2.7.1 生物薬剤学試験及び関連する分析法

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略語及び定義一覧

略語又は用語	省略していない表現又は説明（英語）	省略していない表現又は説明（日本語）
3-OMD	3-O-methyldopa	3-O-メチルドパ
CD	carbidopa	カルビドパ
CDP4'（CD′, CD4′，CDP）	foscarbidopa (carbidopa-4′-monophosphate)	ホスカルビドパ（カルビドパ-4'-一リン酸）
CSCI	continuous subcutaneous infusion	持続皮下注入
K_2EDTA	Ethylenediaminetetra acetic acid dipotassium	エチレンジアミン四酢酸二カリウム
LCIG	levodopa/carbidopa intestinal gel	レボドパ・カルビドパ経腸用液
LC-MS/MS	high performance liquid chromatography tandem mass spectrometory	高速液体クロマトグラフィータンデム質量分析
LD	levodopa	レボドパ
LDP4'（LD′, LD4′，LDP）	foslevodopa (levodopa-4′-monophosphate)	ホスレボドパ（レボドパ-4'-一リン酸）
PD	Parkinson's disease	パーキンソン病

2.7.1.1 背景及び概観

ホスレボドパ・ホスカルビドパ水和物（以下「ABBV-951」）は，高い溶解性をもつ，レボドパ（以下「LD」）及びカルビドパ（以下「CD」）のプロドラッグである。ABBV-951 は，既存の治療では運動症状の日内変動のコントロールが不十分な個々の進行期パーキンソン病（以下「PD」）患者に応じた治療のための持続皮下注入（以下「CSCI」）製剤としてアッヴィが開発した製剤である。

ABBV-951 は携帯型注入ポンプに接続した注入セットを用いて，24 時間連日皮下投与する。ABBV-951 の持続注入では，経口投与とは異なり LD 及び CD の血漿中濃度の変動が少ない。そのため，レボドパ・カルビドパ経腸用液（以下「LCIG」）投与のような外科的介入を必要とせずに，脳内のドパミン受容体を間欠的ではなく持続的に刺激することが可能となる。

ABBV-951 の承認申請における臨床データパッケージでは，バイオアベイラビリティ試験 2 試験（M17-220 試験［5.3.1.2-1 項］及び M18-764 試験［5.3.1.2-2 項］）が実施され，ABBV-951 を CSCI したとき，又は LCIG を空腸から注入したとき（夜間の LD/CD 経口投与を含む，あるいは含まない）の LD の薬物動態を比較した。M17-220 試験はピボタルな薬物動態比較試験であり，ABBV-951 を 24 時間皮下注入したときの LD の曝露量は，LCIG を空腸から 16 時間注入後，夜間に LD/CD を経口投与したときと同程度であった（2.7.2.2.4.1 項）。M18-764 試験は，M17-220 試験での用量を決定するために実施したパイロット薬物動態比較試験であった（2.7.2.2.4.2 項）。結果及び考察は 2.7.2 項に詳述した。

血漿中濃度測定のため，LD，CD，ホスレボドパ，ホスカルビドパ及び 3-O-メチルドパ（以下「3-OMD」）の生体試料分析法を，規制当局の最新の基準に従ってバリデートした。サンプル測定における選択性，精度，真度，感度，頑健性，及びマトリックス中での安定性が十分であることを確認した。第 I 相試験で評価した薬物動態の結果は 2.7.2.2 項に要約した。

なお，本項では，ホスレボドパ及びホスカルビドパの名称を以下のように記載する場合がある。

ホスレボドパ：レボドパ-4'-一リン酸，LD′，LD4′，LDP4′及び LDP

ホスカルビドパ：カルビドパ-4'-一リン酸，CD′，CD4′，CDP4′及び CDP

2.7.1.1.1 物理的化学的特性

ホスレボドパ及びホスカルビドパ水和物の構造式を図 2.7.1-1 及び図 2.7.1-2 に示す。また，ホスレボドパ及びホスカルビドパ水和物の名称及び一般特性を表 2.7.1-1 に示す。

図 2.7.1-1. ホスレボドパの構造式

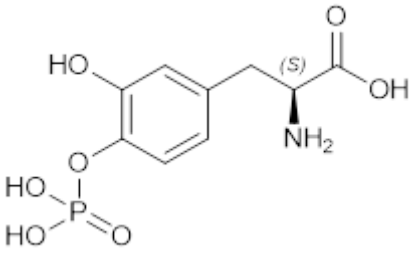


図 2.7.1-2. ホスカルビドパ水和物の構造式

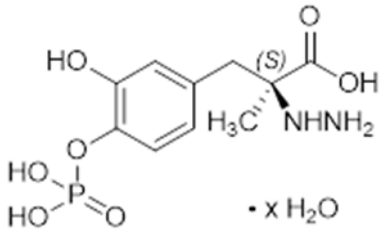


表 2.7.1-1. ABBV-951 の名称及び一般特性

Chemical Name:	Foslevodopa: Levodopa-4′-Monophosphate (LDP4′)	(2*S*)-2-amino-3-[3-hydroxy-4-(phosphonooxy)phenyl]propanoic acid
	Foscarbidopa: Carbidopa-4′-Monophosphate (CDP4′)	(2*S*)-2-hydrazinyl-3-[3-hydroxy-4-(phosphonooxy)phenyl]-2-methylpropanoic acid hydrate
Associated Name(s):	ABBV-951	
Generic Name:	Foslevodopa/foscarbidopa	
INN (International Nonproprietary Name):	Foslevodopa, foscarbidopa	
USAN (United States Adopted Name):	Foslevodopa, foscarbidopa	
Japanese Accepted Name (JAN):	ホスレボドパ，ホスカルビドパ水和物	
British Approved Name (BAN):	Not available	
Molecular Formula:	Foslevodopa	$C_9H_{12}NO_7P$
	Foscarbidopa	$C_{10}H_{15}N_2O_7P$ (anhydrous basis)
Molecular Weight (grams/mole):	Foslevodopa	277.17
	Foscarbidopa	306.21 (anhydrous basis)
Description:	Foslevodopa is a crystalline white to off-white powder and foscarbidopa is a crystalline white to off-white to light yellow powder	
Solubility:	Foslevodopa and foscarbidopa are freely soluble in aqueous media	
Stereoisomerism:	Foslevodopa and foscarbidopa each have a single stereogenic center and are manufactured as a single stereoisomer	

2.7.1.1.2 製剤開発

本承認申請の臨床データパッケージとなる臨床試験 10 試験で使用した ABBV-951 の製剤及び治験機器の要約を表 2.7.1-2 に示す。また，試験に使用した ABBV-951 の製剤組成を表 2.7.1-3 に示す。

製剤開発に関するより詳細な情報は 3.2.P.2 項に示す。

表 2.7.1-2. 臨床試験で用いた ABBV-951 の製剤及び治験機器の要約

	Study									
Formulation and Devices[a]	**M15-733**	**M15-738**	**M15-739**	**M16-769**	**M17-220**	**M18-763**	**M18-764**	**M15-736**	**M15-741**	**M15-737**
107.5/430.0 mg CD′/LD′ lyophilized powder [redacted] pump, model number [redacted]; [redacted] infusion set catheter, model number [redacted]; [redacted] tubing [redacted]	X	X								
20/400 mg CD′/LD′ lyophilized powder [redacted] pump, model number [redacted]; [redacted] infusion set, model number [redacted]		X								
20/400 mg CD′/LD′ lyophilized powder [redacted] ([redacted]) [redacted] syringe pump, model [redacted]; [redacted] infusion set, model number [redacted]		X	X	X		X	X			
12/240 mg/mL CDP/LDP solution for infusion [redacted] syringe pump, model [redacted]; [redacted] infusion set, model number [redacted]					X		X			

表 2.7.1-2. 臨床試験で用いた ABBV-951 の製剤組成及び治験機器の要約（続き）

	Study									
Formulation and Devices[a]	**M15-733**	**M15-738**	**M15-739**	**M16-769**	**M17-220**	**M18-763**	**M18-764**	**M15-736**	**M15-741**	**M15-737**
12/240 mg/mL CDP/LDP solution for infusion [redacted] infusion pump, reference # [redacted], Neria™ Guard infusion set, 6 mm cannula, 60 cm tubing; reference # [redacted] USA (US); Neria™ Guard infusion set, 9 mm cannula, 60 cm tubing; [redacted] Reference # [redacted] USA (US)								X		
12/240 mg/mL CDP/LDP solution for infusion [redacted] S.p.A [redacted], Neria™ Guard infusion set, 6 mm cannula, 60 cm tubing; [redacted] reference # [redacted] USA (US), [redacted] (OUS); Neria™ Guard infusion set, 9 mm cannula, 60 cm tubing; [redacted] reference # [redacted] USA (US), [redacted] (OUS); [redacted] infusion set, 6-mm cannula with inserter, 24-inch tubing with buckle, #[redacted]; [redacted] infusion set, 9-mm cannula with inserter, 24-inch tubing with buckle, #[redacted]									X	X

CDP and CD′ = foscarbidopa; LDP and LD′ = foslevodopa

a. Formulation (strength and dosage form); devices (pump and infusion set).

表 2.7.1-3. 臨床試験で用いた ABBV-951 の製剤組成

Dosage Form 1:	Lyophilized powder for reconstitution
Composition:	Lyophilized Powder Formulation 1 (4:1 ratio foslevodopa:foscarbidopa) 430.0 mg foslevodopa per vial 107.5 mg foscarbidopa per vial Lyophilized Powder Formulation 2 (20:1 ratio foslevodopa:foscarbidopa) 400.0 mg foslevodopa per vial 20.0 mg foscarbidopa per vial
Excipients:	Sucrose, NaOH, Water for Injection
Dosage Form 2:	Solution for infusion
Strength:	240 mg foslevodopa per mL and 12.0 mg foscarbidopa per mL
Excipients:	NaOH, HCl, Water for Injection

2.7.1.1.3 分析法

ヒ酸水素二ナトリウム及びメタ重亜硫酸ナトリウム処置した，エチレンジアミン四酢酸二カリウム（以下「K_2EDTA」）を含むヒト血漿中のホスレボドパ，ホスカルビドパ，LD，CD 及び 3-OMD を定量するため，高速液体クロマトグラフィータンデム質量分析（以下「LC-MS/MS」）を用いた特異的かつ高感度の生体試料分析法を開発し，バリデートした。本分析法では，各分析対象物に対する安定同位体標識した内標準物質を用いた。本バリデーションは，生体試料分析法に関する規制当局によるガイダンス及び社内標準作業手順書に従って実施した。また，アセトン誘導体（アセトンアジン）である血漿中ヒドラジンの定量のため，fit for purpose に基づいた分析法を開発した。各分析対象物のバリデーション試験結果について，付録 A（ホスレボドパ及びホスカルビドパ），付録 B（LD 及び CD），付録 C（3-OMD）及び付録 D（ヒドラジン）にそれぞれ要約した。本承認申請で提出する臨床試験における薬物濃度は，バリデートした分析法を用いて測定した（表 2.7.1-4）。

表 2.7.1-4. 臨床試験で使用した各分析対象物の濃度測定法

Analyte	Validated Method ID	Matrix	Bioanalytical site	Study
LDP4' and CDP4'	R&D/17/1095	Plasma	AbbVie Inc., North Chicago, IL USA	M15-733 (Part 1) M15-733 (Part 2) M15-733 (Part 4) M15-738 M15-739 M16-769 M17-220 M18-763 M18-764
LD and CD	R&D/17/1085			M15-733 (Part 1) M15-733 (Part 2) M15-733 (Part 3) M15-733 (Part 4) M15-738 M15-739 M16-769 M17-220 M18-763 M18-764
3-OMD	R&D/17/0894			M15-733 (Part 1) M15-733 (Part 2) M15-733 (Part 3) M15-733 (Part 4) M15-738 M15-739 M16-769 M17-220 M18-763 M18-764
Hydrazine	R&D/11/678			M15-738

LDP4' = foslevodopa; A-1591706; LD = levodopa; CDP4' = foscarbidopa; A-1610308; CD = carbidopa; 3-OMD = 3-O-methyldopa

2.7.1.2 個々の試験結果の要約

該当なし。

2.7.1.3 全試験を通しての結果の比較と解析

該当なし。

2.7.1.4 付録

付録 A. 分析法バリデーションの概要：ホスレボドパ及びホスカルビドパ

Bioanalytical method validation report name, amendments and hyperlinks	Validation Report for a 96-Well Protein Precipitation Extraction HPLC Tandem Mass Spectrometric Method for the Determination of A-1591706 and A-1610308 in Treated Human Plasma with K_2EDTA as Anticoagulant (R&D/17/1095 [5.3.1.4-1 項]) Validation Update Report for a 96-Well Protein Precipitation Extraction HPLC Tandem Mass Spectrometric Method for the Determination of A-1591706 and A-1610308 in Treated Human Plasma with K_2EDTA as Anticoagulant (R&D/20/1577 [5.3.1.4-2 項])	
Method description	HPLC-MS/MS method for quantitation of A-1591706 (LDP4') and A-1610308 (CDP4') in human plasma with K_2EDTA treated with disodium hydrogen arsenate and sodium metabisulfite	
Materials used for standard calibration curve and concentration (% purity)	A-1591076 (LDP4'), Lots: ABBV-3371-126 (97.9%) ABBV-3510-088 (97.5%) ABBV-3371-126 (97.7%) ABBV-3420-100 (98.3%) RSFT00282721 (98.7%) FT00105980 (97.7%)	A-1610308 (CDP4'), Lots: ABBV-3913-48 (84.1%) ABBV-3510-001 (83.3%) ABBV-3510-001 (83.0%) ABBV-3731-172 (83.8%) ABBV-3913-150 (84.8%) 1000132987 (83.8%)
Validated assay range	8.97 to 3010 ng/mL	3.00 to 3010 ng/mL
Material used for QCs and concentration (% purity)	A-1591076 (LDP4'), Lots: ABBV-3371-126 (97.9%) ABBV-3510-088 (97.5%) ABBV-3371-126 (97.7%) ABBV-3420-100 (98.3%) RSFT00282721 (98.7%) FT00105980 (97.7%)	A-1610308 (CDP4'), Lots: ABBV-3913-48 (84.1%) ABBV-3510-001 (83.3%) ABBV-3510-001 (83.0%) ABBV-3731-172 (83.8%) ABBV-3913-150 (84.8%) 1000132987 (83.8%)
Minimum required dilutions (MRDs)	NA	NA
Source and lot of reagents	NA	NA
Regression model and weighting	Linear, $1/x^2$	Linear, $1/x^2$

付録 A. 分析法バリデーションの概要：ホスレボドパ及びホスカルビドパ（続き）

Validation parameters	**Method Validation Summary**		**A-1591706 (LDP4')**	**A-1610308 (CDP4')**
Standard calibration curve performance during accuracy and precision runs	# std calibrators from LLOQ to ULOQ		8 R&D/17/1095: Table 5	8 R&D/17/1095: Table 7
	% bias from LLOQ to ULOQ		–6.0 to 4.7% R&D/17/1095: Table 5	–10.3 to 8.3% R&D/17/1095: Table 7
	%CV from LLOQ to ULOQ		0.4 to 1.5% R&D/17/1095: Table 5	0.5 to 2.8% R&D/17/1095: Table 7
Performance of QCs during accuracy and precision runs	% bias in 5 QCs	x to y%	–11.9 to 8.0%	–11.0 to 14.3%
	Inter-batch %CV	≤ x%	≤ 10.3% R&D/17/1095: Table 9, Table 11, Table 13, Table 15, Table 17, Table 19	≤ 8.5% R&D/17/1095: Table 10, Table 12, Table 14, Table 16, Table 18, Table 20
	Total Error (TE)	≤ x%	NA	NA

付録 A. 分析法バリデーションの概要：ホスレボドパ及びホスカルビドパ（続き）

	A-1591706 (LDP4')	A-1610308 (CDP4')
Selectivity effect	12 lots; 0.0 to 0.4% of LLOQ PA R&D/17/1095: Table 21 & Table 22	6 lots; 0.1 to 8.0% of LLOQ PA R&D/17/1095: Table 23
Matrix effect	12 lots, 2 concentrations; inter-lot CV ≤ 2.6% R&D/17/1095: Table 30 & Table 31	6 lots, 2 concentrations; inter-lot CV ≤ 2.5% R&D/17/1095: Table 32
Interference	2 evaluations at 3 concentrations –3.4 to 9.0% bias R&D/17/1095: Table 47 & Table 49	1 evaluation at 3 concentrations –9.0 to 7.3% bias R&D/17/1095: Table 50
Specificity	Each analyte (LDP4', CDP4', LD, CD, 3-OMD) evaluated separately and combined provided an average analyte PA < 20% of the LLOQ PA in the presence of the other four analytes R&D/17/1095: Tables 51 through 63	
Hemolysis effect	3 lots at 2 concentrations –6.7 to 5.0% bias R&D/17/1095: Table 41 & Table 42 R&D/20/1577: Table 27	2 lots at 2 concentrations –6.4 to 6.3% bias R&D/17/1095: Table 43 R&D/20/1577: Table 28
Lipemic effect	3 lots at 2 concentrations –4.7 to 11.5% bias R&D/17/1095: Table 44 & Table 45 R&D/20/1577: Table 25	2 lots at 2 concentrations –6.8 to 7.5% bias R&D/17/1095: Table 46 R&D/20/1577: Table 26
Dilution linearity & hook effect	10-fold dilution from 28000 ng/mL 3.6-6.8% bias 20-fold dilution from 28300 ng/mL –3.2 to –1.4% bias R&D/17/1095: Table 33	20-fold dilution from 28300 ng/mL –3.9 to 0.0% bias R&D/17/1095: Table 34
Freeze-Thaw stability (-70°C)	At F/T 4, –3.4 to 10.4% bias R&D/17/1095: Table 76	At F/T 4, –8.6 to 4.3% bias R&D/17/1095: Table 80
Long-term storage	562 days at –70°C; –1.3 to 0.8% bias R&D/20/1577: Table 34	562 days at –70°C; –2.6 to 4.0% bias R&D/20/1577: Table 35
Parallelism	NA	NA
Carry over	0.0% of LLOQ PA following ULOQ R&D/17/1095: Table 35 0.4% of LLOQ PA following ULOQ R&D/17/1095: Table 37	44.1% of LLOQ PA following ULOQ R&D/17/1095: Table 39

PA = peak area; LLOQ = lower limit of quantitation; ULOQ = upper limit of quantitation; NA = not applicable; LDP4' = foslevodopa; LD = levodopa; CDP4' = foscarbidopa; CD = carbidopa; 3-OMD = 3-O-methyldopa; F/T = freeze/thaw

付録 B. 分析法バリデーションの概要：レボドパ及びカルビドパ

Bioanalytical method validation report name, amendments and hyperlinks		Validation Report for a 96-Well Protein Precipitation Extraction HPLC Tandem Mass Spectrometric Method for the Determination of A-21236 and A-39432 in Treated Human Plasma with K_2EDTA as Anticoagulant (R&D/17/1085 [5.3.1.4-3 項]) Validation Update Report for a 96-Well Protein Precipitation Extraction HPLC Tandem Mass Spectrometric Method for the Determination of A-21236 and A-39432 in Treated Human Plasma with K_2EDTA as Anticoagulant (R&D/20/1607 [5.3.1.4-4 項])		
Method description		HPLC-MS/MS method for quantitation of A-21236 (LD) and A-39432 (CD) in human plasma with K_2EDTA treated with disodium hydrogen arsenate and sodium metabisulfite		
Materials used for standard calibration curve and concentration (% purity)		A-21236 (LD), Lots: 1000090231 (99.7%) RS70216 (100%)		A-39432 (CD), Lots: 1000095179 (92.4%) RS0120511 (92.6%) RS0240218 (92.3%)
Validated assay range		9.99 to 9990 ng/mL		9.27 to 9270 ng/mL
Material used for QCs and concentration (% purity)		A-21236 (LD), Lots: 1000090231 (99.7%) RS70216 (100%)		A-39432 (CD), Lots: 1000095179 (92.4%) RS0120511 (92.6%) RS0240218 (92.3%)
Minimum required dilutions (MRDs)		NA		NA
Source and lot of reagents		NA		NA
Regression model and weighting		Linear, $1/x^2$		Linear, $1/x^2$
Validation parameters	**Method Validation Summary**		**A-21236 (LD)**	**A-39432 (CD)**
Standard calibration curve performance during accuracy and precision runs	# std calibrators from LLOQ to ULOQ		8 R&D/17/1085: Table 1, Table 5	8 R&D/17/1085: Table 3, Table 7
	% bias from LLOQ to ULOQ		–10.4 to 9.7% R&D/17/1085: Table 1, Table 5	–9.5 to 7.8% R&D/17/1085: Table 3, Table 7
	%CV from LLOQ to ULOQ		0.1 to 4.3% R&D/17/1085: Table 1, Table 5	0.0 to 2.0% R&D/17/1085: Table 3, Table 7
Performance of QCs during accuracy and precision runs	% bias in 5 QCs	x to y%	–10.2 to 6.8% R&D/17/1085: Table 9, Table 11, Table 13, Table 15, Table 17, Table 19	–8.3 to 7.8% R&D/17/1085: Table 10, Table 12, Table 14, Table 16, Table 18, Table 20
	Inter-batch %CV	≤ x%	≤ 7.3% R&D/17/1085: Table 9, Table 11, Table 13, Table 15, Table 17, Table 19	≤ 7.5% R&D/17/1085: Table 10, Table 12, Table 14, Table 16, Table 18, Table 20
	Total Error (TE)	≤ x%	NA	NA

付録 B. 分析法バリデーションの概要：レボドパ及びカルビドパ（続き）

	A-21236 (LD)	A-39432 (CD)
Selectivity effect	6 lots; 4.1 to 6.8% of LLOQ PA R&D/17/1085: Table 21	6 lots; 0.0 to 0.4% of LLOQ PA R&D/17/1085: Table 22
Matrix effect	6 lots, 2 concentrations; inter-lot CV ≤ 3.3% R&D/17/1085: Table 27	6 lots, 2 concentrations; inter-lot CV ≤ 1.8% R&D/17/1085: Table 28
Interference	1 evaluation at 2 concentrations –3.9 to 12.9% bias R&D/17/1085: Table 105	1 evaluation at 2 concentrations –1.4 to –0.8% bias R&D/17/1085: Table 106
Specificity	Each analyte (LDP4', CDP4', LD, CD, 3-OMD) evaluated separately and combine provided an average analyte PA < 20% of the LLOQ PA in the presence of the other four analytes R&D/17/1085: Tables 107 through 110	
Hemolysis effect	2 lots at 3 concentrations –7.2 to 2.4% bias R&D/17/1085: Table 41 R&D/20/1607: Table 23	2 lots at 3 concentrations –13.0 to 0.9% bias R&D/17/1085: Table 42 R&D/20/1607: Table 24
Lipemic effect	2 lots at 2 concentrations –7.8 to -0.4% bias R&D/17/1085: Table 43 R&D/20/1607: Table 21	2 lots at 2 concentrations –9.9 to 1.9% bias R&D/17/1085: Table 44 R&D/20/1607: Table 22
Dilution linearity & hook effect	10-fold dilution from 40100 ng/mL –10.5 to –6.7% bias R&D/17/1085: Table 29	10-fold dilution from 37200 ng/mL –10.5 to –7.3% bias R&D/17/1085: Table 30
Freeze-Thaw stability (-70°C)	At F/T 5, –7.8 to 10.4% bias; CV ≤ 5.8% R&D/17/1085: Table 61	At F/T 9, –8.1 to -0.8% bias; CV ≤ 8.1% R&D/20/1607: Table 25
Long-term storage	441 days at –70°C; –3.9 to 14.0% bias R&D/20/1607: Table 27	441 days at –70°C; –4.9 to 6.0% bias R&D/20/1607: Table 28
Parallelism	NA	NA
Carry over	8.1% of LLOQ PA following ULOQ R&D/17/1085: Table 37	17.6% of LLOQ PA following ULOQ R&D/17/1085: Table 39

PA = peak area; LLOQ = lower limit of quantitation; ULOQ = upper limit of quantitation; NA = not applicable; LDP4' = foslevodopa; LD = levodopa; CDP4' = foscarbidopa; CD = carbidopa; 3-OMD = 3-O-methyldopa; F/T = freeze/thaw

付録 C. 分析法バリデーションの概要：3-O-メチルドパ

Bioanalytical method validation report name, amendments and hyperlinks	Amended Validation Report for a 96-Well Protein Precipitation Extraction HPLC Tandem Mass Spectrometric Method for the Determination of 3-OMD in Treated Human Plasma with K_2EDTA as Anticoagulant (R&D/17/0894 [5.3.1.4-5 項]) Validation Update Report for a 96-Well Protein Precipitation Extraction HPLC Tandem Mass Spectrometric Method for the Determination of 3-OMD in Treated Human Plasma with K_2EDTA as Anticoagulant (R&D/20/1426 [5.3.1.4-6 項])			
Method description	HPLC-MS/MS method for quantitation of 3-O-methyldoopa (3-OMD) in human plasma with K_2EDTA treated with disodium hydrogen arsenate and sodium metabisulfite			
Materials used for standard calibration curve and concentration (% purity)	3-OMD; lot JIJ299 (87.0%)			
Validated assay range	400 to 40000 ng/mL			
Material used for QCs and concentration	3-OMD; lot JIJ299 (87.0%)			
Minimum required dilutions (MRDs)	NA			
Source and lot of reagents	NA			
Regression model and weighting	Linear; $1/x^2$			
Validation parameters	**Method Validation Summary**			**3-OMD**
Standard calibration curve performance during accuracy and precision runs	# std calibrators from LLOQ to ULOQ		8	R&D/17/0894: Table 2
	% bias from LLOQ to ULOQ		–3.8 to 2.6%	R&D/17/0894: Table 2
	%CV from LLOQ to ULOQ		0.4 to 4.5%	R&D/17/0894: Table 2
Performance of QCs during accuracy and precision runs	% bias in 5 QCs	x to y%	–4.0 to 9.0%	R&D/17/0894: Table 6, Table 8, Table 10
	Inter-batch %CV	≤ x%	≤ 6.4	
	Total Error (TE)	≤ x%	NA	
Selectivity effect				R&D/17/0894: Table 11
Matrix effect	6 lots; 3.2 to 6.2% of LLOQ PA 6 lots, 2 concentrations; inter-lot CV ≤ 4.5%			R&D/17/0894: Table 14, Table 15
Interference	1 evaluation at 2 concentrations; 1.9 to 11.0% bias			R&D/17/0894: Table 29
Specificity	Each analyte (LDP4', CDP4', LD, CD) evaluated separately and combined provided an average analyte PA < 20% of the LLOQ PA in the presence of the other four analytes.			R&D/17/0894: Tables 30 through 34
Hemolysis effect	2 lots at 2 concentrations; –1.0 to 10.0% bias			R&D/17/0894: Table 22 R&D/20/1426: Table 14
Lipemic effect	2 lots at 2 concentrations; 0.0 to 11.0% bias			R&D/17/0894: Table 23 R&D/20/1426: Table 13

付録 C. 分析法バリデーションの概要：3-O-メチルドパ（続き）

Dilution linearity & hook effect	10-fold dilution from 100000 ng/mL 4.0 to 11.0% bias	R&D/17/0894: Table 16
Freeze-thaw stability (-70°C)	At F/T 6, –12.6 to –11.3% bias; CV ≤ 2.8%	R&D/20/1426: Table 15
Long-term storage	1518 days at ~-70°C; –1.3 to 3.0% bias; CV ≤ 1.3%	R&D/20/1426: Table 16
Parallelism	NA	NA
Carry over	8.0% of LLOQ PA following ULOQ	R&D/17/0894: Table 20

