

## Supplementary Online Content

Lees AJ, Ferreira J, Rascol O, et al; BIPARK-2 Study Investigators. Opicapone as adjunct to levodopa therapy in patients with Parkinson disease and motor fluctuations: a randomized clinical trial. *JAMA Neurol*. Published online December 27, 2016. doi:10.1001/jamaneurol.2016.4703

**eTable 1.** Independent Ethics Committees/Institutional Review Boards Consulted

**eTable 2.** Change From Baseline to End Point of the Different On-Time States

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**eFigure.** Change From Baseline to the End of Double-Blind Phase in Absolute Off-Time

This supplementary material has been provided by the authors to give readers additional information about their work.

**eTable 1. Independent Ethics Committees/Institutional Review Boards Consulted****Argentina***Central Ethics Committee*

<b>Centre No</b>	<b>Name and address of IEC/IRB</b>	<b>Chairman of IEC/IRB</b>
1002	Comite de Etica en Investigacion Isntituto de Investigaciones Clinicas Av Colon 3364 Mar del Plata	Jesus Vazquez
1005	Comite de Evaluacion Etica y Cientifica del Departamento de Docencia Av Belgrano 2975 Ciudad Autonoma de Buenos Aires C1209AAB	Luis Maria Zieher
1006	Comité Independiente de Ética para Ensayos en Farmacología Clínica J. E. Uriburu 774 Piso 1 CABA Ciudad Autonoma Buenos Aires C1027AAP	Luis Maria Zieher
1008	Comite de Etica en Investigacion del Instituto Medico Especializado Hidalgo 568 Ciudad Autonoma de Buenos Aires C1405BCH	Maria Victoria Bertolino
1009	Comité Independiente de Ética para Ensayos en Farmacología Clínica J. E. Uriburu 774, 1st Floor Ciudad Autónoma de Bs. As. C1027AAP	Luis Maria Zieher

## Argentina

### *Local Ethics Committees*

<b>Centre No</b>	<b>Name and address of IEC/IRB</b>	<b>Chairman of IEC/IRB</b>
1004	Comite Independiente de Etica e Investigacion Biomedica Uruguay 840 Ciudad Autonoma de Buenos Aire C1015ABR	Mariana Bendersky
1005	Comite de Evaluacion Etica y Cientifica del Departamento de Docencia Av Belgrano 2975 Cidad Autonoma de Buenos Aires C1209AAB	Alicia Miranda
1006	Comite de Docencia e Investigacion del Instituto Av Entre Rios 2144 Ciudad autónoma de Buenos Aires, 1133	Aldo Alberto Calzinari
1007	Comite de Bioetica de la Fundacion Alfredo Thomson Av Diaz Velez 3992 Ciudad Autonoma de Buenos Aire C1200AAT	Fernando Adolfo Alvarez
1008	Comite de Revision Institucional Hidalgo 568 Ciudad Autonoma de Buenos Aires C1405BCH	Amado Jose Bechara

## Australia

### *Central Ethics Committee*

<b>Centre No</b>	<b>Name and address of IEC/IRB</b>	<b>Chairman of IEC/IRB</b>
1102; 1103; 1105; 1108	Austin Health Human Research Ethics Committee Research Ethics Unit, Room 8322 Level 8, Harold Stokes Building 145 Studley Road Victoria, 3084	David Taylor
1106; 1109	St Vincents Hospital Research Governance Office St Vincents Hospital 390 Victoria Street Darlinghurst New South Wales, 2010	Prof Jo-Anne Brien

### *Local Ethics Committees*

<b>Centre No</b>	<b>Name and address of IEC/IRB</b>	<b>Chairman of IEC/IRB</b>
1101	Bellberry Human Research Ethics Committee 34 Brougham Street East Gosford New South Wales, 2250	Michael James
1102	Melbourne Health Research Governance The Royal Melbourne Hospital - city campus 300 Grattan Street Parkville, Victoria, 3050	Prof Peter Colman
1103	Austin Health Research Governance 145 Studley Road Heidelberg Victoria, 3084	David Taylor
1104	Royal Adelaide Hospital Research Ethics Committee Research Ethics Committee Level 3, Hanson Institute, North Terrace Adelaide, South Australia, 5000	A Thorton

