Subcutaneous Pumps for Parkinson's Disease: Foslevodopa/Foscarbidopa

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AMDAPP Conference

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Association of Movement Disorder Advanced Practice Providers

Kinsey McCartney

- Speakers' Bureau, consultant, and/or advisory board member for AbbVie.

All relevant financial relationships have been mitigated

OBJECTIVES:

1. Pump Basics
2. Brief Review of the Literature
3. Practical Considerations
    - Patient Selection
    - Rate Calculations
    - Clinical Integration and Workflow
    - Optimizing Therapy
    - Navigating the Delivery System
    - Managing Side Effects
4. Cases

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Therapy Indications

- Indicated for the treatment of motor fluctuations in adults with advanced Parkinson's Disease
- General guideline summary:
  1. Diagnosis of idiopathic, levodopa-responsive Parkinson's Disease
  2. Currently taking at least 400mg of levodopa equivalents daily
  3. Motor fluctuations are inadequately controlled with carbidopa/levodopa therapy
  4. Minimum daily average "off" time of 2.5 hours per day

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Delivery

- **24 hours/day** continuous infusion of LD-based therapy
  - Replaces LD-containing medications and COMT inhibitors*
  - Can temporarily disconnect for water-based activities†

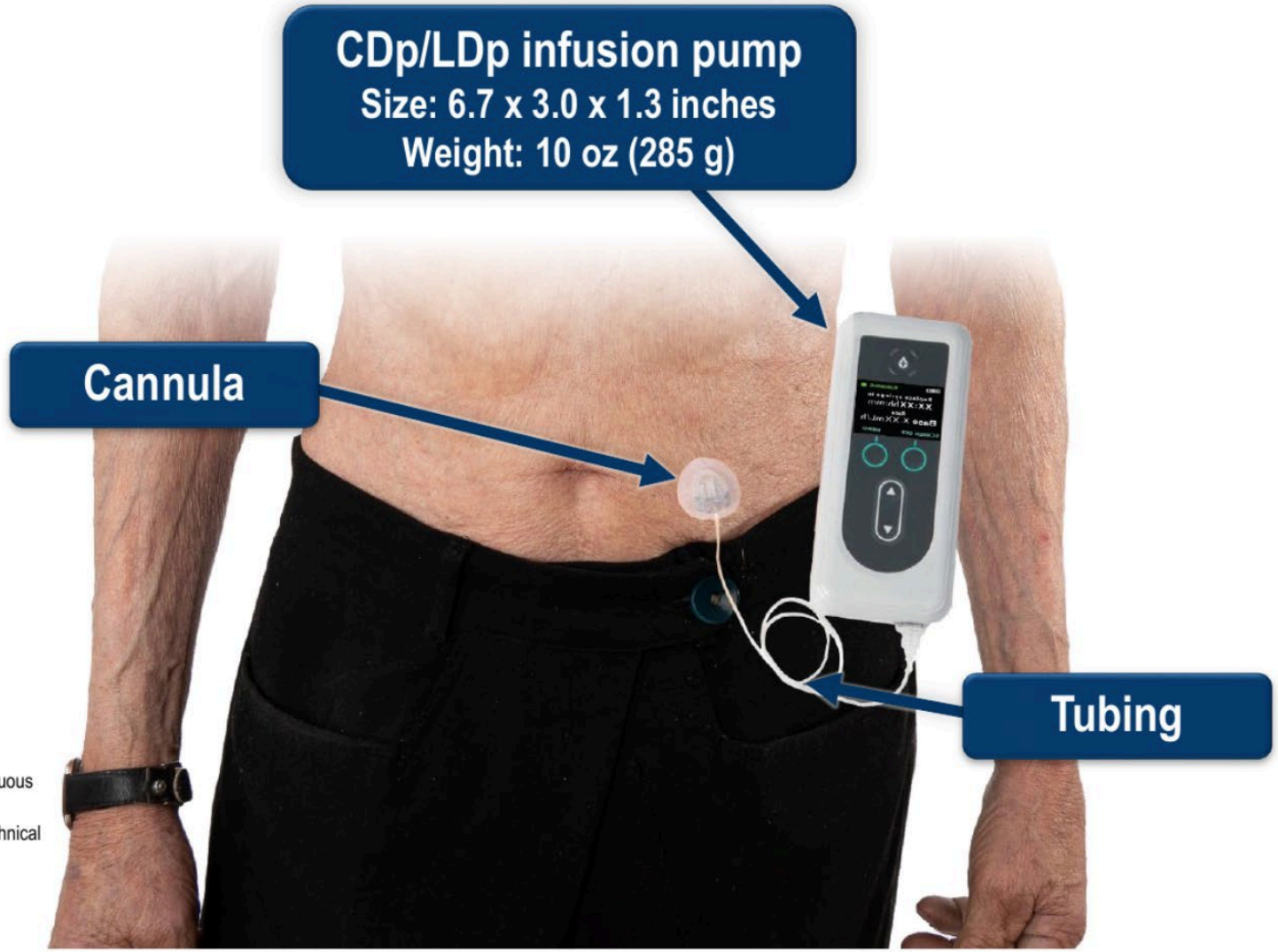
Formulation

- **CDp/LDp is converted** to CD/LD by alkaline phosphatases
- **Bypasses the gut**
  - Absorption or systemic exposure of CD/LD not affected by food or iron salts[3]

Dosing

- **Individualized dosing** to address clinical needs of patients‡
  - **Precise** adjustments to hourly infusion rate by **1.7 mg LE/hr**
  - Account for changes in functional demand with alternative **low/high flow rates**§
  - Self-administered **optional loading dose** and **extra dose** functions§
  - Maximum recommended daily dose of CDp/LDp is ~2500 mg LE (3525 mg LDp)

COMPONENTS OF THE CDp/LDp CSCI SYSTEM[1,2]



CDp/LDp=foscarbidopa/foslevodopa; CSCI=continuous subcutaneous infusion.

1. VYAFUSER™ HCP Technical Manual. Struer, Denmark.
2. VYAFUSER™ Patient Technical Manual. Struer, Denmark.

INDIVIDUAL COMPONENTS OF THE CDp/LDp CSCI SYSTEM[1-3]

Replaced at least once per day

Medication vial

Vial adapter

Syringe

Battery

Replaced at least once every 3 days

Tubing

Cannula insertion device with cannula

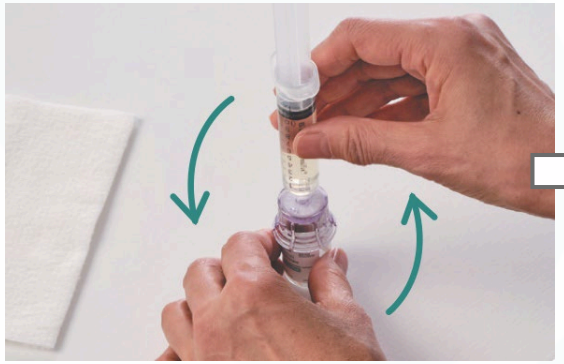
CDp/LDp=foscarbidopa/foslevodopa; CSCI=continuous subcutaneous infusion.

1. CDp/LDp [package insert]. North Chicago, IL: AbbVie Inc. 2. VYAFUSER™ HCP Technical Manual. Struer, Denmark. 3. VYAFUSER™ Patient Technical Manual. Struer, Denmark.





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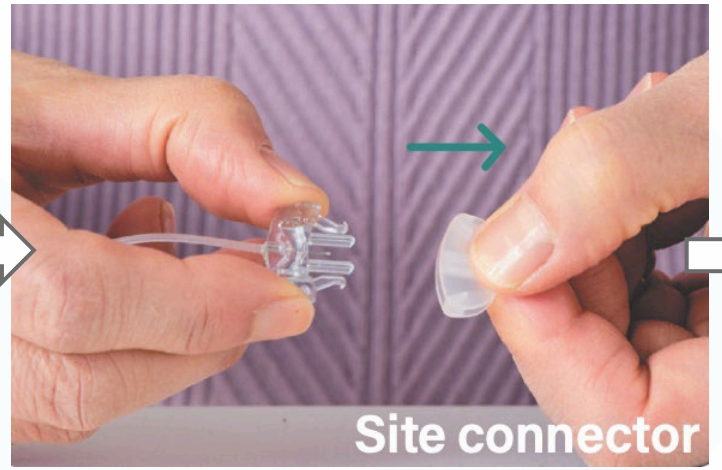

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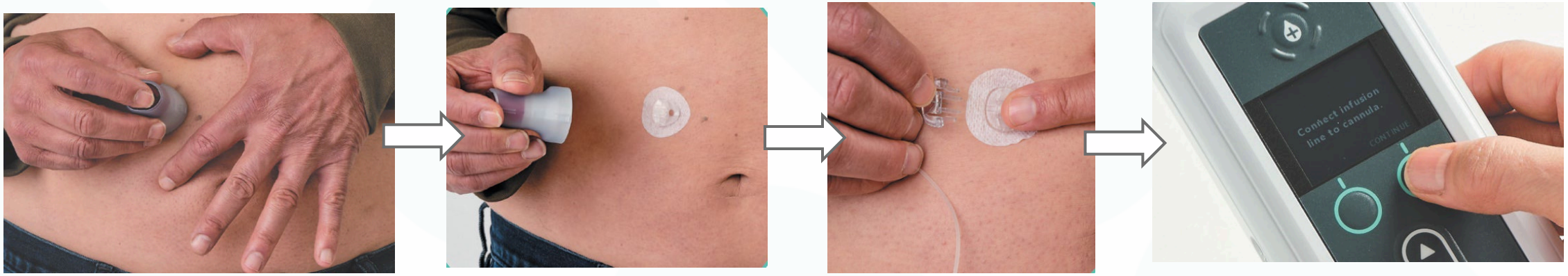