PA = peak area; LLOQ = lower limit of quantitation; ULOQ = upper limit of quantitation; NA not applicable; LDP4' = foslevodopa; LD = levodopa; CDP4' = foscarbidopa; CD carbidopa; 3-OMD = 3-O-methyldopa; F/T = freeze/thaw

付録 D. 分析法バリデーションの概要：ヒドラジン

Bioanalytical method validation report name, amendments and hyperlinks	96-Well Salt-Assisted Liquid/Liquid Extraction HPLC Tandem Mass Spectrometric Method of the Acetone Derivative (Acetone Azine) for the Determination of Hydrazine in Human Plasma (0.5% Sodium Metabisulfite) (R&D/11/678 [5.3.1.4-7 項])			
Method description	Salt-assisted liquid/liquid extraction followed by HPLC-MS/MS of the acetone derivative (acetone azine) for quantitation			
Materials used for standard calibration curve and concentration (% purity)	Sigma-Aldrich, lot MKBD8293V (24.63%)			
Validated assay range	4.87 to 3040 ng/mL			
Material used for QCs and concentration (% purity)	Sigma-Aldrich, lot MKBD8293V (24.63%)			
Minimum required dilutions (MRDs)	NA			
Source and lot of reagents	NA			
Regression model and weighting	Linear, $1/x^2$			
Validation parameters	**Method Validation Summary**			
Standard calibration curve performance during accuracy and precision runs	# std calibrators from LLOQ to ULOQ		8	R&D/11/678: Table 1
	% bias from LLOQ to ULOQ		–4.0 to 2.8%	R&D/11/678: Table 1
	%CV from LLOQ to ULOQ		0.5 to 2.2%	R&D/11/678: Table 1
Performance of QCs during accuracy and precision runs	% bias in 5 QCs	x to y%	–5.7 to 0.8%	R&D/11/678: Table 3, Table 4, Table 5
	Inter-batch %CV	< x%	≤ 4.1%	R&D/11/678: Table 3, Table 4, Table 5
	Total Error (TE)	< x%	NA	NA
Selectivity effect	6 lots; 0% of LLOQ PA			R&D/11/678: Table 6
Matrix effect	6 lots, –5.7 to –1.6% bias			R&D/11/678: Table 7
Interference	Mean bias from carbidopa degradation: –-0.8 to 3.0%			R&D/11/678: Table 23
Specificity				not assessed
Hemolysis effect				not assessed
Lipemic effect				not assessed
Dilution linearity & hook effect	11-fold dilution from 5500 ng/mL; –5.5 to –0.4% bias			R&D/11/678: Table 8
Freeze-Thaw stability (-70°C)	At F/T 6, –8.8 to –6.8% bias			R&D/11/678: Table 14
Long-term storage	148 days at –70°C; –1.9 to 3.9% bias			R&D/11/678: Table 15
Parallelism	NA			NA
Carry over				not assessed

PA = peak area; LLOQ = lower limit of quantitation; ULOQ = upper limit of quantitation; NA = not applicable

2.7.2 臨床薬理試験

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略語及び定義一覧

略語又は用語	省略していない表現又は説明（英語）	省略していない表現又は説明（日本語）
AUC	Area under the plasma concentration-time curve	血漿中濃度－時間曲線下面積
AUC_{0-4}	AUC from hours 0 to 4	投与後 0～4 時間までの AUC
AUC_{0-16}	AUC from hours 0 to 16	投与後 0～16 時間までの AUC
AUC_{0-24}	AUC from hours 0 to 24	投与後 0～24 時間までの AUC
AUC_{inf}	AUC from hours 0 extrapolated to infinity	投与後無限大時間までの AUC
AUC_t	Area under the plasma concentration-time curve from time zero to time of last measurable concentration	投与後最終定量可能時点までの AUC
C_{ave}	average plasma concentration	平均血漿中濃度
CD	carbidopa	カルビドパ
CDP4'（CD′, CD4′，CDP）	foscarbidopa (carbidopa-4′-monophosphate)	ホスカルビドパ（カルビドパ-4'-一リン酸）
C_{max}	Maximum observed plasma concentration	最高血漿中濃度
$C_{max,0-16}$	C_{max} from hours 0 to 16	投与後 0～16 時間までの C_{max}
C_{min}	Minimum observed plasma concentration	最低血漿中濃度
COMT	catechol-O-methyltransferase	カテコール-O-メチルトランスフェラーゼ
CSCI	continuous subcutaneous infusion	持続皮下注入
DFL	degree of fluctuation	変動度
ECG	electrocardiogram	心電図
GLP	Good Laboratory Practice	-
hERG	human ether-à-go-go related gene	ヒト遅延整流性カリウムイオンチャネル遺伝子
ICH	International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use	日米 EU 医薬品規制調和国際会議
LCIG	levodopa/carbidopa intestinal gel	レボドパ・カルビドパ経腸用液
LD	levodopa	レボドパ
LDP4'（LD′, LD4′，LDP）	foslevodopa (levodopa-4′-monophosphate)	ホスレボドパ（レボドパ-4'-一リン酸）
PD	Parkinson's disease	パーキンソン病
PK	pharmacokinetics	薬物動態
PT	preferred term	基本語
QTc	corrected QT	補正 QT 間隔
QTcF	QTc using Fridericia's correction formula Fridericia	Fridericia 補正式による補正 QT 間隔
SC	subcutaneous	皮下

略語又は用語	省略していない表現又は説明（英語）	省略していない表現又は説明（日本語）
SD	standard deviation	標準偏差
SOC	system organ class	器官別大分類
UPDRS	Unified Parkinson's Disease Rating Scale	統一パーキンソン病評価尺度

2.7.2.1 背景及び概観

2.7.2.1.1 背景

ホスレボドパ・ホスカルビドパ水和物（以下「ABBV-951」）は，高い溶解性をもつ，レボドパ（以下「LD」）及びカルビドパ（以下「CD」）のプロドラッグである。ABBV-951 は，既存の治療では運動症状の日内変動のコントロールが不十分な個々の進行期パーキンソン病（以下「PD」）患者に応じた治療のための持続皮下注入（以下「CSCI」）製剤としてアッヴィが開発した製剤である。

ABBV-951 は携帯型注入ポンプに接続した注入セットを用いて，24 時間連日皮下（以下「SC」）投与する。ABBV-951 の持続注入では，経口投与とは異なり LD 及び CD の血漿中濃度の変動が少ない。そのため，レボドパ・カルビドパ経腸用液（以下「LCIG」）投与のような外科的介入を必要とせずに，脳内のドパミン受容体を間欠的ではなく持続的に刺激することが可能となる。

これまでに，LCIG 治療が経口 LD/CD 製剤治療と比べ PD 患者のオフ時間を顕著に短縮させ，PD 患者における LD 及び CD の持続注入のベネフィットが示されている [1]。本邦における ABBV-951 の承認申請における臨床パッケージは第 I 相 7 試験（M15-733 試験，M15-738 試験，M15-739 試験，M16-769 試験，M17-220 試験，M18-763 試験及び M18-764 試験）及び第 III 相 3 試験（M15-736 試験，M15-741 試験及び M15-737 試験）から構成される。第 I 相試験のうち，M18-763 試験（5.3.4.1-1 項）及び M15-739 試験（5.3.3.2-2 項）はいずれも安全性の評価が主要な目的であり，薬物動態（以下「PK」）用検体はスパースサンプリングのみであったことから PK パラメータを算出していない。そのため，これら 2 試験の薬物動態に関する結果は本モジュールに記載しなかった。本モジュールでは，M18-763 試験及び M15-739 試験を除く 5 試験の第 I 相試験について詳述し，その概要を表 2.7.2-1 に示す。

なお，本項では，ホスレボドパ及びホスカルビドパの名称を以下のように記載する場合がある。

ホスレボドパ：レボドパ-4'-一リン酸，LD′，LD4′，LDP4′及び LDP

ホスカルビドパ：カルビドパ-4'-一リン酸，CD′，CD4′，CDP4′及び CDP

表 2.7.2-1. 本モジュールで詳述する第 I 相臨床薬理試験 5 試験の概要

Study (CTD number)	Description	Formulation (Strength and Dosage Form)	Devices (Pump and Infusion Set)
M15-733 (5.3.3.1-1 項)	Pharmacokinetic and initial tolerability in healthy subjects	107.5/430.0 mg carbidopa monophosphate/ levodopa monophosphate lyophilized powder	[redacted] pump, model number [redacted]; [redacted] infusion set catheter, model number [redacted]; [redacted] tubing [redacted]
M15-738 (5.3.3.2-1 項)	Patient pharmacokinetic and initial tolerability	107.5/430.0 mg carbidopa monophosphate/ levodopa monophosphate lyophilized powder 20/400 mg carbidopa monophosphate/ levodopa monophosphate lyophilized powder	[redacted] pump, model number [redacted]; [redacted] infusion set catheter, model number [redacted]; [redacted] tubing [redacted]
M16-769 (5.3.3.3-1 項)	Pharmacokinetic in Asian population	20/400 mg carbidopa monophosphate/ levodopa monophosphate lyophilized powder	[redacted] ([redacted]) [redacted] syringe pump, model [redacted]-[redacted]; [redacted] infusion set, model number [redacted]-[redacted]-[redacted]
M17-220 (5.3.1.2-1 項)	Comparative bioavailability	12/240 mg/mL carbidopa monophosphate/ levodopa monophosphate solution for infusion	[redacted] syringe pump, model [redacted]-[redacted]; [redacted] infusion set, model number [redacted]-[redacted]-[redacted]
M18-764 (5.3.1.2-2 項)	Comparative bioavailability	20/400 mg carbidopa monophosphate/ levodopa monophosphate lyophilized powder 12/240 mg/mL carbidopa monophosphate/ levodopa monophosphate solution for infusion	[redacted] syringe pump, model [redacted]-[redacted]; [redacted] infusion set, model number [redacted]-[redacted]-[redacted]

2.7.2.1.2 臨床薬理試験の概観

ABBV-951 として SC 注入投与されたホスレボドパ及びホスカルビドパは，速やかに吸収された後，アルカリホスファターゼにより活性体である LD 及び CD にそれぞれ変換される。ABBV-951 を単回ボーラス投与したとき，投与後の最初の採血時点（投与後 30 分）で血漿中に LD 及び CD が認められた（M15-733 試験グループ 3 レジメン D［5.3.3.1-1 項］）。また，ホスレボドパ及びホスカルビドパの血漿中濃度は LD 及び CD と比べそれぞれ低く，ホスレボドパ／ホスカルビドパ 960/48～4800/240 mg の用量範囲において，LD の最高血漿中濃度（C_{max}）はホスレボドパと比べ 9～12 倍高く，CD の C_{max} はホスカルビドパと比べ 21～33 倍高かった（M15-738 試験パート 2［5.3.3.2-1 項］）。また，ホスレボドパ／ホスカルビドパ 960/48～4800/240 mg の用量範囲で ABBV-951 を CSCI したときの LD 及び CD の曝露量（C_{max} 及び血漿中濃度－時間曲線下面積［AUC］）は用量に比例して増加した。ABBV-951 注入投与では，LD 及び CD の曝露量が定常状態に達した後，注入期間中は安定した LD 及び CD の曝露量が維持され，変動は極めて小さかった。この結果は，健康被験者（M15-733 試験グループ 4）及び PD 患者（M15-738 試験パート 2）のいずれにおいても同様であった。

First-in-human 試験である M15-733 試験グループ 1 ではホスレボドパ／ホスカルビドパの用量比が 4:1 の ABBV-951 が注入投与され，CD の曝露量は経口 LD/CD 製剤投与時の PK データから想定した曝露量より高く，ホスカルビドパの SC 投与における CD のバイオアベイラビリティは CD の経口投与に比べ高いことが示唆された。そこで，グループ 1 の結果に基づいて，グループ 2 では用量比が 4:1 の経口 LD/CD 製剤を投与したときと同程度の LD：CD の曝露量比（AUC 比）を得るための最適なホスレボドパ／ホスカルビドパの用量比を検討した。その結果，ホスレボドパ／ホスカルビドパの用量比が 20:1 の ABBV-951 を投与したとき，用量比が 4:1 の経口 LD/CD 製剤を投与したときと同程度の LD：CD の曝露量比が認められた。そのため，ホスレボドパ／ホスカルビドパの最適な用量比を 20:1 とし，ABBV-951 の最終用量比とした。

LCIG における有効性及び安全性は既に確立されている。健康被験者を対象とした M17-220 試験（5.3.1.2-1 項）では，ABBV-951 を投与したとき（ABBV-951 投与レジメン），及び，LCIG 投与後夜間に経口 LD/CD 製剤を投与したとき（LCIG 投与レジメン）の LD 及び CD の PK プロファイルを比較した。いずれのレジメンにおいても LD の PK は類似しており，C_{max} 及び AUC の比の点推定値及び 90%信頼区間は 0.8～1.25 の範囲内であった。また，投与後 2～16 時間の定常状態における LD の C_{max} 及び最低血漿中濃度（C_{min}）の差を平均血漿中濃度（C_{ave}）で除した変動度（以下，「DFL」）を算出したところ，LCIG レジメン及び ABBV951 レジメンで，それぞれ 0.404 及び 0.262 であった。この ABBV-951 で見られた LD の曝露量における低い DFL は，進行期 PD 患者の狭い治療域に対する治療に望ましいと考える。同様に，PD 患者に ABBV-951 を投与したとき，試験期間を通じて安定した LD の曝露量が維持された（M15-738 試験）。

ABBV-951 を健康被験者に注入投与したときの LD 及び CD の消失半減期（調和平均）は，それぞれ約 1.5～2.7 時間及び約 2～3 時間であった（M15-733 試験，M16-769 試験［5.3.3.3-1 項］，M17-220 試験及び M18-764 試験［5.3.1.2-2 項］）。これらの値は，これまでに報告されている経口 LD/CD 製剤を投与したときと同程度であった [2,3,4]。LD のクリアランスは，低年齢に比べ高

年齢でやや低いことがこれまでに知られている[5,6]。そのため，健康被験者を対象とした試験は，進行期 PD 患者の年齢に近い 45～75 歳の被験者で実施した。PD 患者では消失半減期を求めるために十分なウォッシュアウト期間を設けることが困難であったことから，LD 及び CD の消失半減期は健康被験者においてのみ評価した。

ABBV-951 は通常，腹部より CSCI するが，3 期クロスオーバーデザインで健康被験者の腹部，腕及び大腿部から ABBV-951 を投与し，異なる SC 投与部位での ABBV-951 の吸収を検討した（M15-733 試験グループ 3）。いずれの部位から投与した場合でも LD 及び CD の曝露量はほぼ同程度であったことから，異なる SC 投与部位でも ABBV-951 の吸収は類似していると考えられる。

ABBV-951 を用いた食事の影響を評価する試験は実施していない。ABBV-951 は SC 投与であり，胃腸を通過しない。そのため，食物の摂取は ABBV-951 の吸収又は LD や CD の全身曝露量に影響を及ぼさないと考えられる。

日本人及び白人に ABBV-951 をホスレボドパ／ホスカルビドパ 480/24～1440/72 mg（一日用量として）の用量で CSCI したときの LD 及び CD の PK は類似していた（M16-769 試験）。また，中国人（漢民族）及び白人に ABBV-951 をホスレボドパ／ホスカルビドパ 1440/72 mg の用量で CSCI したときの LD 及び CD の PK は類似していた（M16-769 試験）。以上より，人種差が ABBV-951 投与後の PK に臨床上重大な影響を及ぼすことは予測されず，日本人を含むアジア人に対する用量調節は不要と考える。

2.7.2.1.3 臨床薬理試験で用いた製剤組成及び関連機器

第 I 相臨床薬理試験で使用した製剤及び治験機器については，2.7.1.1.2 項に記載した。

2.7.2.2 個々の試験結果の要約

2.7.2.2.1 M15-733 試験（健康被験者を対象とした first-in-human 試験）

目的：

本試験の各グループにおける目的を以下に示す。

- グループ 1：
  - ABBV-951 を単回 CSCI したときの安全性，忍容性及び PK を評価する。
  - ABBV-951 を SC 投与したとき及び CD と LD を経口投与したときの CD 及び LD の PK を比較する。
- グループ 2：
  - 高用量の ABBV-951 を単回 CSCI したときの安全性，忍容性及び PK を評価する。
  - 3 つの異なるホスレボドパ／ホスカルビドパ比で SC 投与したときの PK を比較する。
- グループ 3：

- ABBV-951 を異なる投与部位（腹部，腕及び大腿部）から CSCI したとき，及び腹部から注入ポンプを用いて 1 分間で単回ボーラス投与したときの安全性，忍容性及び PK を評価する。

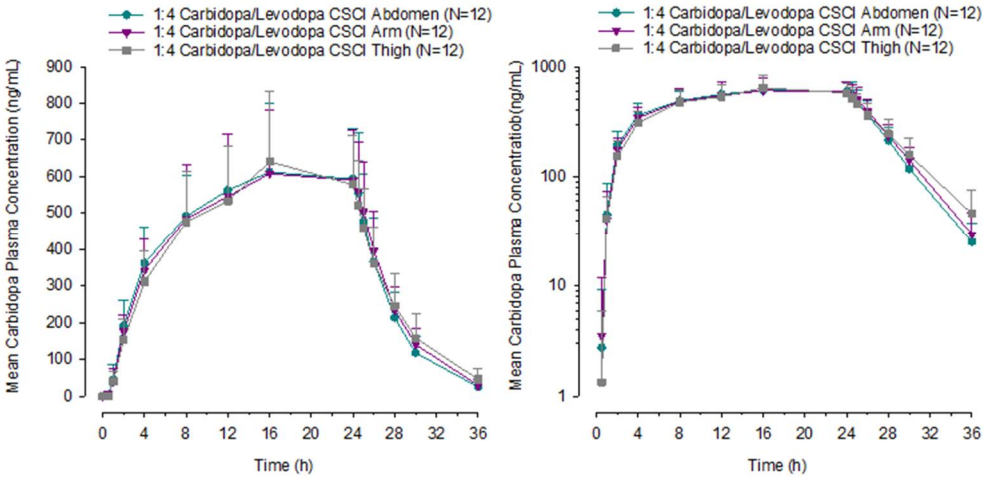
- グループ 4：
  - ABBV-951 を初回 SC ボーラス投与後（負荷投与），72 時間かけて CSCI したときの安全性，忍容性及び PK を評価する。

結果及び結論：

ABBV-951 をホスカルビドパ／ホスレボドパ 90/360～240/960 mg の用量範囲で単回 CSCI したとき，ホスカルビドパ及びホスレボドパは速やかに CD 及び LD に変換され，CD 及び LD は CSCI 後 30 分までに血漿中に検出された。全てのグループにおいて，CD 及び LD の曝露量（AUC）の変動は全体的に小さかった（変動係数 7～26%）。ABBV-951 を SC 投与したときの CD 及び LD の半減期は，それぞれ 2.1～3.0 時間及び 1.8～2.7 時間であった。ホスカルビドパ：ホスレボドパ比が 1：20 の ABBV-951 を投与したときの LD の曝露量は，ホスカルビドパ：ホスレボドパ比が 1：4 の ABBV-951 を投与したときと比べ約 14%低かった。ホスカルビドパ：ホスレボドパ比が 1：20 の ABBV-951 を投与したとき，及び，CD：LD 比が 1：4 の CD/LD 製剤を経口投与したときの CD と LD の曝露量比（CD の投与後無限大時間までの AUC［AUC_{inf}］／LD の AUC_{inf}）は，いずれも約 0.13 と同程度であった（M15-733 試験総括報告書 Table 11 及び Table 12）。

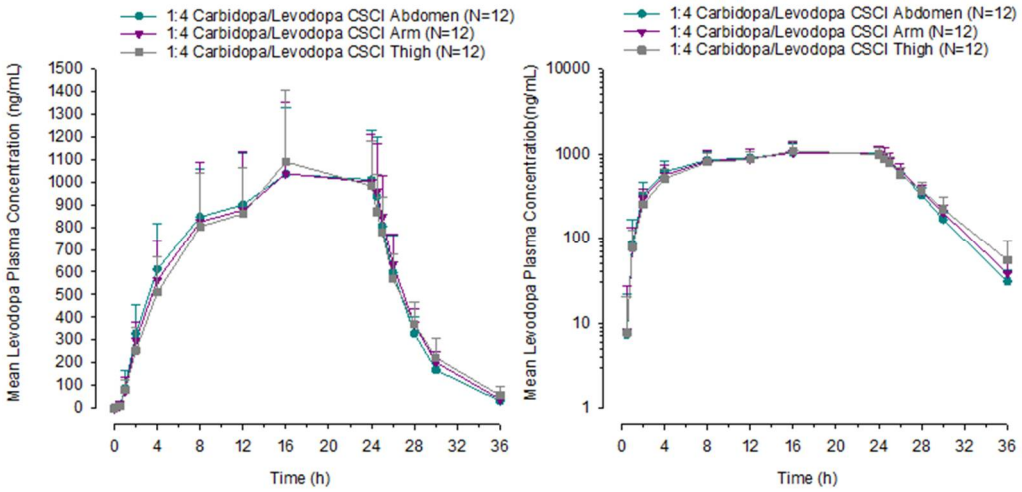
ABBV-951 を 3 つの異なる投与部位（腕，腹部及び大腿部）から投与したとき，CD 及び LD の曝露量，並びに PK の変動はいずれも類似していた（図 2.7.2-1 及び図 2.7.2-2）。

図 2.7.2-1. ABBV-951 を腹部，腕及び大腿部に CSCI したときの血漿中カルビドパ濃度－時間プロファイル（平均値+SD，線形及び片対数，M15-733 試験グループ 3）



CSCI = continuous subcutaneous infusion; SD = standard deviation
240/960 mg CD4'/LD4' ABBV-951 CSCI delivered in the abdomen, arm or thigh at a constant rate over 24 hours

図 2.7.2-2. ABBV-951 を腹部，腕及び大腿部に CSCI したときの血漿中レボドパ濃度－時間プロファイル（平均値+SD，線形及び片対数，M15-733 試験グループ 3）

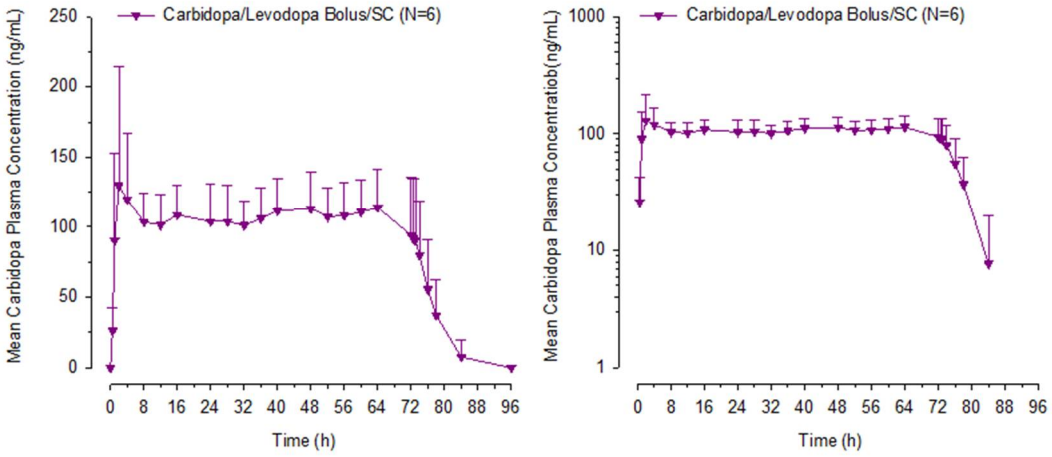


CSCI = continuous subcutaneous infusion; SD = standard deviation
240/960 mg CD4'/LD4' ABBV-951 CSCI delivered in the abdomen, arm or thigh at a constant rate over 24 hours

ABBV-951 をボーラス SC 投与したときの吸収，及び CD 又は LD への変換は速やかであり，CD 及び LD の最高血漿中濃度到達時間は 1.3～1.5 時間であった。

CD 及び LD はいずれも速やかに定常状態に達し，72 時間の投与期間を通して曝露量が維持された（図 2.7.2-3 及び図 2.7.2-4）。ABBV-951 を投与したときの 2～16 時間での LD の DFL は 0.2 であった。過去の試験においてデュオドーパを投与したときの LD の DFL は 0.52 であった（S187-1-002 試験）[15]。

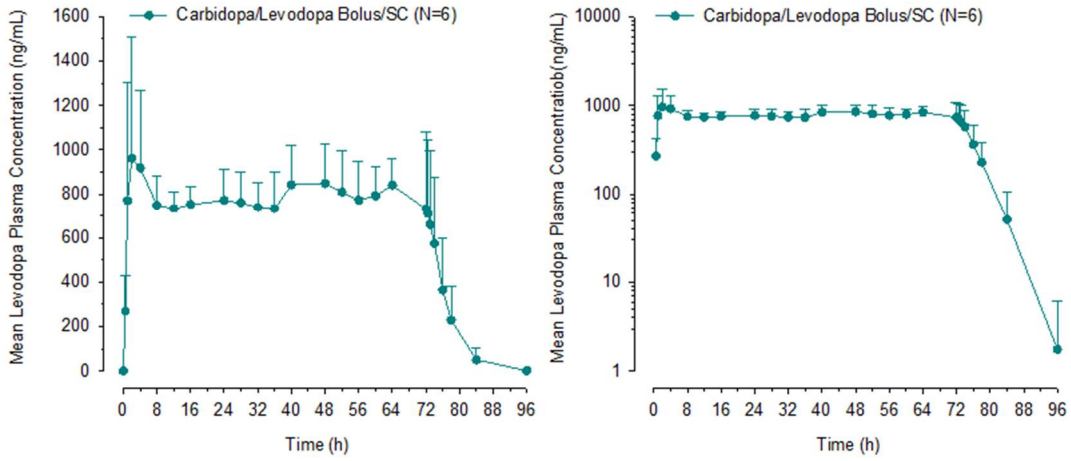
図 2.7.2-3. ABBV-951 を初回ボーラス投与後に CSCI したときの血漿中カルビドパ濃度－時間プロファイル（平均値+SD，線形及び片対数，M15-733 試験グループ 4）



SC = subcutaneous; SD = standard deviation

10/200 mg CD4'/LD4' ABBV-951 delivered as an initial bolus infusion followed by 48/960 mg CD4'/LD4' ABBV-951 per 24 hours (total infusion time 72 hours).

図 2.7.2-4. ABBV-951 を初回ボーラス投与後に CSCI したときの血漿中レボドパ濃度－時間プロファイル（平均値+SD，線形及び片対数，M15-733 試験グループ 4）



SC = subcutaneous; SD = standard deviation
10/200 mg CD4'/LD4' ABBV-951 delivered as an initial bolus infusion followed by 48/960 mg CD4'/LD4' ABBV-951 per 24 hours (total infusion time 72 hours).

