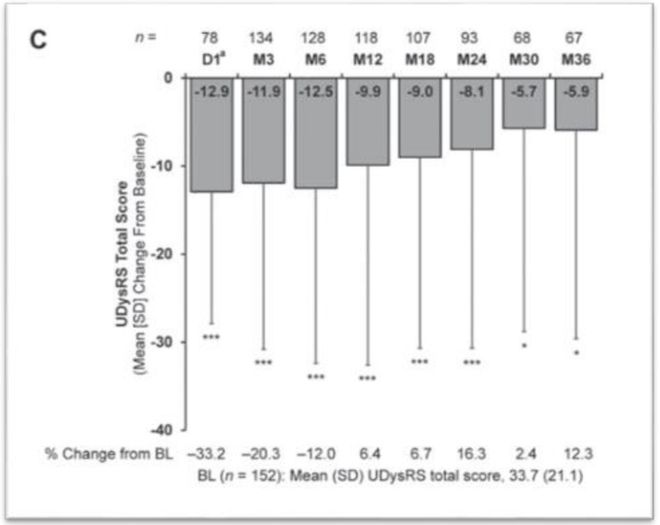

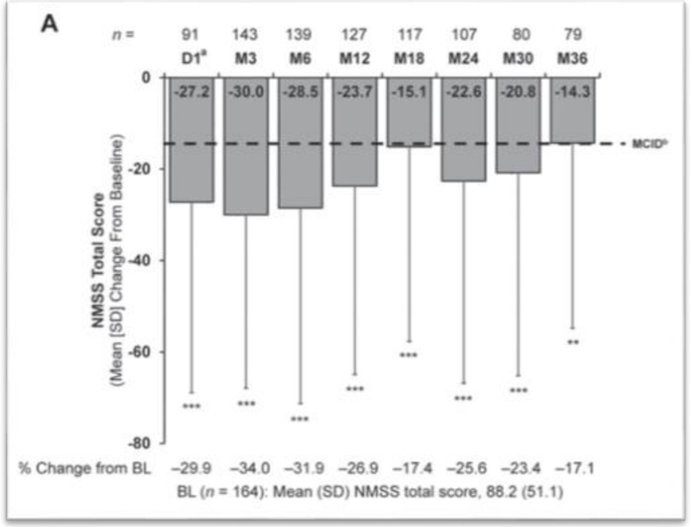

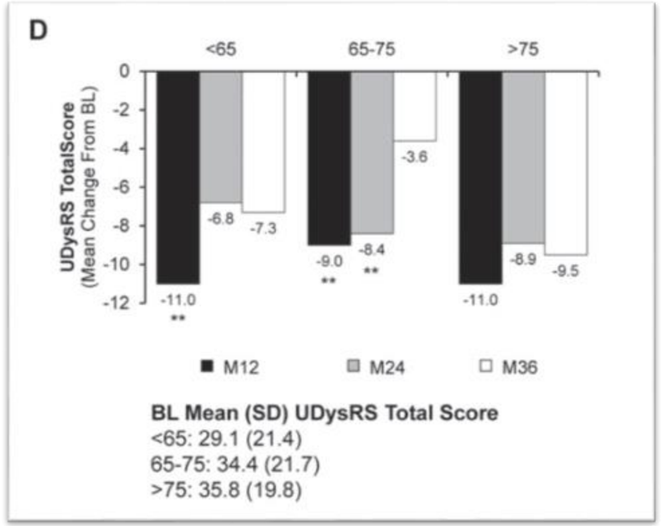

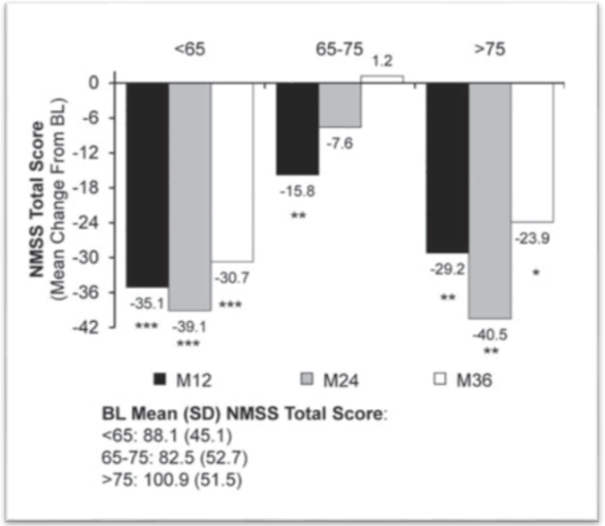

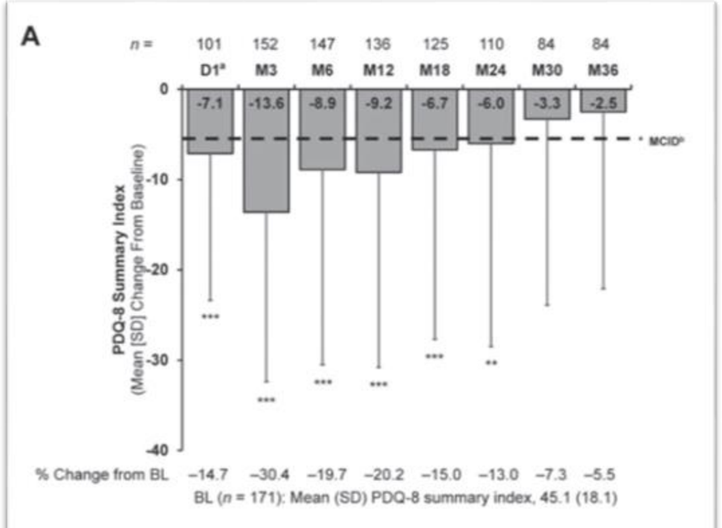

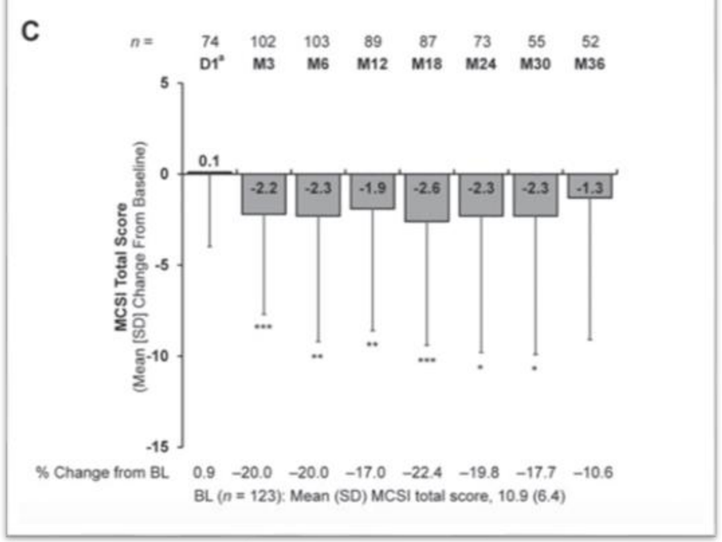

1. Chaudhuri KR *et al. J Parkinsons Dis* 2023;13:769-783.

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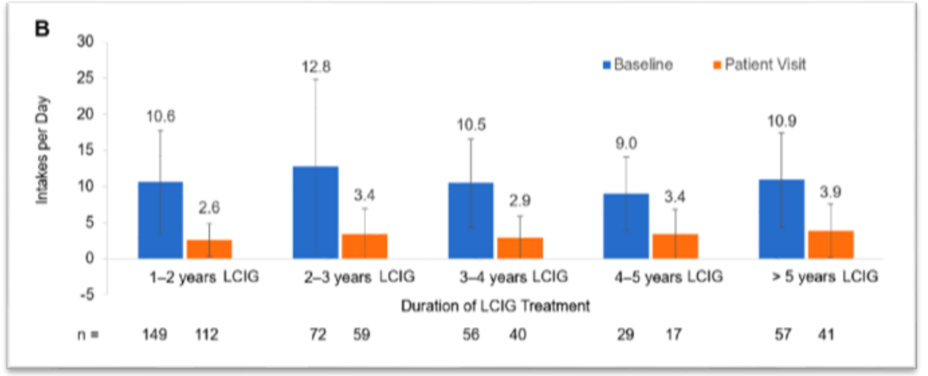
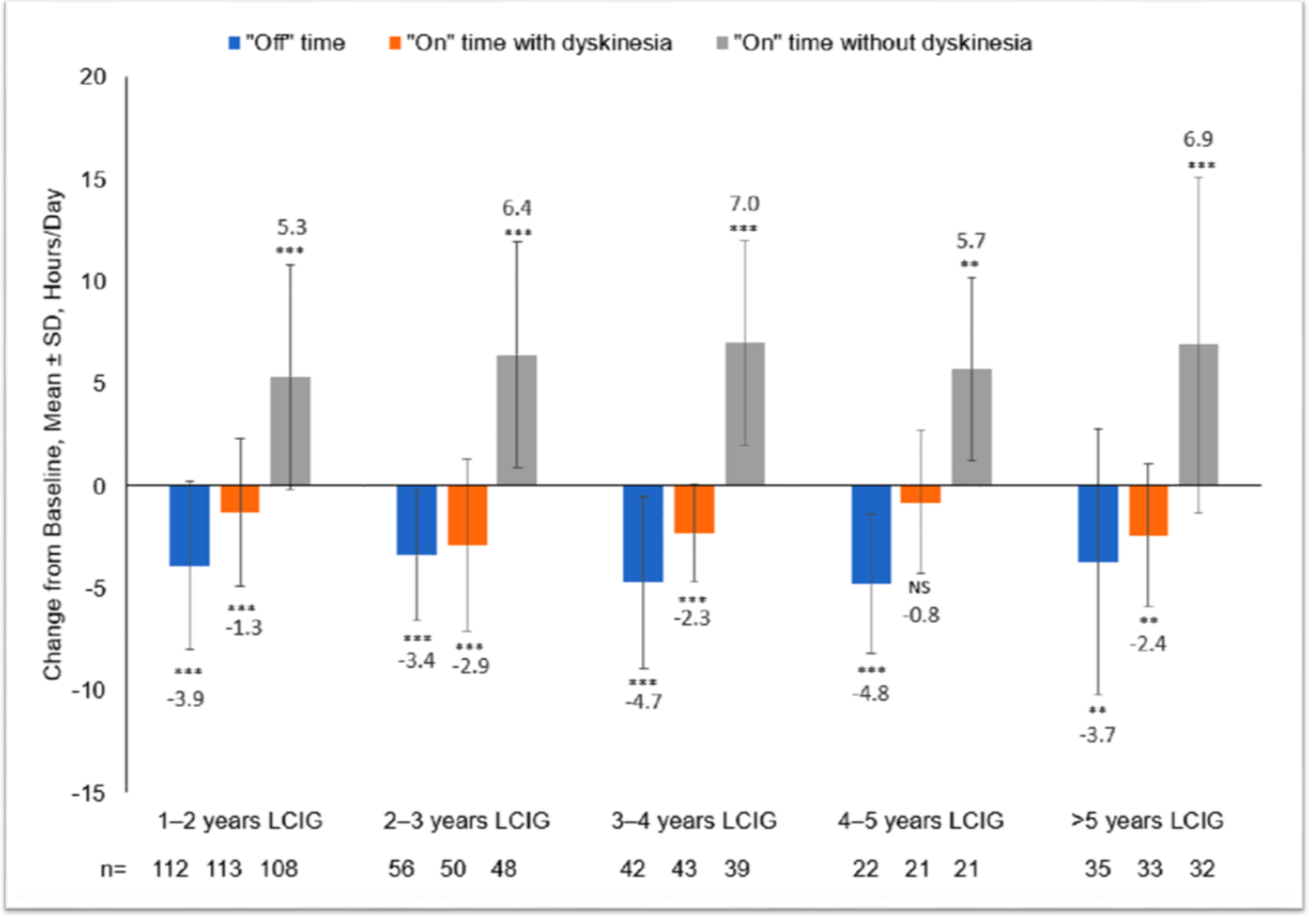