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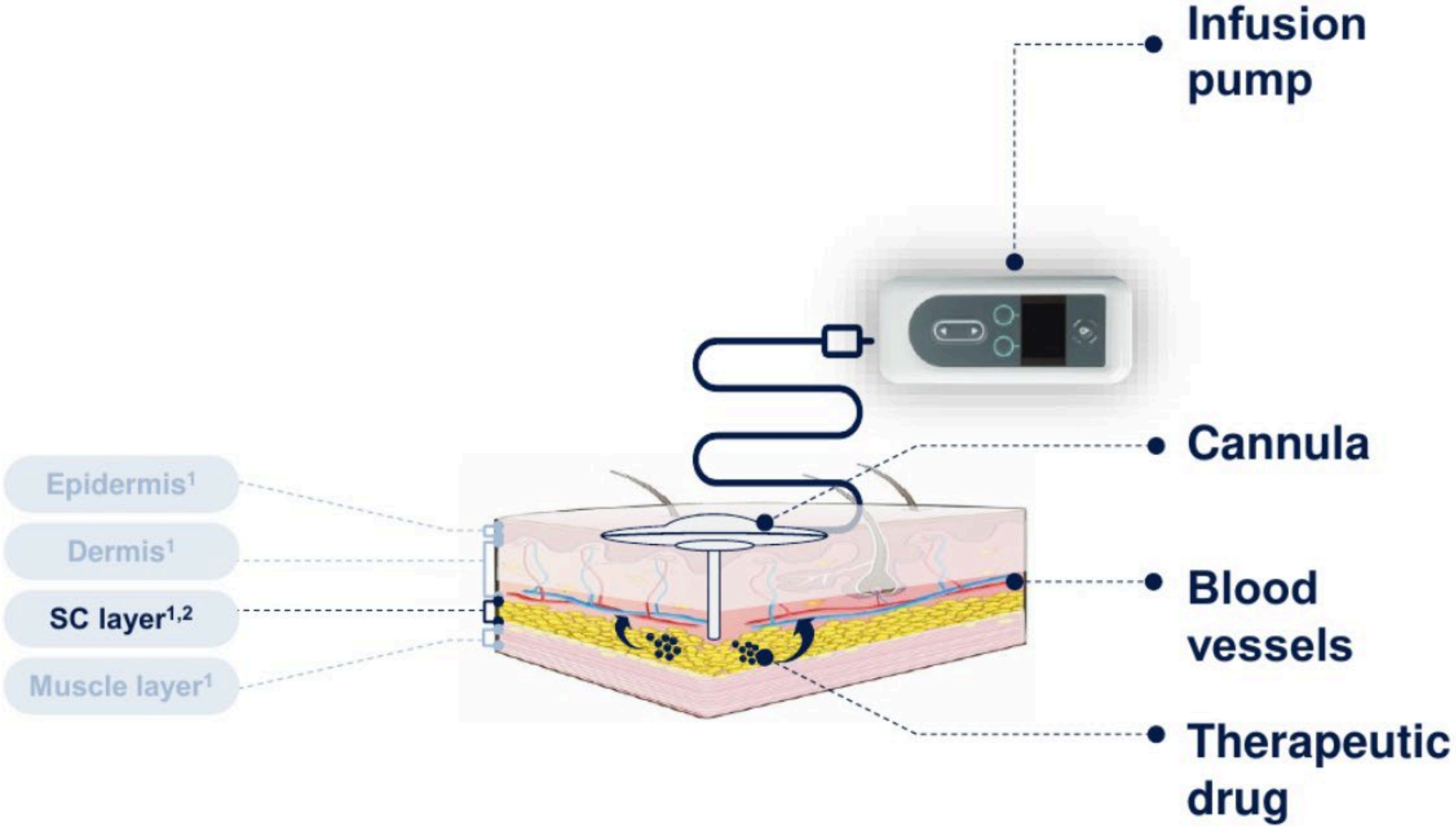


Cutaneous and SC layers are not drawn to scale.

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

Summary

Background Levodopa is the most effective symptomatic therapy for Parkinson's disease, but patients with advanced Parkinson's disease develop motor fluctuations with chronic oral levodopa therapy. Foslevodopa-foscarbidopa is a soluble formulation of levodopa and carbidopa prodrugs that is delivered as a 24-h/day continuous subcutaneous infusion, and we aimed to assess the safety and efficacy of this formulation in patients with advanced Parkinson's disease.

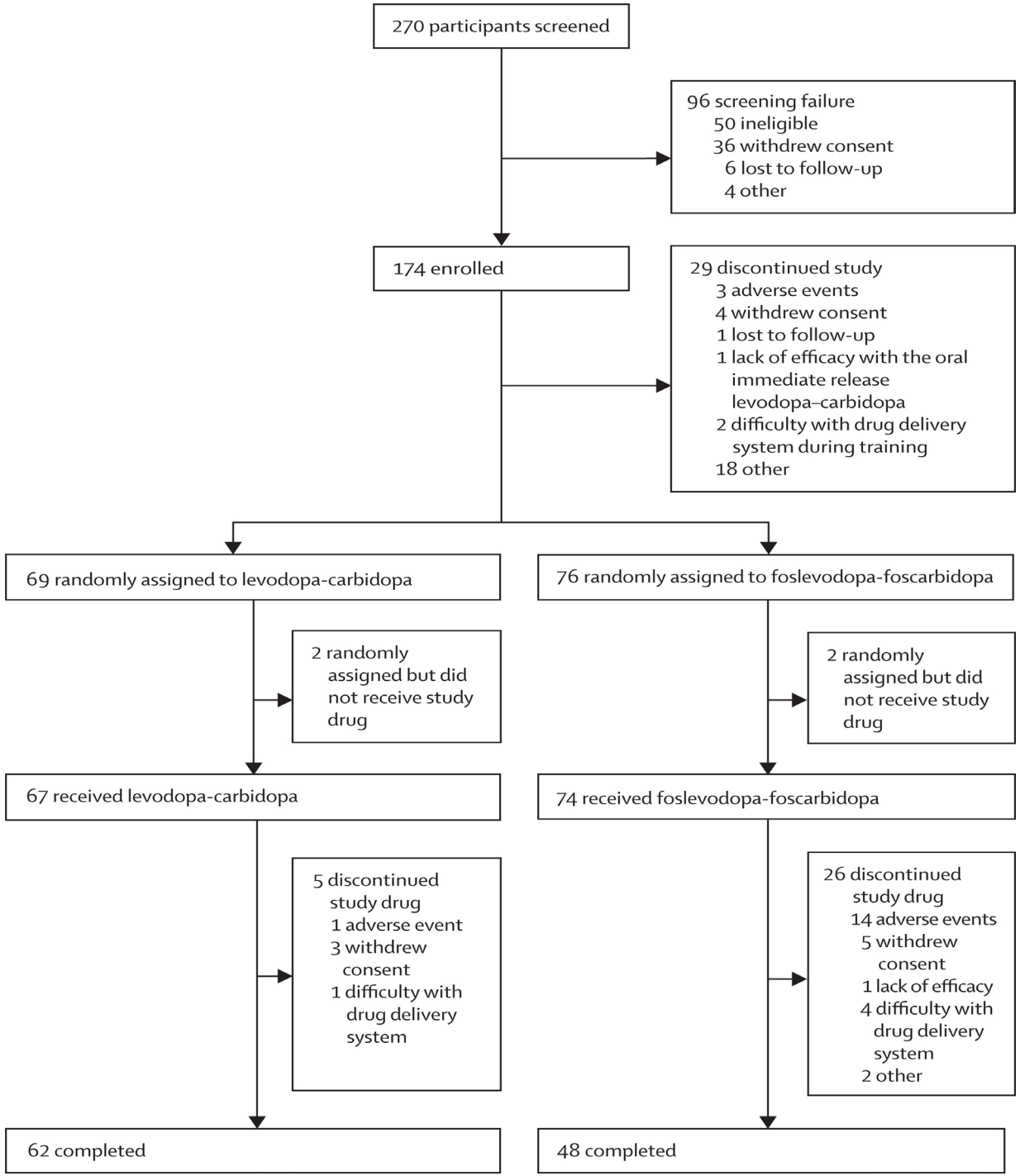
Methods A 12-week randomised, double-blind, double-dummy, active-controlled study was done at 65 academic and community study centres in the USA and Australia. Patients with levodopa-responsive advanced Parkinson's disease inadequately controlled on current therapy, including at least 2·5 h of average daily off time, were randomly assigned (1:1) to continuous subcutaneous infusion of foslevodopa-foscarbidopa plus oral placebo or to oral

Lancet Neurol 2022; 21: 1099–109

This online publication has been corrected. The corrected version first appeared at thelancet.com on Feb 15, 2023

See **Comment** page 1063

Texas Movement Disorder Specialists, Georgetown, TX, USA (M J Soileau MD); **Selkirk**