2.7.2.2.2 M15-738 試験（PD 患者を対象とした薬物動態試験）

目的：

本試験の主要目的を以下に示す。

- ABBV-951 を PD 患者にボーラス SC 投与後，シリンジポンプを用いて 24 時間又は 72 時間単回 CSCI したときの局所及び全身の安全性及び忍容性を評価する。ABBV-951 は臨床的に意味のある 4 用量を投与する。
- ABBV-951 を PD 患者に投与したときの定常状態における CD 及び LD の血漿中濃度を測定する。ABBV-951 は 2 つの製剤を用いて 4 用量を投与する。

副次目的は ABBV-951 を投与したときの曝露量（血漿中濃度）が補正 QT 間隔（QTc）に及ぼす影響を評価する（2.7.2.3.4.1 項）。

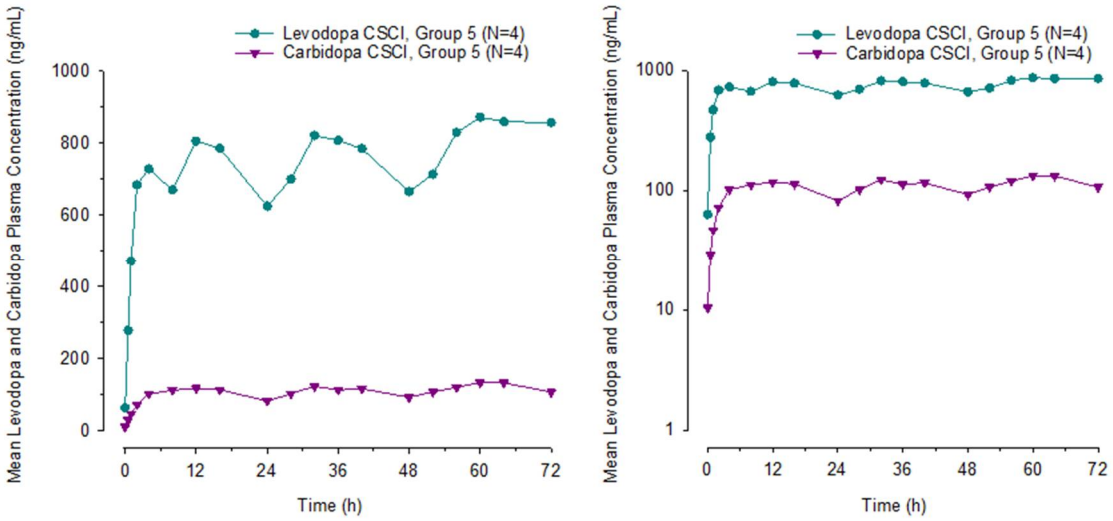
結果及び結論：

最終製剤と同じホスカルビドパ：ホスレボドパ比（1：20）の ABBV-951 が本試験のパート 2 で用いられた。そのため，パート 2 の結果のみを詳述する。

パート 2 において 4 つの異なる注入速度で ABBV-951 を 72 時間にわたり注入投与したとき，72 時間の投与期間を通じて安定した CD 及び LD の曝露量が維持されることが示された（図 2.7.2-5，図 2.7.2-6，図 2.7.2-7 及び図 2.7.2-8）。LD の C_{max} はホスレボドパと比べ 9～12 倍高く，CD の C_{max} はホスカルビドパと比べ 21～33 倍高かった。このことから，プロドラッグ体

であるホスレボドパ及びホスカルビドパは，活性体であるレボドパ及びカルビドパに，それぞれ速やかに変換されることが示唆された。

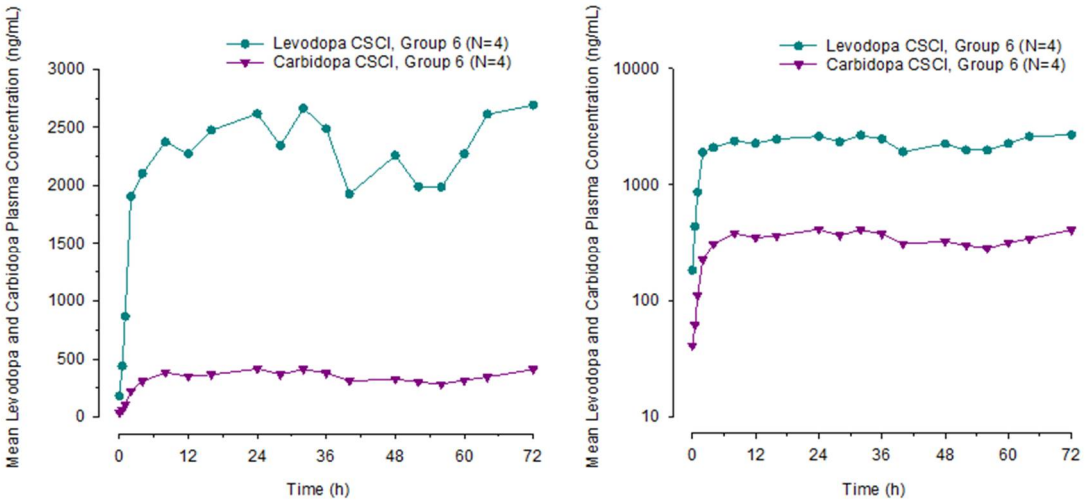
図 2.7.2-5. PD 患者に ABBV-951（ホスカルビドパ／ホスレボドパ 48/960 mg）を CSCI したときの血漿中カルビドパ及びレボドパ濃度ー時間プロファイル（平均値，線形及び片対数，M15-738 試験グループ 5）



CSCI = continuous subcutaneous infusion

Note: ABBV-951 10/200 mg foscarbidopa/foslevodopa loading dose followed by 48/960 mg foscarbidopa/foslevodopa per 24 hours for 72 hours.

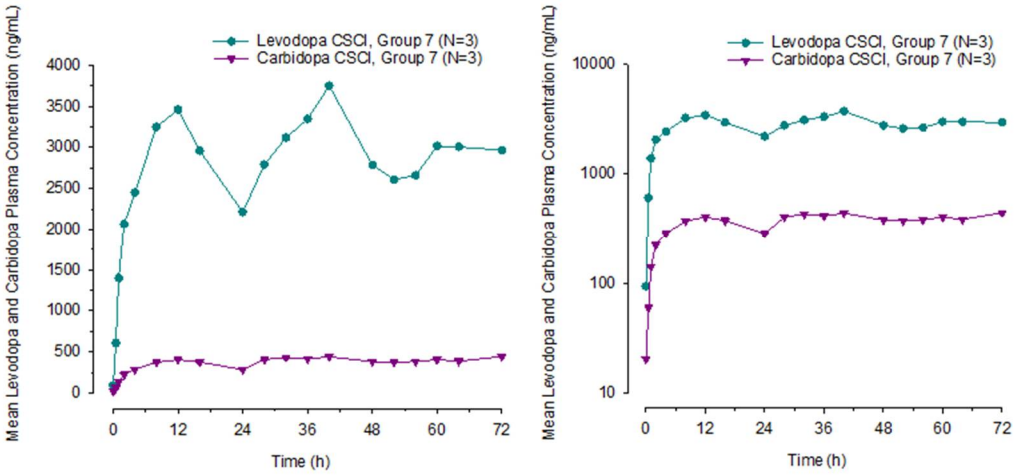
図 2.7.2-6. PD 患者に ABBV-951（ホスカルビドパ／ホスレボドパ 120/2400 mg）を CSCI したときの血漿中カルビドパ及びレボドパ濃度－時間プロファイル（平均値，線形及び片対数，M15-738 試験グループ 6）



CSCI = continuous subcutaneous infusion

Note: ABBV-951 10/200 mg foscarbidopa/foslevodopa loading dose followed by 120/2400 mg foscarbidopa/foslevodopa per 24 hours for 72 hours.

図 2.7.2-7. PD 患者に ABBV-951（ホスカルビドパ／ホスレボドパ 180/3600 mg）を CSCI したときの血漿中カルビドパ及びレボドパ濃度－時間プロファイル（平均値，線形及び片対数，M15-738 試験グループ 7）

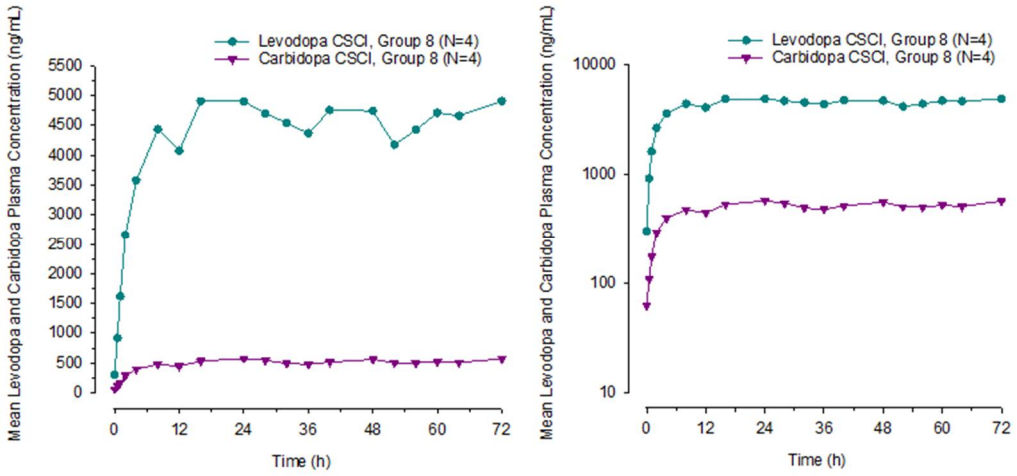


CSCI = continuous subcutaneous infusion

Notes: Plot only includes the first 40 hours of data for Subject 701 because of premature discontinuation.

ABBV-951 10/200 mg foscarbidopa/foslevodopa loading dose followed by 180/3600 mg foscarbidopa/foslevodopa per 24 hours for 72 hours.

図 2.7.2-8. PD 患者に ABBV-951（ホスカルビドパ／ホスレボドパ 240/4800 mg）を CSCI したときの血漿中カルビドパ及びレボドパ濃度－時間プロファイル（平均値，線形及び片対数，M15-738 試験グループ 8）



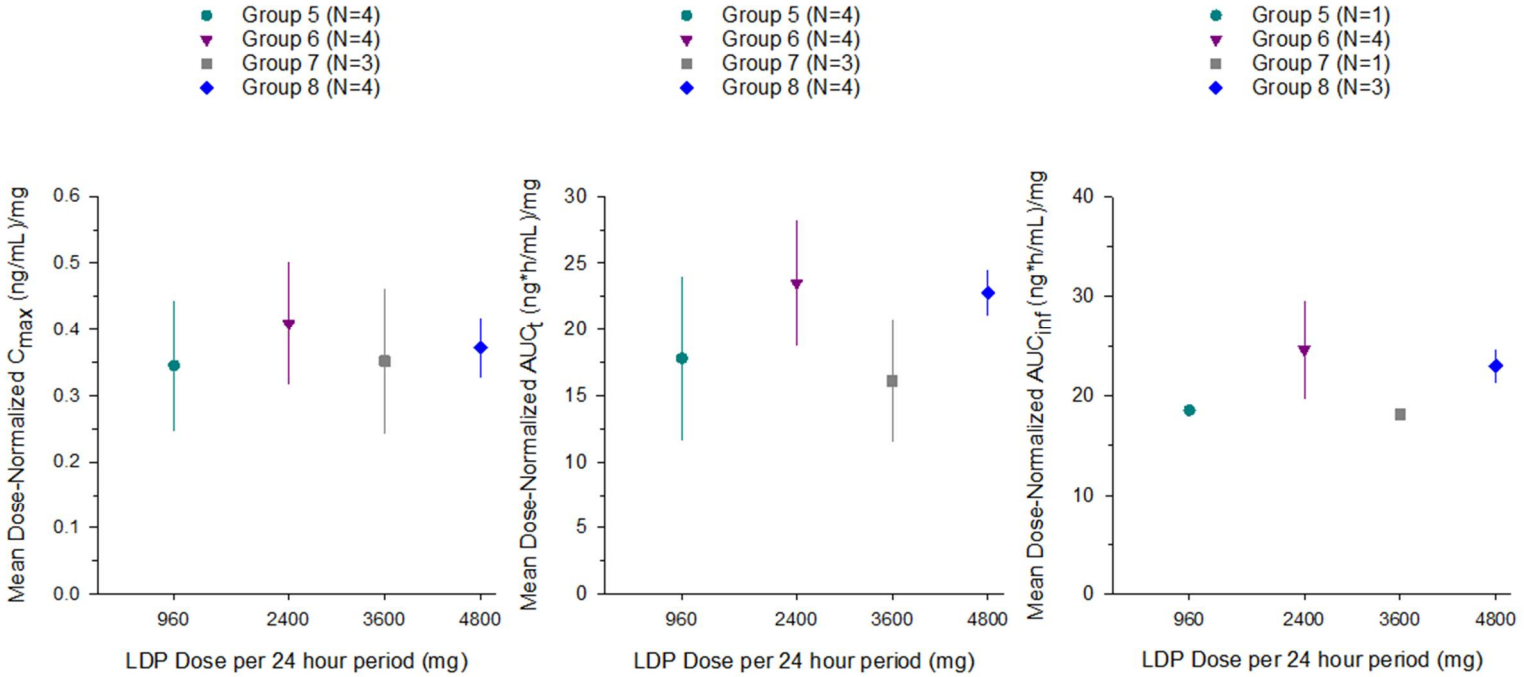
CSCI = continuous subcutaneous infusion

Note: ABBV-951 10/200 mg foscarbidopa/foslevodopa loading dose followed by 240/4800 mg foscarbidopa/foslevodopa per 24 hours for 72 hours.

パート 2 のデータを用いて統計解析により用量比例性を評価した。パート 2 で 4 つの異なる用量の ABBV-951 を注入投与したとき，安定した LD 及び CD の PK を示した。

用量で標準化した LD の曝露量（C_{max}，投与後最終定量可能時点までの AUC［AUC_t］及び AUC_{inf}）は，ホスレボドパの用量範囲（960 mg～4800 mg）にわたり類似したことから，LD の曝露量は検討した用量範囲において用量に比例して増加することが示された（図 2.7.2-9）。同様に，CD の曝露量も検討した用量範囲（ホスカルビドパ 48 mg～240 mg）でホスカルビドパの用量に比例した増加が示された。ホスカルビドパ/ホスレボドパ 48/960～240/4800 mg の用量範囲において，用量で標準化した LD 及び CD の曝露量に統計的に有意な差はなかった（*p* 値 ≥0.192）。

図 2.7.2-9. 用量で標準化したレボドパの曝露量（C_{max}，AUC_t 及び AUC_{inf}）と用量との関係性（平均値±SD，M15-738 試験パート 2）



AUC_t = area under the plasma concentration-time curve from time zero to time of last measurable concentration C_{max} = maximum observed plasma concentration; AUC_∞ = area under the plasma concentration-time curve from time zero to infinite time; LDP = foslevodopa; SD = standard deviation

Note: AUC_∞ could not be estimated for all subjects because of oral carbidopa/levodopa dosing during the intended washout period to control patient's symptoms.

2.7.2.2.3 M16-769 試験（日本人を含むアジア人を対象とした薬物動態試験）

目的：

異なる用量の ABBV-951 を単回 24 時間 CSCI したときの安全性，忍容性及び PK を評価し，また，日本人及び中国人（漢民族）の健康被験者の PK を白人の健康被験者の PK と比較する。

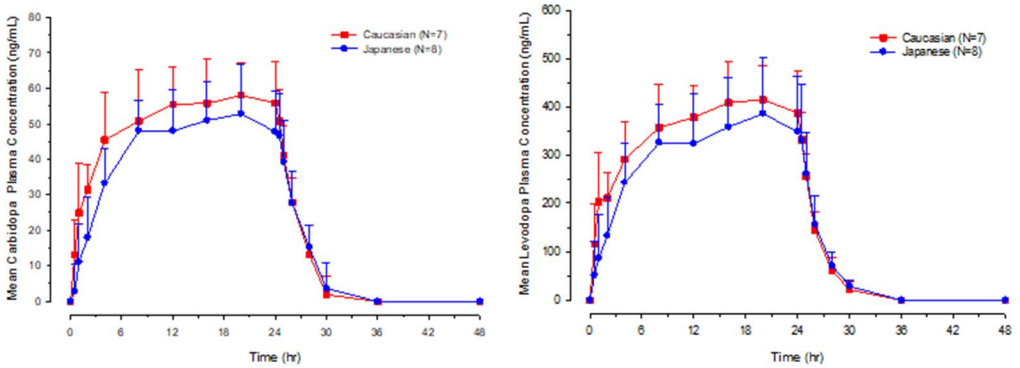
結果及び結論：

日本人に ABBV-951 を投与したときの CD 及び LD の曝露量（C_{max} 及び AUC）は，白人と同程度であり，中心値の比の点推定値及び 95%信頼区間の結果から日本人と白人の差はわずかであった（10%未満）（表 2.7.2-2）。異なる用量の ABBV-951 を日本人及び白人に CSCI したときのカルビドパ及びレボドパの血漿中濃度推移を図 2.7.2-10，図 2.7.2-11 及び図 2.7.2-12 に示す。

表 2.7.2-2. 日本人及び白人に ABBV-951 を投与したときのカルビドパ及びレボドパの曝露量の中心値の比の点推定値及び 95%信頼区間（M16-769 試験グループ 1，2 及び 3）

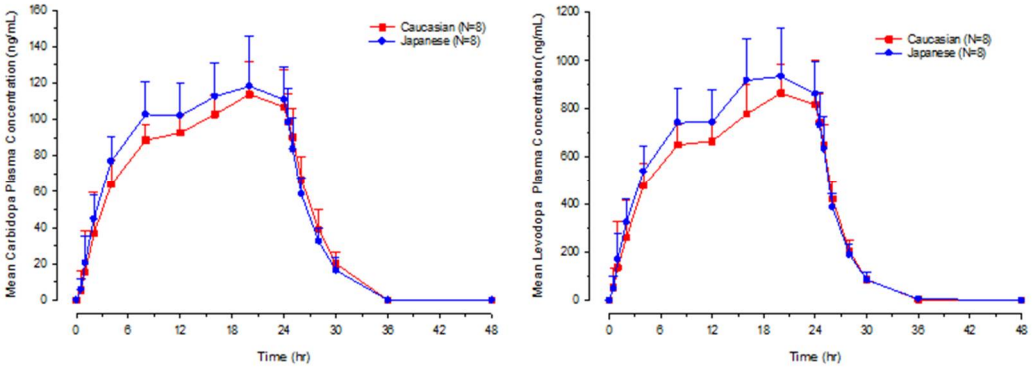
Ethnicity Test vs. Reference	Dose-Normalized Pharmacokinetic Parameter	Central Value		Ratio of Central Values	
		Test	Reference	Point Estimate	95% Confidence Interval
Carbidopa					
Japanese vs. Caucasian	C_{max}	2.30	2.54	0.905	0.828, 0.989
	AUC_t	49.4	54.0	0.914	0.842, 0.993
	AUC_{inf}	50.9	55.7	0.914	0.842, 0.991
	AUC_{0-16}	25.9	28.0	0.928	0.856, 1.01
	AUC_{0-24}	43.4	47.0	0.923	0.852, 1.00
Levodopa					
Japanese vs. Caucasian	C_{max}	0.883	0.944	0.935	0.863, 1.01
	AUC_t	18.4	19.6	0.935	0.866, 1.01
	AUC_{inf}	18.5	19.7	0.937	0.867, 1.01
	AUC_{0-16}	9.52	10.2	0.935	0.865, 1.01
	AUC_{0-24}	16.2	17.3	0.937	0.868, 1.01

図 2.7.2-10. 日本人及び白人に ABBV-951（ホスカルビドパ／ホスレボドパ 24/480 mg）を CSCI したときの血漿中カルビドパ及びレボドパ濃度－時間プロファイル（平均値+SD，M16-769 試験グループ 1）



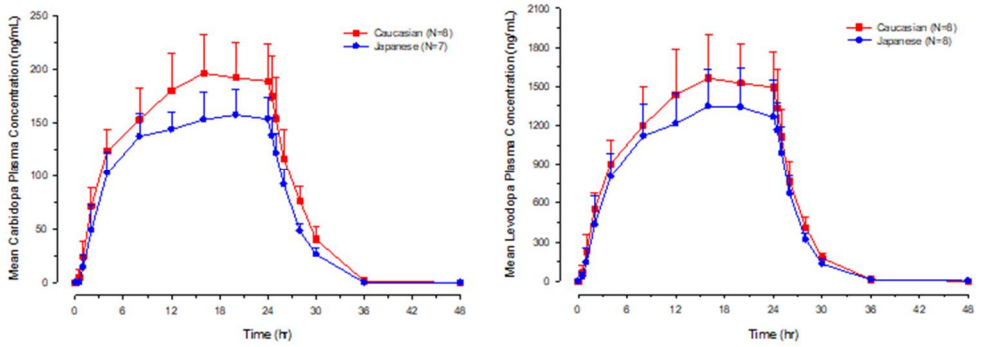
SD = standard deviation

図 2.7.2-11. 日本人及び白人に ABBV-951（ホスカルビドパ／ホスレボドパ 48/960 mg）を CSCI したときの血漿中カルビドパ及びレボドパ濃度－時間プロファイル（平均値+SD，M16-769 試験グループ 2）



SD = standard deviation

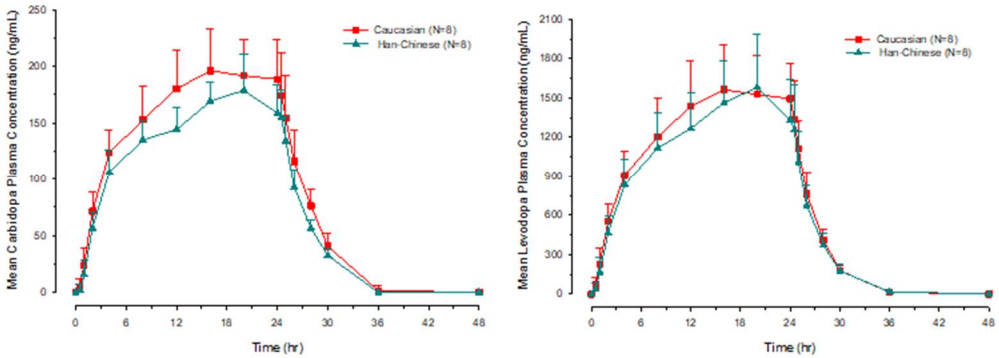
図 2.7.2-12. 日本人及び白人に ABBV-951（ホスカルビドパ／ホスレボドパ 72/1440 mg）を CSCI したときの血漿中カルビドパ及びレボドパ濃度－時間プロファイル（平均値+SD，M16-769 試験グループ 3）



SD = standard deviation

また，中国人（漢民族）に ABBV-951 を投与したときの CD 及び LD の曝露量（C_{max} 及び AUC）は白人と比べ同程度であり，中国人（漢民族）と白人の間で LD の PK パラメータに統計的な差は認められなかった（M16-769 試験総括報告書 Table 9［5.3.3.3-1 項］）。ABBV-951 を中国人（漢民族）及び白人に CSCI したときのカルビドパ及びレボドパの血漿中濃度推移を図 2.7.2-13 に示す。

図 2.7.2-13. 中国人（漢民族）及び白人に ABBV-951（ホスカルビドパ／ホスレボドパ 72/1440 mg）を CSCI したときの血漿中カルビドパ及びレボドパ濃度－時間プロファイル（平均値+SD，M16-769 試験グループ 3）



SD = standard deviation

2.7.2.2.4 薬物動態比較試験

2.7.2.2.4.1 M17-220 試験

目的：

ABBV-951 を 24 時間持続注入したとき（ABBV-951 投与レジメン）の LD の PK とデュオドーパを 16 時間持続注入後に夜間に経口 LD/CD 製剤を投与したとき（LCIG 投与レジメン）の LD の PK を比較する。

結果及び結論：

ABBV-951 投与レジメン及び LCIG 投与レジメンにおける LD の相対的バイオアベイラビリティを表 2.7.2-3 に示す。なお，相対的バイオアベイラビリティは，ABBV-951 投与レジメン及び LCIG 投与レジメンのいずれのレジメンも完了した被験者のデータのみを用いて解析した。

表 2.7.2-3. ABBV-951 投与レジメン（レジメン B）及び LCIG 投与レジメン（レジメン A）におけるレボドパの相対的バイオアベイラビリティと 90%信頼区間（M17-220 試験）

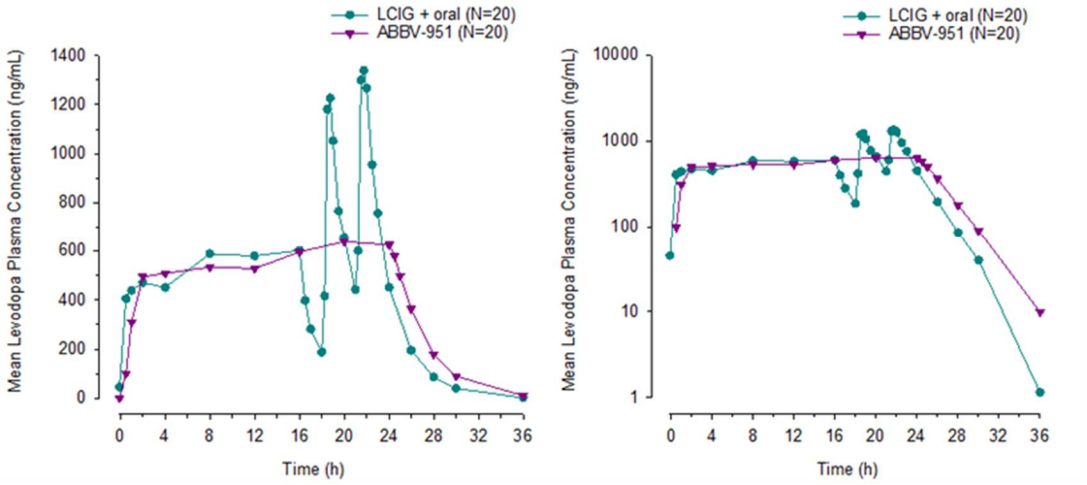
Regimens Test vs. Reference	Pharmacokinetic Parameter	Central Value		Relative Bioavailability	
		Test	Reference	Point Estimate	90% Confidence Interval
Regimen B vs. Regimen A	$C_{max,0-16}$	606	656	0.923	0.873, 0.975
	AUC_{0-16}	7810	8220	0.951	0.893, 1.012
	AUC_{inf}	14900	14700	1.009	0.969, 1.049

Regimen A: Levodopa/carbidopa intestinal gel (12.5/50 mg carbidopa/levodopa loading dose followed by 87.5/350 mg carbidopa/levodopa over 16 hours followed by two 25/100 mg carbidopa/levodopa oral doses at 18 and 21 hours after the start of infusion). Levodopa/carbidopa intestinal gel was delivered via a portable infusion pump through a nasojejunal tube.

Regimen B: ABBV-951 (4/80 mg foscarbidopa/foslevodopa loading dose followed by 35/700 mg foscarbidopa/foslevodopa over 24 hours). ABBV-951 was delivered via a portable infusion pump subcutaneous into the abdomen.