ORIGINAL COMMUNICATION

Levodopa–carbidopa intestinal gel in advanced Parkinson's disease: long-term results from COSMOS

Alfonso Fasano[1,2] · Rocío García-Ramos[3] · Tanya Gurevich[4] · Robert Jech[5] · Lars Bergmann[6] · Olga Sanchez-Soliño[6] · Juan Carlos Parra[6] · Mihaela Simu[7]

Cross sectional study
N=387



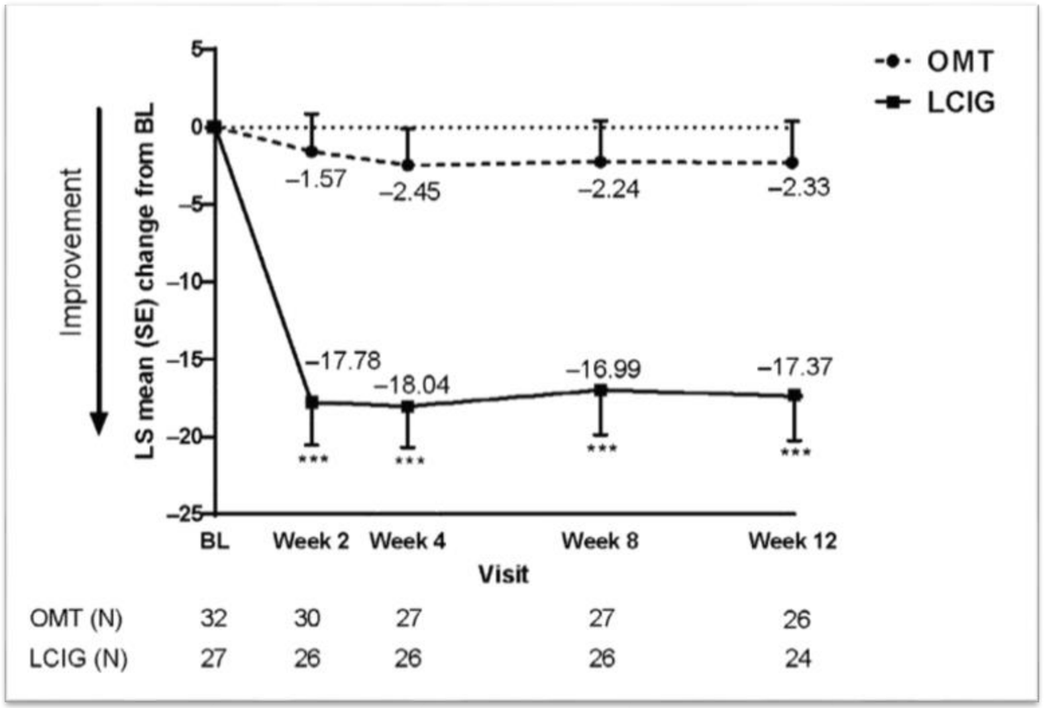


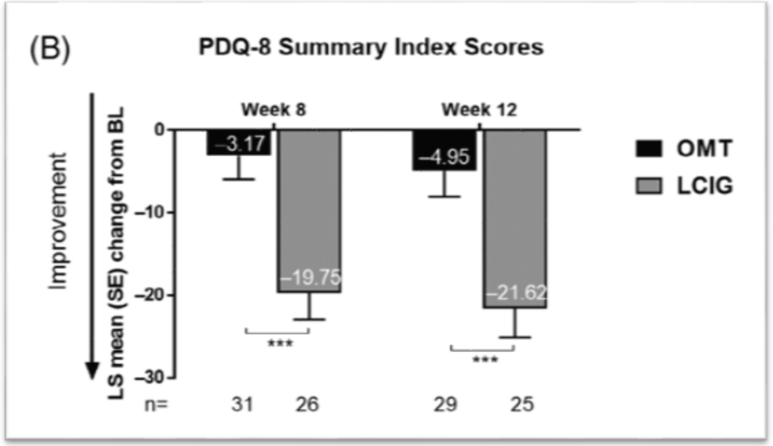
Fasano A *et al. J Neurol* 2023;270:2765-2775.