## Australia

### *Local Ethics Committee - Continued*

<b>Centre No</b>	<b>Name and address of IEC/IRB</b>	<b>Chairman of IEC/IRB</b>
1105	St Vincent's Melbourne Research Governance Unit Research Governance Unit PO Box 2900 FITZROY, Victoria, 3065	Ms Kelly Hoffman
1106	Sydney West Area Health Research Governance Research Office, Level 6, de Lacy Building 390 Victoria Street Darlinghurst New South Wales, 2010	Julie Charlton
1108	Southern Health Research Governance Southern Health 246 Clayton Rd CLAYTON Victoria, 3168	Dr Sally Middleton
1109	St Vincents Hospital Human Research Ethics Committee Level 6 de Lacey Building 390 Victoria Street Darlinghurst New South Wales, 2010	Ms Julie Charlton

## Belgium

### *Central Ethics Committee*

<b>Centre No</b>	<b>Name and address of IEC/IRB</b>	<b>Chairman of IEC/IRB</b>
1202- 1206	Ethisch Comité UZA (CEC) Wilrijkstraat 10 Edegem, 2650	Prof. Dr Patrick Cras

### *Local Ethics Committees*

<b>Centre No</b>	<b>Name and address of IEC/IRB</b>	<b>Chairman of IEC/IRB</b>
1202	Med Ethische Commissie H-Hartziekenhuis Roeselare-Menen (LEC) Wilgenstraat 2 Roeselare, 8800	Dr L. Marcelis
1203	Ethische Toetsingscommissie Jessa Ziekenhuis Stadsomvaart 11 Hasselt, 3500	Dr Koen Magerman
1204	Commission d'Ethique Biomédicale Hospitalo- Facultaire de l'UCL Avenue Hippocrate 55.14, Tour Harvey - niveau 0 Bruxelles, 1200	Prof. Dr Maloteaux
1205	Ethisch Comité UZA (LEC) Wilrijkstraat 10 Edegem, 2650	Prof. Dr Patrick Cras
1206	Lokale Commissie voor Ethiek Sint- Andriesziekenhuis (LEC) Krommewalstraat 9-11 Tielt, 8700	Dr Jozef Verhamme

## Chile

### *Central Ethics Committee*

<b>Centre No</b>	<b>Name and address of IEC/IRB</b>	<b>Chairman of IEC/IRB</b>
1301	Comite de Etica de la Investigacion SSM Norte Calle San José 1053 Independencia, Santiago	Dr Carlos Navarro
1302	Comite Etico-Cientifico SS Viña del Mar-Quillota Calle Limache 1307 Esquina Peñablanca 2º, Viña del Mar	Paola Fossa Corvalan
1303	Comite Etico Cientifico SSM Sur-Oriente Av. Concha y Toro 3459 Puente Alto, Santiago	Dr Patricio Michaud
1304	Comite Etico-Cientifico SSM Central Santa Rosa 1234, Santiago	Dr Emiliano Soto Romo
1305	Comite Etico-Científico SSM Oriente Av. Salvador 364 Providencia, Santiago	Dr Andrés Stuardo
1306	Comite Etico- Cientifico SSM Sur Santa Rosa 3453, Parad.5 San Miguel, Santiago	Dr Verónica Rivera
1307	Comite Etico de Investigacion SS Valdivia Maipu 550, Piso 3, Of.307 Valdivia	Dr Ginette Grandjean Obando
1308	Comite Etico-Científico SSM Oriente Av. Salvador 364 Providencia, Santiago	Dr Andrés Stuardo

### *Local Ethics Committees*

<b>Centre No</b>	<b>Name and address of IEC/IRB</b>	<b>Chairman of IEC/IRB</b>
1304	Comité de Ética en Inv, Esc. Med, PUC Marcoleta 391, Piso 1, Santiago	Dr Eduardo Guarda

## Czech Republic

### *Central Ethics Committee*

<b>Centre No</b>	<b>Name and address of IEC/IRB</b>	<b>Chairman of IEC/IRB</b>
1401; 1402; 1404; 1406	Eticka komise Vseobecne fakultni nemocnice v Praze Na Bojisti 1 Prague, 128 08	Josef Sedivy, MD, PhD