ABBV-951 を 24 時間持続注入したとき（ABBV-951 投与レジメン）及び LCIG を 16 時間持続注入後に夜間に経口 LD/CD 製剤を投与したとき（LCIG 投与レジメン）の LD の血漿中濃度推移を図 2.7.2-14 に示す。ABBV-951 を投与したとき，血漿中 LD 濃度は速やかに定常状態に達し，注入期間を通して維持された。ホスカルビドパ／ホスレボドパ 35/700 mg の ABBV-951 を 24 時間かけて注入投与したとき，LD の投与後 0～16 時間までの C_{max}（$C_{max,0-16}$）及び AUC（AUC_{0-16}）は，CD/LD 87.5/350 mg の LCIG を 16 時間かけて注入投与したときと同程度であった。また ABBV-951 投与レジメンでの LD の AUC_{inf} は，CD/LD 87.5/350 mg の LCIG を 16 時間かけて注入投与した後，投与開始後 18 及び 21 時間後に CD/LD 25/100 mg を経口投与したときと同程度であった。各投与レジメンでの LD の PK パラメータの比の点推定値及び 90%信頼区間は 0.8～1.25 の範囲内であった（表 2.7.2-3）。

図 2.7.2-14. ABBV-951 を 24 時間持続注入したとき及び LCIG を 16 時間持続注入後に夜間に経口 LD/CD 製剤を投与したときのレボドパの濃度－時間プロファイル（平均値，線形及び片対数，M17-220 試験）



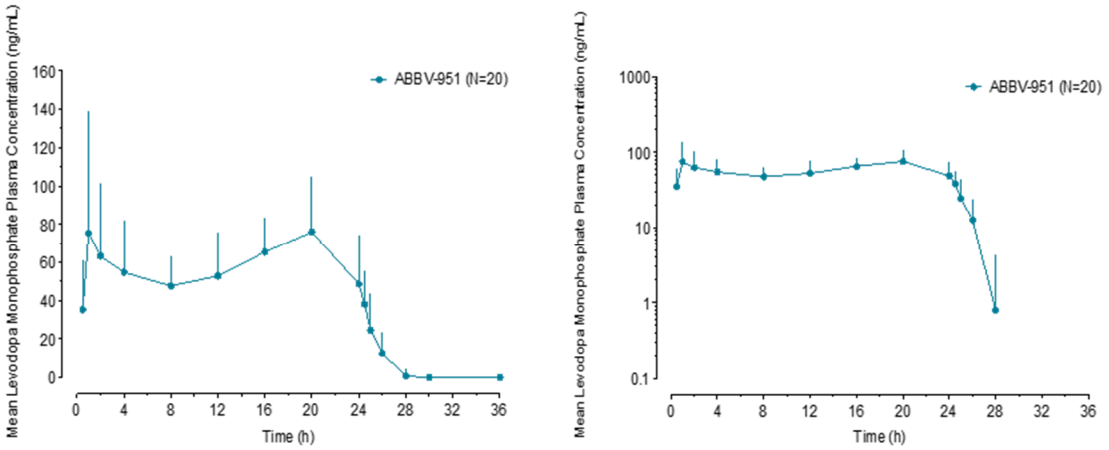
LCIG + oral: 12.5/50 mg CD/LD loading dose followed by 87.5/350 mg CD/LD over 16 hours followed by two 25/100 mg CD/LD oral doses at 18 and 21 hours after the start of infusion

ABBV-951: 4/80 mg CDP/LDP loading dose followed by 35/700 mg CDP/LDP over 24 hours

ABBV-951 投与レジメンにおける LD の DFL は，LCIG 投与レジメンと比べ小さかった。ABBV-951 投与レジメン及び LCIG 投与レジメンでの投与後 2～16 時間の LD の DFL（中心値）はそれぞれ 0.262 及び 0.404 であり，有意な差ではなかったものの ABBV-951 投与レジメンで小さかった（*p* 値=0.064）。ABBV-951 投与レジメン及び LCIG 投与レジメンでの投与後 2～24 時間の LD の DFL（中心値）はそれぞれ 0.359 及び 2.906 であり，ABBV-951 投与レジメンで有意に小さかった（*p* 値<0.001）。

ABBV-951 投与レジメンにおけるホスレボドパの曝露量は LD と比べ低かった（図 2.7.2-14 及び図 2.7.2-15）。ABBV-951 注入終了後にホスレボドパ濃度は急速に減少したことから，ホスレボドパは速やかに活性体である LD に変換されることが示唆された。また，ABBV-951 投与レジメンにおけるホスカルビドパの曝露量は CD と比べ低く，ABBV-951 注入中及び注入終了後のいずれにおいてもほとんどの時点でホスカルビドパ濃度は検出限界である 3 ng/mL 未満であった。

図 2.7.2-15. ABBV-951 を投与したときの血漿中ホスレボドパ濃度－時間プロファイル（平均値+SD，線形及び片対数，M17-220 試験）



ABBV-951 = 4/80 mg CDP/LDP loading dose followed by foscarbidopa/foslevodopa 35/700 mg ABBV-951

2.7.2.2.4.2 M18-764 試験

目的：

本試験の目的を以下に示す。

- 健康成人に ABBV-951 又は LCIG を 16 時間注入投与したときの CD 及び LD のバイオアベイラビリティを比較する。
- 健康成人に ABBV-951 を 24 時間注入投与，又は LCIG を 16 時間注入投与後に夜間に CD/LD を 2 回経口投与したときの CD 及び LD のバイオアベイラビリティを比較する。
- 低用量の ABBV-951 を 24 時間注入投与，又は LCIG を 16 時間注入投与後に夜間に CD/LD を 2 回経口投与したときの CD 及び LD のバイオアベイラビリティを比較する。

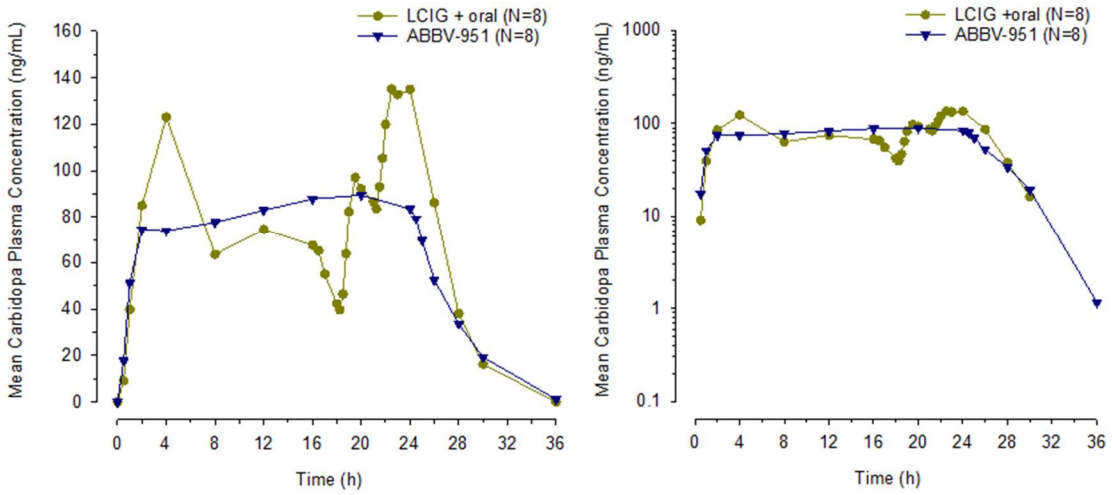
結果及び結論：

ホスカルビドパ/ホスレボドパ 37.5/750 mg の ABBV-951 を 16 時間かけて注入投与したとき（レジメン B）の CD 及び LD の曝露量（$AUC_{0\text{-}16}$，AUC_t 及び AUC_{inf}）は，CD/LD 125/500 mg の LCIG を 16 時間かけて注入投与したとき（レジメン A）と比べ，19%～37%高かった。

ホスカルビドパ/ホスレボドパ 42.5/850 mg の ABBV-951 を 24 時間かけて注入投与したとき（レジメン D）の CD 及び LD の曝露量（$AUC_{0\text{-}16}$，投与後 0～24 時間までの AUC［$AUC_{0\text{-}24}$］，AUC_t 及び AUC_{inf}）は，CD/LD 87.5/350 mg の LCIG を 16 時間かけて注入投与後，25/100 mg の CD/LD を投与開始後 18 時間及び 21 時間に経口投与したとき（レジメン C）と比べ，21%～46%高かった。

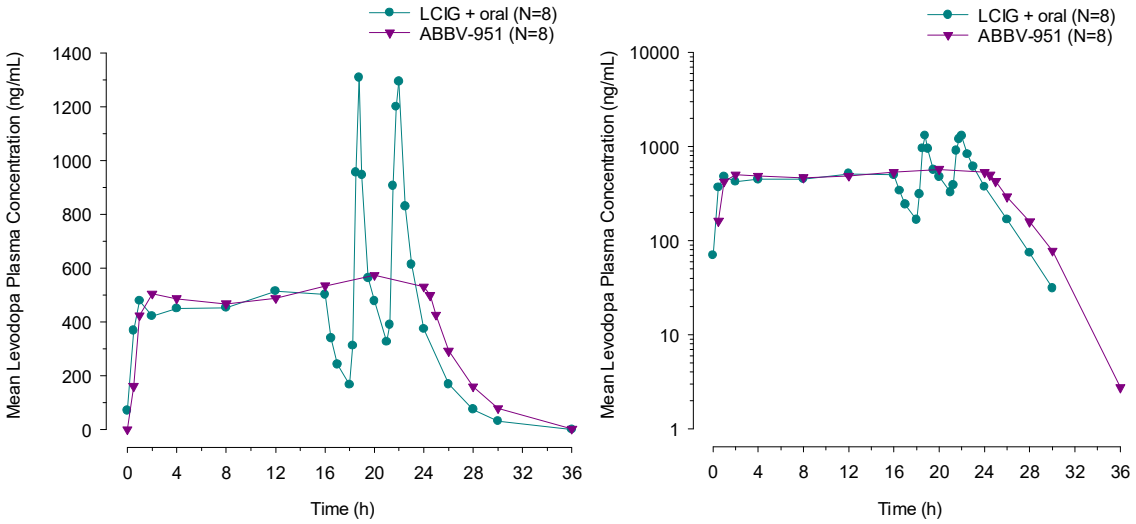
ホスカルビドパ/ホスレボドパ 35/700 mg の ABBV-951 を 24 時間かけて注入投与したとき（レジメン F）の CD の $C_{max,0-16}$ は，CD/LD 87.5/350 mg の LCIG を 16 時間かけて注入投与後，CD/LD 25/100 mg を投与開始後 18 時間及び 21 時間に経口投与したとき（レジメン E）と比べ，低かった。CD の AUC_{0-16}，AUC_{0-24}，AUC_t 及び AUC_{inf}，並びに，LD の $C_{max,0-16}$，AUC_{0-16}，AUC_{0-24}，AUC_t 及び AUC_{inf} の中心値の比の点推定値は 1.00 に近く，90%信頼区間は狭かった（図 2.7.2-16 及び図 2.7.2-17，M18-764 試験総括報告書 Table 11［5.3.1.2-2 項］）。

図 2.7.2-16. ABBV-951 を 24 時間かけて注入投与したとき及び LCIG を 16 時間かけて注入投与後 CD/LD を 2 回経口投与したときの血漿中カルビドパ濃度ー時間プロファイル（平均値，線形及び片対数，M18-764 試験パート 3）



LCIG = levodopa/carbidopa intestinal gel
LCIG + oral = CD/LD 12.5/50 mg loading dose followed by CD/LD 87.5/350 mg LCIG + two 25/100 mg oral doses
ABBV-951 = foscarbidopa/foslevodopa 4/80 mg loading dose followed by foscarbidopa/foslevodopa 35/700 mg ABBV-951

図 2.7.2-17. ABBV-951 を 24 時間かけて注入投与したとき及び LCIG を 16 時間かけて注入投与後 CD/LD を 2 回経口投与したときの血漿中レボドパ濃度－時間プロファイル（平均値，線形及び片対数，M18-764 試験パート 3）



LCIG = levodopa/carbidopa intestinal gel
LCIG + oral = CD/LD 12.5/50 mg loading dose followed by CD/LD 87.5/350 mg LCIG + two 25/100 mg oral doses
ABBV-951 = foscarbidopa/foslevodopa 4/80 mg loading dose followed by foscarbidopa/foslevodopa 35/700 mg ABBV-951

2.7.2.3 全試験を通しての結果の比較と解析

健康被験者に ABBV-951 を持続注入したときと，LCIG を持続注入後に夜間に経口 LD/CD 製剤を投与したときの PK を比較した（M17-220 試験［2.7.2.2.4.1 項］）。ABBV-951 を投与したとき，血漿中 LD 濃度は速やかに定常状態に達し，注入期間を通して維持された。ABBV-951 を 24 時間持続注入したとき（ABBV-951 投与レジメン）及び LCIG を 16 時間持続注入後に夜間に経口 LD/CD 製剤を投与したとき（LCIG 投与レジメン）の LD の血漿中濃度推移を図 2.7.2-14 に示す。2 つの投与レジメンから得られた LD の PK パラメータ（$C_{max,0-16}$，AUC_{0-16} 及び AUC_{inf}）は同程度であり，これらのパラメータの比の点推定値及び 90%信頼区間は 0.8～1.25 の範囲内であった（表 2.7.2-3）。

M17-220 試験では血漿中 LD 濃度を速やかに定常状態に到達させるため，LCIG 投与レジメンでは LCIG を用いて，また，ABBV-951 投与レジメンでは ABBV-951 を用いて負荷投与した。LCIG 投与レジメン及び ABBV-951 投与レジメンにおける LD の投与後 0～4 時間までの AUC（AUC_{0-4}）の幾何平均値は，それぞれ 1510 及び 1530 ng•hr/mL であった。この結果から，LCIG 及び ABBV-951 のいずれの負荷投与においても血漿中 LD 濃度は速やかに定常状態に達し，LD の PK は類似していた。

同様に，LCIG 投与レジメン及び ABBV-951 投与レジメンにおける CD の曝露量も類似しており，$AUC_{0\text{-}16}$ の幾何平均値はそれぞれ 1080 及び 1120 ng•hr/mL，AUC_{inf} の幾何平均値はそれぞれ 2370 及び 2170 ng•hr/mL であった。

M17-220 試験における ABBV-951 及び LCIG（デュオドーパ）の持続注入速度は，それぞれ 0.12 及び 1.1 mL/hour であり，ABBV-951 では LCIG の約 10%の注入速度で同程度の LD の曝露量が得られた。

M17-220 試験において，LCIG 投与レジメンでは 16 時間までに 100/400 mg の CD/LD が投与され（負荷投与及び持続注入），ABBV-951 投与レジメンでは 16 時間までに 27/547 mg のホスカルビドパ／ホスレボドパが投与された（負荷投与及び持続注入）。LCIG 投与レジメンにおいて 16 時間までの LD 投与量が 400 mg であるのに対し，ABBV-951 投与レジメンにおける 16 時間までの LD 投与量は 388 mg であった（分子量を用いてホスレボドパ投与量から換算）。いずれのレジメンでの $AUC_{0\text{-}16}$ も同程度であったことから，LCIG 及び ABBV-951 での LD のバイオアベイラビリティは類似していることが示された。

2.7.2.3.1 薬物動態特性

2.7.2.3.1.1 吸収

ABBV-951 は皮下腔に直接投与された後，速やかに吸収され，LD 及び CD に変換される。健康被験者を対象とした第 I 相試験では，最初の血漿中濃度測定時点（投与後 30 分）で LD 及び CD は検出された。また，ABBV-951 を負荷投与後に持続注入したとき，大部分の被験者で 2 時間以内に血漿中 LD 濃度が定常状態に到達した（M15-733 試験グループ 4，2.7.2.2.1 項）。

異なる SC 投与部位からの ABBV-951 の吸収を検討するため，クロスオーバーデザインを用いて健康被験者に ABBV-951 を腹部，腕及び大腿部から投与したところ，3 つの投与部位における LD 及び CD の曝露量は類似していた（M15-733 試験グループ 3，2.7.2.2.1 項）。このことから，これらの異なる投与部位においても ABBV-951 の吸収は同程度であることが示された。

ABBV-951 は CSCI されるため，消化管を経由しない。そのため，ABBV-951 の吸収，並びに LD 及び CD の全身曝露量に対し，食事の影響はほとんどないと考えられる。

2.7.2.3.1.2 分布

プロドラッグ体であるホスレボドパ及びホスカルビドパは，アルカリホスファターゼによりそれぞれ LD 及び CD に速やかに変換されるため，循環血中から速やかに消失する。血漿中におけるホスレボドパ及びホスカルビドパのタンパク非結合率は 2.6.4.4 項に記載した。

LD の分布容積はやや低く，血漿タンパク結合率は約 10～30%と非常に低い。CD の血漿タンパクへの結合率は約 36%である。LD は大型中性アミノ酸担体を介して脳内に移行するが，CD は血液脳関門を通過しない（デュオドーパ申請時 CTD2.6.4.4 項）。

2.7.2.3.1.3 代謝及び排泄

プロドラッグ体であるホスレボドパ及びホスカルビドパは，アルカリホスファターゼによりそれぞれ LD 及び CD に速やかに変換されるため，循環血中から速やかに消失する。M17-220 試験において，ABBV-951 注入投与終了後 4 時間以降で血漿中ホスレボドパは検出されず（図 2.7.2-15），また，血漿中ホスカルビドパは大部分の検体で検出限界未満であった。

LD 及び CD の代謝及び排泄はこれまでに記述されている（デュオドーパ申請時 CTD2.6.4.5, 2.6.4.6 項）。

2.7.2.3.2 内因性要因の影響

2.7.2.3.2.1 年齢の影響

ABBV-951 注入後の LD の PK に対する年齢の影響の評価は実施していない。健康被験者を対象としたすべての第 I 相試験は，進行期 PD 患者集団の年齢層とおおむね一致する 45～75 歳の被験者を対象として実施した。LCIG 製剤でこれまでに評価された母集団 PK モデルの結果では，年齢は LD のクリアランスに対し統計的有意に近い程度の影響を示した [7]。また，Contin らの報告によると，65 歳未満（21 例）と 65 歳超（19 例）の PD 患者に LD を経口投与したときの PK を比較したところ，高年齢群で AUC は 28%高く，半減期は 24%長く，また，見かけの経口クリアランスは 24%低かった [5]。

ABBV-951 は LD 治療未経験の進行期 PD 患者への治療を対象とせず，ABBV-951 の開始用量は各患者個別のこれまでの経口 LD 治療レジメンを基に設定する（2.7.2.3.5 項）。したがって，LD のクリアランスに対する年齢の影響は，各患者の経口 LD 治療レジメンに既に反映されていると考えられる。また，運動症状を最適にコントロールするため，ABBV-951 の投与開始後に個々の患者で投与速度が調節される。

2.7.2.3.2.2 体重の影響

ABBV-951 注入後の LD の PK に対する体重の影響の評価は実施していない。LCIG 製剤でこれまでに評価された母集団 PK モデルでは，分布容積に対し体重は有意な共変量であった（$p < 0.005$）[7]。

ABBV-951 は，LD 治療未経験の進行期 PD 患者への治療を対象とせず，ABBV-951 の開始用量は各患者個別のこれまでの経口 LD 治療レジメンを基に設定する（2.7.2.3.5 項）。したがって，LD の曝露量に対する体重の影響は，各患者の経口 LD 治療レジメンに既に反映されていると考えられる。また，運動症状を最適にコントロールするため，ABBV-951 の投与開始後に個々の患者で投与速度が調節される。

2.7.2.3.2.3 被験者対象集団の影響（健康被験者 vs.パーキンソン病患者）

M15-733 試験グループ 4 の健康被験者及び M15-738 試験グループ 5 の PD 患者では，同じ製剤組成の ABBV-951 が 72 時間にわたりそれぞれ投与された。すなわち，200/10 mg のホスレボドパ／ホスカルビドパを負荷投与後，24 時間あたり 960/48 mg のホスレボドパ／ホスカルビドパを投与された。定常状態における LD 及び CD の曝露量は，健康被験者と PD 患者のいずれにおいてもおおむね同程度であったことから，健康被験者と PD 患者に PK の差はほとんどないことが示された。

2.7.2.3.2.4 人種の影響

第 I 相 M16-769 試験で，日本人及び中国人（漢民族）の健康被験者に ABBV-951 を注入したときの PK を評価した（2.7.2.2.3 項）。ABBV-951 を投与したときの日本人における CD 及び LD の曝露量（C_{max} 及び AUC）は白人と比べ同程度であり，中心値の比の点推定値及び 95%信頼区間の結果では日本人と白人の曝露量の差はわずかであった（10%未満）。また，中国人における CD 及び LD の曝露量（C_{max} 及び AUC）も白人と比べ同程度であり，中心値の比の点推定値及び 95%信頼区間の結果では中国人と白人の曝露量の差はわずかであった（14%未満）。

2.7.2.3.2.5 性別の影響

ABBV-951 注入後の PK に対する性別の影響の評価は実施していない。LCIG 製剤でこれまでに評価された母集団 PK モデルの結果では，性別は LD のクリアランスに対し統計的に有意な影響を示さなかった [7]。LD の PK に対する性別の影響についてはこれまでに複数の研究で評価されている。Kompoliti らの研究では，100/25 mg の LD/CD を単回投与したとき，女性 PD 患者（14 例）における体重で標準化した LD の AUC は，男性 PD 患者（12 例）と比べて 80%高かった [8]。しかしながら，この LD 曝露量における見かけの差は，用量ではなく AUC を体重で標準化したことにより過大評価された可能性が高い [9]。また，Kompoliti らの同研究では，統一パーキンソン病評価尺度（以下「UPDRS」）パート III 及び運動課題所用時間測定により評価した臨床効果において，見かけの LD の曝露量の差に伴う顕著な性差は認められなかった [8]。Martinelli らは，115 例（男性 67 例及び女性 49 例）の PD 患者に標準的な LD／ベンセラジド（100/25 mg）を経口投与したとき，LD の用量で標準化した AUC 及びジスキネジアの発現における性差について検討した [10]。その結果，LD の AUC における性差はわずかであり（女性における用量で標準化した AUC は，男性と比べて約 13%高い），ジスキネジアの発現割合に性差は認められなかった。更に Chen らの研究では，PD 患者（男性 7 例及び女性 18 例）に徐放性 LD/CD 製剤を投与したとき，体重で標準化した用量で補正した LD の AUC に顕著な性差は認められなかった [9]。

以上より，LD の曝露量において臨床的に意味のある性差はないと考えられる。

2.7.2.3.2.6 肝機能及び腎機能障害の影響

肝機能障害及び腎機能障害を有する被験者における ABBV-951 の PK は確立していない。

2.7.2.3.3 外因性要因の影響

2.7.2.3.3.1 食事の影響

ABBV-951 を用いた食事の影響を評価する試験は実施していない。ABBV-951 は SC 投与であり，胃腸を通過しない。そのため，食物の摂取は ABBV-951 の吸収又は LD や CD の全身曝露量に影響を及ぼさないと考えられる。

食物性タンパク質と共に LD を経口投与したとき，定常状態における血漿中 LD 濃度は変化しないにも関わらず，効果が減弱することがこれまでに報告されている [11,12]。そのため，タンパク質豊富な食事が血液脳関門における LD の輸送を競合阻害することで LD による治療効果が減弱する可能性がある。ABBV-951 を用いた血液脳関門における LD の輸送に対する食事の影響の評価は実施していない。

2.7.2.3.3.2 薬物動態的薬物相互作用

ホスレボドパ及びホスカルビドパに臨床的に意味のある薬物相互作用は予想されない。ホスレボドパ及びホスカルビドパは生体内で速やかに LD 及び CD に変換される。そのため，ABBV-951 に関する薬物相互作用は，LD/CD 製剤であるデュオドーパにおいてこれまでに特定されているものと同様と考えられる。詳細は 2.6.4.7 項に記載した。

2.7.2.3.4 QT 評価

LD 及び CD は 50 年以上前より確立された PD の治療薬である [13]。現在市販されているデュオドーパを含む様々な LD/CD 製剤において，QT 間隔延長に関する安全性の懸念は特定されていない。ABBV-951 の非臨床及び臨床成績から心臓安全性に対するリスクは特定されなかった。この結果は LD/CD 製剤でこれまでに確立された安全性プロファイルと同様であった。

GLP 適合 *in vitro* ヒト遅延整流性カリウムイオンチャネル遺伝子（以下「hERG」）試験で QT 間隔延長の可能性を評価した結果，ホスレボドパ（8.3 µg/mL）及びホスカルビドパ（9.2 µg/mL）はいずれも hERG に対し明らかな影響を示さなかった。また，溶解度に近い濃度の LD（6.75 µg/mL）及び CD（5.42 µg/mL）も hERG に対し明らかな影響を示さなかった（2.6.2.4 項）。PD 患者を対象とした M15-741 試験では最高用量となるホスレボドパ／ホスカルビドパ 6000/300 mg（24 時間あたり）が投与され，この最高用量で予測されるホスレボドパ及びホスカルビドパの C_{max} と hERG 試験で用いた濃度とのマージンは，それぞれ 21 倍及び 484 倍であった。同様に，最高用量で予測される LD 及び CD の C_{max} と hERG 試験で用いた濃度とのマージンは，それぞれ 1.2 倍及び 8.0 倍であった。

ABBV-951 の心臓安全性を評価するため，ホスレボドパ及びホスカルビドパの臨床最大推定曝露量を超える用量を用いた非臨床安全性薬理試験を実施した。麻酔イヌ及び覚醒サルにおける安全性薬理試験において，ABBV-951 が QT 延長を引き起こすことは示唆されなかった（2.6.2.4 項）。

以上より，高濃度のホスレボドパ及びホスカルビドパにおいても hERG 及び安全性薬理に影響を及ぼさなかったことから，他の LD/CD 製剤と同様に ABBV-951 による QT 間隔延長のリスクは低いと考えられる。

2.7.2.3.4.1 パーキンソン病患者を対象とした第 I 相試験における QT 間隔延長評価

PD 患者の PK を評価した M15-738 試験では，3 回の心電図（以下「ECG」）データを用いて，ABBV-951 注入投与後の Fridericia 補正式による補正 QT 間隔（以下「QTcF」）における曝露－反応解析を実施した。PD 患者を対象とした本試験は，患者個別の経口 LD 製剤を投与される 24 時間の LD/CD 経口投与期，及び，ABBV-951 が 72 時間 CSCI される ABBV-951 注入投与期があり，いずれの期間においても PK 評価用検体の頻回採取及び 3 回の ECG 測定を実施した。以下の項目については，日米 EU 医薬品規制調和国際会議（ICH）E14「非抗不整脈薬における QT/QTc 間隔の延長と催不整脈作用の潜在的可能性に関する臨床評価」で推奨されているものの，PD 患者に対する制限，並びに，LD 及び CD の薬力学的特性を考慮し，M15-738 試験では実施しなかった。

- プラセボ対照期：
  - PD 患者に非常に負荷のかかる運動症状を引き起こし，また，その結果生じる振戦又はオフ時間により，3 回の心電図測定及び採血に支障をきたす可能性がある。
  - 食事による ECG 測定値への影響を避けるため，通常 ECG 測定は食事を考慮して規定した時間に実施するが，投薬中止期間では，運動症状により食事がより困難となる可能性がある。
  - 倫理的な理由により，ウォッシュアウト期間が治験審査委員会に承認されない可能性がある。
  - 患者の登録が困難となる。
- 治療用量を超える投与期間：
  - 治療用量を超える LD の用量では，重度のジスキネジア及び悪心を引き起こす。
- 陽性対照期：
  - モキシフロキサシンは QT 延長を引き起こすことが知られており，PD 患者のような高年齢層に対してはよりリスクの高い薬物である。また，陽性対照では，通常，その他の薬剤を投与しないため，プラセボ対照期と同様の PD 患者に対する問題が生じる。

以上の点より，実用的及び倫理的な観点を考慮し，一般的な thorough QT 試験で実施される QT 延長の評価は困難であった。そこで，M15-738 試験では薬物濃度と対応した 3 回の ECG を用いて QT に対する ABBV-951 の影響を評価した（M15-738 試験総括報告書 12.4.3 項［5.3.3.2-1 項］）。

ABBV-951 の注入開始前後に観察された QTcF 間隔の最大値が高値のカテゴリーに分類された被験者の例数及び割合を表 2.7.2-4 に示す。ABBV-951 の注入開始前では 4 例の被験者に高値の QTcF 値が認められ，ABBV-951 の注入開始後では 3 例の被験者に高値の QTcF 値が認められた。これらの値は，治験責任医師又は AbbVie のメディカルモニターにより臨床的に重大と判断されず，有害事象又は試験の中止に関連しなかった。

表 2.7.2-4. ABBV-951 の注入開始前後における QTcF 値が高値のカテゴリーに分類された被験者の例数（例数／全例数，M15-738 試験）

QTcF Interval (msec)	Before ABBV-951 Initiation	After ABBV-951 Initiation
> 450 and ≤ 480	2/26	2/26
> 480 and ≤ 500	1/26	1/26
> 500	1/26	0/26

本試験の PD 患者における QTcF の解析結果から，LD/CD 経口投与期及び ABBV-951 投与期の全体の平均 QTcF は，それぞれ 422 msec 及び 421 msec と類似していた。

M15-738 試験では QTcF を評価するため，LD 濃度と QTcF 値の関係性を検討した Analysis 1，LD 濃度と LC/CD 経口投与期からの QTcF 変化量の関係性を検討した Analysis 2，及び LD 濃度とベースラインからの QTcF 変化量の関係性を検討した Analysis 3 の 3 つの曝露－反応解析を実施した。3 つの曝露－反応解析の概要を表 2.7.2-7 に示す。

Analysis 1 では，LD 濃度（及び CD 濃度）と QTcF 値の関係性を評価した。初期モデルでは，施設，時間，LD 濃度，CD 濃度及び LD 及び CD 濃度の積が含まれた。SAS procedure PROC MIXED を用いてモデルをフィッティングして重要でないと特定された項目を順次モデルから省いた結果，最終モデルでは LD 濃度のみが含まれた。QTcF に及ぼす影響を LD 濃度の線形関数により推定した。線形曝露－反応解析を用いた QTcF における影響の統計学的評価の結果を表 2.7.2-5 に示す。QTcF は LD 濃度と有意な関係性が認められた（p 値=0.003）。LD の C_{max}（6000 ng/mL：1 日量としてホスレボドパ／ホスカルビドパ 4800/240 mg の用量で ABBV-951 を投与したとき）における QTcF への影響の推定値は 17.05 msec であり，95%信頼上限は 26.16 msec であった。

表 2.7.2-5. 血漿中レボドパ濃度と QTcF 値の関係性（Analysis 1，M15-738 試験）

Analyte	Label	Estimate	95% One-Sided Upper Confidence Interval	Pr > |t|
Levodopa	Intercept	419.22	--	--
	Slope of Levodopa concentration	0.0028	--	0.003
	QTcF Effect at C_{max}[a]	17.05	26.16	--

a. Levodopa C_{max} = 6000 ng/mL for dose of 240 mg/4800 mg carbidopa monophosphate/levodopa monophosphate per 24 hours.