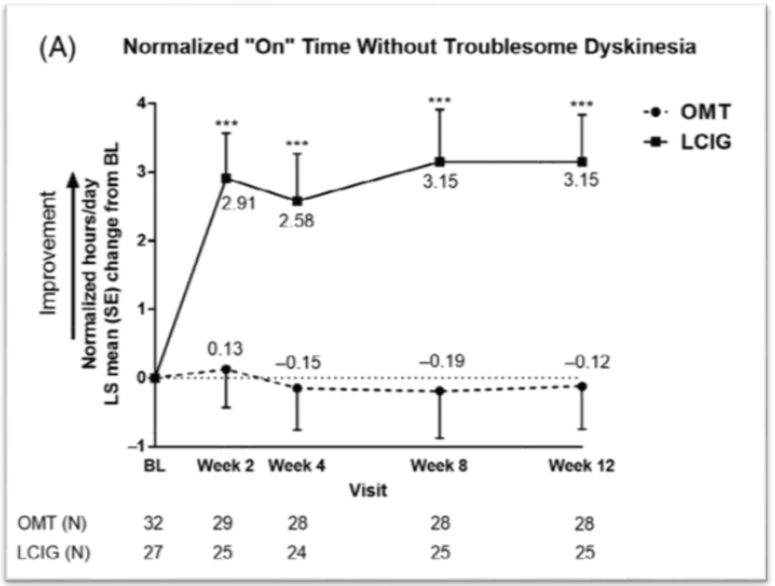
RESEARCH ARTICLE

Levodopa-Carbidopa Intestinal Gel Reduces Dyskinesia in Parkinson's Disease in a Randomized Trial

Eric Freire-Alvarez, MD,[1*] Egon Kurča, PhD, MUDr,[2] Lydia Lopez Manzanares, MD,[3] Eero Pekkonen, MD, PhD,[4] Cleanthe Spanaki, MD, PhD,[5] Paola Vanni, MD,[6] Yang Liu, PhD,[7] Olga Sánchez-Soliño, MD,[8] and Luigi M. Barbato, MD[8]







Open label RCT
OMT n=33
LCIG n=30
Mean age 69y

Freire-Alvarez E *et al. Mov Disord* 2021;36:2615-2623.

LCIG safety and retention

RESEARCH ARTICLE

Long-Term Safety and Efficacy of Levodopa-Carbidopa Intestinal Gel in Advanced Parkinson's Disease

Hubert H. Fernandez, MD,[1*] James T. Boyd, MD,[2] Victor S. C. Fung, MBBS, PhD,[3] Mark F. Lew, MD,[4] Ramon L. Rodriguez, MD,[5] John T. Slevin, MD,[6] David G. Standaert, MD, PhD,[7] Cindy Zadikoff, MD,[8] Arvydas D. Vanagunas, MD,[8] Krai Chatamra, PhD,[9] Susan Eaton, PharmD,[9] Maurizio F. Facheris, MD,[9] Coleen Hall, MS,[9] Weining Z. Robieson, PhD,[9] Janet Benesh, BSMT,[9] and Alberto J. Espay, MD[10]

Open-label extension (n=262)

- Median duration 4.3y[1]
- 34% discontinued LCIG

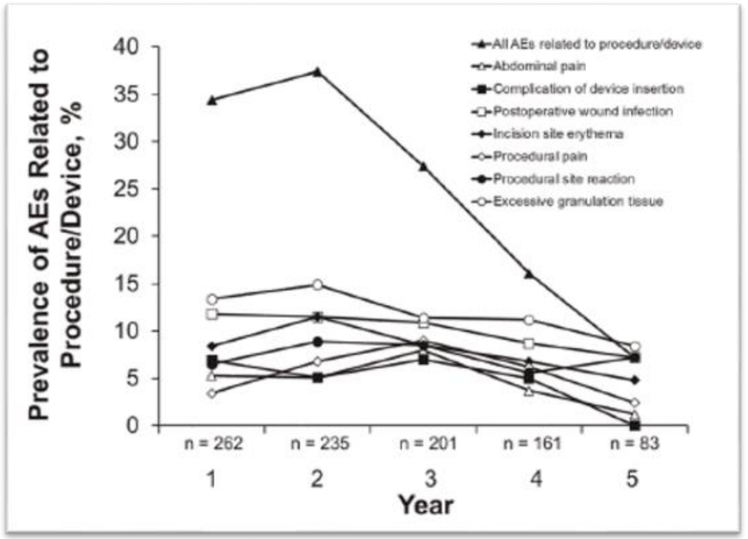


TABLE 2. Adverse events (AEs) and serious AEs

Parameter[a,b]	n = 262 n (%)
AEs occurring in ≥10% of patients	
Postoperative wound infection	*59 (23)*
Vitamin B_6 decreased	58 (22)
Fall	55 (21)
Urinary tract infection	50 (19)
Blood homocysteine increased	48 (18)
Excessive granulation tissue	*41 (16)*
Incision-site erythema	*38 (15)*
Weight decreased	36 (14)
Complication of device insertion[c]	*33 (13)*
Parkinson's disease[d]	33 (13)
Procedural-site reaction	*33 (13)*
Nausea	32 (12)
Depression	30 (11)
Constipation	29 (11)
Insomnia	29 (11)
Abdominal pain	*27 (10)*
Dyskinesia	27 (10)
Procedural pain	*27 (10)*
Serious AEs occurring in ≥3% of patients	
Pneumonia	17 (6)
Complication of device insertion[c]	*14 (5)*
Fall	12 (5)
Pneumonia aspiration	8 (3)
Postoperative wound infection	*8 (3)*
Weight decreased	8 (3)

1. Fernandez HH *et al. Mov Disord* 2018;33:928-936.

LCIG safety and retention

- 19 (24%) discontinued LCIG
- Most commonly in first 2y
- Weight loss in 56%
- Peristomal complications predict discontinuation

ORIGINAL COMMUNICATION

Long-term safety, discontinuation and mortality in an Italian cohort with advanced Parkinson's disease on levodopa/carbidopa intestinal gel infusion

