Efficacy and safety of subcutaneous L-dopa/carbidopa (ND0612) infusion in fluctuating PD patients

(24-hour vs. 14-hour continuous delivery)

Alberto Espay, C. Warren Olanow, Fabrizio Stocchi, Werner Poewe, Aaron Ellenbogen, Ruth Djaldetti, Tami Rachmilewitz-Minei, Yael Cohen, Sheila Oren, Karl Kieburtz

Alberto J. Espay, MD, MSc, FAAN

Professor of Neurology

Director and Endowed Chair, James J. and Joan A. Gardner Family Center for Parkinson's Disease and Movement Disorders

University of Cincinnati Academic Health Center

Author disclosures

- **Research**: NIH, Great Lakes Neurotechnologies, and the Michael J Fox Foundation
- **Consultant/scientific advisory board**: NeuroDerm, Abbvie, Chelsea Therapeutics, TEVA, Impax, Merz, Pfizer, Acadia, Acorda, Cynapsus, Solstice Neurosciences, Eli Lilly, Lundbeck, and USWorldMeds
- **Honoraria**: Abbvie, UCB, USWorldMeds, Lundbeck, the American Academy of Neurology, and the Movement Disorders Society
- **Royalties**: Lippincott Williams & Wilkins, Cambridge University Press, and Springer

Disclaimer

This presentation is intended for educational and informational purposes only.

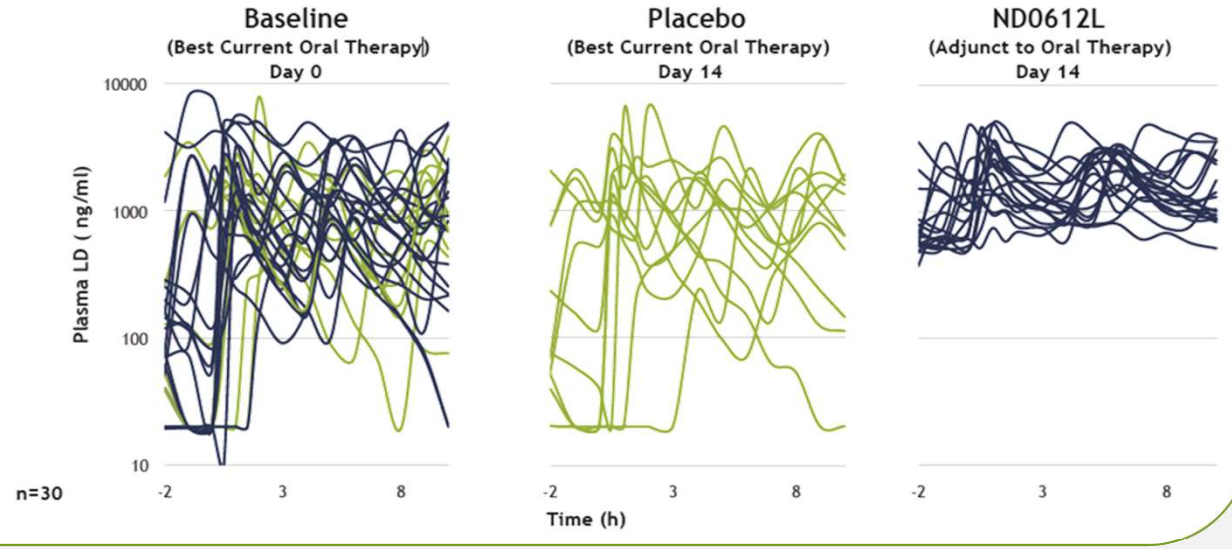
*It contains information on an **unapproved investigational** treatment.*

The clinical research described in this presentation was sponsored by NeuroDerm, a wholly owned subsidiary of Mitsubishi Tanabe Pharma Corp, Inc.

Background

- ND0612 is a drug-device combination that continuously delivers liquid levodopa/carbidopa (60/7.5 mg/mL) by subcutaneous infusion through a non-surgical mini-pump system.
- Early Phase 2 studies vs. oral levodopa demonstrated:[1]
  - Stable levodopa plasma levels with reduced fluctuations
  - Reduced OFF time