### *Local Ethics Committees*

<b>Centre No</b>	<b>Name and address of IEC/IRB</b>	<b>Chairman of IEC/IRB</b>
1401	Lokalni eticka komise Mestske nemocnice Ostrava Nemocnicni 20 Ostrava, 728 80	Jan Nieslanik, MD
1402	Eticka komise Centrum neurologicke pece s.r.o. Jiraskova 1389 Rychnov nad Kneznou, 516 01	Radomir Strupl, MD
1404	Eticka komise Vseobecne fakultni nemocnice v Praze Na Bojisti 1 Prague, 128 08	Josef Sedivy, MD, PhD
1406	Eticka komise Vseobecne fakultni nemocnice v Praze Na Bojisti 1 Prague, 128 08	Josef Sedivy, MD, PhD



**Estonia***Central Ethics Committee*

<b>Centre No</b>	<b>Name and address of IEC/IRB</b>	<b>Chairman of IEC/IRB</b>
1501 - 1504	Tallinn Medical Research Ethics Committee Hiiu 42 Tallinn 11619	J. Põlluste

## India

### *Local Ethics Committees*

<b>Centre No</b>	<b>Name and address of IEC/IRB</b>	<b>Chairman of IEC/IRB</b>
1702	Vidyasagar Institute of Mental Health & Neurosciences 1, Institutional Area Nehru Nagar New Delhi, 110065	Mr Ravindra Bana
1703	Institutional Ethics Committee Sri Aurobindo Seva Kendra, 1H, Gariahat Road South Kolkata West Bengal	Mrs Manjula Bose
1704	Ethics Committee of Manipal Hospital & Manipal Heart Foundation Airport Road Bangalore, 560017	Dr Justice SR Bannurmath
1705	Mallikatta Ethical Committee Mamatha Residency, No. 305, 2-15-1265/29, Bejai, Anegundi, 1st Cross Road Mangalore Karnataka, 575004	Professor N Krishnamoorthy
1706	Lalitha Super Specialities Hospital Ethics Committee Lalitha Super Specialities Hospital (P) Ltd, Heart & Brain Centre, Kothapet, Guntur Andhra Pradesh, 522001	Dr C Nageswararao
1707	Ethics Committee Sahyadri Hospitals, 30 C, Erandwane Karve Road Pune Maharashtra, 411004	Dr BG Sahastrabudhe

**India***Local Ethics Committees - Continued*

<b>Centre No</b>	<b>Name and address of IEC/IRB</b>	<b>Chairman of IEC/IRB</b>
1708	Global Independent Ethics Committee 1-C, Bhuyandev Society Near Bhuyandev Croos road, Ghatlodia Ahmedabad Gujarat, 380061	Mr Shashikant Sharma
1709	Kovai Medical Center and Hospital Ethics Committee Kovai Medical Center and Hospital Limited Post Box No. 3209, Avanashi Road, Coimbatore Tamilnadu, 641 014	Dr Muthuswamy PR

## Israel

### *Local Ethics Committees*

<b>Centre No</b>	<b>Name and address of IEC/IRB</b>	<b>Chairman of IEC/IRB</b>
1601	Rabin Medical Center Helsinki Committee 39 Jabutinsky st. Petach Tikva 49100	Prof Meir Lahav
1602	The Chaim sheba Medical Cnter Helsinki Committee Tel Hashomer Ramat Gan 52621	Prof Dror Haretz
1605	Rambam Medical Center Helsinki Committee 12 Aliya st. Bat Galim Haifa	Prof Moshe Barnet
1606	Tel Aviv Sourasky Ethics committee 6 Weizman st Tel Aviv, 64239	Prof Marsel Topilasky

## Russia

### *Central Ethics Committee*

<b>Centre No</b>	<b>Name and address of IEC/IRB</b>	<b>Chairman of IEC/IRB</b>
1801 – 1804; 1807	Ethical Council at the Ministry of Health and Social Development of RF 3, Rakhmanovskiy lane Moscow, 127994	Ramenskaya G.V.