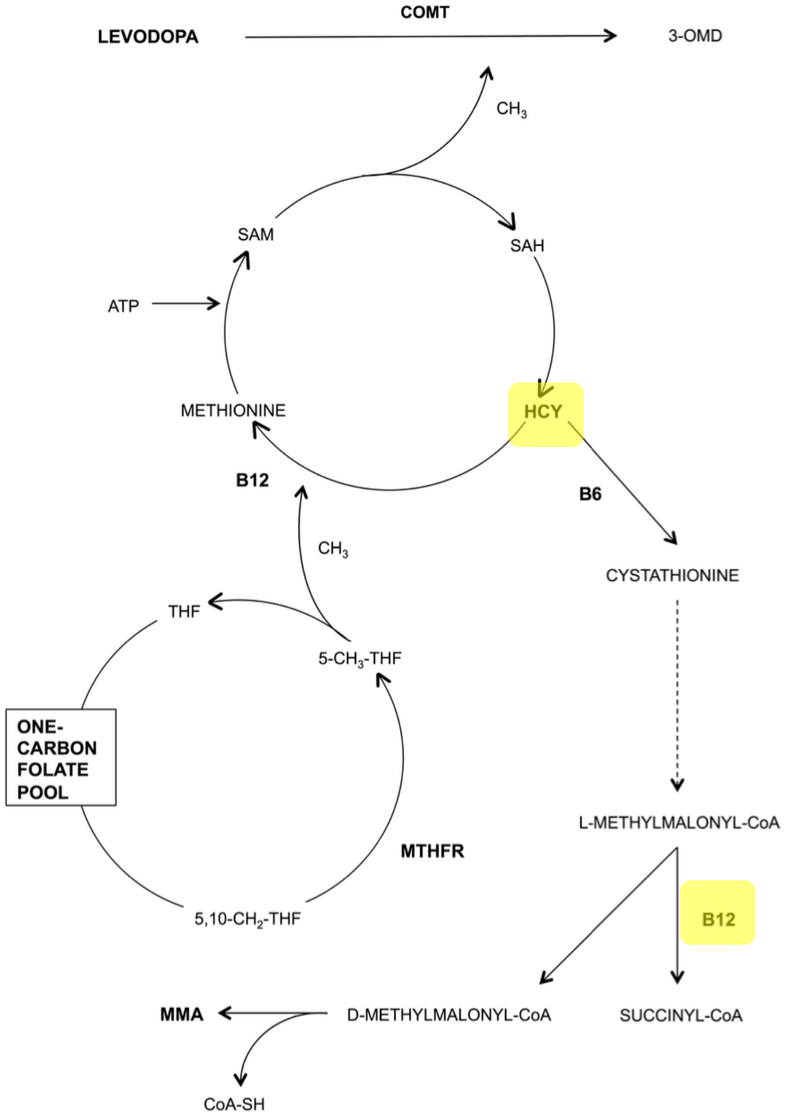
Multicentre cohort study (n=79)

Long term adverse events (AES)	*N*=63 Patients	Discontinued
Peristomal complications	**34**	
Erythema	22	
Granulation tissue	20	
Peristomal infections	2	2 (24; 81 mo)
Leakage	8	
Tube complications	**21**	
Occlusions	8	
Deterioration	10	
Dislocations/Accidental removal	12	
Tube Damage	12	
Other complications	**13**	

Garrì F *et al. J Neurol* 2022;269:5606-5614

Peripheral neuropathy and LCIG

- Neuropathy in 8% of long-term series[2]
  - Only one SAE
- Subacute/acute cases less common
- Recommended to check B12, folate, Hcy/MMA at baseline
- Consider supplementation if evidence of deficiency
- Check if new neuropathy symptoms occur



1. Romagnolo A *et al. Mov Disord Clin Pract* 2019;6:96-103.
2. Fernandez HH *et al. Mov Disord* 2018;33:928-936.

Levodopa-carbidopa-entacapone intestinal gel

- Addition of entacapone→blocks conversion to 3-O-methyldopa
- Increased plasma levodopa, reduced daily dose
- Estimated 35% reduction in levodopa exposure[1]