Analysis 2 では，LD/CD 経口投与期で対応する時間におけるベースラインで補正を行い，ABBV-951 注入開始後の QTcF 変化量を評価した。線形混合効果回帰分析を用いて曝露－反応解析を実施し，LD の曝露量と QTcF 変化量の関係の傾きを 95%信頼区間とともに推定した。この解析では，本試験における全血漿中 LD 濃度時間推移及び 3 回の ECG 測定値を用いた。その結果，血漿中 LD 濃度の影響を示す傾きのモデル推定値（母集団）は 0.138 msec•mL/µg で，その 95%信頼区間は-1.24～1.51 msec•mL/µg であり，統計的に有意な影響は示されなかった（表 2.7.2-6）。また，この傾きを用いた場合，予測される LD の最大曝露量（C_{max}）においても QTcF 変化量の片側 95%信頼上限は閾値である 10 msec を下回った。

表 2.7.2-6. 血漿中レボドパ濃度と LD/CD 経口投与期からの QTcF 変化量の関係性：曝露－反応解析の最終モデルにおけるパラメータ推定値及び誤差（Analysis 2，M15-738 試験）

Parameter	Population Estimate (SEE)	%RSE	95% CI
Slope (msec•mL/µg)	0.138 (0.701)	507	–1.24, 1.51
IIV of Slope (Additive)	2.54 (NA)	NA	NA
RUV (Additive)	10.0 (NA)	NA	NA

SEE = Standard error of estimate; RSE = Relative standard error; CI = Confidence interval; IIV = Inter-individual variability; RUV = Residual unexplained variability; NA = Not applicable

Analysis 3 では，ベースライン（0 時間：ABBV-951 投与開始時）からの QTcF 変化量と薬物濃度（LD 及び/又は CD）との関係性を検討するため，QTcF 変化量を応答変数とした線形混合効果モデルを用いて解析した。初期モデルでは，LD 濃度，CD 濃度及び施設を固定効果として，症例をランダム効果とした。各症例の実測値についての共分散行列構造は複合対称とした。モデルからの変数の除去は順次行い，施設の効果は重要性が認められなかった場合にモデルから除くこととし，CD 濃度又は LD 濃度の効果は，重要でないと特定された場合（回帰係数の推定値が有意水準 0.20 で有意でなかった場合），モデルから除くこととした。最終モデルでは，説明変数は LD 濃度のみであり，QTcF 変化量に及ぼす影響は LD 濃度の線形関数として推定した。

最終モデルのフレームワークでは，高曝露量（最大 6000 ng/mL）での LD 濃度の効果の点推定値及び 95%信頼上限を評価した。LD 濃度の回帰係数について有意水準 0.050 で両側仮説検定を実施した。

日内変動を考慮し，ベースライン時の ECG 測定時刻から 2 時間以内にベースライン後の ECG を測定したデータポイントのみを本解析のデータセットに含めた。また，食事の影響を考慮し，ベースライン時及びベースライン後の ECG データはいずれも朝食前に実施することと規定した。さらに，ABBV-951 注入終了後の ECG データは，ABBV-951 注入終了後から ECG 測定までに LD/CD 経口製剤が投与されていないデータに限り，データセットに含めた。本解析のデータセットでは，被験者 16 名から得られた 47 のベースライン（0 時間）からの QTcF 変化量データが含まれた。

ベースラインからの QTcF 変化量に対する LD 濃度の回帰係数の推定値は 0.0006（標準誤差は 0.0014）で，有意な関係性は認められなかった（$p = 0.647$）。また，ベースラインからの QTcF 変化量に対する 6000 ng/mL の LD 濃度の効果の点推定値は 3.8 msec，95%信頼上限は 17.63 msec であった。

上述したように M15-738 試験では，Analysis 1，Analysis 2 及び Analysis 3 の 3 つの曝露－反応解析を用いて ABBV-951 の QT 間隔に及ぼす影響を評価した。説明変数はいずれの解析でも LD 濃度であったが，応答変数は各解析で異なり，Analysis 1 では QTcF 値，Analysis 2 では LD/CD 経口投与期からの QTcF 変化量，また，Analysis 3 ではベースラインからの QTcF 変化量をそれぞれ用いた。3 つの曝露－反応解析の概要を表 2.7.2-7 に示す。応答変数に QTcF 値を用いた Analysis 1 では，LD 濃度との間に有意な関係が認められた一方，応答変数に LD/CD 経口投与期からの QTcF 変化量を用いた Analysis 2 及びベースラインからの QTcF 変化量を用いた Analysis 3 では，有意な関係は認められなかった。Analysis 2 は取得した 170 の ECG 測定値のうち 98%に当たる 166 の測定値を含む，最も多くの ECG 測定値を用いた解析であり（表 2.7.2-7），また，Analysis 3 は M15-738 試験の治験実施計画書に予定していた解析であった。本曝露－反応解析の目的は，パーキンソン病患者が ABBV-951 の治療を開始した際に QTcF の変化が生じる可能性を評価することであり，各解析の背景から得られた結果の重要度を考慮すると，ABBV-951 が QT 延長を引き起こす可能性は極めて低いと考えられる。

表 2.7.2-7. QT 評価のために M15-738 試験で実施した 3 つの曝露－反応解析の概要

	Analysis 1	Analysis 2	Analysis 3
Prespecified in Protocol	No	No	Yes
Subjects Included	20	24	16[a]
Number of QTcF Values Included	65	166	47[b]
Explanatory Variable	Levodopa Concentration	Levodopa Concentration	Levodopa Concentration
Response Variable	QTcF Value	QTcF Change from Oral Period	QTcF Change from Baseline
Statistically Significant Slope Estimate	Yes	No	No
Predicted Effect at Maximum LD Exposure, 6000 ng/mL (95% Upper Confidence Bound)	17.05 (26.16) msec	0.83 (9.06) msec	3.8 (17.63) msec

QTcF = QT interval corrected for heart rate using Fridericia's formula

a. Only subjects with both baseline and post-baseline electrocardiograms (ECGs) were included in the analysis.

b. Number of QTcF values as change from baseline.

2.7.2.3.4.2 第 III 相試験における心臓における安全性及び ECG 評価

2021 年 3 月 30 日時点で M15-741 試験及び M15-737 試験における器官別大分類（SOC）の心臓障害に関する全ての事象及び ECG パラメータを評価した。M15-741 試験では，ABBV-951 が投与された 223 例中 11 例（4.9%）に心イベントが認められた。M15-737 試験では心イベントが認められた被験者はいなかった。M15-741 試験で報告された 11 例の基本語（PT）は，冠動脈疾患及び動悸が各 2 例（0.9%），急性心筋梗塞，狭心症，心房細動，徐脈，心停止，心肺停止，冠動脈狭窄，期外収縮，左室肥大及び心筋梗塞が各 1 例（0.4%）であった。これらの被験者の大部分（11 例中 9 例）では，認められた事象と ABBV-951 との因果関係は「関連なし」と判断した。心イベントが認められた 11 例のうち，QTcF の同時変化が認められた被験者はいなかった。

M15-741 試験の ECG の結果から，QTcF 間隔の平均変化量（ベースライン後の最大値）は 8.3（標準偏差［SD］：15.38）msec であった。最低用量（ABBV-951 の最頻用量が LD 量として 1200 mg/day 未満）と最高用量（ABBV-951 の最頻用量が LD 量として 2200 mg/day 以上）の間での四分位間において，QTcF を含む ECG パラメータに意味のある差は認められなかった。QTcF 間隔に臨床的に意味のある可能性がある基準（480 msec 以上又はベースラインから 60 msec 以上延長）に該当した被験者は 2 例であった。1 例の被験者では，QTcF がベースラインから 60 msec 以上延長し（388 msec から 448 msec），もう 1 例の被験者では，ベースライン後の値が 491 msec であった（ただし，この被験者では，ABBV-951 初回投与の 39 日前に 512 msec の

QTcF，また，Day 1 に 482 msec の QTcF が認められた）。この 2 例の被験者のいずれにおいても心臓に関する有害事象は認められなかった。M15-741 試験及び M15-737 試験のいずれにおいても，ABBV-951 を投与した被験者に Torsades de pointes は報告されなかった。また，QTcF 延長に関連した心室性不整脈又は心臓死は報告されなかった。

以上，M15-741 試験及び M15-737 試験の臨床データを評価した結果，ABBV-951 投与と QT 延長に関連性はみられなかった。

2.7.2.3.5 用量設定

2.7.2.3.5.1 CD/LD 経口用量から ABBV-951 用量への換算

ABBV-951 は CD/LD 療法歴のない PD 患者の治療に用いることは想定していない。そのため，ABBV-951 の推奨開始用量は，患者個別の LD 含有製剤の一日用量及びカテコール-O-メチルトランスフェラーゼ（以下「COMT」）阻害薬の使用に基づく。なお，オン時間を最大にし，かつ，オフエピソード並びに日常生活に支障をきたすジスキネジアを伴うオンエピソードの回数及び期間を最小にする臨床反応が得られるよう，最適な ABBV-951 の用量に調節可能である。

以下に示す ABBV-951 の開始用量を設定するためのアルゴリズムの妥当性について，長期投与試験である M15-741 試験での各患者における ABBV-951 の初回から最終回までの LD（等価量）注入量（mg/hr）の変化（初回から増量，減量，または変化なし）から評価した。治療開始後，LD 注入量の中央値は用量調節により 10.2 mg/hr 増加し，25 パーセンタイルは変化がなく，75 パーセンタイルは 22.2 mg/hr 増加した。治療開始時での日常生活に支障をきたすジスキネジアを回避するため，用量調節は減量よりも増量が望ましい。また，この軽度な用量の中央値の増加には，ドパミン作動薬などの併用薬の中止が関与している可能性がある。

全体として，このアルゴリズムによる ABBV-951 の開始用量の設定が，本試験の患者に十分に機能したことが示された。

ABBV-951 の推奨開始用量の設定には以下を考慮する。

1. LD 含有製剤での患者個別の治療用量を基に，文献で報告されている各 LD 含有製剤での換算係数を用いて LD 等価量を算出する [14]
2. COMT 阻害薬併用時では LD のクリアランスが低下するため，COMT 阻害薬を併用していた場合には補正係数（1.33）を用いて LD 等価量を補正する [14]
3. ホスレボドパ及び LD の分子量の差（1.41 mg のホスレボドパは 1 mg の LD に相当）
4. わずかではあるが ABBV-951 と LCIG の LD のバイオアベイラビリティの差（M17-220 試験において ABBV-951 の LD のバイオアベイラビリティは 8%高い）
5. ABBV-951 製剤の濃度（240/12 mg/mL ホスレボドパ／ホスカルビドパ）
6. 患者個別の起床中時間

以上を考慮し，ABBV-951 の時間あたりの推奨注入速度を以下のように設定する。

時間あたりの ABBV-951 注入速度（mL/hr）＝[(LE_X × 0.92 × 1.41)／240]/X

LE_X は起床中時間（X）において患者個別に必要な LD 等価量である。0.92 及び 1.41 は ABBV-951 と LCIG の LD のバイオアベイラビリティの差，及び，ホスレボドパと LD の分子量の差に基づく。240 は ABBV-951 製剤のホスレボドパ濃度（mg/mL）であり，重量から容量へ変換する。

2.7.2.3.5.2 負荷投与

治療の開始時に患者がオフ状態である場合，あるいは，ABBV-951 の投与を 3 時間以上中断し，かつ，中断期間中に補助的な LD 含有製剤を服用していない場合，ABBV-951 の負荷投与が推奨される。負荷投与の用量（LD 用量として）は，ABBV-951 の治療以前に起床時間中に服用していた初回経口 CD/LD 投与時の用量である。負荷投与は，CD/LD 経口製剤投与，又は，ABBV-951 のボーラス SC 投与のいずかで実施する。ABBV-951 を用いて負荷投与する場合，負荷投与に必要な用量（LD 用量）から ABBV-951 の容量を表 2.7.2-8 を用いて換算することができる。

表 2.7.2-8. ABBV-951 を用いた負荷投与量（容量）設定

Recommended Loading Dose Volume (mL)	Approximate Corresponding Levodopa Amount (mg)
0.6	100
0.9 – 1.2	150 – 200
1.5 – 1.8	250 – 300
2.0	350

Notes: 0.1 mL of ABBV-951 contains 24 mg levodopa monophosphate (equivalent to approximately 17 mg of levodopa). The pump is capable of delivering a loading dose ranging from 0.1 mL to a maximum of 3.0 mL, in increments of 0.1 mL.

負荷投与は ABBV-951 持続注入を開始する直前に実施し，負荷投与により速やかな症状のコントロールが可能となると考えられる。負荷投与を実施しない場合，LD の曝露量は 12～16 時間後に定常状態に達したが，負荷投与を実施した場合では 2 時間以内であった（M15-733 試験パート 3 及びパート 4）。そのため，オフ状態では負荷投与の実施が推奨され，オフ状態で負荷投与を実施しない場合では PD 患者の症状のコントロールが遅れる可能性がある。

ABBV-951 の負荷投与量（容量）はホスレボドパ及び LD の分子量を用いて換算する（0.6 mL の ABBV-951 は 144 mg のホスレボドパを含み，これは約 100 mg の LD 等価量となる）。持続注入時と同様に，運動症状のコントールに応じて患者個別に ABBV-951 の負荷投与量を調節することが可能である。

2.7.2.3.5.3 LCIG 用量から ABBV-951 用量への換算

M17-220 試験では，LCIG の LD 用量と比べ約 1.3 倍高いホスレボドパ用量の ABBV-951 を投与した結果，同程度の LD の曝露量が得られた。そのため，16 時間の LCIG 投与における CD/LD の用量が 250/1000 mg の場合，ホスカルビドパ／ホスレボドパ 65/1300 mg の ABBV-951 が等価用量となる。また，ABBV-951 は 24 時間注入投与が推奨されるため，更に 1.5 倍高いホスカルビドパ/ホスレボドパ 97.5/1950 mg が 24 時間あたりの ABBV-951 の等価用量となる。したがって，LCIG 用量から ABBV-951 用量への換算式は以下となる。

16 時間あたりの LCIG での LD 用量（mg）× 1.3 × 1.5 = 24 時間あたりの ABBV-951 でのホスレボドパ用量（mg）

また，時間あたりの ABBV-951 注入速度については，以下の式を用いて LCIG 注入速度から換算することができる。

LCIG 投与における時間あたりの LD 用量（mg/hour）× 1.3 = ABBV-951 投与における時間あたりのホスレボドパ用量（mg/hour）

オン時間を最大にし，かつ，オフエピソード及び日常生活に支障をきたすジスキネジアを伴うオンエピソードの回数及び期間を最小にする臨床反応が得られるよう，ABBV-951 投与開始後に用量を調節することが可能である。

2.7.2.4 参考文献

1. Olanow CW, Kieburtz K, Odin P, et al. Continuous intrajejunal infusion of levodopa-carbidopa intestinal gel for patients with advanced Parkinson's disease: a randomised, controlled, double-blind, double-dummy study. Lancet Neurol. 2014;13(2):141-9.
2. Hardie RJ, Malcolm SL, Lees AJ, et al. The pharmacokinetics of intravenous and oral levodopa in patients with Parkinson's disease who exhibit on-off fluctuations. Br J Clin Pharmacol. 1986;22(4):429-36.
3. Nutt JG, Woodward WR, Anderson JL. The effect of carbidopa on the pharmacokinetics of intravenously administered levodopa: the mechanism of action in the treatment of Parkinsonism. Ann Neurol. 1985;18(5):537-43.
4. Yeh KC, August TF, Bush DF, et al. Pharmacokinetics and bioavailability of Sinemet CR: a summary of human studies. Neurology. 1989;39 (11 Suppl 2):25-38.
5. Contin M, Riva R, Martinelli P, et al. Effect of age on the pharmacokinetics of oral levodopa in patients with Parkinson's disease. Eur J Clin Pharmacol. 1991;41(5):463-6.
6. Robertson DR, Wood ND, Everest H, et al. The effect of age on the pharmacokinetics of levodopa administered alone and in the presence of carbidopa. Br J Clin Pharmacol. 1989;28(1):61-9.
7. Othman AA, Dutta S. Population pharmacokinetics of levodopa in subjects with advanced Parkinson's disease: levodopa-carbidopa intestinal gel infusion vs. oral tablets. Br J Clin Pharmacol. 2014;78(1):94-105.
8. Kompoliti K, Adler CH, Raman R, et al. Gender and pramipexole effects on levodopa pharmacokinetics and pharmacodynamics. Neurology. 2002;58(9):1418-22.
9. Chen C, Cowles VE, Sweeney M, et al. Pharmacokinetics of levodopa/carbidopa delivered from gastric-retentive extended-release formulations in patients with Parkinson's disease. J Clin Pharmacol. 2012;52(7):1069-77.
10. Martinelli P, Contin M, Scaglione C, et al. Levodopa pharmacokinetics and dyskinesias: are there sex-related differences? Neurol Sci. 2003;24(3):192-3.
11. Nutt JG, Woodward WR, Hammerstad JP, et al. The "On-Off" phenomenon in parkinson's disease: relationship to levodopa absorption and transport. New Engl J Med. 1984;310(8):483-8.
12. Frankel JP, Kempster PA, Bovingdon M, et al. The effects of oral protein on the absorption of intraduodenal levodopa and motor performance. J Neurol Neurosurg Psychiatry. 1989;52(9):1063-7.

13. Fahn S, Poewe W. Levodopa: 50 years of a revolutionary drug for Parkinson disease. Mov Disord. 2015;30(1):1-3.

14. Tomlinson CL, Stowe R, Patel S, et al. Systematic review of levodopa dose equivalency reporting in Parkinson's disease. Mov Disord. 2010;25(15):2649-53.

15. Nyholm D, Odin P, Johansson A, et al. Pharmacokinetics of levodopa, carbidopa, and 3-O-methyldopa following 16-hour jejunal infusion of levodopa-carbidopa intestinal gel in advanced Parkinson's disease patients. AAPS J. 2013;15(2):316-23.

2.7.3 臨床的有効性

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略語及び定義一覧

略語又は用語	省略していない表現又は説明（英語）	省略していない表現又は説明（日本語）
ABBV-951	Foslevodopa/Foscarbidopa hydrate	ホスレボドパ・ホスカルビドパ水和物
AESI	adverse events of special interest	特に注目すべき有害事象
CD/LD	carbidopa/levodopa	カルビドパ／レボドパ
COMT	catechol-O-methyltransferase	カテコール–O–メチル基転移酵素
CSCI	continuous subcutaneous infusion	持続皮下注入
CSR	clinical study report	治験総括報告書
DDCI	DOPA decarboxylase inhibitor	ドパ脱炭酸酵素阻害薬
EQ-5D-5L	EuroQol 5-dimensions questionnaire	EuroQol 5 項目質問票
F1	-	標準注入速度
F2	-	F1 の+20%以内で F1 より高い注入速度
F3	-	F1 の–20%以内で F1 より低い注入速度
FAS	Full Analysis Set	最大の解析対象集団
IR	immediate release	速放性の
LD	levodopa	レボドパ
LED	levodopa equivalent dose	レボドパ換算投与量
MDS-UPDRS	Movement Disorder Society-Unified Parkinson's Disease Rating Scale	国際パーキンソン病・運動障害学会統一パーキンソン病評価尺度
M-EDL	Motor Aspects of Experiences of Daily Living	日常生活における運動症状
MMRM	mixed model repeated measures	反復測定のある混合効果モデル
MMSE	Mini-Mental State Examination	ミニメンタルステート検査
PD	Parkinson's disease	パーキンソン病
PDQ-39	PD Questionnaire-39 item	パーキンソン病質問票
PDSS-2	PD Sleep Scale-2	パーキンソン病における睡眠評価尺度改訂版
[redacted]	[redacted] or [redacted] (United States)	[redacted] 又は [redacted] （米国）
UPDRS	Unified Parkinson's Disease Rating Scale	統一パーキンソン病評価尺度
VAS	visual analog scale	視覚的評価尺度

2.7.3.1 背景及び概観

2.7.3.1.1 有効性の評価に用いた臨床試験

ABBV-951（ホスレボドパ・ホスカルビドパ水和物）の有効性は，臨床データパッケージのうち，パーキンソン病（以下「PD」）患者を対象とした 3 つの第 III 相試験から評価した。有効性評価に用いた臨床試験の一覧を表 2.7.3-1 に示す。

3 つの第 III 相試験はいずれも評価資料であり，ABBV-951 単群の日本人を含む非盲検国際共同試験の M15-741 試験（5.3.5.2-1 項［申請時］及び 5.3.5.2-1-2 項［更新時］）及びその継続試験であり，ABBV-951 単群の日本人を含む非盲検国際共同試験である M15-737 試験（5.3.5.2-2 項［申請時］及び 5.3.5.2-2-2 項［更新時］），並びに海外で経口薬と比較した二重盲検実薬対照並行群間比較試験の M15-736 試験（5.3.5.1-1 項）であった。試験対象は，M15-741 試験が経口 PD 治療薬では運動症状を十分にコントロールできないレボドパ（以下「LD」）反応性の特発性 PD と診断された患者であり，M15-737 試験が M15-741 試験を完了した成人被験者，また，検証的解析である M15-736 試験が現在の治療ではコントロール不十分な運動症状の日内変動を持つ進行期 PD 患者であった。本申請時点で，M15-741 試験及び M15-737 試験は実施中であり，M15-736 試験は終了している。実施中の M15-741 試験及び M15-737 試験の治験総括報告書（以下「CSR」）のデータカットオフ日は，いずれも 20[redacted] 年 [redacted] 月 [redacted] 日であった。申請後に更新した M15-741 試験及び M15-737 試験の CSR（CSR update）のデータカットオフ日は，いずれも 20[redacted] 年 [redacted] 月 [redacted] 日であった。本臨床的有効性の評価は，M15-741 試験及び M15-737 試験のデータカットオフまでの結果並びに M15-736 試験の結果に基づき行った。

表 2.7.3-1. 有効性評価に用いた臨床試験の概要（評価資料）（1/6）

試験番号/ 施設数/ 実施国/ 実施期間	開始日/ 登録状況/ 終了日/ 登録例数/ 登録目標例数	デザイン 対照の種類	治験薬及び 対照薬の用量 投与経路及び 投与方法	試験の目的	投与群ごとの 投与例数/ 完了例数	性別： 男性/女性 年齢の中央値 （範囲）	診断 選択基準	主要評価項目
M15-741/ 60/ オーストラリア， ベルギー， カナダ， デンマーク， ドイツ， イタリア， 日本， オランダ， ロシア， スペイン， スウェーデン， 英国， 米国/ 最大 52 週	20[redacted]年[redacted]月[redacted]日/ 実施中/ 未完了/ 244 / 240	第 III 相，非盲検，単群，多施設共同	被験者ごとに設定した ABBV-951，CSCI，1 日 24 時間持続	<u>主要目的</u> 最大 52 週間にわたり 1 日 24 時間 CSCI により送達する ABBV-951 の局所及び全身の安全性及び忍容性を評価する <u>副次目的</u> 被験者報告及び評価者が評価した有効性評価項目を指標として ABBV-951 の有効性を評価する	申請時 244 / 115 更新時 244 / 125	146 / 98 65.0 歳 （34～86）	スクリーニング時に 30 歳以上であり，LD 反応性の特発性 PD と診断された成人男女 治験責任（分担）医師により，現在の治療ではコントロール不十分と判断され，識別可能なはっきりとした「オフ」と「オン」の状態（運動症状の日内変動）があり，1 日あたりの「オフ」時間が 2.5 時間以上ある被験者	本試験期間中に有害事象及び重篤な有害事象が認められた被験者の割合 本試験期間中に AESI が認められた被験者の割合 本試験期間中のいずれかの時点で，注入部位評価尺度（Infusion Site Evaluation Scale）で 5 以上に相当する数値グレード及び D 以上に相当する

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表 2.7.3-1. 有効性評価に用いた臨床試験の概要（評価資料）（2/6）

試験番号/ 施設数/ 実施国/ 実施期間	開始日/ 登録状況/ 終了日/ 登録例数/ 登録目標例数	デザイン 対照の種類	治験薬及び 対照薬の用量 投与経路及び 投与方法	試験の目的	投与群ごとの 投与例数/ 完了例数	性別： 男性/女性 年齢の中央値 （範囲）	診断 選択基準	主要評価項目
								レターグレードの注入部位反応が認められた被験者の割合 臨床検査値のベースラインから試験終了時までの変化量 バイタルサイン測定値のベースラインから試験終了時までの変化量 心電図のベースラインから試験終了時までの変化量

表 2.7.3-1. 有効性評価に用いた臨床試験の概要（評価資料）（3/6）

試験番号/ 施設数/ 実施国/ 実施期間	開始日/ 登録状況/ 終了日/ 登録例数/ 登録目標例数	デザイン 対照の種類	治験薬及び 対照薬の用量 投与経路及び 投与方法	試験の目的	投与群ごとの 投与例数/ 完了例数	性別： 男性/女性 年齢の中央値 （範囲）	診断 選択基準	主要評価項目
M15-737/ 41（申請時）， 44（更新時）/ オーストラリア， ベルギー， カナダ， デンマーク， ドイツ， イタリア， 日本， オランダ， スペイン， スウェーデン， 英国， 米国/ 最大 144（96 週＋48 週）	20[redacted]年[redacted]月[redacted]日/ 実施中/ 未完了/ 105（申請時）， 116（更新時）/ 130	第 III 相，非盲検，単群，多施設共同， M15-741 試験の継続試験	被験者ごとに設定した ABBV-951， CSCI，1 日 24 時間持続	CSCI として 1 日 24 時間， ABBV-951 を持続投与した場合の局所及び全身の安全性及び忍容性を評価する	申請時 105 / 0 更新時 116 / 0	申請時 68 / 37 63.0 歳 （34～86） 更新時 74 / 42 63.0 歳 （34～86）	M15-741 試験を完了した成人被験者	本試験期間中に有害事象及び重篤な有害事象が認められた被験者の割合 本試験期間中に AESI が認められた被験者の割合 本試験期間中のいずれかの時点で，注入部位評価尺度（Infusion Site Evaluation Scale）で 5 以上に相当する数値グレード及び D 以上に相当するレターグレード