270 participants screened
96 screening failure
50 ineligible
36 withdrew consent
6 lost to follow-up
4 other
174 enrolled
29 discontinued study
3 adverse events
4 withdrew consent
1 lost to follow-up
1 lack of efficacy with the oral immediate release levodopa–carbidopa
2 difficulty with drug delivery system during training
18 other
69 randomly assigned to levodopa-carbidopa
76 randomly assigned to foslevodopa-foscarbidopa
2 randomly assigned but did not receive study drug
2 randomly assigned but did not receive study drug
67 received levodopa-carbidopa
74 received foslevodopa-foscarbidopa
5 discontinued study drug
1 adverse event
3 withdrew consent
1 difficulty with drug delivery system
26 discontinued study drug
14 adverse events
5 withdrew consent
1 lack of efficacy
4 difficulty with drug delivery system
2 other
62 completed
48 completed

	Oral levodopa–carbidopa group (n=67)	Foslevodopa–foscarbidopa group (n=74)	Total (n=141)
Sex			
Male	49 (73%)	50 (68%)	99 (70%)
Female	18 (27%)	24 (32%)	42 (30%)
Age, years	66·6 (9·8)	66·3 (9·2)	66·4 (9·5)
<65 years	24 (36%)	27 (36%)	51 (36%)
≥65 years	43 (64%)	47 (64%)	90 (64%)
Race			
White	61 (91%)	70 (95%)	131 (93%)
Black or African American	2 (3%)	2 (3%)	4 (3%)
Asian	3 (4%)	0	3 (2%)
American Indian or Alaska Native	0	1 (1%)	1 (1%)
Native Hawaiian or other Pacific Islander	1 (1%)	1 (1%)	2 (1%)
Country			
Australia	9 (13%)	12 (16%)	21 (15%)
USA	58 (87%)	62 (84%)	120 (85%)
Body mass index, kg/m²	26·34 (23·33–31·19)	26·31 (22·73–29·88)	26·34 (23·01–30·29)
MMSE score	28·83 (1·27)	28·72 (1·60)	28·77 (1·45)
Duration since Parkinson's disease diagnosis, years	8·79 (5·49)	8·38 (4·22)	8·58 (4·85)
<10 years	44 (66%)	51 (69%)	95 (67%)
≥10 years	23 (34%)	23 (31%)	46 (33%)
Hoehn and Yahr stage (MDS-UPDRS)			
0	1 (1%)	0	1 (1%)
1	4 (6%)	9 (12%)	13 (9%)
2	45 (67%)	43 (58%)	88 (62%)
3	14 (21%)	20 (27%)	34 (24%)
4	2 (3%)	2 (3%)	4 (3%)
5	1 (1%)	0	1 (1%)
Levodopa,* mg/day	1000 (600–1500)	1050 (800–1500)	1000 (800–1500)

Baseline Characteristics Part 1

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Baseline Characteristics Part 2

	Oral levodopa–carbidopa group (n=67)	Foslevodopa–foscarbidopa group (n=74)	Total (n=141)
(Continued from previous page)			
Parkinson's disease diary outcomes, †normalised hours			
Off time	5·91 (1·88)	6·34 (2·27)‡	6·13 (2·10)§
On time without troublesome dyskinesia	9·49 (2·62)	9·20 (2·42)‡	9·34 (2·51)§
On time without dyskinesia	7·47 (3·73)	7·23 (3·14)‡	7·35 (3·42)§
On time with non-troublesome dyskinesia	2·02 (2·75)	1·97 (2·47)‡	1·99 (2·60)§
On time with troublesome dyskinesia	0·60 (1·46)	0·46 (0·86)‡	0·53 (1·18)§
Presence of morning akinesia	51/67 (76%)	56/71 (79%)	107/138 (78%)
MDS-UPDRS part II score	13·27 (6·37)	15·31 (6·93)	14·34 (6·73)
PDSS-2 total score	18·88 (9·25)¶	21·19 (8·80)‖	20·09 (9·06)**
PDQ-39 summary index	26·15 (14·46)¶	30·68 (16·05)‡	28·53 (15·43)**

Summary of Efficacy Findings

	Oral levodopa-carbidopa group (n=67)	Foslevodopa-foscarbidopa group (n=74)	Treatment difference (SE; 95% CI)	p value
Primary efficacy measure				
On time without troublesome dyskinesia, h/day	0·97 (0·50)	2·72 (0·52)*	1·75 (0·65; 0·46 to 3·05)	0·0083
Key secondary efficacy measures				
Off time, h/day	−0·96 (0·49)	−2·75 (0·50)*	−1·79 (0·63; −3·03 to −0·54)	0·0054
MDS-UPDRS part II score	−1·06 (0·79)	−2·65 (0·82)	−1·58 (1·05; −3·65 to 0·48)	0·13
Morning akinesia, n/N (%)	38/60 (63%)	8/47 (17%)	0·12 (0·49; 0·04 to 0·31)	..

Adverse Event Data

	Oral levodopa-carbidopa group (n=67)	Foslevodopa-foscarbidopa group (n=74)
Adverse events	42 (63%)	63 (85%)
Deaths	1 (1%)	0
Serious adverse events	4 (6%)	6 (8%)
Severe adverse events	1 (1%)	7 (9%)
Any adverse event leading to death	1 (1%)*	0
Any adverse event leading to premature study drug discontinuation†	1 (1%)	16 (22%)
Any adverse event considered related to study drug	15 (22%)	52 (70%)
Adverse events of special interest		
Infusion site events	8 (12%)	53 (72%)
Hallucinations or psychosis	2 (3%)	11 (15%)
Falls and associated injuries	17 (25%)	13 (18%)
Somnolence	1 (1%)	1 (1%)
Polyneuropathy	2 (3%)	2 (3%)
Weight loss	1 (1%)	1 (1%)

	Oral levodopa-carbidopa group (n=67)	Foslevodopa-foscarbidopa group (n=74)
Most frequent adverse events‡		
Infusion site erythema	1 (1%)	20 (27%)
Infusion site pain	1 (1%)	19 (26%)
Infusion site cellulitis	0	14 (19%)
Infusion site oedema	0	9 (12%)
Dyskinesia	4 (6%)	8 (11%)
Fall	12 (18%)	6 (8%)
Infusion site bruising	2 (3%)	6 (8%)
Infusion site haemorrhage	0	6 (8%)
Infusion site nodule	0	6 (8%)
On and off phenomena	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%)

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Movement Disorders
CLINICAL PRACTICE

RESEARCH ARTICLE

Efficacy and Safety of Foslevodopa/Foscarbidopa Monotherapy in Patients with Parkinson's Disease

Jason Aldred, MD,[1,] Manon Bouchard, MD,[2] Juan Carlos Martínez-Castrillo, MD, PhD,[3] Michael J. Soileau, MD,[4] Amy M. Spiegel, PhD,[5] Lars Bergmann, MD,[5] Resmi Gupta, PhD,[5] Megha B. Shah, PharmD,[5] Pavnit Kukreja, PharmD,[5] David G. Standaert, MD, PhD,[6] Stuart H. Isaacson, MD,[7] and Tove Henriksen, MD[8]*

Abstract: Background: As Parkinson's disease (PD) progresses, managing symptoms becomes increasingly difficult. Foslevodopa/foscarbidopa (LDp/CDp), a 24-hour/day continuous subcutaneous infusion of levodopa/carbidopa (LD/CD) prodrugs, improves motor complications. The feasibility and sustainability of LDp/CDp monotherapy warrants investigation.

Objective: The aim was to report the efficacy and safety of LDp/CDp monotherapy and combination therapy.

Methods: This post hoc analysis assessed patients with PD and ≥2.5 "Off" hours/day receiving LDp/CDp monotherapy or combination therapy in 3 trials: a 12-week randomized active-controlled trial (RCT) comparing

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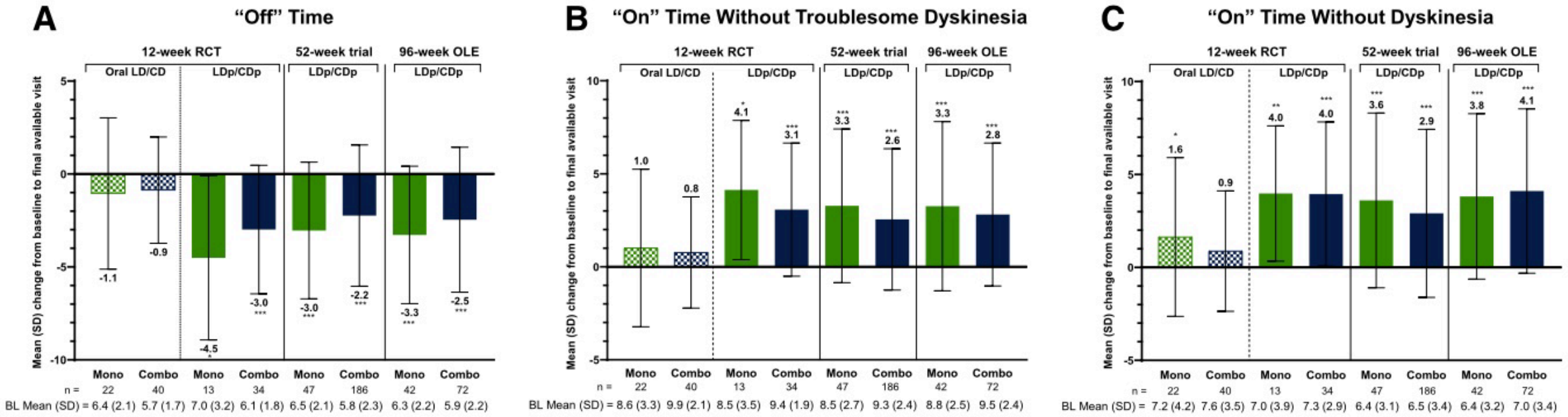


FIG. 2. Change from baseline to final visit in (**A**) "Off" time, (**B**) "On" time without troublesome dyskinesia, and (**C**) "On" time without dyskinesia. Reported values are mean (SD [standard deviation]) change from baseline to week 12 for the RCT and mean (SD) change from baseline to final available visit for the 52-week trial and 96-week OLE. The baseline of the 96-week OLE corresponds to the start of the 52-week trial. *$P \leq 0.05$, **$P \leq 0.01$, and ***$P \leq 0.001$ versus baseline. BL, baseline; Combo, combination therapy; LD/CD, levodopa/carbidopa; LDp/CDp, foslevodopa/foscarbidopa; Mono, monotherapy; OLE, open-label extension; RCT, randomized active-controlled trial.