1. Senek M *et al. Sci Rep* 2020;10:18057

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Movement Disorders

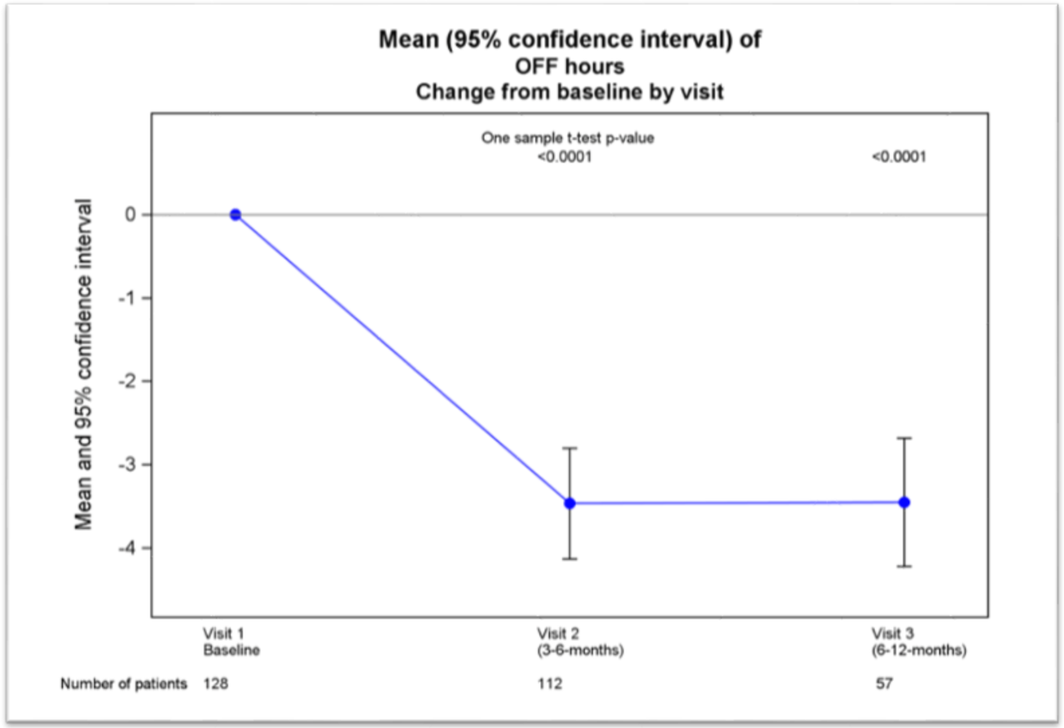
CLINICAL PRACTICE

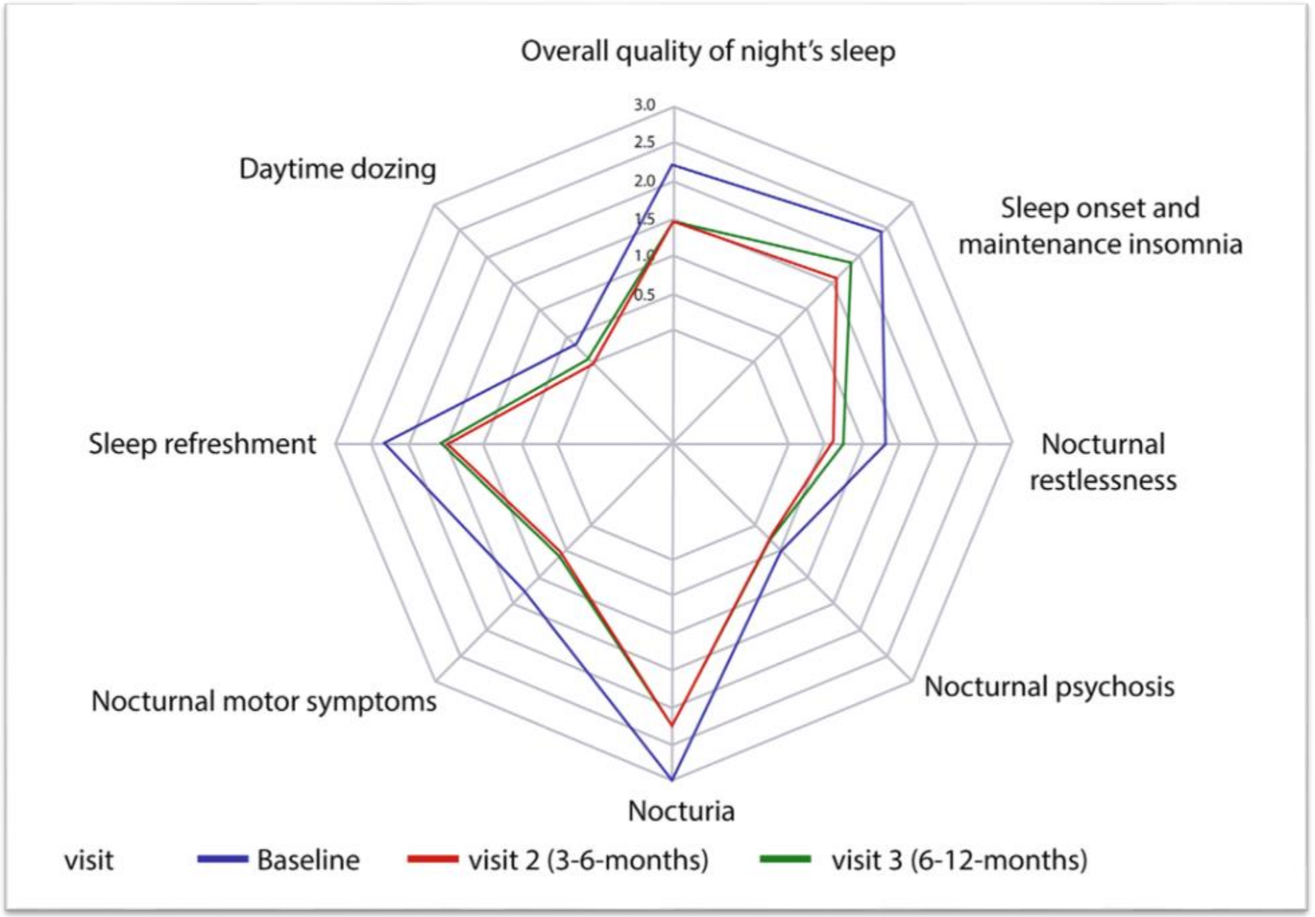
RESEARCH ARTICLE

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]

Registry study
n=167





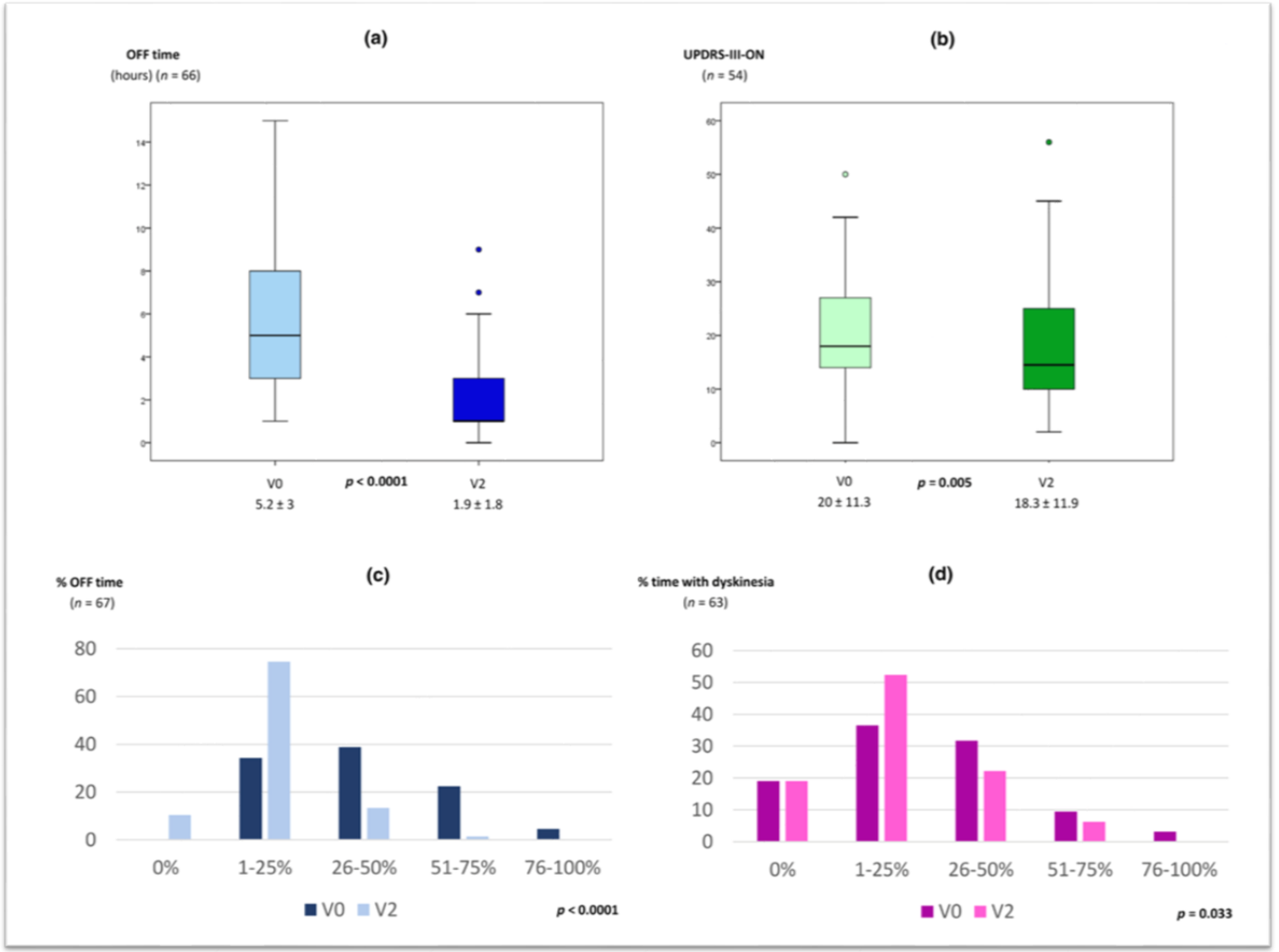
Weiss D *et al. Mov Disord Clin Pract* 2025;12:1075-1085.

ORIGINAL ARTICLE

european journal of neurology

Effectiveness and safety of levodopa–entacapone–carbidopa infusion in Parkinson disease: A real-world data study

Multicentre observational study
n=73
n=26 switch from LCIG



Santos-García D *et al. Eur J Neurol* 2025;32:e16535.

Neuropsychiatric profile – impulse control disorders

Infusion Therapies and Development of Impulse Control Disorders in Advanced Parkinson Disease: Clinical Experience After 3 Years' Follow-up

Antoniya Todorova, PhD, Michael Samuel, MD, FRCP,* Richard G. Brown, PhD,†‡ and Kallol Ray Chaudhuri, DSc*‡*