Levodopa pharmacokinetics

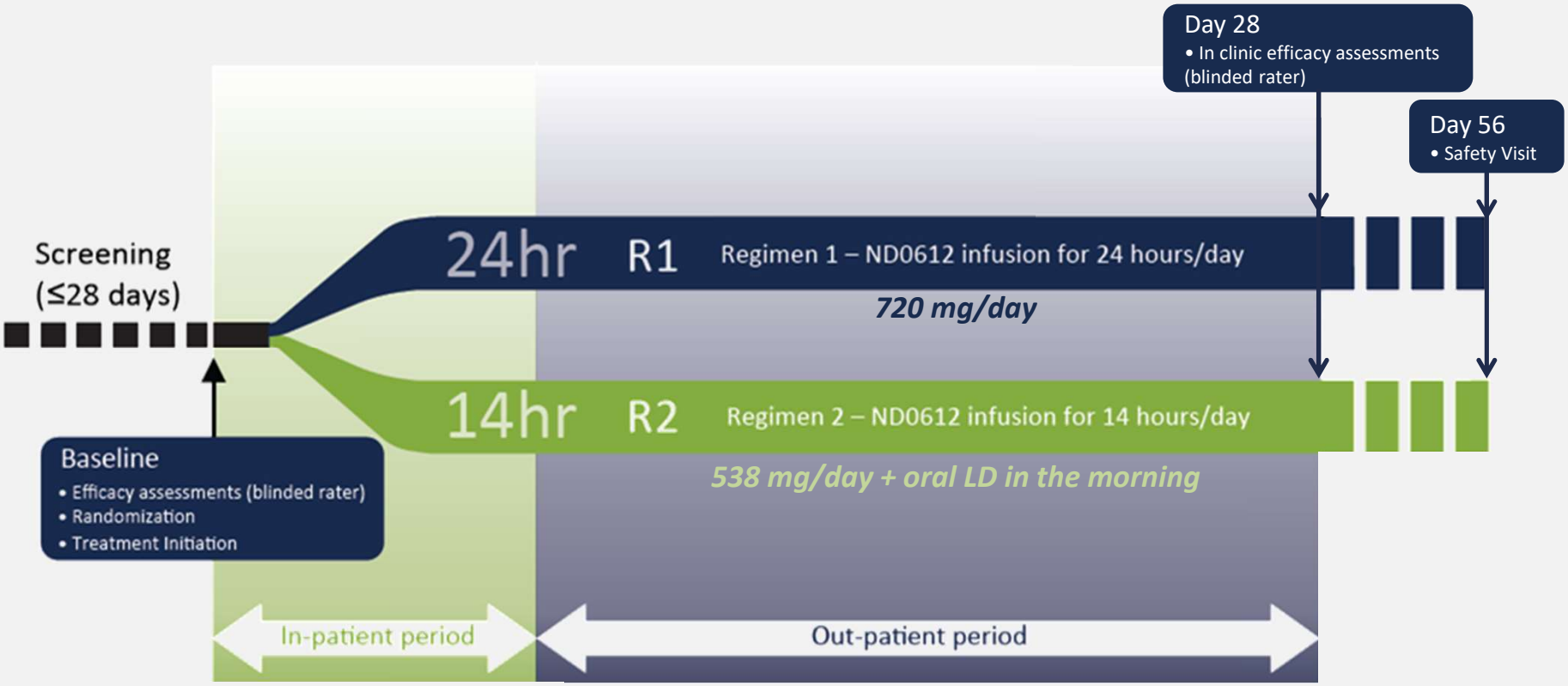


1. Giladi et al. Poster 1386 at MDS 2017. Available for download at Neuroderm.com

Aim

- It is currently unknown whether providing ‘round the clock’ levodopa delivery provides additional benefits to patients versus a ‘waking day’ regimen
- This Phase 2a clinical study evaluated whether continuous **24-hour** SQ delivery of ND0612 offers differential benefits versus waking-day **14-hour** delivery