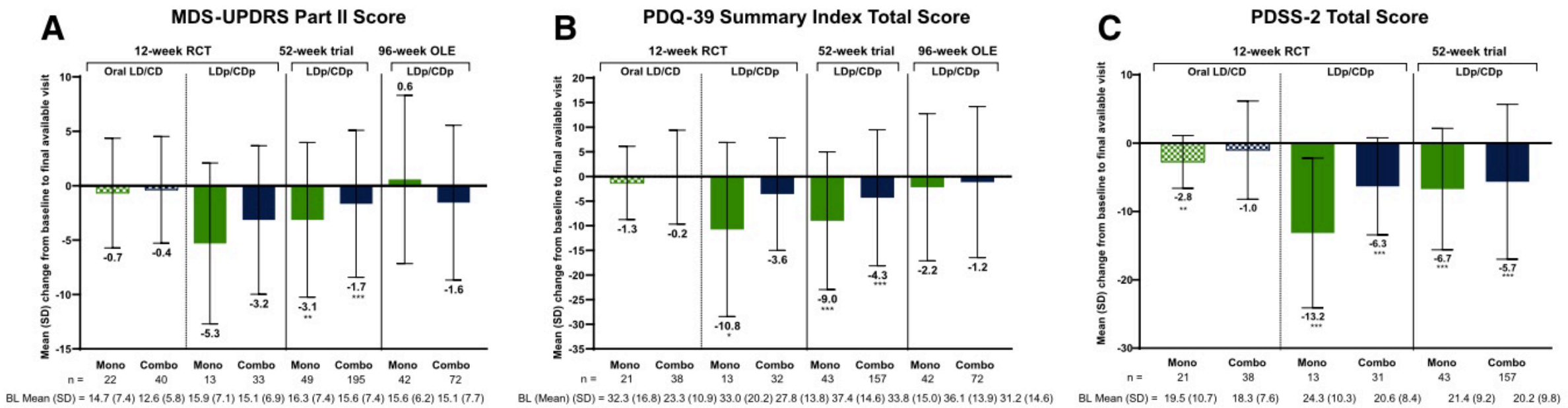


FIG. 3. Change from baseline to final visit in (**A**) MDS-UPDRS Part II score, (**B**) PDQ-39 summary index total score, and (**C**) PDSS-2 total score.[a] Reported values are mean (SD [standard deviation]) change from baseline to final available visit except for MDS-UPDRS Part II data for the 12-week RCT, which is change from baseline to week 12. Baseline of the 96-week trial corresponds to the start of the 52-week trial. *$P \leq 0.05$, **$P \leq 0.01$, and ***$P \leq 0.001$ versus baseline. BL, baseline; Combo, combination therapy; LD/CD, levodopa/carbidopa; LDp/CDp, foslevodopa/foscarbidopa; MDS-UPDRS, Movement Disorder Society-Unified Parkinson's Disease Rating Scale; Mono, monotherapy; OLE, open-label extension; PDQ-39, 39-item Parkinson's Disease Questionnaire; PDSS-2, Parkinson's Disease Sleep Scale-2; RCT, randomized active-controlled trial. [a]PDSS-2 was not evaluated in the OLE.

	12-week RCT				52-week trial		96-week OLE	
	Oral LD/CD (n = 67)		LDp/CDp (n = 74)		LDp/CDp (N = 244)		LDp/CDp (N = 129)	
TEAE,* n (%)	Mono (n = 22)	Combo (n = 45)	Mono (n = 19)	Combo (n = 55)	Mono (n = 49)	Combo (n = 195)	Mono (n = 46)	Combo (n = 83)
Any TEAE	6 (27.3)	27 (60.0)	15 (78.9)	47 (85.5)	46 (93.9)	184 (94.4)	41 (89.1)	67 (80.7)
Severe TEAE	0	1 (2.2)	1 (5.3)	6 (10.9)	13 (26.5)	50 (25.6)	11 (23.9)	18 (21.7)
Serious TEAE	0	4 (8.9)	0	6 (10.9)	11 (22.4)	52 (26.7)	13 (28.3)	22 (26.5)
TEAE leading to study drug discontinuation	0	1 (2.2)	2 (10.5)	14 (25.5)	14 (28.6)	50 (25.6)	4 (8.7)	5 (6.0)

Note: Data shown include all patients who received the study drug.

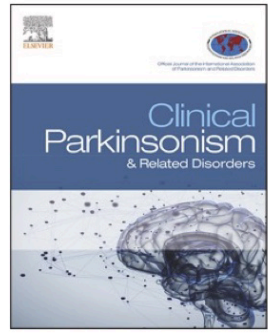
Abbreviations: RCT, randomized active-controlled trial; OLE, open-label extension; LD/CD, levodopa/carbidopa; LDp/CDp, foslevodopa/foscarbidopa; mono, monotherapy; combo, combination therapy; TEAE, treatment-emergent adverse event.

*Patients are counted once in each row, regardless of the number of events they may have had.

Contents lists available at ScienceDirect

Clinical Parkinsonism & Related Disorders

journal homepage: www.sciencedirect.com/journal/clinical-parkinsonism-and-related-disorders



Review

Continuous subcutaneous foslevodopa/foscarbidopa infusion for the treatment of motor fluctuations in Parkinson's disease: Considerations for initiation and maintenance

Victor S.C. Fung [a,b,*], Jason Aldred [c,d], Martha P. Arroyo [e], Filip Bergquist [f,g], Agnita J.W. Boon [h], Manon Bouchard [i,j], Sarah Bray [a], Sara Dhanani [k], Maurizio F. Facheris [l], Nahome Fisseha [m], Eric Freire-Alvarez [n], Robert A. Hauser [o], Anna Jeong [l], Jia Jia [l], Pavnit Kukreja [l], Michael J. Soileau [p], Amy M. Spiegel [l], Saritha Talapala [l], Arjun Tarakad [q], Enrique Urrea-Mendoza [r,s,1], Jorge Zamudio [l], Rajesh Pahwa [t]

Patient Selection

- “A general consensus for good candidates across all device-aided therapies include patients typically < 70 years of age, with good levodopa response, who may or may not have troublesome dyskinesia, and who still have good cognitive function”
- Use caution and discretion with the following:
  - Presence of mild hallucinations
  - Orthostatic hypotension
  - Mild cognitive impairment, especially when care partner presence is lacking

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Determining Infusion Rates

- The continuous infusion rate is based on the total levodopa dosage (TDL) during waking hours
  - Calculations to include all levodopa-containing medications that LDp/CDp is replacing
- The hourly base continuous infusion rate (mL/hr)= [(TLD x 1.3)/240] / [number of hours patient is typically awake]
- The maximum recommended daily dose of foslevodopa is 3,525mg which is equivalent to approximately 2,500mg immediate release levodopa

Calculating LD Equivalents From LD-Containing Medications.[a]

Medication	Dose Multiplication Factor
Immediate-release LD, including enteral suspension	No adjustment needed (i.e., multiply by 1)
Sustained-release LD, controlled-release or prolonged-release	Multiply by 0.75
Extended-release LD (Rytary®), mg	Multiply by:
0 – 855	0.42
856 – 1755	0.48
1756 – 2340	0.56
≥ 2341	0.67
If any COMT inhibitor is used, multiply sum of calculated LD equivalents from above by 1.33	

LD = levodopa. CD = carbidopa. IR = immediate release. COMT = catechol-*O*-methyltransferase.