表 2.7.3-1. 有効性評価に用いた臨床試験の概要（評価資料）（4/6）

試験番号/ 施設数/ 実施国/ 実施期間	開始日/ 登録状況/ 終了日/ 登録例数/ 登録目標例数	デザイン 対照の種類	治験薬及び 対照薬の用量 投与経路及び 投与方法	試験の目的	投与群ごとの 投与例数/ 完了例数	性別： 男性/女性 年齢の中央値 （範囲）	診断 選択基準	主要評価項目
								の注入部位反応が認められた被験者の割合 臨床検査値のベースラインから試験終了時までの変化量 バイタルサイン測定値のベースラインから試験終了時までの変化量 心電図のベースラインから試験終了時までの変化量

表 2.7.3-1. 有効性評価に用いた臨床試験の概要（評価資料）（5/6）

試験番号/ 施設数/ 実施国/ 実施期間	開始日/ 登録状況/ 終了日/ 登録例数/ 登録目標例数	デザイン 対照の種類	治験薬及び 対照薬の用量 投与経路及び 投与方法	試験の目的	投与群ごとの 投与例数/ 完了例数	性別： 男性/女性 年齢の中央値 （範囲）	診断 選択基準	主要評価項目
M15-736/ 65/ オーストラリア， 米国/ 12 週	2020 年 10 月 19 日/ 完了/ 2021 年 9 月 29 日 145 / 130	第 III 相，ランダム化，二重盲検，ダブルダミー，並行群，実薬対照，多施設共同	ABBV-951 群 ABBV-951 24 時間 CSCI 及び CD/LD IR 製剤に対応するプラセボカプセル 対照群 ABBV-951 に対応するプラセボ注射液 24 時間 CSCI 及び CD/LD IR 製剤充填カプセル	主要目的 進行期 PD 患者における投与 12 週時の運動症状の日内変動について，CD/LD IR 製剤経口投与に対する，ABBV-951 CSCI 投与の優越性を確認すること 副次目的 ABBV-951 を 12 週間 24 時間 CSCI したときの，局所及び全身の安全性，並びに忍容性を評価すること	ABBV-951 群 74 / 48 対照群 67 / 62	99 / 42 68.0 歳 （39～85）	スクリーニング時に 30 歳以上であり，LD 反応性の特発性 PD と診断された成人男女 少なくとも 1 日 400 mg 相当の LD 投与を受け，治験責任（分担）医師により現在の治療ではコントロール不十分な運動症状を持つと判断され，識別可能なはっきりとした「オフ」と「オン」の状態（運動症状の日内変動）があり，スクリーニング期の連続する 3 日間	PD 日誌に基づく日常生活に支障のあるジスキネジアを伴わない「オン」時間（ジスキネジアを伴わない「オン」時間と日常生活に支障のないジスキネジアを伴う「オン」時間の合計）の，ベースラインから二重盲検期の投与 12 週時までの変化量（「オン」時間は，覚醒 16 時間に標準化した時間の，連続 3 日間の平均）

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表 2.7.3-1. 有効性評価に用いた臨床試験の概要（評価資料）（6/6）

試験番号/ 施設数/ 実施国/ 実施期間	開始日/ 登録状況/ 終了日/ 登録例数/ 登録目標例数	デザイン 対照の種類	治験薬及び 対照薬の用量 投与経路及び 投与方法	試験の目的	投与群ごとの 投与例数/ 完了例数	性別： 男性/女性 年齢の中央値 （範囲）	診断 選択基準	主要評価項目
							の PD 日誌で，1 日あたり平均 2.5 時間以上の「オフ」時間があり，かつ各日の「オフ」時間が 2 時間以上である患者 スクリーニング期の間，被験者（又はその介護者）が，被験者胃内へのカニューレ挿入を含む投与器具の正しい使用方法及びその理解を持つと，治験責任（分担）医師又はその被指名者によって判断された場合	

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ABBV-951 = ホスレボドパ・ホスカルビドパ水和物，AESI = 特に注目すべき有害事象，CD/LD = カルビドパ／レボドパ，CSCI = 持続皮下注入，IR = 速放性の，LD = レボドパ，PD = パーキンソン病

Cross References：M15-741 試験 CSR Table 14.1__2（申請時），M15-741 試験 CSR update Table 14.1__1.1.1 及び Table 14.1__2.1（更新時），M15-737 試験 CSR Table 14.1__2（申請時），M15-737 試験 CSR update Table 14.1__1.1 及び Table 14.1__2（更新時），並びに M15-736 試験 CSR Table 14.1__2.1

2.7.3.1.2 有効性の評価項目

2.7.3.1.2.1 各評価項目の定義

M15-741 試験，M15-737 試験及び M15-736 試験における有効性評価項目を以下に示す。

- PD 日誌に基づく標準化した 1 日あたりの平均「オフ」時間及び「オン」時間
- Movement Disorder Society Unified Parkinson's Disease Rating Scale（国際パーキンソン病・運動障害学会統一パーキンソン病評価尺度，以下「MDS-UPDRS」）Part I-IV（又は MDS-UPDRS の検証済み翻訳を利用できない国では UPDRS Part I-V）により評価した PD 症状
- パーキンソン病質問票（以下「PDQ-39」）により評価した生活の質
- EuroQol 5 項目質問票（以下「EQ-5D-5L」）により評価した健康に関連した生活の質
- パーキンソン病における睡眠評価尺度改訂版（以下「PDSS-2」）により評価した睡眠症状（M15-741 試験及び M15-736 試験）
- ミニメンタルステート検査（以下「MMSE」）により評価した認知障害（M15-737 試験のみ）
- PD 日誌に基づく朝の無動（起床時以降に観察された最初の朝の症状としての「オフ」状態）の有無
- [redacted]（以下「[redacted]」）[redacted]（各国規制による）を用いて評価した PD 症状（M15-736 試験のみ）

2.7.3.1.2.2 評価項目

2.7.3.1.2.2.1 M15-741 試験

####### 2.7.3.1.2.2.1.1 主要評価項目

本試験の主要評価項目は，以下の安全性評価項目とした。

1. 本試験期間中に有害事象及び重篤な有害事象が認められた被験者の割合
2. 本試験期間中に特に注目すべき有害事象（以下「AESI」）が認められた被験者の割合
3. 本試験期間中のいずれかの時点で，注入部位評価尺度（Infusion Site Evaluation Scale）で 5 以上に相当する数値グレード及び D 以上に相当するレターグレードの注入部位反応が認められた被験者の割合
4. 臨床検査値のベースラインから試験終了時までの変化量
5. バイタルサイン測定値のベースラインから試験終了時までの変化量
6. 心電図のベースラインから試験終了時までの変化量

2.7.3.1.2.2.1.2 副次評価項目

本試験の副次評価項目は有効性評価項目であり，以下に関するベースラインから試験終了時までの変化量とした。

1. PD 日誌に基づく標準化した 1 日あたりの平均「オフ」時間及び「オン」時間
2. MDS-UPDRS Part I–IV（又は MDS-UPDRS の検証済み翻訳を利用できない国では UPDRS Part I-V）により評価した PD 症状
3. PDSS-2 により評価した睡眠症状
4. PDQ-39 により評価した生活の質
5. EQ-5D-5L により評価した健康に関連した生活の質

2.7.3.1.2.2.2 M15-737 試験

2.7.3.1.2.2.2.1 主要評価項目

本試験の主要評価項目は，以下の安全性評価項目とした。

1. 本試験期間中に有害事象及び重篤な有害事象が認められた被験者の割合
2. 本試験期間中に AESI が認められた被験者の割合
3. 本試験期間中のいずれかの時点で，注入部位評価尺度（Infusion Site Evaluation Scale）で 5 以上に相当する数値グレード及び D 以上に相当するレターグレードの注入部位反応が認められた被験者の割合
4. 臨床検査値のベースラインから試験終了時までの変化量
5. バイタルサイン測定値のベースラインから試験終了時までの変化量
6. 心電図のベースラインから試験終了時までの変化量

2.7.3.1.2.2.2.2 副次評価項目

本試験の副次評価項目は有効性評価項目であり，以下に関するベースラインから試験終了時までの変化量とした。

1. PD 日誌に基づく標準化した 1 日あたりの平均「オフ」時間及び「オン」時間
2. MDS-UPDRS Part I–IV により評価した PD 症状
3. PDQ-39 により評価した生活の質
4. EQ-5D-5L により評価した健康に関連した生活の質
5. MMSE により評価した認知障害

2.7.3.1.2.2.3 M15-736 試験

2.7.3.1.2.2.3.1 主要評価項目

本試験の主要評価項目は，PD 日誌に基づく日常生活に支障のあるジスキネジアを伴わない「オン」時間（ジスキネジアを伴わない「オン」時間と日常生活に支障のないジスキネジアを伴う「オン」時間の合計）の，ベースラインから二重盲検期の投与 12 週時までの変化量（「オン」時間は，覚醒 16 時間に標準化した時間の連続 3 日間の平均）とした。ベースラインは，ランダム化前の PD 日誌 3 日間から収集した日常生活に支障のあるジスキネジアを伴わない標準化「オン」時間の平均とした。

2.7.3.1.2.2.3.2 副次評価項目

<u>主な副次評価項目</u>

- PD 日誌に基づく標準化した 1 日あたりの平均「オフ」時間のベースラインから二重盲検期の投与 12 週時までの変化量
- MDS-UPDRS Part II による日常生活における運動症状（以下「M-EDL」）スコアのベースラインから二重盲検期の投与 12 週時までの変化量
- PD 日誌に基づく投与 12 週時における朝の無動（起床時以降に観察された最初の朝の症状としての「オフ」状態）の有無

<u>その他の副次評価項目</u>

- PD 日誌に基づく標準化した 1 日あたりのジスキネジアを伴わない平均「オン」時間のベースラインから投与 12 週時までの変化量
- PDSS-2 合計スコアにより評価された睡眠症状のベースラインから最終来院日までの変化量
- PDQ-39 要約指標により評価された PD に関連した生活の質のベースラインから最終来院日までの変化量
- EQ-5D-5L 要約指標により評価された健康に関連した生活の質のベースラインから最終来院日までの変化量
- [redacted]（各国規制による）を用いて評価した PD 症状のベースラインから投与 12 週時までの変化量

2.7.3.1.3 解析対象集団

2.7.3.1.3.1 個々の試験の解析対象集団

臨床的有効性を評価した M15-741 試験，M15-737 試験及び M15-736 試験における，有効性解析対象集団（最大の解析対象集団，以下「FAS」）の概略を以下に示す。

M15-741 試験及び M15-737 試験においては，「ABBV-951 の注入を 1 回以上受け，かつ有効性の結果指標に関するベースライン及び投与期間中の 1 つ以上の評価値が得られたすべての被験者」を FAS と定義した。M15-736 試験においては，「二重盲検期に ABBV-951 の注入を 1 回以上受け，かつベースライン及び 1 回以上のベースライン後の有効性評価を受けたすべてのランダム化された被験者」を FAS と定義した。

2.7.3.1.3.2 日本人部分集団

M15-741 試験及び M15-737 試験には日本人被験者がそれぞれ 27 例及び 11 例（申請時），27 例及び 12 例（更新時）含まれ，日本人部分集団における有効性評価に関する解析を実施している。

日本人部分集団は，症例報告書に入力された治験実施医療機関が所在する国に基づいて設定した。

2.7.3.1.4 統計解析

2.7.3.1.4.1 M15-741 試験

M15-741 試験は，単群，非盲検試験である。別途記載がない限り，有効性評価項目に関するすべての解析は，ABBV-951 の注入終了後 1 日までに収集されたデータを含む FAS に対して実施された。ベースラインからの変化量については，対応のある t 検定を実施した。なお，全体集団及び日本人部分集団ともに多重性の調整は行わず，すべての有効性解析について nominal *P* 値のみを示した。

全被験者及び以下に示す各部分集団について，すべての有効性評価項目の各規定来院日まで，及び最終来院日までのベースラインからの変化量を記述統計量で要約した。統計量には，観察回数，平均値，標準偏差，最小値，中央値及び最大値が含まれる。

- 用量
- 性別
- 人種（白人，アジア人及びその他）。その他（白人及びアジア人以外）については，同一人種として 3 例以上の場合に解析を実施する。
- 年齢（65 歳未満及び 65 歳以上）
- 地域（北米，オーストラリア及び欧州，又は日本）
- PD 罹病期間（診断後経過期間，10 年未満及び 10 年以上）

また，欠測データの取扱いについては，以下のとおりである。

<u>PD 日誌</u>

ベースライン（Day 1）前又はベースライン後来院日に 2 日間を超える有効な PD 日誌がある場合は，来院日（又は Day 1）に近い 2 日間の PD 日誌を使用した。有効な PD 日誌が 1 日のみ

の場合は，その PD 日誌を用いた。有効な PD 日誌がない場合は，その来院日における標準化した 1 日あたりの平均「オフ」又は「オン」時間は欠測とした。

MDS-UPDRS

MDS-UPDRS の合計スコア及び各 Part スコアについては，回答の 15%に満たない場合は欠測として扱った。欠測項目は同一の MDS-UPDRS の非欠測項目の平均で補完した。Part I，Part II，Part III 又は Part IV スコアの補完には，当該 Part 内の非欠測項目を用いるが，Part I から Part III の合計スコアは，3 つの Part にわたる全 59 項目から，非欠測項目を補完した。

PDSS-2

欠測値は補完しなかった。項目スコアのいずれもが欠測した場合は，合計スコア及び当該ドメインスコアは計算しなかった。

PDQ-39

PDQ-39 の要約指標については，回答の 15%（すなわち 5 項目）に満たない場合は欠測として扱った。欠測値の補完には，同一 PDQ-39 評価の非欠測項目の平均を用いた。ドメインスコアは，当該ドメインの質問すべてに回答がある場合にのみ計算された。

EQ-5D-5L

EQ-5D-5L 要約指標は，個々の質問 5 つすべてに回答が得られた場合にのみ計算された。EQ-5D-5L 視覚的評価尺度（以下「VAS」）は，単一値として収集され，欠測値は補完しなかった。

2.7.3.1.4.2 M15-737 試験

M15-737 試験は，単群，非盲検継続試験である。別途記載がない限り，ABBV-951 の注入終了後 1 日までに収集されたデータを用いて，FAS を対象にすべての有効性評価項目を解析した。ベースラインは，M15-737 試験で治験薬の投与を開始する前の最後の評価値と定義した。

全被験者及び各部分集団に関する記述統計量の要約及び統計量は，M15-741 試験と同様とした。

また，欠測データの取扱いについては，以下に示す MMSE を除き，M15-741 試験と同様とした（2.7.3.1.4.1 項）。

MMSE

MMSE 総スコアについては，回答の 15%（すなわち 4 項目）に満たない場合は欠測として扱った。欠測値の補完には，同一 MMSE 評価の非欠測項目の平均を用いた。ドメインスコアは，当該ドメインの質問すべてに回答がある場合にのみ計算された。

2.7.3.1.4.3 M15-736 試験

主要評価項目

有効な PD 日誌は，日誌 24 時間のうち，欠測データが 2 時間を超えないもの（30 分の欠測が 4 回又はそれ未満）と定義した。有効な PD 日誌の各日で収集された，ジスキネジアを伴わない「オン」時間と日常生活に支障のないジスキネジアを伴う「オン」時間の合計は，各被験者で異なる睡眠時間の影響を除外するために，典型的な 1 日における覚醒時間（16 時間）に標準化した。

また，連続 3 日間の PD 日誌を平均し，各来院日における日常生活に支障のあるジスキネジアを伴わない標準化した 1 日あたりの平均「オン」時間を求めた。

主要解析には反復測定混合効果モデル（以下「MMRM」）を用い，ベースライン後の各来院日における，PD 日誌から得られた標準化した 1 日あたりの日常生活に支障のあるジスキネジアを伴わない平均「オン」時間のベースラインからの変化量をデータとして含めた。この混合モデルにはカテゴリカルな固定効果として，投与群，実施国，来院日，投与群と来院日の交互作用，投与群とベースラインの交互作用，連続値の固定効果としてベースライン測定値を含めた。分散共分散行列は無構造とした。二重盲検期中に試験を完了せず中止された被験者の欠測データは，ランダムな欠測と仮定した MMRM で取り扱われた。モデルパラメータは，制限付き最尤推定法を用いて推定した。なお，二重盲検期の投与 12 週時における，ABBV-951 24 時間持続皮下注入群（以下「ABBV-951 投与群」）とカルビドパ／レボドパ（以下「CD/LD」）速放性製剤経口投与群（以下「CD/LD 経口投与群」）の対比を主要な比較とした。

副次評価項目

以下の主な副次評価項目及びその他の副次評価項目には，試験全体について両側有意水準 0.05 のファミリーワイズエラー率を制御するために，第一種過誤の多重比較調整を適用した。これらの副次評価項目は，ゲートキーピング法により以下の固定順位で検定した。なお，主な副次評価項目（第 2 順位）である「MDS-UPDRS Part II による M-EDL スコアのベースラインから二重盲検期の投与 12 週時までの変化量」において，統計学的有意差が認められなかったことから，その後の順位の副次評価項目の結果及び nominal *P* 値を参考として記載することとした。また，[redacted]による評価については，本項には記載しなかった。

- 主な副次評価項目
  - PD 日誌に基づく標準化した 1 日あたりの平均「オフ」時間のベースラインから二重盲検期の投与 12 週時までの変化量

- MDS-UPDRS Part II による M-EDL スコアのベースラインから二重盲検期の投与 12 週時までの変化量
- PD 日誌に基づく投与 12 週時における朝の無動の有無

- その他の副次評価項目
  - PD 日誌に基づく標準化した 1 日あたりのジスキネジアを伴わない平均「オン」時間のベースラインから投与 12 週時までの変化量
  - PDSS-2 合計スコアにより評価された睡眠症状のベースラインから最終来院日までの変化量
  - PDQ-39 要約指標により評価された PD に関連した生活の質のベースラインから最終来院日までの変化量
  - EQ-5D-5L 要約指標により評価された健康に関連した生活の質のベースラインから最終来院日までの変化量
  - [redacted]評価による動作緩慢スコア中央値（BK50）のベースラインから投与 12 週時までの変化量
  - [redacted]評価による動作緩慢スコア 75～25%タイル（BK75-BK25）のベースラインから投与 12 週時までの変化量
  - [redacted]評価によるジスキネジアスコア中央値（DK50）のベースラインから投与 12 週時までの変化量
  - [redacted]評価によるジスキネジアスコア 75～25%タイル（DK75-DK25）のベースラインから投与 12 週時までの変化量

標準化した 1 日あたりの平均「オフ」時間，MDS-UPDRS Part II スコア，標準化した 1 日あたりのジスキネジアを伴わない平均「オン」時間及び[redacted]データのベースラインから投与 12 週時までの変化量については，主要有効性解析と同様の MMRM を適用した。

PDSS-2 合計スコア，PDQ-39 要約指標及び EQ-5D-5L 要約指標のベースラインから最終来院日までの変化量については，カテゴリデータとして投与群及び実施国を固定効果，並びにベースラインスコアを共変量とした共分散分析モデルを適用した。

ベースライン後の各来院日における朝の無動の有無については，投与群間の朝の無動状態を呈する被験者の割合を比較するために，固定効果として投与群，実施国，来院日，来院日・投与群交互作用及び朝の無動のベースラインのカテゴリデータを含む，ロジットリンク関数による一般化線形モデルを適用した。分散共分散行列は無構造とした。なお，投与 12 週時における，ABBV-951 投与群と CD/LD 経口投与群のオッズ比を主要な比較とした。

また，欠測データの取扱いについては，以下に示す PD 日誌を除き，M15-741 試験と同様とした（2.7.3.1.4.1 項）。

PD 日誌

ベースライン又はベースライン後の来院日に 3 日間を超える有効な PD 日誌がある場合は，来院日に最も近い 3 日間の PD 日誌を使用した。有効な PD 日誌が 2 日間しか入手できない場合は，

その 2 日間のデータを用いて 1 日の標準化した「オフ」又は「オン」時間の平均値を算出した。有効な PD 日誌が 1 日のみの場合は，その PD 日誌を用いた。各来院日に有効な PD 日誌がない場合は，その来院日における標準化した 1 日あたりの平均「オフ」又は「オン」時間は欠測とした。

部分集団解析

主要評価項目，すなわち標準化した 1 日あたりの日常生活に支障のあるジスキネジアを伴わない平均「オン」時間のベースラインから二重盲検期における投与 12 週時までの変化量について，以下の部分集団解析を実施した。

- 年齢（65 歳未満又は 65 歳以上）
- 性別（男性又は女性）
- 人種（白人又はその他）
- 実施国
- PD 罹病期間（10 年未満又は 10 年以上）
- ドパミンアゴニストの併用の有無
- LD の用量（低用量又は高用量）。詳細については M15-736 試験 CSR（5.3.5.1-1 項）の統計解析計画書を参照

部分集団変数の 1 カテゴリが FAS の 20%に満たない場合は，部分集団解析を実施しなかった。

2.7.3.2 個々の試験結果の要約

2.7.3.2.1 M15-741 試験

M15-741 試験は，PD 患者を対象とした ABBV-951 の持続皮下注入（以下「CSCI」）による 1 日 24 時間投与時の安全性及び忍容性を評価する 52 週間，非盲検，単群試験であり，主要目的は，最大 52 週間，1 日 24 時間 CSCI したときの ABBV-951 の局所及び全身の安全性及び忍容性を評価すること，また，副次目的は，被験者報告及び評価者が評価した有効性評価項目を指標として ABBV-951 の有効性を評価することとして実施した。

試験デザインの概略を図 2.7.3-1 に示す。

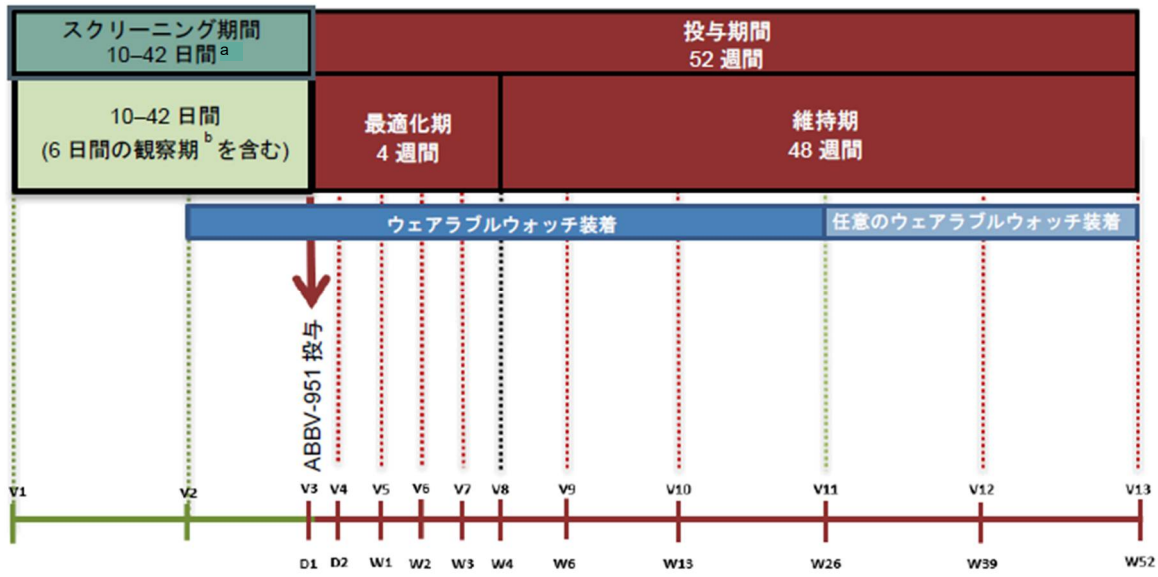
治験薬投与期間は最大 52 週（最適化期 4 週及び維持期 48 週），用法・用量は治験責任医師が事前に被験者ごとに設定した上で，ABBV-951（ホスカルビドパ／ホスレボドパ：12/240 mg/mL）の CSCI とした。治験薬投与は，経口負荷投与及び CSCI で構成され，経口負荷投与は，治験開始時又は CSCI を 3 時間以上中断した際に，被験者の LD 及びドパ脱炭酸酵素阻害薬（以下「DDCI」）の朝投与量に可能な限り近い量を速放性（以下「IR」）製剤を用いて実施した。また，CSCI については，被験者ごとに標準注入速度（以下「F1」）を LD 換算投与量（以下「LED」）及び ABBV-951 の薬物動態によって考案されたアルゴリズムに基づき設定し，必要に応じて F1 の ± 20%以内で F1 より高い注入速度（以下「F2」）及び F1 より低い注入速度（以

下「F3」）を規定に従って設定した。治験開始時の注入速度は 0.70 mL/時間を超えないこととした。F1，F2 及び F3 の許容範囲は 0.17～1.04 mL/時間とし，F2 又は F3 が不要な場合は OFF に設定しなければならなかった。被験者は，治験責任医師によって事前に設定されたこれら 3 種類の注入速度から 1 日の持続注入速度を選択することができた。更に，運動機能の急速な悪化などの緊急的な医学的必要性に対処するため，事前に許可された場合，被験者は事前に設定された量の ABBV-951 の追加投与を自己投与できることとした。治験責任医師は，0.11，0.15，0.19，0.24，0.3 mL（それぞれ約 20，25，33，40，50 mg の LD に相当）から追加投与量を選択できた。最短のロックアウト時間（追加投与の間隔）は 60 分であり，1 時間から 24 時間まで 15 分刻みで設定可能であった。追加投与の必要性が 1 日 5 回を超える場合，治験責任医師は F1 の増加及びロックアウト時間の延長を検討することとした。また，治験責任医師は，被験者の来院時に有効性及び安全性を評価した後，規定に従って用量調節及び追加投与の設定を可能とした。治験中のいかなる状況下でも，ホスカルビドパ水和物の投与量の上限は 6000 mg/日（LD として 4260 mg/日に相当）とした。LED の計算に用いる換算係数を表 2.7.3-2 に，治験開始時に選択する注入速度を表 2.7.3-3 に，追加の注入速度，又は追加投与量と追加投与のロックアウト時間を設定する際に考慮すべき上限のガイダンスを表 2.7.3-4 に示した。なお，CSCI 機器として，[redacted]，20 mL シリンジ，及び Neria Guard 注入セット又は [redacted] 注入セット（カニューレ，チューブ）を用いた。また，LD 又はカテコール-O-メチル基転移酵素（以下「COMT」）阻害薬を含まない PD 治療薬は，ABBV-951 開始前に中止する必要がないものの，治験責任医師の判断又は当該薬の添付文書に従って，最適化期において併用 PD 治療薬の漸減を考慮した。

また，M15-741 試験では，予想を上回る脱落・中止例が認められ，その根本原因は注入部位の有害事象の発現及び投与システム使用の困難が考えられたことから，無菌操作を含む注入セットの使用方法に関する再教育を実施するとともに，使いやすさがより優れていると考えられる注入セット（Neria Guard）も使用できるように治験実施計画書の改訂（20[redacted] 年 [redacted] 月 [redacted] 日）を行った。これらの改善策は 20[redacted] 年 [redacted] 月 [redacted] 日までに完全に実施されたことから，それよりも前に登録された被験者（以下「Sample 1」），及びそれ以降に登録された被験者（以下「Sample 2」）ごとに各評価項目を要約した。