An open-label, rater-blinded, parallel-group, randomized study



N=38 PD patients

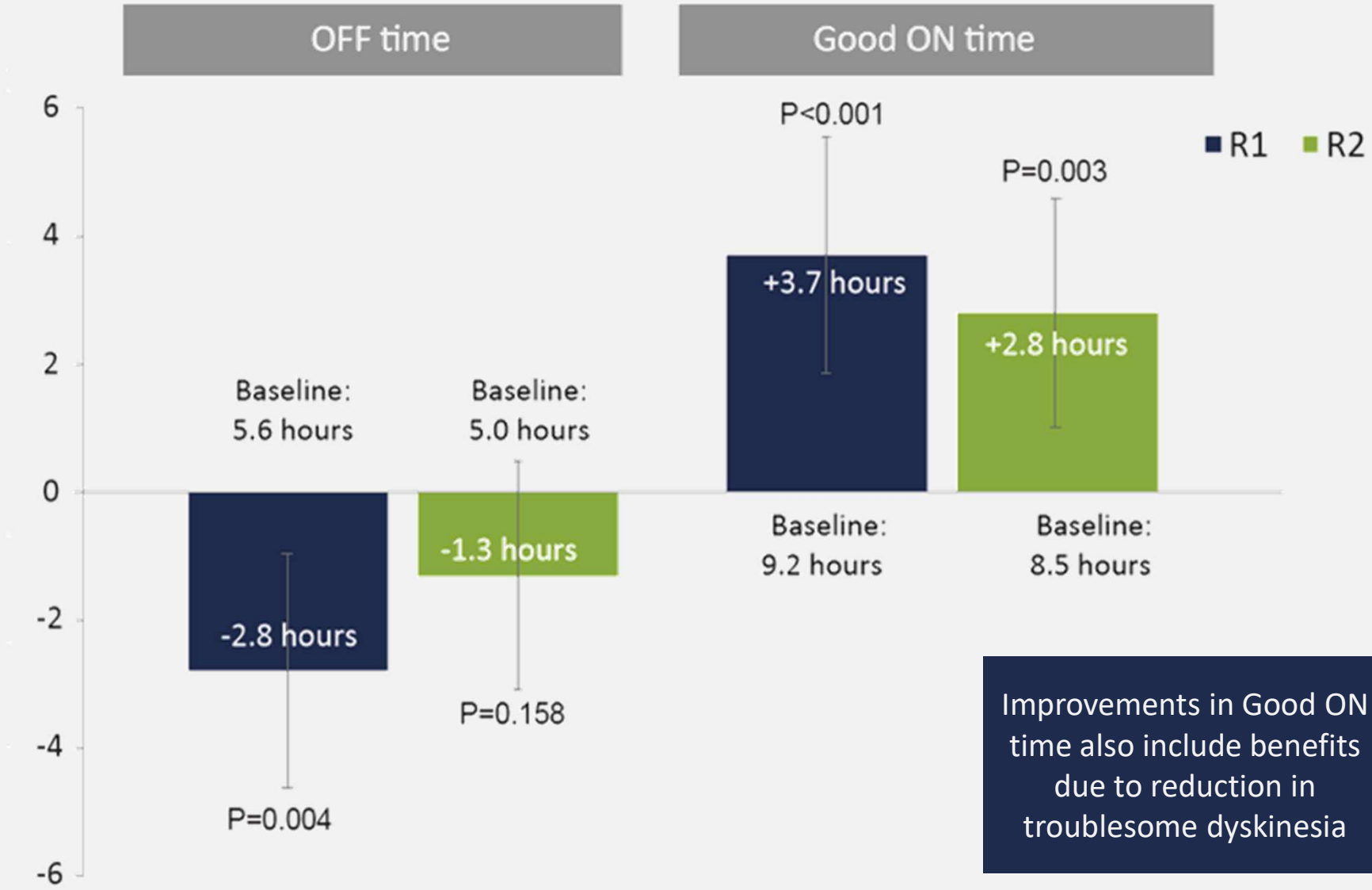
- H&Y ≤3 (ON)
- ≥4 levodopa doses/day
- ≥ 2.5h/day OFF time
- Predictable early morning OFF

Baseline characteristics

	R1 (24 hours) (N=19)	R2 (14 hours) (N=19)	Overall (N=38)
Age (years)	63.0 (10.07)	64.0 (8.47)	63.5 (9.19)
Sex (n, % men)	12 (63.2)	14 (73.7)	26 (68.4)
Years since PD diagnosis	10.7 (5.5)	12.2 (5.0)	11.5 (5.2)
Years with motor fluctuations	5.7 (1.0)	5.5 (4.8)	5.6 (5.9)
Years with dyskinesia	3.1 (2.7)	4.2 (3.4)	3.7 (3.1)
OFF time (hours/day)	5.6 (2.1)	5.0 (2.4)	5.3 (2.2)
Moderate or severe dyskinesia (hours/day)	1.2 (2.8)	2.5 (3.7)	1.9 (3.3)
UPDRS Part III (motor) score	37.4 (14.5)	37.3 (13.3)	37.3 (13.7)
Levodopa dose (mg)	1135.8 (818.0)	1054.1 (567.3)	1094.9 (695.5)
Frequency levodopa dosing	6.8 (3.2)	6.9 (2.2)	6.8 (2.7)