TABLE 2. Results

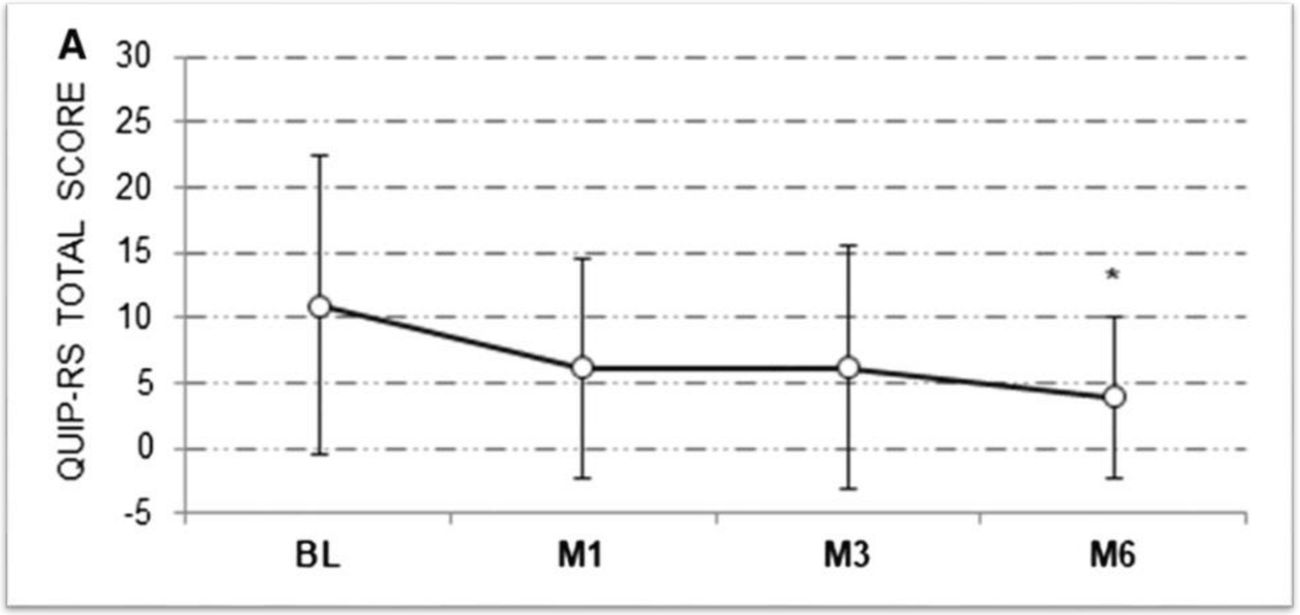
	Apo Group, n (%)	IJLI Group, n (%)
Preexisting ICDs	4 (10)	8 (42)
Preexisting ICDs- resolved	1 (2.4)	6 (32)
Preexisting ICDs- attenuated	3 (7.3)	2 (10)
New troublesome ICDs	4 (9.7)	0
Treatment stopped due to ICDs	1 (2.4)	0

Single centre cohort
CSAI n=41
LCIG n=19

ORIGINAL COMMUNICATION

Improvement of impulse control disorders associated with levodopa–carbidopa intestinal gel treatment in advanced Parkinson's disease

Maria Jose Catalan[1] · Jose Antonio Molina-Arjona[2] · Pablo Mir[3] · Esther Cubo[4] · Jose Matias Arbelo[5] · Pablo Martinez-Martin[6] · On behalf of the EDIS Study Group



Single centre cohort
n=62

1. Todorova A et al. Clin Neuropharm 2015;38:132-134..
2. Catalan MJ *et al. J Neurol* 2018;265:1279-1287.

Genetic factors in response to LCIG

Contents lists available at ScienceDirect
Parkinsonism and Related Disorders
journal homepage: www.elsevier.com/locate/parkreldis

Short communication

Levodopa-carbidopa intestinal gel for advanced Parkinson's disease: Impact of *LRRK2* and *GBA1* mutations

	iPD	*LRRK2*-PD	*GBA1*-PD	Significance
Number of participants	52	15	23	
Male/Female	39/13	10/5	14/9	0.44
Age	74.24 (8.74)	72.57 (8.91)	71.52 (6.15)	0.39
Age at diagnosis	55.82 (8.85)	50.50 (9.37)	57.65 (8.54)	0.06
Disease duration	18.50 (6.60)	21.33 (6.24)	13.87 (6.43)	<0.01[a]
H&Y	3.40 (1.01)	3.37 (1.01)	3.33 (1.12)	0.29
Disease duration until LCIG	13.96 (5.66)	15.07 (5.31)	10.04 (6.22)	0.01[a]
Years treated with LCIG	4.88 (3.60)	6.20 (3.34)	3.47 (2.01)	<0.01[a]
LCIG dosage	1441.78 (526.05)	1372.40 (470.94)	1396.87 (537.53)	0.88
LEDD	1661.41 (612.36)	1599.93 (528.07)	1586.14 (672.90)	0.67
Number of participants still treated at last visit	35	9	19	<0.01[a]
Deceased	14	5	4	0.51
Elected to stop LCIG treatment	3	1	0	0.83
hallucinations %	0.47	0.38	0.81	0.03[a]

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Should we start integrating genetic data in decision-making on device-aided therapies in Parkinson disease? A point of view

Philippe A. Salles[a,c], Ignacio F. Mata[b], Hubert H. Fernandez[a,*]

Device	Eligibility Prediction								
	SNCA Triplication	*SNCA* Duplication	*SNCA* missense	LRRK2	VPS35	PRKN	PINK1	DJ1	Pathogenic GBA variants
DBS	Poor	Fair	Fair	**Good**	Fair	**Good**	Fair	Fair	Fair *
LCIG	Poor	Fair	Fair	**Good**	**Good**	Fair	Fair	Fair	Fair *
CASI	Poor	Poor	Fair	**Good**	Fair	Fair	Fair	Fair	Fair *

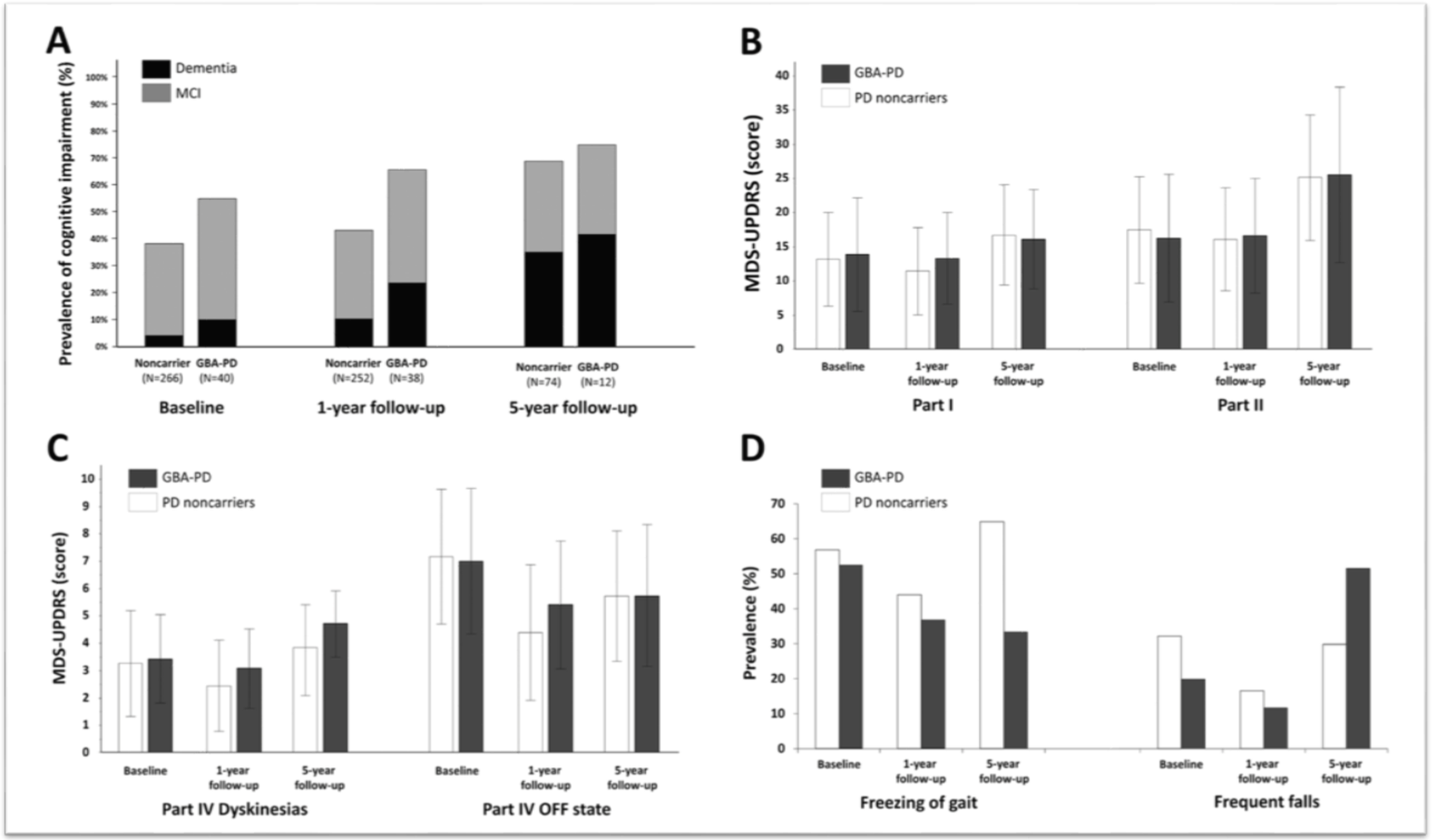
1. Thaler A *et al. Parkinsonism Relat Disord* 2024;127:107115.
2. Salles PA *et al. Parkinsonism Relat Disord* 2021;88:51-57.