### *Local Ethics Committees*

<b>Centre No</b>	<b>Name and address of IEC/IRB</b>	<b>Chairman of IEC/IRB</b>
1801	EC of Siberian State Medical University of MoH and SD of RF 2, Moskovsky trakt Tomsk, 634050	Bukreeva E.B.
1802	Ethics and Evidence Committee of "Kemerovo Regional Clinical Hospital" 22, Oktyabrsky prospect Kemerovo, 650066	Khimchenko L.A.
1803	Ethics Committee of "Territorial Clinical Hospital" 1, Lyapidevskogo str Barnaul, 656024	Berestov S.A.
1804	EC of SEI HPE KrasSMU named after Prof. V.F. Voyno-Yasenetsky 1, Partizana Zheleznyaka str Krasnoyarsk, 660022	Demko I.V.
1807	Ethics Committee at the NSMU 52, Krasny prospect Novosibirsk, 630091	Poteryaeva E.L.

## South Africa

### *Central Ethics Committee*

<b>Centre No</b>	<b>Name and address of IEC/IRB</b>	<b>Chairman of IEC/IRB</b>
1902 – 1904; 1906 – 1908; 1910 - 1911	Pharma-Ethics (Pty)Ltd 123 Amcor Road Lyttelton Manor Pretoria Gauteng, 0157	Dr CSJ Duvenage

### *Local Ethics Committees*

<b>Centre No</b>	<b>Name and address of IEC/IRB</b>	<b>Chairman of IEC/IRB</b>
1901	University of Stellenbosch Ethics Tygerberg Cape Town Western Cape 7505	Dr JAM de Roubaix
1905	University of Pretoria Ethics 31 Bophela Road, HW Snyman South Building Level 2-Rooms 2.33, 2.34 & 2.35 Pretoria Gauteng 0001	Dr CSJ Duvenage

## South Korea

### *Local Ethics Committees*

<b>Centre No</b>	<b>Name and address of IEC/IRB</b>	<b>Chairman of IEC/IRB</b>
2001	Samsung Medical Center IRB 50, Irwon-Dong, Gangnam-Gu Seoul, 135-710	Lee, Suk-Koo
2002	Asan Medical Center IRB 388-1 Pungnap-2 dong, Songpa-gu Seoul, 138-736	Jong Woo Chung
2003	Dong-A University Medical Center IRB Dongdaesindong 3ga-1, Seo-gu Busan, 602-715	Lee, Soo-il
2004	Severance Hospital IRB 250 Seongsan-no, Seodaemun-gu, Seoul, 120-752	Seung Min Kim

**UK**

*Central Ethics Committee*

<b>Centre No</b>	<b>Name and address of IEC/IRB</b>	<b>Chairman of IEC/IRB</b>
2101 - 2102; 2104 - 2105	Southampton & South West Hampshire REC University of Reading London Road Reading RG1 5AQ	Dr Iain MacIntosh



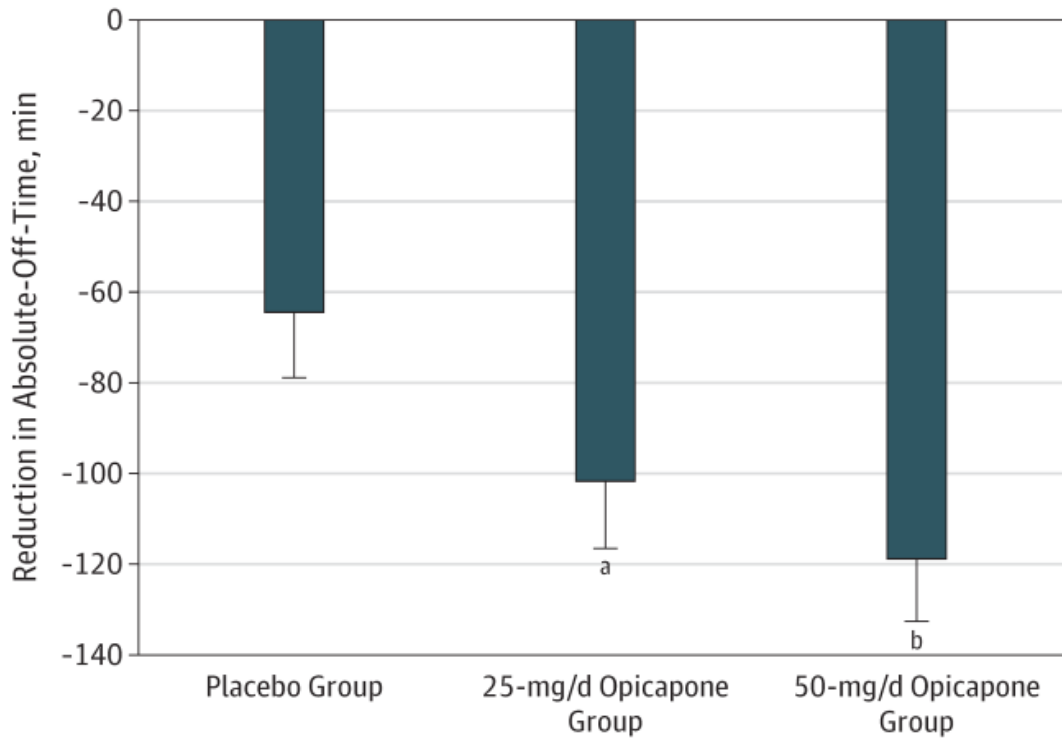
**eTable 2.** Change From Baseline to End Point of the Different On-Time States