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Pump Settings

- The pump can be programmed to allow for 3 continuous rates of infusion: “High,” “Base,” and “Low”
  - Infusion rates are adjusted in increments of 0.01mL/hr
  - One approach based on clinical trial experience is to adjust the infusion rate as a percentage of the Base rate, with +/- 10 % as a reasonable starting point for titration
- Loading dose: if foslevodopa/foscarbidopa is being initiated in the “off” state or patient has not been receiving their base continuous infusion for more than 3 hours, a loading dose can be administered immediately prior to starting or re-starting continuous hourly infusion
- An “extra dose” can be programmed to 1 of 5 options and the feature is limited to no more than 1 extra dose per hour

Foslevodopa Extra Dose Volume	Approximate Equivalent Levodopa Dose
0.1mL	17mg
0.15mL	25.5mg
0.2mL	34mg
0.25mL	42.5mg
0.30mL	51mg

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Optimizing Therapy

- In the clinical trials, optimization was considered complete when no changes to the infusion rate were made for at least 15 days
- Mean number of visits for initial optimization in the phase 3 clinical trials ranged from 2.4 to 3.5 visits
- No established protocol on how to initiate and optimize a patient's therapy. Several factors, including patient's distance from clinic and availability of providers will influence this
- Decision to taper or discontinue concomitant medications, along with the timing of such changes, is highly dependent on the individual patient profile and must be considered on a case-by-case basis

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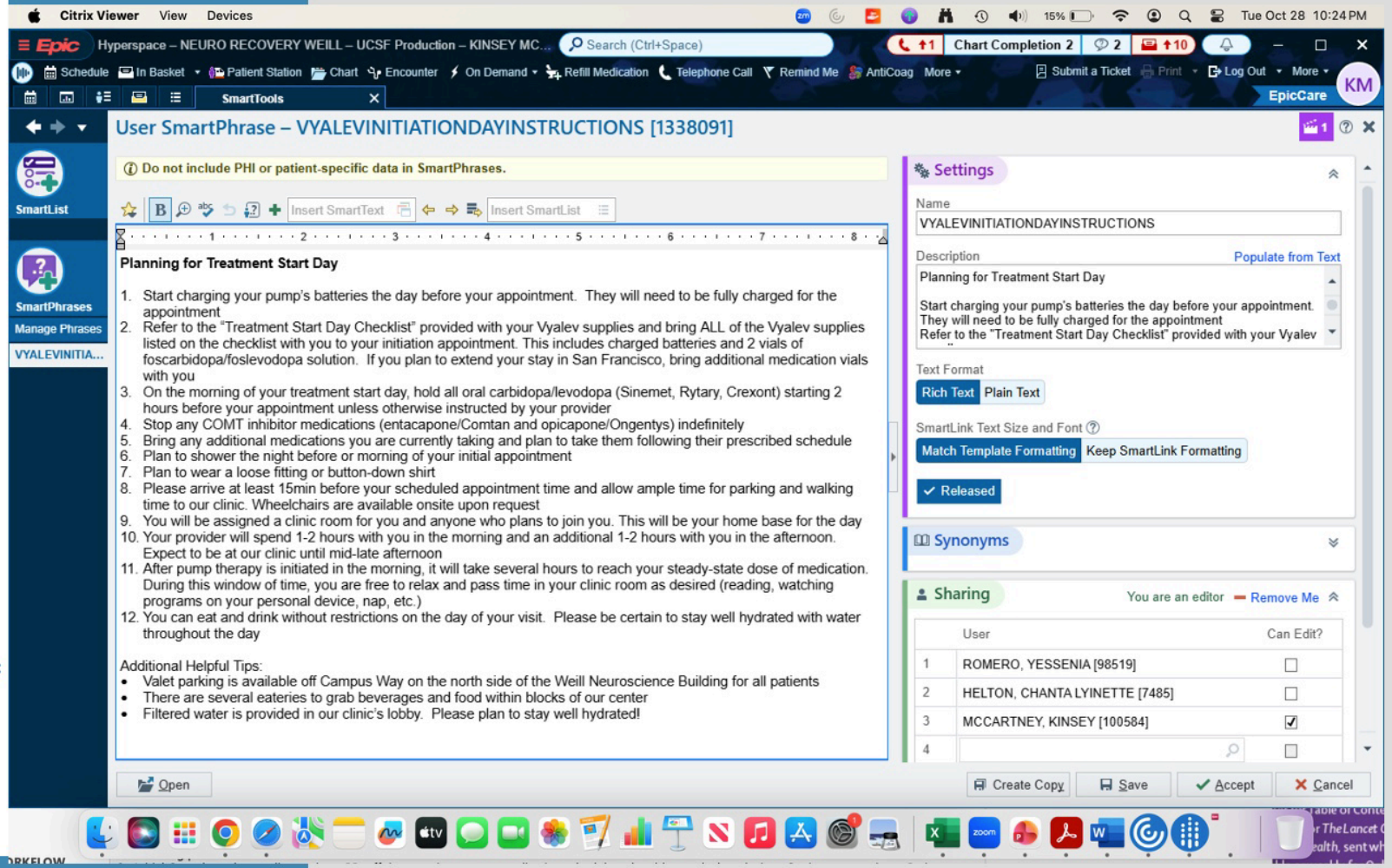
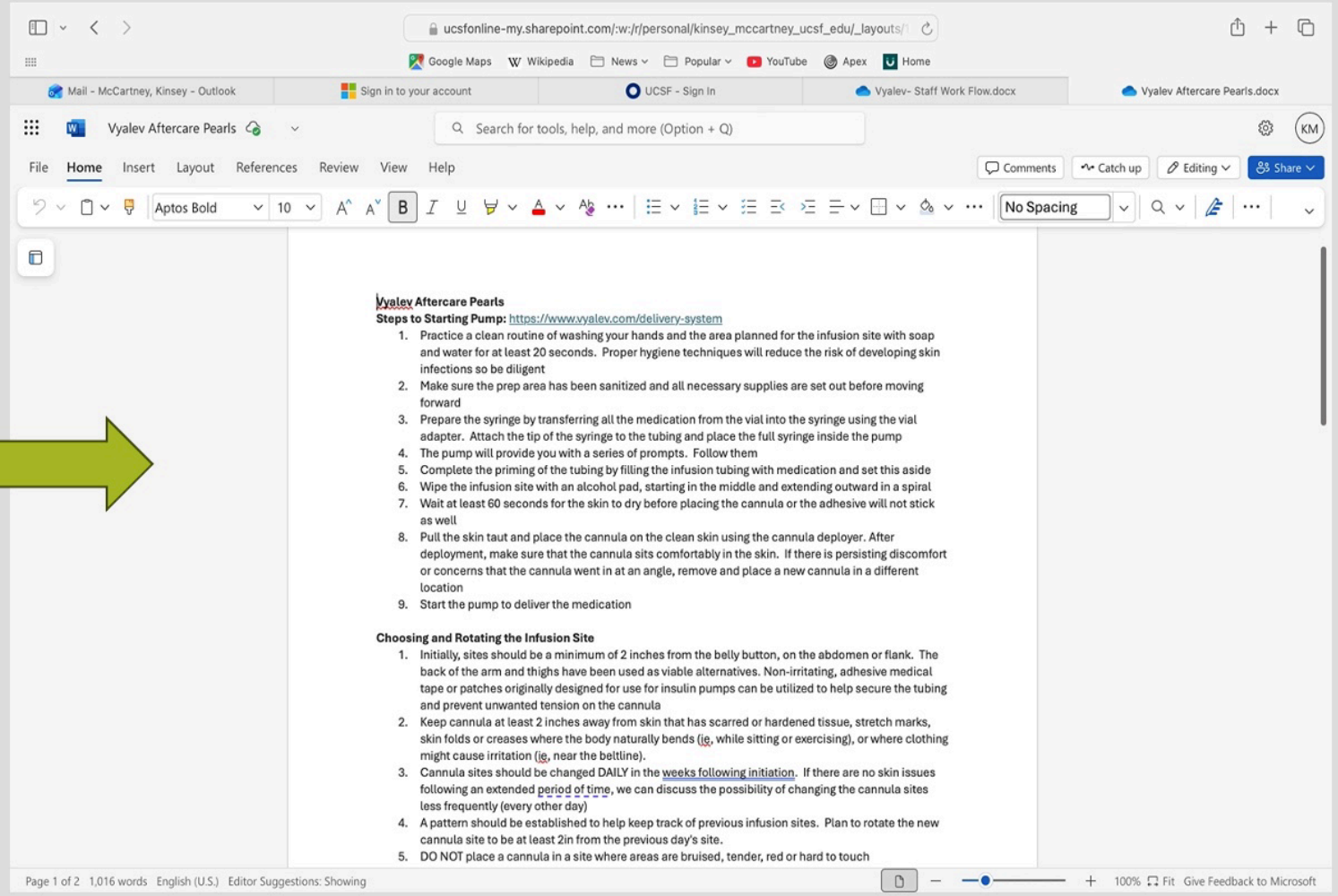
CURRENT WORK FLOW

1. Referral for initial consult
2. Initial consult + education
3. Patient Education Webinar
4. Dose calculation
5. Enrollment form completion, including patient signature
6. Insurance authorization process
7. In-home Nurse Ambassador training
8. Appointment scheduling: initiation + 2 follow up visits at 1 week and 2 or 3 weeks s/p initiation
9. Initiation Day Instructions sent to patient via mychart



INITIATION DAY

- Evolving Process
  - Bringing patients in in an "ON" state
  - Time blocked in morning and afternoon
  - Avoid the loading dose
  - +/- "extra dose" once connecting
- "Vyalev Aftercare Pearls" handout
  - Morning: Education: "Steps to Starting Pump" and "Choosing and Rotating Infusion Site"
  - Afternoon Education: "Skin Concerns" and "Routine Reminders"
- Abbvie™ provided diary to track rates, extra doses, "on" and "off" times