試験結果の詳細は，2.7.3.3 項に示す。

図 2.7.3-1. 試験デザインの概略（M15-741 試験）



ABBV-951 = ホスレボドパ・ホスカルビドパ水和物，D = 投与 X 日目，PD = パーキンソン病，V = 来院，W = 投与 X 週時

a. 考慮すべき状況（供給上の制約など）がある場合は，スクリーニング期間を計 90 日間まで延長することができる。

b. 観察期は V3 までのいずれかの時点で 6 日間連日で実施。また，PD 日誌も観察期に 2 日以上連日で記入する。[redacted]が未承認の国では，PD 日誌の記入及び注入ポンプのトレーニングを考慮し，観察期を 2 日間以上に短縮できる。

注意：各国の規制で許容される場合，被験者はスクリーニング来院 1（V1）後に[redacted]を受領し，観察期中及び少なくとも 26 週来院（V11）完了まで[redacted]（最新の承認された製造元の指示を参照）を着用した。以降の[redacted]の使用は任意とした。観察期はスクリーニング期間（V3 前まで）に 6 日間以上連日で実施し，被験者は PD 日誌の記入と[redacted]の着用を同時に求められた。本治験実施計画書，付録を通してすべてのウェアラブルウォッチの使用には「各国の規制で許容される場合」が適用された。治験責任医師の判断で，[redacted]の使用を妨げる可能性の状況（宗教上の理由，アトピー性皮膚炎の問題など）がある場合は，治験依頼者の治験担当医学専門家（TA MD）に相談することとした。輸送上の問題により[redacted]の入手が困難で着用できない被験者の場合であっても，本試験への参加は可能とした。

Cross References：M15-741 試験 Protocol Figure 1

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表 2.7.3-2. レボドパ換算投与量（LED）の範囲

薬剤	LED の計算に用いる換算係数	
レボドパ放出制御製剤 (シネメット CR，マドパーCR など)	レボドパ放出制御製剤を使用している被験者の場合，レボドパ放出制御製剤の 1 日量に **0.75 を乗じて**各被験者の LED を求める	
レボドパ徐放性製剤 (Rytary)	レボドパ徐放性製剤を使用している被験者の場合，Rytary の総 1 日投与量に，以下の表に記載されている変換率を**乗じて**各被験者の LED を求める	
	Rytary 投与量範囲 (mg)	**変換率(LED に対する Rytary の比)**
	0–855	**0.42**
	856–1755	**0.48**
	1756–2340	**0.56**
	2341 以上	**0.67**
エンタカポン (コムタン又はスタレボなど) 又は tolcapone (Tasmar) などの COMT 阻害剤を使用している被験者に対する調節	被験者がエンタカポン又は tolcapone を使用している場合，レボドパ含有製剤から算出する LED はすべて，**1.33 を乗じて**求めなければならない 注：スタレボ中に含まれるレボドパは IR とみなす	

COMT = カテコール–*O*–メチル基転移酵素；CR = 放出制御；IR = 速放性；LED = レボドパ換算投与量

Cross References：M15-741 試験 Protocol Table 2

表 2.7.3-3. 推奨される ABBV-951 の開始注入速度

起きている時間 (16 時間) に投与したすべての経口 LD 含有治療薬に基づく LED (mg)[a]	推奨される ABBV-951 の時間当たりの開始注入速度 (mL/時間)[b]	対応する時間当たりの概算 LD 投与量 (mL/時間)[c]
< 500	0.17	29
500–599	0.17–0.20	30–34
600–699	0.20–0.24	34–41
700–799	0.24–0.27	41–46
800–899	0.27–0.30	46–51
900–999	0.30–0.34	51–58
1000–1099	0.34–0.37	58–63
1100–1199	0.37–0.40	63–68
1200–1299	0.40–0.44	68–75
1300–1399	0.44–0.47	75–80
1400–1499	0.47–0.51	80–87
1500–1599	0.51–0.54	87–92
1600–1699	0.54–0.57	92–97
1700–1799	0.57–0.61	97–104
1800–1899	0.61–0.64	104–109
1900–1999	0.64–0.68	109–116
> 2000	0.70	119

LD = レボドパ；LED = レボドパ換算投与量

a. 表 2.7.3-2 に基づく。

b. 推奨される注入速度は参照する範囲の中間点より算出される。

c. LDP 240 mg/mL の ABBV-951 濃度と分子量換算係数 LD 100 mg = LDP 141 mg に基づく。

Cross References：M15-741 試験 Protocol Table 3

表 2.7.3-4. 標準注入速度に基づく追加の注入速度の制限と追加投与の回数に関するガイダンス

F1 標準注入速度 (mL/時間)	F2 上限 (mL/時間)	F3 下限 (mL/時間)	許容される追加投与回数 [a]
0.17	≤ 0.20	OFF	23
0.2	≤ 0.24	≥ 0.17	23
0.23	≤ 0.28	≥ 0.18	23
0.27	≤ 0.32	≥ 0.22	23
0.3	≤ 0.36	≥ 0.24	23
0.33	≤ 0.40	≥ 0.26	23
0.37	≤ 0.44	≥ 0.30	23
0.4	≤ 0.48	≥ 0.32	23
0.43	≤ 0.52	≥ 0.34	23
0.47	≤ 0.56	≥ 0.38	23
0.5	≤ 0.60	≥ 0.40	23
0.53	≤ 0.64	≥ 0.42	23
0.57	≤ 0.68	≥ 0.46	23
0.6	≤ 0.72	≥ 0.48	23
0.63	≤ 0.76	≥ 0.50	23
0.67	≤ 0.80	≥ 0.54	19
0.7	≤ 0.84	≥ 0.56	16
0.73	≤ 0.88	≥ 0.58	13
0.77	≤ 0.92	≥ 0.62	9
0.8	≤ 0.96	≥ 0.64	7
0.83	≤ 1.00	≥ 0.66	4
0.86	≤ 1.02	≥ 0.69	1
0.89	≤ 1.04	≥ 0.71	0
0.92	≤ 1.04	≥ 0.74	0
0.95	≤ 1.04	≥ 0.76	0
0.98	≤ 1.04	≥ 0.78	0
1	≤ 1.04	≥ 0.80	0
1.04	OFF	≥ 0.83	0

a. 追加の高い注入速度（F2）が有効でその上限が設定されており，ロックアウト時間が最短の 60 分に設定されていると仮定した場合（すなわち 1 日に 23 回の追加投与が可能）の最大追加投与量（0.3 mL）に対する値

Cross References：M15-741 試験 Protocol Table 4

2.7.3.2.2 M15-737 試験

M15-737 試験は，PD 患者を対象とした ABBV-951 の CSCI による 1 日 24 時間投与時の安全性及び忍容性を評価する M15-741 試験の非盲検継続試験であり，CSCI として 1 日 24 時間，ABBV-951 を投与した場合の局所及び全身の安全性及び忍容性の評価を目的として実施した。

試験デザインの概略を図 2.7.3-2 に示す。

治験薬投与期間は最大 144 週（96 週の投与期間＋48 週の延長投与期間），用法・用量は被験者ごとに M15-741 試験を継続した上で，ABBV-951 の CSCI とした。M15-737 試験で投与する開始時の持続注入速度（F1，F2，F3）及び追加投与量は，M15-741 試験で最終日に処方された注入速度，追加投与量，及びロックアウト時間を反映した。用量調節及び追加投与の設定方法は，M15-741 試験と同様であった。ただし，治験責任医師の判断により臨床効果を最適化させるため，追加注入速度の範囲について，標準注入速度の±20%のしばりを削除し，柔軟性を高めた。CSCI を 3 時間以上中断した場合に限り，被験者の M15-741 試験開始前の LD 及び DDCI の朝投与量に可能な限り近い量の IR 製剤を経口負荷投与した。なお，CSCI 機器として，[redacted]，20 mL シリンジ，及び Neria Guard 注入セット又は [redacted] 注入セット（カニューレ，チューブ）を用いた。

試験結果の詳細は，2.7.3.3 項に示す。

図 2.7.3-2. 試験デザインの概略（M15-737 試験）



Cross References：M15-737 試験 Protocol Figure 1

2.7.3.2.3 M15-736 試験

M15-736 試験は，進行期 PD 患者を対象として，経口 CD/LD 製剤に対する ABBV-951 の有効性，安全性及び忍容性を比較する，ランダム化，二重盲検，ダブルダミー，実薬対照試験であり，主要目的を，投与 12 週時の運動症状の日内変動について，CD/LD IR 製剤経口投与に対する，ABBV-951 CSCI 投与の優越性を確認すること，また，副次目的を，ABBV-951 を 12 週間 24 時間 CSCI したときの，局所及び全身の安全性，並びに忍容性を評価することとして実施した。

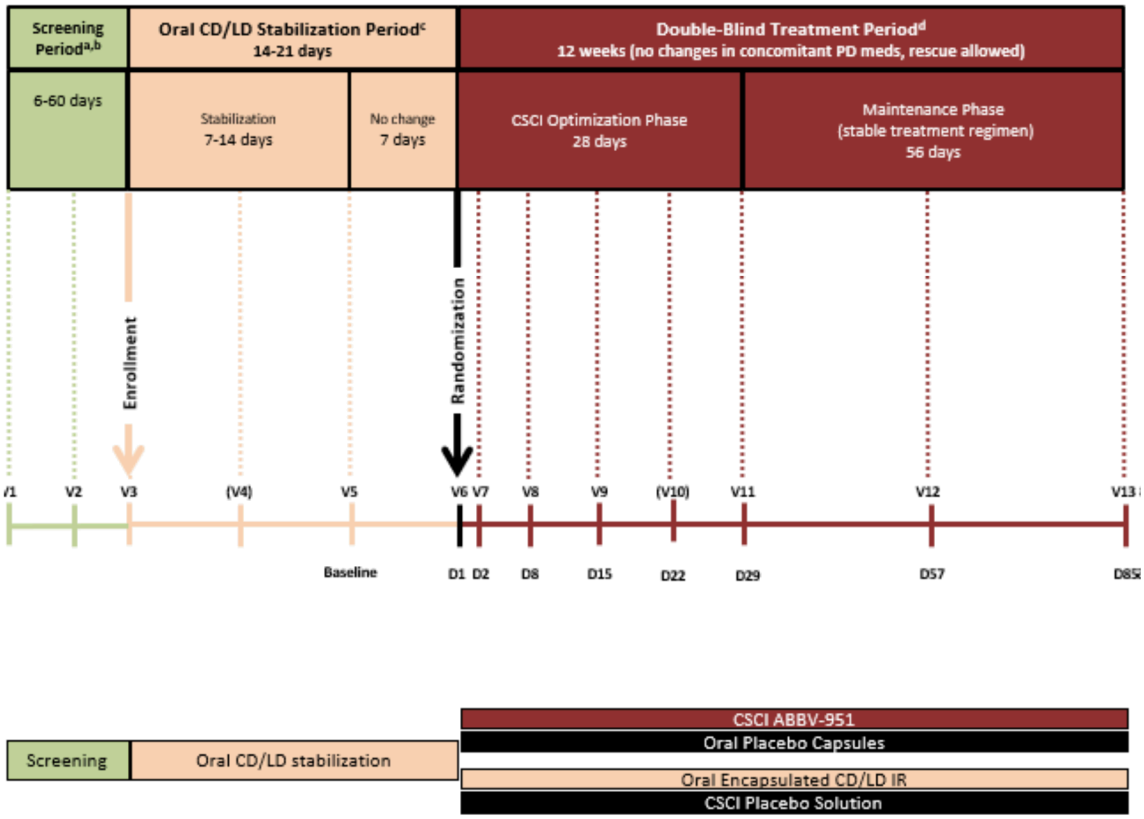
試験デザインの概略を図 2.7.3-3 に示す。

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治験薬投与期間は経口 CD/LD 安定化期（最大 21 日）及び二重盲検期 12 週（CSCI 最適化期 28 日，維持期 56 日），用法・用量は，前 PD 治療薬を経口 CD/LD IR 製剤（CD/LD：25/100 mg）に相当量換算した上で，経口 CD/LD 安定化期において症状及び安全性評価に基づき CD/LD 用量を調節した。二重盲検期は CSCI 最適化期及び維持期で構成され，CSCI 最適化期において，まず，規定に従って経口投与及び皮下投与の負荷投与を実施した後，安定化期における経口 CD/LD 製剤相当量の ABBV-951 の CSCI 及び経口 CD/LD IR 製剤のプラセボ（以下「ABBV-951 投与」），又は ABBV-951 プラセボの CSCI 及び経口 CD/LD IR 製剤（以下「経口 CD/LD IR 投与」）のいずれかを開始し，CSCI についてのみ，PD 症状及び安全性を評価した上で用量調節可とした。また，維持期においては，ABBV-951 の用量は不変としたが，PD 症状によって緊急的対応が必要となった場合は，CD/LD IR 製剤の使用を可能とした。なお，CSCI 機器として，[redacted]，[redacted]シリンジ 10 mL，及び Neria Guard 注入セット（カニューレ，チューブ）を用いた。また，前 PD 治療薬の併用については，COMT 阻害薬を除き，症状に応じて非 LD 製剤の併用可としたが，治験期間中の用法・用法変更は原則不可とした。

試験結果の詳細は，2.7.3.3 項に示す。

図 2.7.3-3. 試験デザインの概略（M15-736）



ABBV-951＝ホスレボドパ・ホスカルビドパ水和物，CD/LD＝カルビドパ／レボドパ，CSCI＝持続皮下注入，D＝投与 X 日目，IR＝速放性の，[redacted]＝[redacted]又は[redacted]（米国），PD＝パーキンソン病，V＝来院

a. V3 は，V1 の結果に基づいて十分なレビューを可能とし，また，被験者が持続投与機器の操作を習熟し，かつこれを確認する意味で，V1 から少なくとも 6 日後以降とした。

b. スクリーニング期は，6 日間以上継続した。PD 日誌は，スクリーニング期の間，V2 までに 3 連続日以上記録した。PD 日誌記録は，必要に応じて，経口 CD/LD 安定化期開始前，かつ V3 までの間に追加の 3 連続日について 1 回のみ実施された。

c. 経口 CD/LD 安定化期は，スケジュールの遵守，予定外の追加来院及び必要に応じて実施される評価に対応するため，14 日から 21 日間確保された。PD 日誌は，ランダム化までに 3 連続日以上記録した。

d. 治験を完了せずに中止となった，又は治験は完了したが非盲検継続試験 M20-098 に組入れられなかった被験者については，すべての治験薬投与による（重篤な）有害事象に対処するため，被験者の同意が得られた場合，最終投与後 30 日に追跡調査のための来院又は電話対応を実施した。

注：各国の規制で許容される場合，被験者はスクリーニング来院 1（V1）後に[redacted]を受領し，Day 85 来院（V13）まで[redacted]（最新の承認された製造元の指示を参照）を着用した。本治験実施計画書，付録を通してすべてのウェアラブルウォッチの使用には「各国の規制で許容される場合」が適用された。治験責任医師の判断で，[redacted]の使用を妨げる可能性の状況（宗教上の理由，アトピー性皮膚炎の問題など）がある場合は，治験依頼者の治験担当医学専門家（TA MD）に相談することとした。

Cross References：M15-736 試験 Protocol Figure 1

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2.7.3.3 全試験を通しての結果の比較と解析

2.7.3.3.1 試験対象集団

2.7.3.3.1.1 被験者の内訳

2.7.3.3.1.1.1 M15-741 試験

申請時

M15-741 試験の被験者の内訳を表 2.7.3-5 及び表 2.7.3-6 に示す。

本試験では，244 例が登録され，全被験者が治験薬を投与された。

解析対象集団については，FAS が 244 例であった。

治験薬の投与を完了した被験者は 115 例（47.1%），治験薬投与継続中は 26 例（10.7%），治験薬投与中止は 103 例（42.2%）であった。治験薬の投与を中止した主な理由で最も多かったのは有害事象 55 例（22.5%）であった（表 2.7.3-5）。

投与開始後 12 週時点の被験者の治験薬投与状況は，Sample 1（157 例）では，治験薬の投与を中止した被験者は 49 例（31.2%），治験薬投与継続中は 108 例（68.8%）であった。一方，Sample 2（87 例）では，治験薬の投与を中止した被験者は 17 例（19.5%），治験薬投与継続中は 70 例（80.5%）であった（表 2.7.3-6）。

更新時

M15-741 試験の被験者の内訳を表 2.7.3-7 に示す。

本試験では，244 例が登録され，全被験者が治験薬を投与された。

解析対象集団については，FAS が 244 例であった。

治験薬の投与を完了した被験者は 125 例（51.2%），治験薬投与継続中は 12 例（4.9%），治験薬投与中止は 107 例（43.9%）であった。治験薬の投与を中止した主な理由で最も多かったのは有害事象 56 例（23.0%）であった（表 2.7.3-7）。

投与開始後 12 週時点の被験者の治験薬投与状況は申請時と同様であった（M15-741 試験 CSR update Table 14.1__1.1.2）。

表 2.7.3-5. 被験者の内訳（All Enrolled Subjects）：M15-741 試験

	Number (%) of Subjects
	Total (N=244)
Total subjects enrolled	244 (100)
Full analysis set	244 (100)
Safety analysis set	244 (100)
ABBV-951 ongoing	26 (10.7)
ABBV-951 completed	115 (47.1)
ABBV-951 prematurely discontinued	103 (42.2)
Primary reasons for prematurely discontinued [a]	
Adverse event	55 (22.5)
Infusion site related infections	12 (4.9)
Infusion site related non infection reactions	18 (7.4)
Hallucinations/psychosis	12 (4.9)
Withdrew consent	28 (11.5)
Lost to follow-up	1 (0.4)
Lack of efficacy	10 (4.1)
Difficulty with drug delivery system	5 (2.0)
Other	4 (1.6)

a. One subject can be only counted once.

Cross References：M15-741 試験 CSR Table 14.1__1.1.1

表 2.7.3-6. 治験薬投与開始後 12 週間の登録時期別の被験者の内訳（All Enrolled Subjects）：M15-741 試験

	Number (%) of Subjects		
	Sample 1 (N=157)	Sample 2 (N=87)	Total (N=244)
ABBV-951 ongoing	108 (68.8)	70 (80.5)	178 (73.0)
ABBV-951 prematurely discontinued	49 (31.2)	17 (19.5)	66 (27.0)
Primary reasons for prematurely discontinued [a]			
Adverse event	26 (16.6)	7 (8.0)	33 (13.5)
Infusion site related infections	8 (5.1)	0	8 (3.3)
Infusion site related non infection reactions	10 (6.4)	1 (1.1)	11 (4.5)
Hallucinations/psychosis	6 (3.8)	2 (2.3)	8 (3.3)
Withdrew consent	14 (8.9)	5 (5.7)	19 (7.8)
Lost to follow-up	1 (0.6)	0	1 (0.4)
Lack of efficacy	5 (3.2)	3 (3.4)	8 (3.3)
Difficulty with drug delivery system	3 (1.9)	1 (1.1)	4 (1.6)
Other	0	1 (1.1)	1 (0.4)

Sample 1 = subjects enrolled before [redacted] 20[redacted], Sample 2 = subjects enrolled on or after [redacted] 20[redacted]

a. One subject can be only counted once.

Cross References：M15-741 試験 CSR Table 14.1__1.1.2

表 2.7.3-7. 被験者の内訳（All Enrolled Subjects）：M15-741 試験（更新時）

	Number (%) of Subjects
	Total (N = 244)
Total subjects enrolled	244 (100)
Full analysis set	244 (100)
Safety analysis set	244 (100)
ABBV-951 ongoing	12 (4.9)
ABBV-951 completed	125 (51.2)
ABBV-951 prematurely discontinued	107 (43.9)
Primary reasons for prematurely discontinued [a]	
Adverse event	56 (23.0)
Infusion site related infections	12 (4.9)
Infusion site related non infection reactions	18 (7.4)
Hallucinations / psychosis	12 (4.9)
Withdrew consent	30 (12.3)
Lost to follow-up	1 (0.4)
Lack of efficacy	11 (4.5)
Difficulty with drug delivery system	5 (2.0)
Other	4 (1.6)

a. One subject can be only counted once.

Cross References：M15-741 試験 CSR update Table 14.1__1.1.1

2.7.3.3.1.1.2 M15-737 試験

申請時

M15-737 試験の被験者の内訳を表 2.7.3-8 に示す。

本試験では，M15-741 試験を完了した 105 例が登録された。

解析対象集団については，FAS が 81 例であった。

治験薬の投与を完了した被験者はおらず，治験薬投与継続中は 97 例（92.4%），治験薬投与中止は 8 例（7.6%）であった。治験薬の投与を中止した主な理由で最も多かったのは有害事象 5 例（4.8%）であった。

更新時

M15-737 試験の被験者の内訳を表 2.7.3-9 に示す。

本試験では，M15-741 試験を完了した 116 例が登録された。

解析対象集団については，FAS が 106 例であった。

治験薬の投与を完了した被験者はおらず，治験薬投与継続中は 105 例（90.5%），治験薬投与中止は 11 例（9.5%）であった。治験薬の投与を中止した主な理由で最も多かったのは有害事象 7 例（6.0%）であった。

表 2.7.3-8. 被験者の内訳（All Enrolled Subjects）：M15-737 試験

	Number (%) of Subjects
	Total (N=105)
Total subjects enrolled	105 (100)
Full analysis set	81 (77.1)
Safety analysis set	105 (100)
ABBV-951 ongoing	97 (92.4)
ABBV-951 completed	0
ABBV-951 prematurely discontinued	8 (7.6)
Primary reasons for prematurely discontinued [a]	
Adverse event	5 (4.8)
Infusion site related infections	1 (1.0)
Infusion site related non infection reactions	1 (1.0)
Withdrew consent	0
Lost to follow-up	0
Lack of efficacy	1 (1.0)
Difficulty with drug delivery system	0
Other	2 (1.9)

a. One subject can be only counted once.

Cross Reference：M15-737 試験 CSR Table 14.1__1.1

表 2.7.3-9. 被験者の内訳（All Enrolled Subjects）：M15-737 試験（更新時）

	Number (%) of Subjects
	Total (N = 116)
Total subjects enrolled	116 (100)
Full analysis set	106 (91.4)
Safety analysis set	116 (100)
ABBV-951 ongoing	105 (90.5)
ABBV-951 completed	0
ABBV-951 prematurely discontinued	11 (9.5)
Primary reasons for prematurely discontinued [a]	
Adverse event	7 (6.0)
Infusion site related infections	3 (2.6)
Infusion site related non infection reactions	1 (0.9)
Withdrew consent	1 (0.9)
Lost to follow-up	0
Lack of efficacy	1 (0.9)
Difficulty with drug delivery system	0
Other	2 (1.7)

a. One subject can be only counted once.

Cross Reference：M15-737 試験 CSR update Table 14.1　1.1

2.7.3.3.1.1.3 M15-736 試験

M15-736 試験の被験者の内訳を表 2.7.3-10 に示す。

本試験では 145 例がランダム化され，141 例に盲検下での治験薬が投与された。

解析対象集団については，FAS が 141 例であった。

治験薬の投与を完了した被験者は 110 例（78.0%），治験薬の投与を中止した被験者は 31 例（22.0%）であった。治験薬の投与を中止した主な理由で最も多かったのは有害事象 15 例（10.6%）であった。投与群別では，ABBV-951 投与群（74 例）で治験薬の投与を完了した被験者は 48 例（64.9%），治験薬の投与を中止した被験者は 26 例（35.1%）で，治験薬の投与を中止した主な理由で最も多かったのは有害事象 14 例（18.9%）であった。CD/LD 経口投与群（67 例）で治験薬の投与を完了した被験者は 62 例（92.5%），治験薬の投与を中止した被験者は 5 例（7.5%）で，治験薬の投与を中止した主な理由で最も多かったのは同意の撤回 3 例（4.5%）であった。

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表 2.7.3-10. 被験者の内訳（All Screened Subjects）：M15-736 試験

	Number (%) of Subjects				
	Randomized and Received any Blinded Study Drug			Total Randomized (N=145)	Total Screened (N=270)
	Oral CD/LD (N=67)	ABBV-951 (N=74)	Total (N=141)		
Total subject screened					270 (100)
Total subject screened failed					96 (35.6)
Total enrolled in Oral CD/LD stabilization period					174 (64.4)
Study prematurely discontinued					29 (10.7)
Total randomized in treatment period				145 (100)	
Not received any blinded study drug					4 (1.5)
Took any blinded study drug	67 (100)	74 (100)	141 (100)		
Full analysis set	67 (100)	74 (100)	141 (100)		
Safety analysis set	67 (100)	74 (100)	141 (100)		
ABBV-951 completed	62 (92.5)	48 (64.9)	110 (78.0)		
ABBV-951 prematurely discontinued	5 (7.5)	26 (35.1)	31 (22.0)		
Primary reasons for prematurely discontinued					
Adverse event	1 (1.5)	14 (18.9)	15 (10.6)		
Infusion site related infections	1 (1.5)	4 (5.4)	5 (3.5)		
Infusion site related non infection reactions	0	6 (8.1)	6 (4.3)		
Hallucinations/psychosis	0	1 (1.4)	1 (0.7)		
Falls and associated injuries	0	1 (1.4)	1 (0.7)		
Withdrew consent	3 (4.5)	5 (6.8)	8 (5.7)		
Lost to follow-up	0	0	0		
Lack of efficacy	0	1 (1.4)	1 (0.7)		
Difficulty with drug delivery system	1 (1.5)	4 (5.4)	5 (3.5)		
Other	0	2 (2.7)	2 (1.4)		

CD/LD = carbidopa/levodopa

Note: One subject can be counted multiple times.