ORIGINAL ARTICLE OPEN ACCESS

Effects of *GBA1* Variants in Patients With Parkinson's Disease and Levodopa–Carbidopa Intestinal Gel: A Nation-Wide, Multicenter, Longitudinal, "Real-World" Study. The EPIC Study

Registry study
N=266 GBA negative
N=40 GBA positive

- No difference in discontinuation rates
- Faster progression of MoCA in GBA+
- Faster decline in MDS-UPDRS part I, II, IV in GBA+



Cilia R *et al. Eur J Neurol* 2025;32:e70179.

Selection for LCIG/LECIG

NHS England

Exclusion criteria

The presence of one or more of the following would exclude both LCIG or LECIG therapy:

- Abnormal upper gastro-intestinal anatomy causing difficulty with device implantation
- Significant dementia
- Significant PD related non transitory psychotic symptoms
- Significant co-morbidities that are likely to compromise the potential benefit of LCIG/LECIG (severe low body weight, severe skeletal or postural deformities)
- The presence of any contraindication as detailed in the LCIG/LECIG summary of product characteristics (SPC)
- Lack of social support / appropriate carer to administer the LCIG/LECIG if appropriate

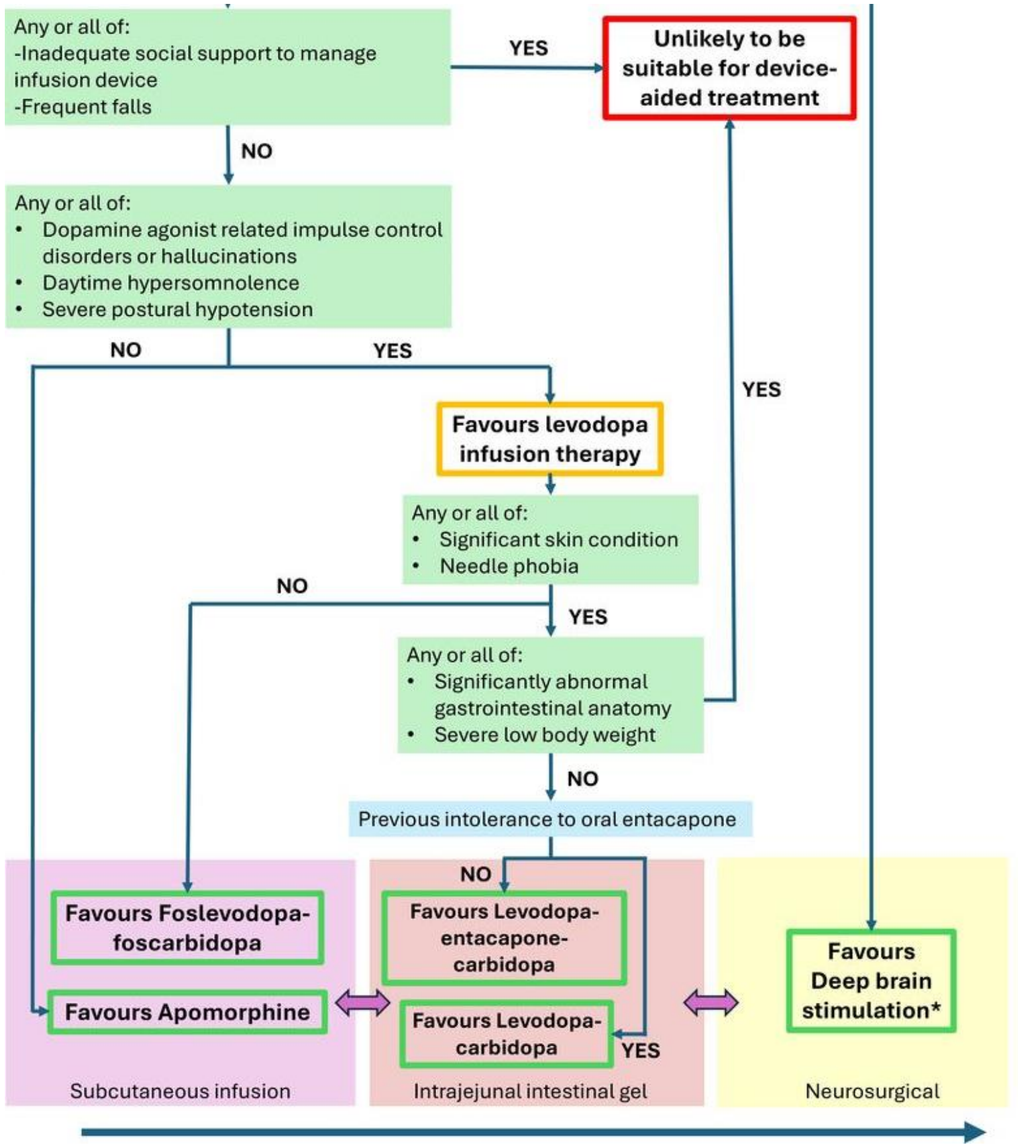
The following criterion excludes the use of LECIG therapy only:

- Previous intolerance (severe resistant diarrhoea, dyskinesias) to oral entacapone

https://www.england.nhs.uk/wp-content/uploads/2015/07/levodopa-carbidopa-intestinal-gel-lcig-and-levodopa-carbidopa-entacapone-intestinal-gel-lecig-for-parkinsons-d.pdf
Accessed 18/11/2025

Issues for consideration

- National/regional funding arrangements
- Nurse support for titration/follow-up
- Links to gastro/endoscopy