Vyalev Aftercare Pearls

Steps to Starting Pump: https://www.vyalev.com/delivery-system

1. Practice a clean routine of washing your hands and the area planned for the infusion site with soap and water for at least 20 seconds. Proper hygiene techniques will reduce the risk of developing skin infections so be diligent
2. Make sure the prep area has been sanitized and all necessary supplies are set out before moving forward
3. Prepare the syringe by transferring all the medication from the vial into the syringe using the vial adapter. Attach the tip of the syringe to the tubing and place the full syringe inside the pump
4. The pump will provide you with a series of prompts. Follow them
5. Complete the priming of the tubing by filling the infusion tubing with medication and set this aside
6. Wipe the infusion site with an alcohol pad, starting in the middle and extending outward in a spiral
7. Wait at least 60 seconds for the skin to dry before placing the cannula or the adhesive will not stick as well
8. Pull the skin taut and place the cannula on the clean skin using the cannula deployer. After deployment, make sure that the cannula sits comfortably in the skin. If there is persisting discomfort or concerns that the cannula went in at an angle, remove and place a new cannula in a different location
9. Start the pump to deliver the medication

Choosing and Rotating the Infusion Site

1. Initially, sites should be a minimum of 2 inches from the belly button, on the abdomen or flank. The back of the arm and thighs have been used as viable alternatives. Non-irritating, adhesive medical tape or patches originally designed for use for insulin pumps can be utilized to help secure the tubing and prevent unwanted tension on the cannula
2. Keep cannula at least 2 inches away from skin that has scarred or hardened tissue, stretch marks, skin folds or creases where the body naturally bends (ie, while sitting or exercising), or where clothing might cause irritation (ie, near the beltline).
3. Cannula sites should be changed DAILY in the weeks following initiation. If there are no skin issues following an extended period of time, we can discuss the possibility of changing the cannula sites less frequently (every other day)
4. A pattern should be established to help keep track of previous infusion sites. Plan to rotate the new cannula site to be at least 2in from the previous day's site.
5. DO NOT place a cannula in a site where areas are bruised, tender, red or hard to touch

Navigating the Delivery System

1. Aseptic Technique

- Prior to preparing the infusion set for use, wash hands with soap and water
- Use a clean workspace when laying out the infusion set components
- Clean the vial top with an alcohol wipe prior to puncturing with vial adapter
- Clean the infusion site with soap and water prior to use. Then, before placing the cannula, wipe the skin with an alcohol wipe in an outward spiral formation to avoid contaminating the insertion site
- Avoid touching the tip of any disposable component (eg, syringe tip)
- Allow the area to air dry (approximately 1 min) before placing the cannula

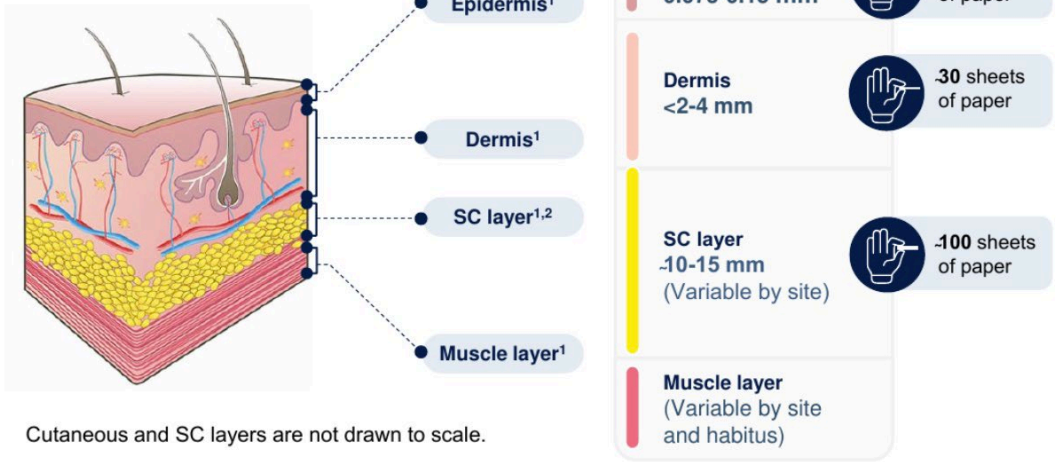
Navigating the Delivery System

2. Infusion Site Selection

- “The periumbilical area of the abdomen is the preferred infusion site for LDp/CDp due to its ample subcutaneous tissue”
- A pharmacokinetic study in patients with PD showed that administration of LDp/CDp via the arm, thigh, and flank resulted in nearly equivalent exposure to the abdomen
- Avoid area within 2 inches of the navel and areas of scaring, tenderness, bruising, inflammation or hard to the touch
- New infusion sites should be at least 1 inch from infusion sites used in previous 12 days

Skin and SC tissue thickness may vary according to:[1,2]

- Body habitus
- Body site
- Gender
- Age



Cutaneous and SC layers are not drawn to scale.

[a]Based on ultrasound measurement of skin and SC layer thickness in adults.
SC, subcutaneous.
1. Laurent A, et al. *Vaccine*. 2007;25(34):6423-6430. 2. Gibney MA, et al. *Curr Med Res Opin*. 2010;26(6):1519-1530.

Navigating the Delivery System

3. Cannula Selection, Management and Dislodgement

- Cannulas come in 2 sizes: 6mm and 9mm
- If infusion-site events develop frequently, adequate delivery into the subcutaneous space should be assessed and cannula length may need to be re-evaluated
- An infusion site should be used for a maximum of 3 days but it was noted by some HCPs participating in the phase 3 clinical trials that it was helpful to instruct patients to change the infusion site more frequently
- The infusion site and infusion set must be changed if the pump is disconnected for > 1 hour or blockage of the cannula or tubing may occur
- Change the cannula and the infusion site immediately if unusual discomfort or irritation at the infusion site occurs
- Non-irritating, adhesive medical tape or patches originally designed for use for insulin pumps can be utilized to help secure the tubing and prevent unwanted tension on the cannula

Navigating the Delivery System

4. Syringe Changes

- The solution vial contains 10 mL of LDp/CDp solution, with an LDp concentration of 240 mg/mL of solution, for a total of 2400 mg LDp and 120 mg CDp (equivalent to approximately 1700 mg LD and 89 mg CD
- Depending on the total daily dose, the patient may require more than one vial per 24 hours
- A continuous rate of 0.42mL/hr is the rough threshold of when a patient will need 2 vs. 1 medication vials daily
- Discuss the best timing for syringe changes, to avoid disruptions during nighttime sleep hours and to accommodate the patient's daily schedule and routine

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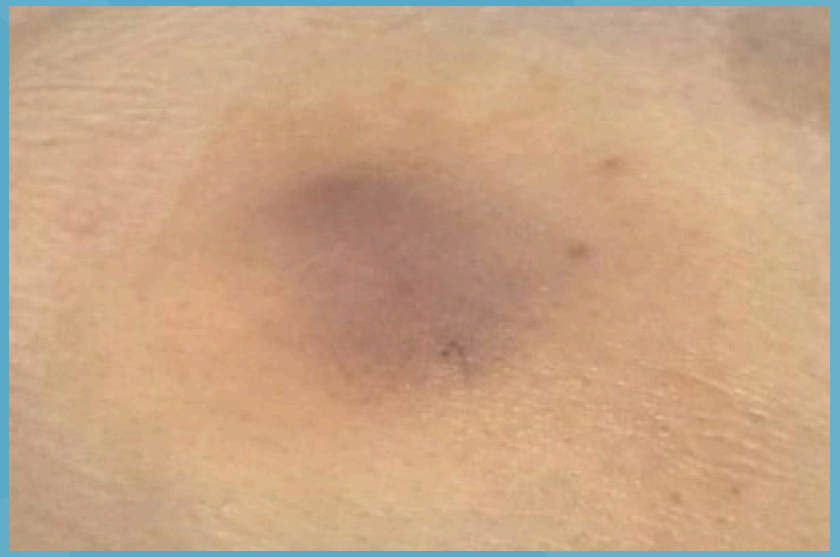
Adverse Skin Events: Bleeding, Bruising and Nodules

- Recurrent bleeding or bruising is possible. In some cases, it may indicate an inadequately secured cannula, leading to dislodgement and trauma
- If pain occurs with cannula insertion and persists, change it immediately. Cannula length may need to be reconsidered if a this is a recurring problem
- Nodules may also develop. A majority of skin nodules were nonserious, mild or moderate in severity, and resolved. It may take weeks for nodules to resolve. Local skin massage may be helpful
- Inform patients to select a new infusion site away from the nodule, as LDp/CDp infusion near the nodule can be painful and may impact drug absorption
- Non-irritating, adhesive medical tape or patches originally designed for use for insulin pumps can be utilized to help secure the tubing and prevent accidental tension and tugging on the cannula