<b>Parameter</b>	<b>Placebo (N=135)</b>	<b>OPC 25mg (N=125)</b>	<b>OPC 50mg (N=147)</b>
<b>ON time without dyskinesia or with non-troublesome dyskinesia (minutes)</b>			
LS Mean change from baseline	48.1	84.1	85.6
LS mean difference vs. placebo (95%CI)		36.0 (-5.6, 77.5)	37.4 (-2.4, 77.2)
<i>P</i> value vs. placebo		.090	.065
<b>ON time with troublesome dyskinesia (minutes)</b>			
LS Mean change from baseline	11.2	19.4	25.6
LS mean difference vs. placebo (95%CI)		8.2 (-15.1, 31.5)	14.4 (-8.0, 36.8)
<i>P</i> value vs. placebo		.490	.206

**eTable 3.** Change From Double-Blind and Open-Label Baseline to End of Open-Label Follow-up Period in Scale-Based Secondary Efficacy Outcomes

<b>Parameter</b>	<b>Vs. Double-Blind Baseline</b>	<b>Vs. Open-Label Baseline</b>
UPDRS Total scores; Mean ± SD baseline score Mean ± SD change from baseline	N=302 31.2 ± 17.8 -3.3 ± 10.4	N=302 27.9 ± 17.1 0.1 ± 8.6
UPDRS Part II (ADL) scores (OFF); Mean ± SD baseline score Mean ± SD change from baseline	N=333 17.4 ± 7.0 -2.8 ± 5.5	N=336 14.7 ± 7.0 0.0 ± 4.4
UPDRS Part II (ADL) scores (ON); Mean ± SD baseline score Mean ± SD change from baseline	N=339 7.4 ± 5.7 -0.8 ± 3.8	N=339 6.3 ± 5.0 0.4 ± 3.0
UPDRS Part III (motor) scores (ON); Mean ± SD baseline score Mean ± SD change from baseline	N=339 22.2 ± 12.4 -2.4 ± 7.7	N=339 19.9 ± 12.4 0.0 ± 6.3
PDSS scores; Mean ± SD baseline score Mean ± SD change from baseline	N=313 101.69 ± 25.3 -0.51 ± 25.5	N=322 104.64 ± 25.6 -3.51 ± 23.3
PDQ-39 scores; Mean ± SD baseline score Mean ± SD change from baseline	N=325 30.6 ± 15.1 -2.2 ± 12.7	N=327 26.0 ± 14.6 2.4 ± 10.5
NMSS scores; Mean ± SD baseline score Mean ± SE change from baseline	N=325 37.9 ± 28.7 -4.2 ± 23.6	N=329 31.5 ± 26.7 1.9 ± 20.2

**eFigure.** Change From Baseline to the End of Double-Blind Phase in Absolute Off-Time



The analysis of covariance model included treatment group and region as fixed effects and baseline off-time as a covariate. Error bars indicate SD.

<sup>a</sup> $P = .11$ , Dunnett  $\alpha$  level adjustment.

<sup>b</sup> $P = .008$ , Dunnett  $\alpha$  level adjustment.