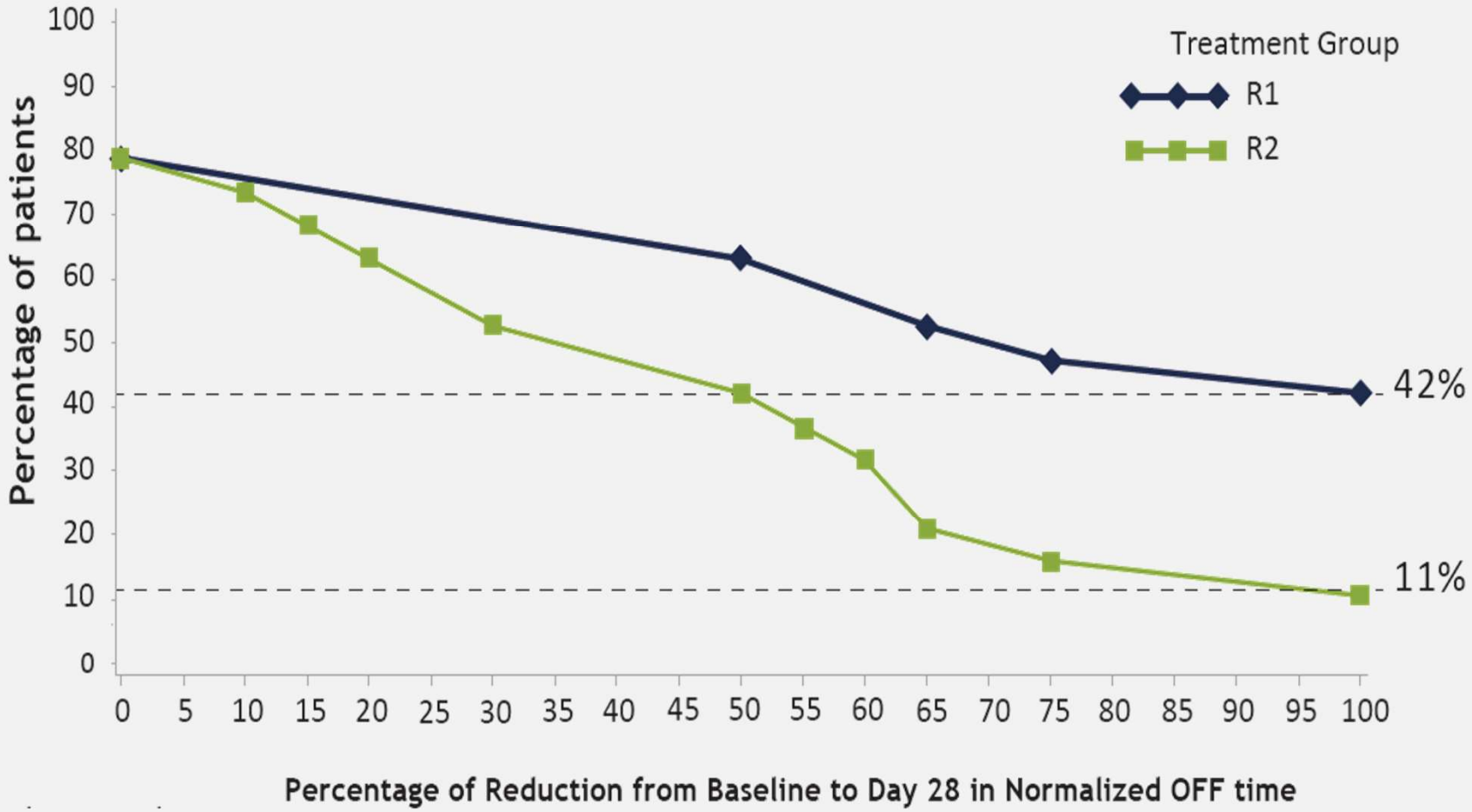
Data are mean (SD) unless otherwise specified

R1 significantly reduced OFF time (primary endpoint) and increased good ON time



Good ON time = ON time with no or mild dyskinesia

42% of R1 patients achieved complete resolution of OFF time* (*post-hoc* analysis)