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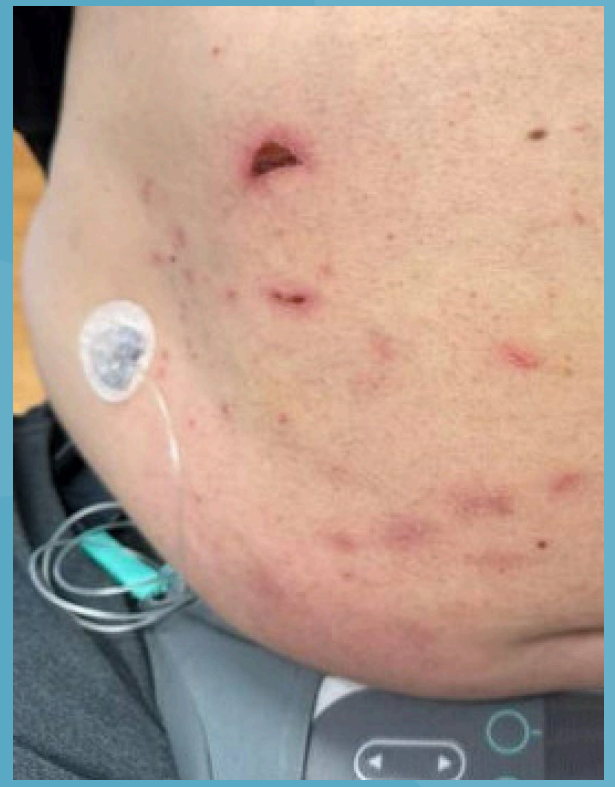
Adverse Skin Events: Drug Pooling

- Drug pooling may appear as swelling and erythema (with or without drug leakage) at the infusion site. This may be related to cannula removal, dislodgement, inappropriate cannula length, or drug volume
- Additional recommendations include:
  - Rotating the infusion site more frequently
  - Switching to a longer cannula to avoid intradermal delivery (and subsequent drug pooling)
  - Gently massaging the infusion site to remove any remaining drug product using aseptic practices
  - Minimizing use of extra foslevodopa doses*
- Anecdotally, leaving previously used cannula in place for a minimum of several hours after transitioning to new cannula/infusion site seems to help to optimize absorption of the medication



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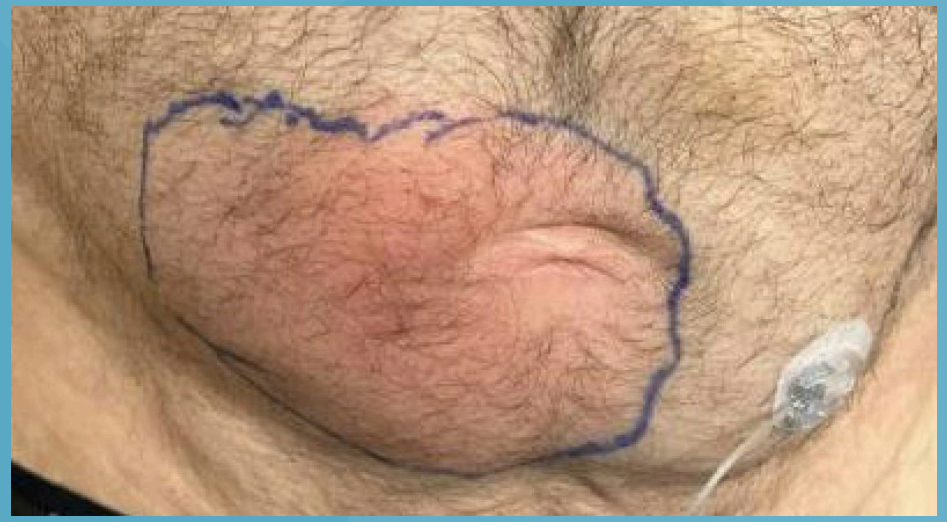
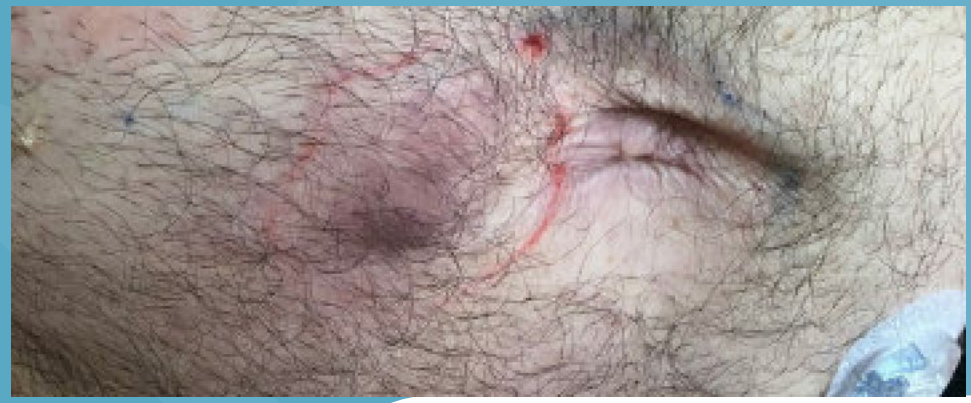
Adverse Skin Events: Infusion Site Reactions vs. Cellulitis

- Inflammatory skin reactions and cellulitis are difficult to distinguish between
- If an infusion site is becoming red, hard or painful, place a new cannula away from the area and rotate the infusion site immediately
- Clues to a diagnosis of cellulitis include spreading erythema, expansion of erythema even after relocation of the cannula and infusion set, and warmth or associated systemic symptoms such as fever
- If infusion-site cellulitis is suspected, the HCP should either initiate appropriate therapy or refer the patient for evaluation and treatment
- Penicillins and cephalosporins were the most frequently prescribed classes of antibiotics in the clinical trials





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Managing Systemic Events

- Hallucinations
  - Hallucinations are a common symptom in patients with PD and can be associated with disease progression, comorbid pathologies, and medication
  - In patients who experience hallucinations following LDp/CDp therapy, a reduction of LDp/CDp, including nighttime infusion rates, may help avoid the risks of new-onset or worsening hallucinations, psychosis, and nightmares
  - If hallucinations or psychosis are encountered, careful tapering or discontinuation of concomitant medications such as dopamine agonists should be considered
- Most of the “systemic” events were present during the optimization period, while clinicians determined the most appropriate dose of LDp/CDp, and these events mostly subsided in the maintenance phase of the studies

Helpful Reminders

- Patients should always have a backup supply of oral carbidopa/levodopa in the event they are not able to continue with infusion therapy
  - Delivery interruptions due to weather
  - Insurance Delays
  - Shipments not including all the necessary supplies
  - Patients leaving battery chargers at TSA
  - International travel exceeding 1 month without the appropriate planning in advance of the trip
- The pump must not be submerged in water and should be disconnected before showering or swimming
- The cannula is designed to be waterproof with or without the site connector but it is preferred to use the site connector when available
- Anytime pump interruption is >1 hour, a new infusion set (tubing + cannula) should be used and rotated to a different infusion site

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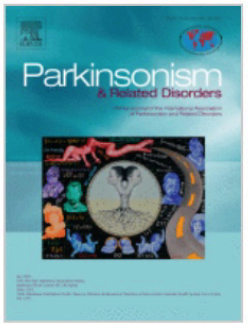

Predictors of discontinuation in foslevodopa/foscarbidopa therapy for Parkinson's disease

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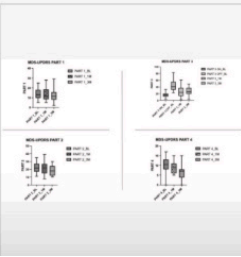
Article Info

Show Outline

Foslevodopa/foscarbidopa (LDp/CDp), a continuous subcutaneous infusion of a soluble levodopa/carbidopa prodrug, has demonstrated efficacy in reducing motor complications in advanced Parkinson's disease (PD) [1]. However, discontinuation is not uncommon in clinical practice, often attributed to perceived lack of benefit, device-related issues, or psychiatric and dermatological side effects [2]. To better understand factors influencing treatment continuation, we retrospectively analyzed patients who either continued or discontinued LDp/CDp therapy.

Twenty-six patients with advanced PD who initiated LDp/CDp between July 2023 and August 2024 were included. All met MDS 2015 diagnostic criteria and the Delphi 5-2-1 criteria for device-aided therapy [3]. Eighteen patients continued treatment for at least six months, while eight discontinued within that timeframe. Clinical characteristics and

Figures (1) Figure Viewer



Demographic and baseline clinical characteristics of patients initiating LDp/CDp therapy.

	ALL		continuation		discontinuation	
numbers of Pt	26		18		8	
numbers of Female Pt(n, %)	11	42.3	6	33.3	5	62.5
	mean	sd	mean	sd	mean	sd
age (years old)	60.3	10.2	58.3	9.4	64.6	11.1
BMI	21.2	3.3	21.7	3.4	20.1	3.1
Disease Duration (years)	14.2	9.1	14.1	10.2	14.4	6.6
HY off	4.0	0.7	4.2	0.6	3.6	0.9
HY on	2.4	0.6	2.3	0.5	2.6	0.7
MDS-UPDRS part I	13.8	5.5	13.1	5.6	15.5	5.3
MDS-UPDRS part II	21.8	6.4	21.8	6.4	21.9	6.9
MDS-UPDRS part III on	17.1	7.6	18.2	7.3	14.8	8.1
MDS-UPDRS part III off	44.6	14.9	48.6	14.9	35.9	11.4
ΔMDS-UPDRS oart III off-on	27.4	14.6	30.4	16.6	21.1	5.6
MDS-UPDRS part IV	10.3	3.6	11.4	2.9	8.5	2.4
LEDD (mg)	1255.7	428.1	1347.2	404.8	1057.6	463.5

Observations from Nishikawa et al.