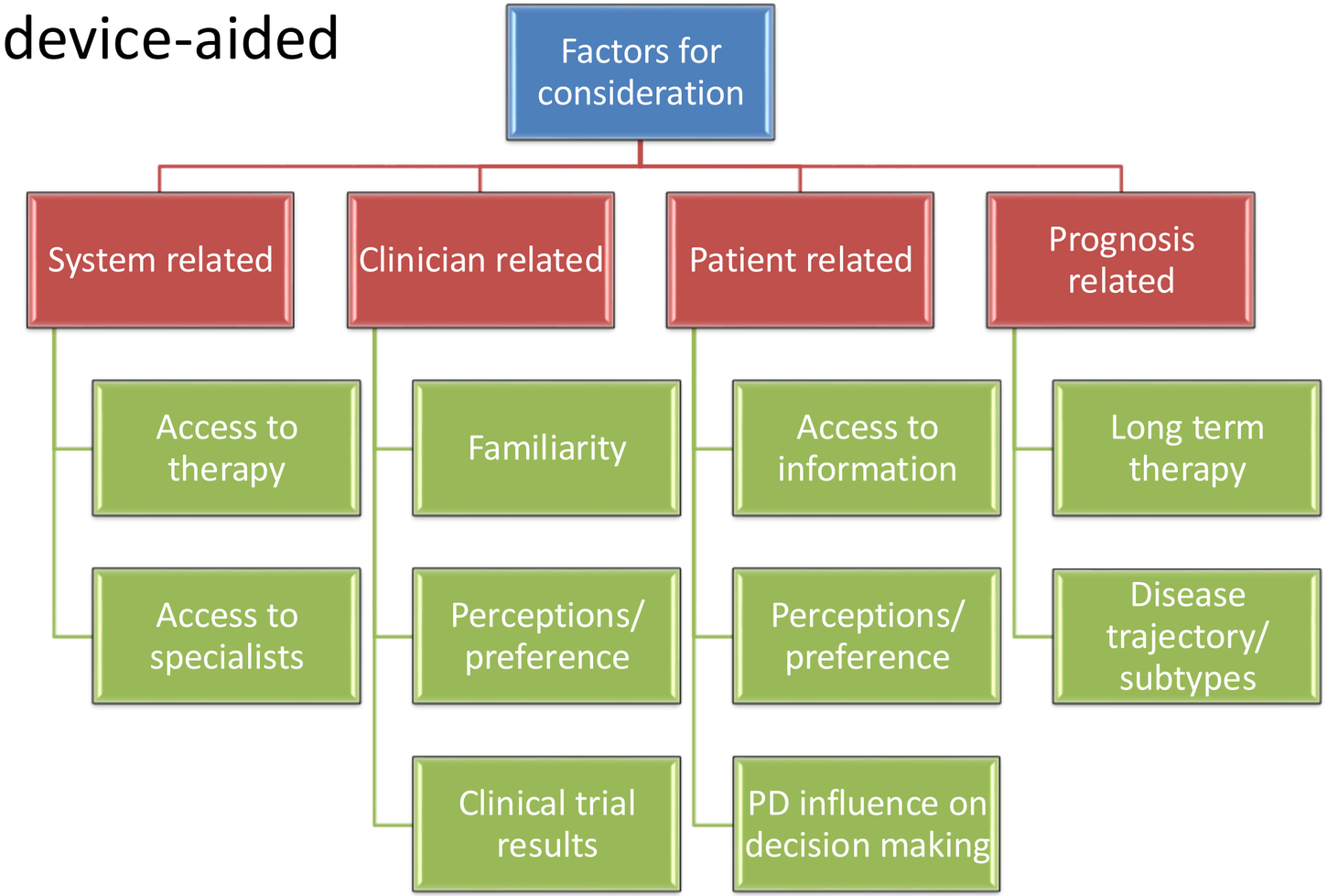


Street D *et al. Pract Neurol.* 2025 Oct 20:pn-2025-004777.

Symptom	Apomorphine pump	LCIG/LECIG	DBS
Dyskinesia	+	+	++
Refractory tremor	-	-	++
Psychosis	-	+/-	-
Impulse control disorders	-	+	+
Hypersomnolence	-	+/-	+/-
Mild cognitive impairment	+/-	+	+/-
Dementia	-	+/-	-
Severe depression	+	+	-
Non-motor fluctuations	+	+	+
Dysarthria	+	+	-
Postural instability	+/-	+/-	-
Orthostatic hypotension	-	+/-	+/-
Peripheral neuropathy	+/-	-	+/-

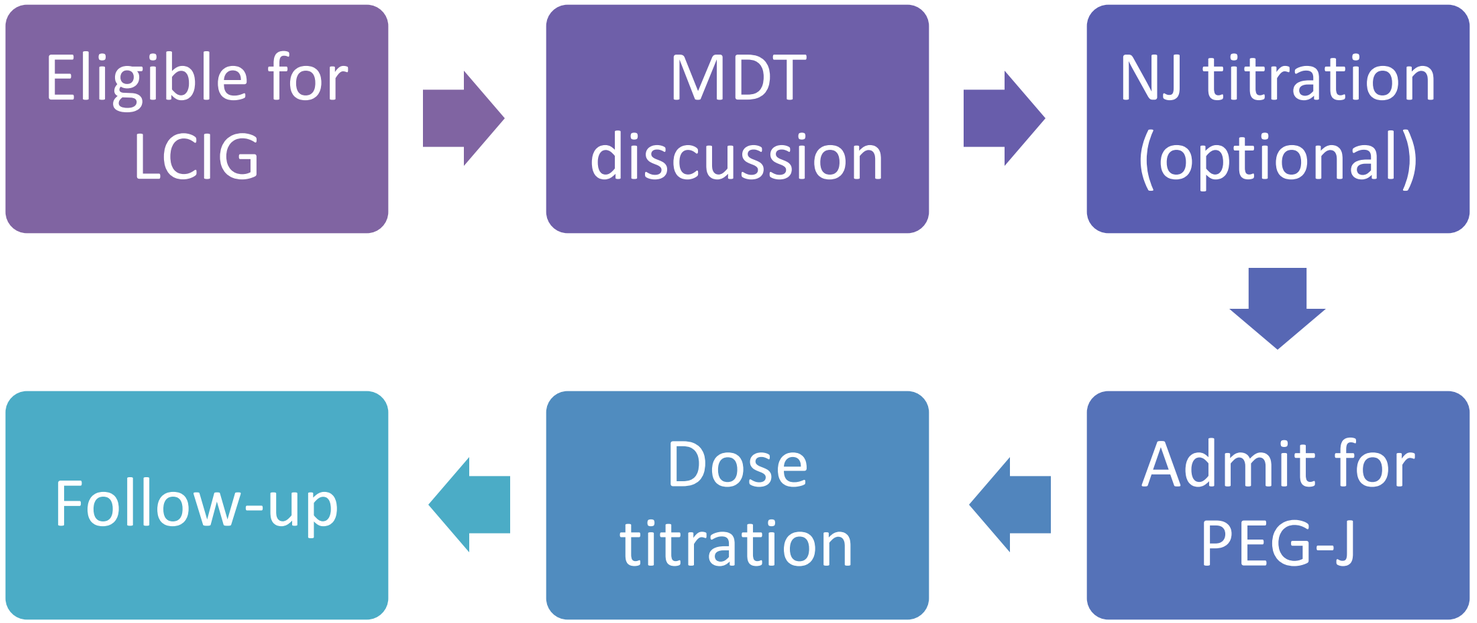
++ strong support for selection; + support for selection; +/- requires further investigation; - evidence against selection
Adapted from Odin *et al. Parkinsonism Relat Disord* 2015;21:1133-1144.

Decision-making for device-aided therapies



Adapted from Auffret M *et al. J Neural Transm* 2023;130:1411-1432.

Process for initiation



Key points for follow-up

- Support with dose changes
- Pump/tube issues
- Ensure rescue treatment plan in place
- Recording of outcomes

Stopping criteria

- Unacceptable adverse effects
- Gait impairment without significant ongoing benefit to limb parkinsonism
- Severe neuropsychiatric issues
- Subacute or acute peripheral neuropathy
- Patient choice
- Recurrent hardware problems e.g. PEG/ jejunal tube displacement
- Severe weight loss
- Significant diarrhoea on LECIG

Conclusions

- LCIG is an effective evidence-based treatment for complex PD
- Selection based on motor and non-motor profile vs other therapies
- Support with titration and PEG-J management is critical
- Potential long-term treatment option

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Thank you

Any questions?