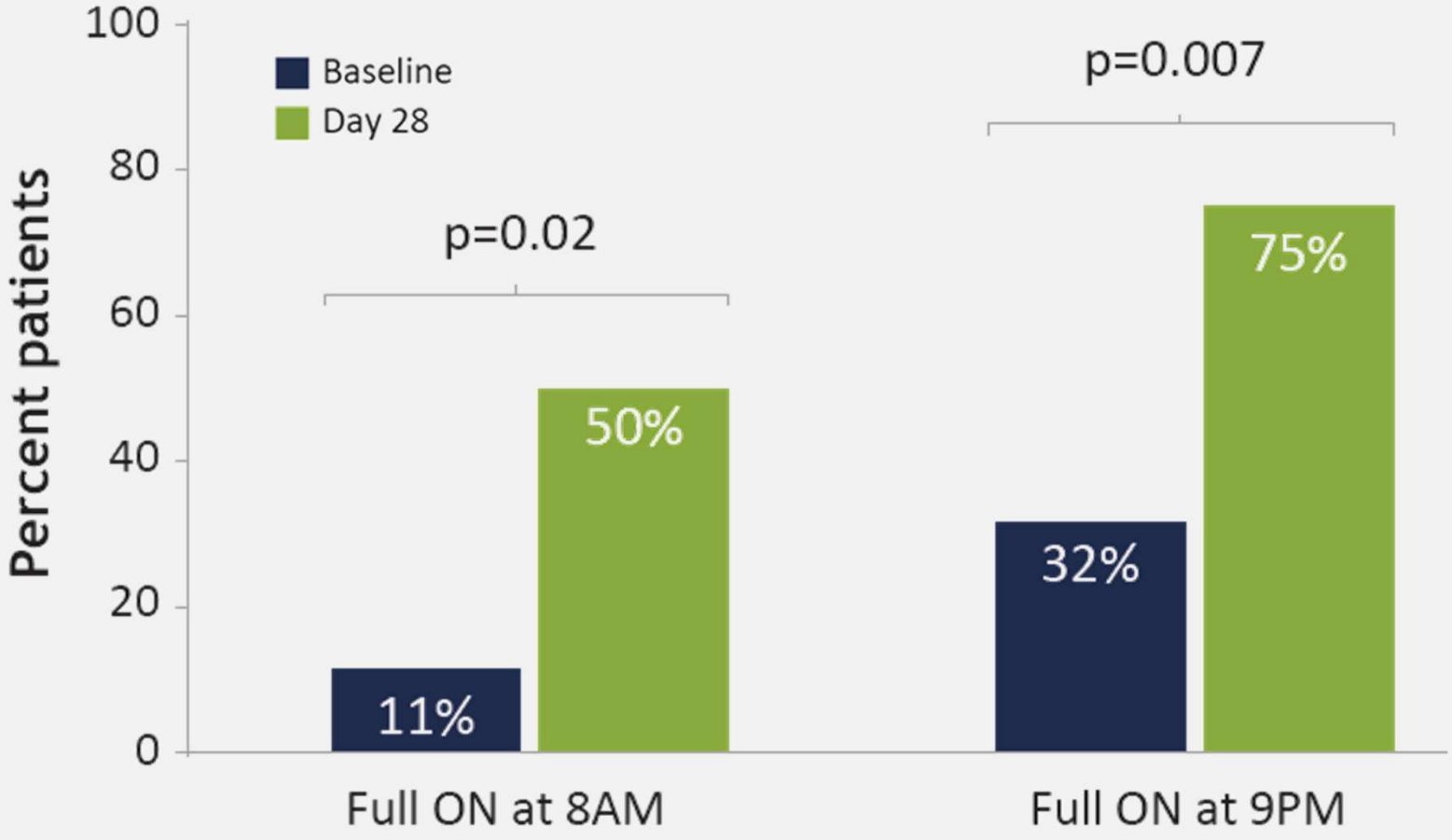


*during 8 hours observation

R1 significantly reduced early morning OFF

(Key secondary endpoint)

Achievement of ON at 8am and 9am with R1



Adverse events

Adverse event	R1 (24 hours) (N=19)	R2 (14 hours) (N=19)	Overall (N=38)
Any AE - n (%)	15 (79%)	14 (74%)	29 (76%)
Serious AE - n (%)	2 (11%)	2 (11%)	4 (11%)
Discontinued due to an AE	1 (5%)	1 (5%)	2 (5%)
Skin tolerability			
Infusion site nodules	11 (58%)	7 (37%)	16 (42%)
Infusion site bruising	4 (21%)	2 (16%)	7 (18%)
Infusion site erythema	5 (26%)	2 (11%)	6 (16%)
Infusion site hemorrhage	2 (11%)	3 (16%)	5 (13%)

- ND0612 infusion pump systems were reliable with only few minor, correctable malfunctions reported

Conclusions

- 24 hour infusion of ND0612H (R1) significantly reduced daily OFF time and morning akinesia and increased good ON time
- No safety concerns were identified. Infusion site adverse events were common, yet generally well tolerated
- ND0612 may provide a novel non-surgical option for continuous 24-hour levodopa/carbidopa delivery in patients with PD and motor fluctuations