- Initial rates of infusion were similar, as were plasma levodopa concentrations at ~10.5 nmol/mL. Within one month, patients in the discontinuation group increased their infusion rate, resulting in higher plasma concentrations (mean: 14.8nmol/mL) while the continuation groups rates held more stable
- Despite higher average doses and elevated plasma concentrations in the discontinuation group, there was no corresponding improvement in motor symptoms
- The delta between off- and on-state MDS-UPDRS Part III scores was lower in the discontinuation group (mean: 21.1) compared to the continuation group (mean: 30.4)
- All patients in the discontinuation group used LDp/CDp monotherapy with identical day and night doses. In contrast, half of the continuation group received reduced nighttime doses and adjunctive therapies
- Among the 8 patients who discontinued, six cited insufficient efficacy, two reported difficulty handling the device, two expressed aversion to the device, one developed cellulitis and some listed multiple reasons for discontinuing

Case 1

- 71yo Caucasian male with hx of idiopathic Parkinson's Disease x 21 years with an "on" state MDS-UPDRS Part III score around 30
- He is a physician who continues to work full time in a leadership position
- He maintains an active lifestyle, walking 2 miles most days but has had to stop activities like boxing due to imbalance. Falls are becoming more frequent, and he is relying more on a walker, occasionally needing a wheelchair
- He is becoming increasingly challenged by severe freezing episodes, fine motor difficulties, an internal "rumbling" sensation in the "off" state and increasing dyskinesia, particularly notable during speaking engagements. Mild levels of generalized anxiety and compulsiveness present at baseline.
- Notes history of skin sensitivity and allergic reaction to an adhesive used following back surgery several years ago
- He reports low level nausea which he attributes to the pramipexole he was started on years ago
- Sleep is "okay" though he finds he feels "glued" to the bed and must wake from sleep to take a sinemet at least 1hr prior to starting his day
- He estimates spending 3 hours of his day in the "off" state with 30min of dyskinesia daily
- His goal of therapy is for improved motor symptom control and being in good shape for his son's upcoming wedding

Case 1

- He maintains a very demanding medication regimen in order to keep symptoms as well controlled as possible

	5:30am	6am	7am	8:15am	10:30am	12:45pm	3pm	5:15pm	7:30pm	9:30pm
Carbidopa/levodopa 25/100 IR	2						¼			½
Carbidopa/levodopa 25/100 CR		1		1	1	1	1	1	1	
Entacapone 200		½		½	½	½	½	½	½	
Pramipexole ER 1.5mg			1							
Rasagiline 1mg			1							

- Also receiving botulinum toxin injections every 3 months for toe curling dystonia with ~2mo efficacy per round

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Case 1

- Foslevodopa/foscarbidopa therapy initiated on 7/16/25
- Initial Settings:
  - High Rate: 0.40mL/hr (10% higher on base rate)
  - Base Rate: 0.36mL/hr
  - Low Rate: 0.29mL/hr (20% lower than base rate)
  - Extra dose 0.15mL/hr
  - Cannula Size: 9mm
- Week 1 follow up report: notable increases in dyskinesia to the point he is stopping the pump for hours of his day, mobility is worse, continued "rumbling" sensation but some improvements to fluctuations, sleep quality and morning akinesia
- Adjustments made at week 1 visit:
  - High rate: 0.40→0.29mL/hr
  - Base rate: 0.36→0.26mL/hr
  - Low rate: 0.29→0.23mL/hr

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Case 1

- Week 2 previous rate adjustments did NOT improve dyskinesia, worsened “rumbling” and mobility challenges. It’s now clear he is not experiencing “peak dose dyskinesia” and begin titrating his dose in the correct direction
- Weeks 3-8
  - Reported benefits: “almost flawless days” with minimal “off” time, improvements to texting, typing, handwriting, resolution of nausea, reports to a “dramatic improvement to quality of life,” mentions that he can now go for extended periods without remembering he has Parkinson's disease. Reports therapy is a “game changer”
  - Reported side effects: adhesive reaction to the tape he was using to secure tubing, medication pooling, infusion site reactions, slight increases in baseline anxiety and irritability
  - Helpful adjustments: transitioning infusion sites from abdomen to thigh, leaving the previously used cannula in place for several hours following discontinuation of use at that site, finding an adhesive he was not sensitive to

Case 1

6 month Follow Up

- Settings
  - High Rate: 0.47mL/hr (+0.07)
  - Base: 0.45mL/hr (+0.11)
  - Low Rate: 0.42mL/hr (+0.13)
- Continues using thigh as preferred infusion site, 9mm cannulas with cannula changes q 24-48hrs
- Occasional infusion site reactions with one event concerning for cellulitis for which he took a course of oral antibiotics
- Fully transitioned from using extra doses of foslevodopa to oral levodopa IR to reduce skin events- using <100mg prn oral med daily
- Stopped rasagiline, has reduced pramipexole
- Marked improvements overall in lower extremity dystonia, freezing of gait and fall frequency
- Average step count increased from 7-8k to 11-12k daily and he's reconsidering a return to Rock Steady Boxing after a 4-5 year hiatus
- Wedding was "fabulous"

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Case 2

- 52yo Hispanic male with a five year history of Parkinson's Disease symptoms
- He previously worked as a painter but stopped painting in 2023 due to disabling PD symptoms
- PD course has been marked by bradykinesia, rigidity, dystonia, gait freezing, speech and swallowing difficulties, all of which worsen in the "off" state and respond to levodopa therapy. Falls are occurring most days, largely related to freezing of gait in the "off" state
- Non-motor symptoms include constipation, orthostatic light-headedness, drooling and sleep challenges with frequent disruptions due to medication doses and nocturia
- Denies cognitive changes but endorses a period of isolated hallucinations in the past
- MDS-UPDRS part III score of 36 in the "on" state, well over 50 in the off state
- Initial gait exam conducted while in process of wearing "off" revealing for marked difficulties with initiation, a mildly stooped posture, cane-assisted gait that is slow, slightly wide-based with shortened stride length and shuffling. He turns en bloc with both festination and freezing observed. Requires being caught on a pull test.

Case 2

- Current medication schedule

	7am	10am	1pm	4pm	7pm	10pm	1am	4am
Carbidopa/levodopa IR 25/100	3	3	3	3				
Levodopa-carbidopa-entacapone 150/37.5/200					1	1	1	1

Inhaled levodopa 84mg prn, on average TID

- Initial LDp/CDp Rates
  - High: 0.55mL/hr (10% higher)
  - Base: 0.50mL/hr
  - Low: 0.45mL/hr (10% lower)
  - Extra dose: 0.3mL, lockout time 1hr
  - Cannula size: 6mm

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Case 2

- Week 1 Follow Up
  - He has been on the base rate (0.50mL/hr) day and night after feeling that his low dose (0.45mL/hr) was too low. He is averaging use of 2-3 extra doses a day with noted benefits. He has yet to try his high rate (0.55mL/hr)
  - He's reports improvements to rigidity, mobility, dystonia, speech, swallowing and sleep
  - He reports he is only waking once overnight to use the bathroom and shares that he "has not slept this well in over three years"
  - Gait exam: arises from chair independently. Able to walk without cane. Mildly stooped posture, shortened stride length with slightly wide based gait. Low foot to ground clearance but no shuffling. Turns en block with freezing. Catches himself in 3 steps on pull test
- Week 1 Adjustments
  - High: 0.55mL/hr→ 0.57mL/hr
  - Base: 0.50mL/hr→ 0.53mL/hr
  - Low: 0.45mL/hr→ 0.48mL/hr
  - Extra dose: 0.3mL, lockout time 1hr
  - Cannula size: 6mm

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Case 2

- Week 5 Follow Up (2nd visit following initiation)
  - Continues to note improvements to his dystonia, mobility, speech, swallowing and sleep
  - Noting some mild fluctuations with “off” time presenting now with speech changes, drooling, “weakness” and increased anxiety
  - He has been using the base dose (0.53mL/hr) 24/7, reporting low rate was too low overnight. He is using extra doses, ~3x/day and reports improvements within 10-15 minutes
  - He reports being low on cannulas and thus elected to transition cannula site changes to q 3 days. With this, he developed reddened and indurated skin twice

- Week 5 Adjustments
  - High: 0.57mL/hr – kept the same
  - Base: 0.53mL/hr →0.55mL/hr
  - Low: 0.48mL/hr – kept the same
  - Extra dose: 0.3mL, lockout time 1hr
  - Cannula size: 6mm→9mm

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Case 2

- Two Month Follow Up via Telehealth (3rd visit following initiation)
  - Reports using the base rate of 0.55mL/hr around the clock. He reports that lowering the dose at night resulted in weakness and jaw tightness
  - Fluctuations are improved, using extra dose once daily on average
  - Transition to 9mm cannula resulted in reduced nodules and redness. He is changing the cannula site every two days on average
- Eight Month Follow Up Visit
  - Symptom control remains stable on 0.55mL/hr rate
  - Use of extra doses down to 1-2x/week
  - Recent falls concerning for orthostatic hypotension which were being targeted with behavioral modifications
  - Skin issues remain infrequent since the transition to 9mm cannulas and not going beyond 48hrs between changes

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Case Take Aways

- Know your patients “on” and “off” states, as much as possible, prior to initiating therapy
- Some starts will be bumpier than others – prepare both yourself and the patient for this possibility
- Troubleshooting is likely to be necessary and will need to be customized to each patient
- Having the option for frequent touch points in the first 1-2 months seems to be helpful during the transition to pump therapy

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THANK YOU

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