Cross Reference：M15-736 試験 CSR Table 14.1__1.1

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2.7.3.3.1.2 人口統計学的特性及びその他のベースラインの特性

2.7.3.3.1.2.1 M15-741 試験

申請時

M15-741 試験の人口統計学的特性及びベースラインの疾患特性の要約を表 2.7.3-11 に示す。

安全性解析対象集団では，年齢の平均値が 63.9 歳（範囲：34～86 歳），65 歳以上の割合が 51.2%，体重の平均値が 72.10 kg（範囲：34.1～120.7 kg），居住地域は欧米及びオーストラリア合わせて 88.9%，女性が 40.2%，民族は非ヒスパニック（非ラテン含む）が 91.8%，人種は白人が 84.8%，アジア人が 13.9%，PD 罹病期間は 10 年以上が 46.3%であった。

更新時

M15-741 試験の人口統計学的特性及びベースラインの疾患特性の要約を M15-741 試験 CSR update Table 14.1__2.2 及び Table 14.1__3.1.2 に示す。

安全性解析対象集団の人口統計学的特性は，申請時と同様であった。

表 2.7.3-11. 人口統計学的特性及びその他のベースラインの特性（安全性解析対象集団）：M15-741 試験

		Sample 1 (N=157)	Sample 2 (N=87)	Total (N=244)
Age, year	Mean (SD)	64.0 (9.51)	63.8 (8.60)	63.9 (9.18)
	Median (min, max)	65.0 (34, 86)	65.0 (44, 82)	65.0 (34, 86)
Age category, n (%)	< 65 years	76 (48.4)	43 (49.4)	119 (48.8)
	≥ 65 years	81 (51.6)	44 (50.6)	125 (51.2)
Weight, kg	Mean (SD)	72.40 (17.654)	71.55 (16.925)	72.10 (17.367)
	Median (min, max)	73.20 (34.1, 120.7)	70.31 (38.9, 110.9)	72.00 (34.1, 120.7)
Geographic region, n (%)	North America	64 (40.8)	26 (29.9)	90 (36.9)
	Europe and Australia	75 (47.8)	52 (59.8)	127 (52.0)
	Japan	18 (11.5)	9 (10.3)	27 (11.1)
Sex, n (%)	Female	61 (38.9)	37 (42.5)	98 (40.2)
	Male	96 (61.1)	50 (57.5)	146 (59.8)
Ethnicity, n (%)	Hispanic or Latino	16 (10.2)	4 (4.6)	20 (8.2)
	Not Hispanic or Latino	141 (89.8)	83 (95.4)	224 (91.8)

表 2.7.3-11. 人口統計学的特性及びその他のベースラインの特性（安全性解析対象集団）：M15-741 試験（続き）

		Sample 1 (N=157)	Sample 2 (N=87)	Total (N=244)
Race, n (%)	White	135 (86.0)	72 (82.8)	207 (84.8)
	Black or African American	0	1 (1.1)	1 (0.4)
	Asian	21 (13.4)	13 (14.9)	34 (13.9)
	American Indian or Alaska Native	1 (0.6)	0	1 (0.4)
	Native Hawaiian or Other Pacific Islander	0	0	0
	Multiple	0	1 (1.1)	1 (0.4)
Duration of PD since diagnosis, n (%)	< 10 years	83 (52.9)	48 (55.2)	131 (53.7)
	≥ 10 years	74 (47.1)	39 (44.8)	113 (46.3)

PD = Parkinson's disease, Sample 1 = subjects enrolled before [redacted] 20[redacted], Sample 2 = subjects enrolled on or after [redacted] 20[redacted], SD = standard deviation

Cross References：M15-741 試験 CSR Table 14.1__2 及び Table 14.1__3.1

2.7.3.3.1.2.2 M15-737 試験

申請時

M15-737 試験の人口統計学的特性及びベースラインの疾患特性の要約を表 2.7.3-12 に示す。

安全性解析対象集団では，年齢の平均値が 62.4 歳（範囲：34～86 歳），65 歳以上の割合が 42.9%，体重の平均値が 74.50 kg（範囲：38.9～110.9 kg），居住地域は欧米及びオーストラリア合わせて 89.5%，女性が 35.2%，民族は非ヒスパニック（非ラテン含む）が 93.3%，人種は白人が 85.7%，アジア人が 13.3%，PD 罹病期間は 10 年以上が 41.0%であった。

更新時

M15-737 試験の人口統計学的特性及びベースラインの疾患特性の要約を表 2.7.3-13 に示す。

安全性解析対象集団では，年齢の平均値が 62.7 歳（範囲：34～86 歳），65 歳以上の割合が 44.8%，体重の平均値が 74.34 kg（範囲：38.9～110.9 kg），居住地域は欧米及びオーストラリア合わせて 89.7%，女性が 36.2%，民族は非ヒスパニック（非ラテン含む）が 92.2%，人種は白人が 85.3%，アジア人が 13.8%，PD 罹病期間は 10 年以上が 44.0%であった。

表 2.7.3-12. 人口統計学的特性及びその他のベースラインの特性（安全性解析対象集団）：M15-737 試験

		Total (N=105)
Age, year	Mean (SD)	62.4 (9.38)
	Median (min, max)	63.0 (34, 86)
Age category, n (%)	< 65 years	60 (57.1)
	≥ 65 years	45 (42.9)
Weight, kg	Mean (SD)	74.50 (17.315)
	Median (min, max)	75.80 (38.9, 110.9)
Geographic region, n (%)	North America	47 (44.8)
	Europe and Australia	47 (44.8)
	Japan	11 (10.5)
Sex, n (%)	Female	37 (35.2)
	Male	68 (64.8)
Ethnicity, n (%)	Hispanic or Latino	7 (6.7)
	Not Hispanic or Latino	98 (93.3)
Race, n (%)	White	90 (85.7)
	Black or African American	0
	Asian	14 (13.3)
	American Indian or Alaska Native	1 (1.0)
	Native Hawaiian or Other Pacific Islander	0
Duration of PD since diagnosis, n (%)	< 10 years	62 (59.0)
	≥ 10 years	43 (41.0)

PD = Parkinson's disease, SD = standard deviation

Cross References：M15-737 試験 CSR Table 14.1__2 及び Table 14.1__3.1

表 2.7.3-13. 人口統計学的特性及びその他のベースラインの特性（安全性解析対象集団）：M15-737 試験（更新時）

		Total (N = 116)
Age, year	Mean (SD)	62.7 (9.39)
	Median (min, max)	63.0 (34, 86)
Age category, n (%)	< 65 years	64 (55.2)
	≥ 65 years	52 (44.8)
Weight, kg	Mean (SD)	74.34 (17.409)
	Median (min, max)	75.65 (38.9, 110.9)
Geographic region, n (%)	North America	49 (42.2)
	Europe and Australia	55 (47.4)
	Japan	12 (10.3)
Sex, n (%)	Female	42 (36.2)
	Male	74 (63.8)
Ethnicity, n (%)	Hispanic or Latino	9 (7.8)
	Not Hispanic or Latino	107 (92.2)
Race, n (%)	White	99 (85.3)
	Black or African American	0
	Asian	16 (13.8)
	American Indian or Alaska Native	1 (0.9)
	Native Hawaiian or Other Pacific Islander	0
Duration of PD since diagnosis, n (%)	< 10 years	65 (56.0)
	≥ 10 years	51 (44.0)

PD = Parkinson's disease, SD = standard deviation
Cross References：M15-737 試験 CSR update Table 14.1__2 及び Table 14.1__3.1

2.7.3.3.1.2.3 M15-736 試験

M15-736 試験の人口統計学的特性及びベースラインの疾患特性の要約を表 2.7.3-14 に示す。

安全性解析対象集団では，年齢の平均値が 66.4 歳（範囲：39～85 歳），65 歳以上の割合が 63.8%，体重の平均値が 80.65 kg（範囲：39.1～142.6 kg），居住地域は米国 85.1%，女性が 29.8%，民族は非ヒスパニック（非ラテン含む）が 96.5%，人種は白人が 92.9%，アジア人が 2.1%，PD 罹病期間は 10 年以上が 32.6%であった。投与群別では，ABBV-951 投与群で年齢の平均値が 66.3 歳（範囲：39～83 歳），65 歳以上の割合が 63.5%，体重の平均値が 79.57 kg（範囲：39.1～142.6 kg），居住地域は米国 83.8%，女性が 32.4%，民族は非ヒスパニック（非ラテン

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含む）が 94.6%，人種は白人が 94.6%，アジア人が 0%，PD 罹病期間は 10 年以上が 31.1%であった。CD/LD 経口投与群では年齢の平均値が 66.6 歳（範囲：45～85 歳），65 歳以上の割合が 64.2%，体重の平均値が 81.85 kg（範囲：51.3～138.2 kg），居住地域は米国 86.6%，女性が 26.9%，民族は非ヒスパニック（非ラテン含む）が 98.5%，人種は白人が 91.0%，アジア人が 4.5%，PD 罹病期間は 10 年以上が 34.3%であり，被験者背景は投与群間でおおむね同様であった。

表 2.7.3-14. 人口統計学的特性及びその他のベースラインの特性（安全性解析対象集団）：M15-736 試験

		Oral CD/LD (N=67)	ABBV-951 (N=74)	Total (N=141)
Age, years	Mean (SD)	66.6 (9.82)	66.3 (9.20)	66.4 (9.47)
	Median (min, max)	69.0 (45, 85)	67.0 (39, 83)	68.0 (39, 85)
Age category, n (%)	< 65 years	24 (35.8)	27 (36.5)	51 (36.2)
	≥ 65 years	43 (64.2)	47 (63.5)	90 (63.8)
Weight, kg	Mean (SD)	81.85 (18.320)	79.57 (18.077)	80.65 (18.164)
	Median (min, max)	79.60 (51.3, 138.2)	80.04 (39.1, 142.6)	79.79 (39.1, 142.6)
Country, n (%)	Australia	9 (13.4)	12 (16.2)	21 (14.9)
	United States	58 (86.6)	62 (83.8)	120 (85.1)
Sex, n (%)	Male	49 (73.1)	50 (67.6)	99 (70.2)
	Female	18 (26.9)	24 (32.4)	42 (29.8)
Ethnicity, n (%)	Hispanic or Latino	1 (1.5)	4 (5.4)	5 (3.5)
	Not Hispanic or Latino	66 (98.5)	70 (94.6)	136 (96.5)
Race, n (%)	White	61 (91.0)	70 (94.6)	131 (92.9)
	Black or African American	2 (3.0)	2 (2.7)	4 (2.8)
	Asian	3 (4.5)	0	3 (2.1)
	American Indian or Alaska Native	0	1 (1.4)	1 (0.7)
	Native Hawaiian or Other Pacific Islander	1 (1.5)	1 (1.4)	2 (1.4)
Duration of PD since diagnosis, n (%)	< 10 years	44 (65.7)	51 (68.9)	95 (67.4)
	≥ 10 years	23 (34.3)	23 (31.1)	46 (32.6)

CD/LD = carbidopa/levodopa, PD = Parkinson's disease, SD = standard deviation

Cross References：M15-736 試験 CSR Table 14.1__2.1 及び Table 14.1__3.1

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2.7.3.3.2 全有効性試験の結果の比較検討

2.7.3.3.2.1 パーキンソン病日誌

2.7.3.3.2.1.1 M15-741 試験

申請時

標準化した 1 日あたりの日常生活に支障のあるジスキネジアを伴わない平均「オン」時間（ジスキネジアを伴わない平均「オン」時間と日常生活に支障のないジスキネジアを伴う平均「オン」時間の合計）及び標準化した 1 日あたりの平均「オフ」時間は，ベースラインと比較してすべての評価時点において改善した（nominal $P < 0.001$）。これらの改善は，ベースライン後の最初の評価時点である投与 1 週時から認められ，投与 26 週時まで経時的に改善し，その後安定した。標準化した 1 日あたりの日常生活に支障のあるジスキネジアを伴わない平均「オン」時間は，ベースラインと比較して投与 26 週時に 3.65 時間，投与 52 週時に 3.58 時間増加し，標準化した 1 日あたりの平均「オフ」時間は，投与 26 週時に 3.27 時間，投与 52 週時に 3.39 時間減少した。標準化した 1 日あたりの平均「オフ」時間と同様に，（日常生活に支障があるか否かにかかわらず）標準化した 1 日あたりのジスキネジアを伴う平均「オン」時間も減少した。標準化した 1 日あたりのジスキネジアを伴わない平均「オン」時間は，ベースラインと比較して投与 26 週時に 4.31 時間，投与 52 週時に 3.78 時間増加した（図 2.7.3-4 及び表 2.7.3.6-1）。

また，登録時期別（Sample 1 及び Sample 2）でも同様に，標準化した 1 日あたりの日常生活に支障のあるジスキネジアを伴わない平均「オン」時間及び標準化した 1 日あたりのジスキネジアを伴わない平均「オン」時間は増加し，標準化した 1 日あたりの平均「オフ」時間及び標準化した 1 日あたりの日常生活に支障のあるジスキネジアを伴う平均「オン」時間は減少した（表 2.7.3.6-2）。

朝の無動状態を呈する被験者の割合は，ベースラインと比較して著しく減少した。朝の無動状態を呈する被験者の割合は，ベースラインの 77.7%に対して投与 1 週時には 31.0%，投与 26 週時で 19.4%であり，その後安定した。朝の無動状態の改善傾向と連動して，覚醒時にジスキネジアを伴わない「オン」状態を呈する被験者の割合は，ベースラインの 17.5%に対して投与 1 週時には 50.0%，投与 26 週時で 67.4%に増加し，その後安定した（図 2.7.3-5）。

更新時

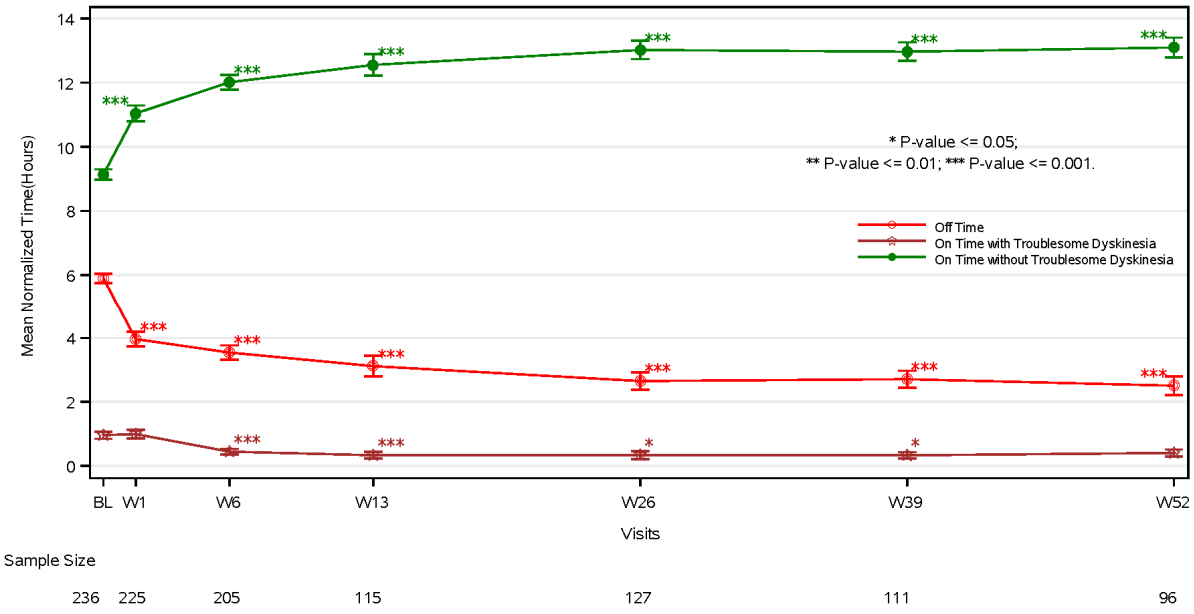
標準化した 1 日あたりの日常生活に支障のあるジスキネジアを伴わない平均「オン」時間（ジスキネジアを伴わない平均「オン」時間と日常生活に支障のないジスキネジアを伴う平均「オン」時間の合計）及び標準化した 1 日あたりの平均「オフ」時間は，ベースラインと比較してすべての評価時点において改善した（nominal $P < 0.001$）。これらの改善は，ベースライン後の最初の評価時点である投与 1 週時から認められ，投与 26 週時まで経時的に改善し，その後安定した。標準化した 1 日あたりの日常生活に支障のあるジスキネジアを伴わない平均「オン」時間は，ベースラインと比較して投与 26 週時に 3.79 時間，投与 52 週時に 3.46 時間増加し，標準化した 1 日あたりの平均「オフ」時間は，投与 26 週時に 3.34 時間，投与 52 週時に 3.36 時間減少した。

標準化した 1 日あたりの平均「オフ」時間と同様に，（日常生活に支障があるか否かにかかわらず）標準化した 1 日あたりのジスキネジアを伴う平均「オン」時間も減少した。標準化した 1 日あたりのジスキネジアを伴わない平均「オン」時間は，ベースラインと比較して投与 26 週時に 4.44 時間，投与 52 週時に 3.79 時間増加した（図 2.7.3-6 及び表 2.7.3.6-18）。

また，登録時期別（Sample 1 及び Sample 2）でも同様に，標準化した 1 日あたりの日常生活に支障のあるジスキネジアを伴わない平均「オン」時間及び標準化した 1 日あたりのジスキネジアを伴わない平均「オン」時間は増加し，標準化した 1 日あたりの平均「オフ」時間及び標準化した 1 日あたりの日常生活に支障のあるジスキネジアを伴う平均「オン」時間は減少した（表 2.7.3.6-19）。

朝の無動状態を呈する被験者の割合は，ベースラインと比較して著しく減少した。朝の無動状態を呈する被験者の割合は，ベースラインの 77.7%に対して投与 1 週時には 31.0%，投与 26 週時で 19.2%であり，その後安定した。朝の無動状態の改善傾向と連動して，覚醒時にジスキネジアを伴わない「オン」状態を呈する被験者の割合は，ベースラインの 17.5%に対して投与 1 週時には 50.0%，投与 26 週時で 68.3%に増加し，その後安定した（図 2.7.3-7）。

図 2.7.3-4. PD 日誌に基づく，標準化した 1 日あたりの平均「オフ」時間及び「オン」時間の推移（FAS）：M15-741 試験



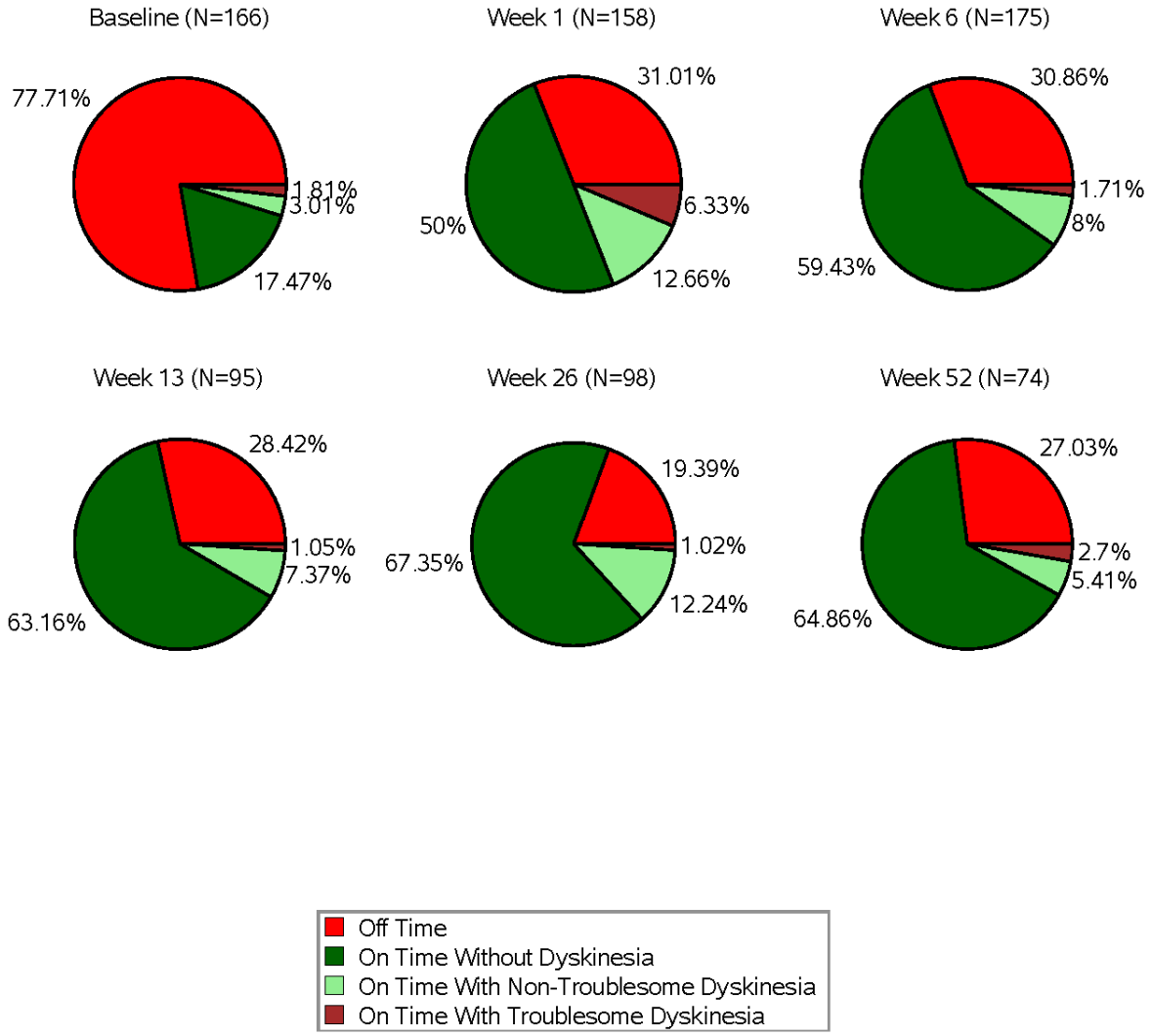
BL = Baseline; FAS = Full Analysis Set; PD = Parkinson's disease; W = Week

Notes: "On" time without troublesome dyskinesia is the sum of "On" time without dyskinesia and "On" time with non-troublesome dyskinesia.

Cross References：M15-741 試験 CSR Figure 14.2__7.1

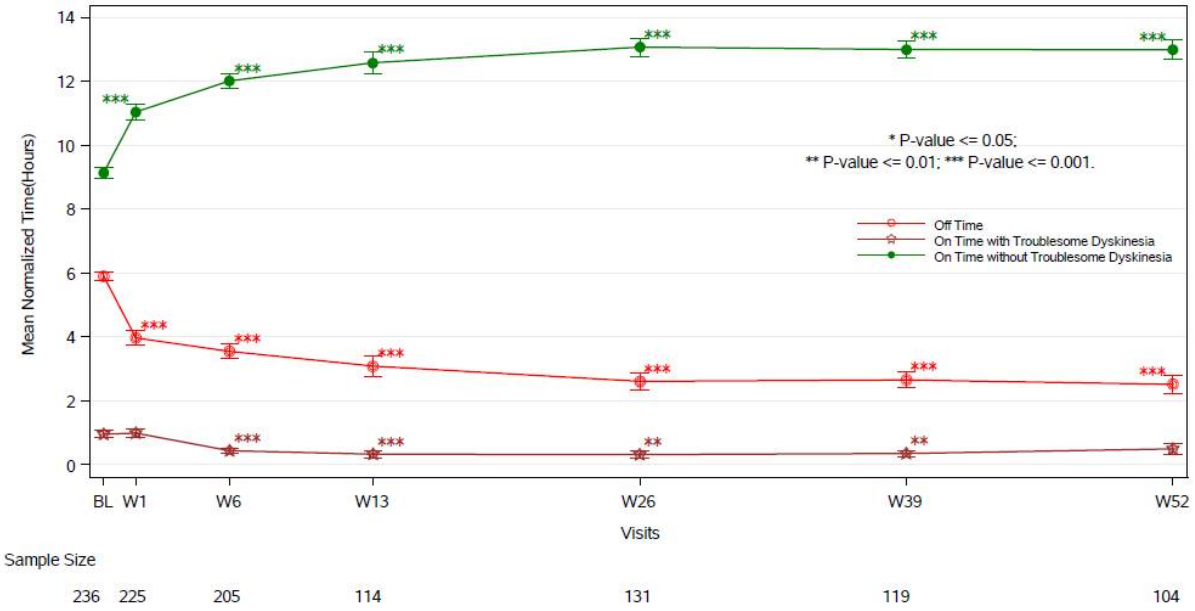
42

図 2.7.3-5. PD 日誌に基づく，早朝覚醒時状態の分布（FAS）：M15-741 試験



FAS = Full Analysis Set, PD = Parkinson's disease
Cross References：M15-741 試験 CSR Figure 14.2__7.3

図 2.7.3-6. PD 日誌に基づく，標準化した 1 日あたりの平均「オフ」時間及び「オン」時間の推移（FAS）：M15-741 試験（更新時）



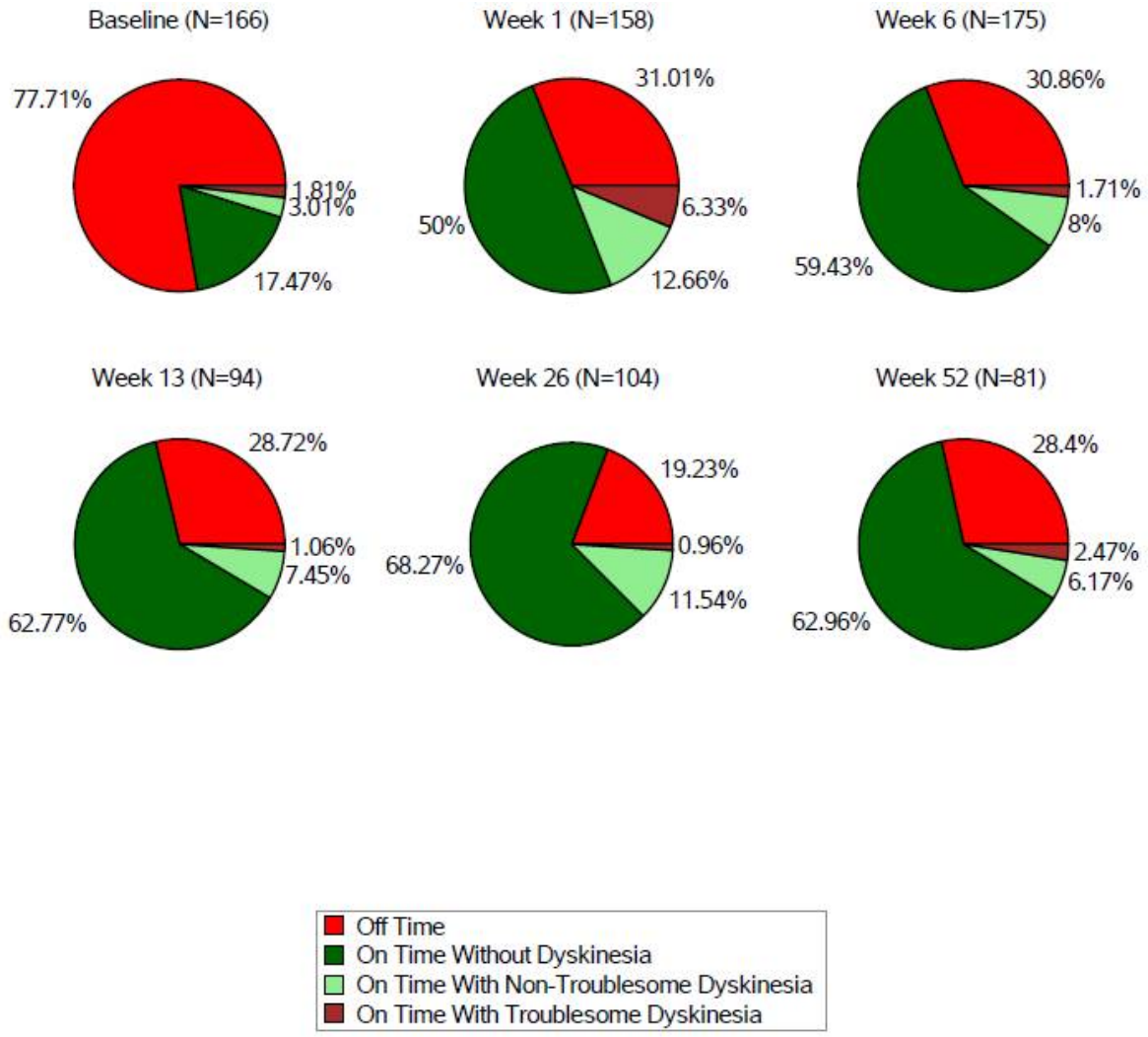
BL = Baseline; FAS = Full Analysis Set; PD = Parkinson's disease; W = Week

Notes: "On" time without troublesome dyskinesia is the sum of "On" time without dyskinesia and "On" time with non-troublesome dyskinesia.

Cross References：M15-741 試験 CSR update Figure 14.2__7.1

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図 2.7.3-7.　　PD 日誌に基づく，早朝覚醒時状態の分布（FAS）：M15-741 試験（更新時）



FAS = Full Analysis Set, PD = Parkinson's disease
Cross References：M15-741 試験 CSR update Figure 14.2__7.3

2.7.3.3.2.1.2　　M15-737 試験

申請時

標準化した 1 日あたりの平均「オフ」時間，標準化した 1 日あたりの日常生活に支障のないジスキネジアを伴う平均「オン」時間及び標準化した 1 日あたりの日常生活に支障のあるジスキネジアを伴う平均「オン」時間の M15-737 試験のベースライン（すなわち親試験である M15-741 試験の最終評価）からの変化量は小さく，M15-741 試験で ABBV-951 を 12 ヵ月間投与した後も投与 48 週にわたって効果が維持されていた（図 2.7.3-8 及び表 2.7.3.6-3）。

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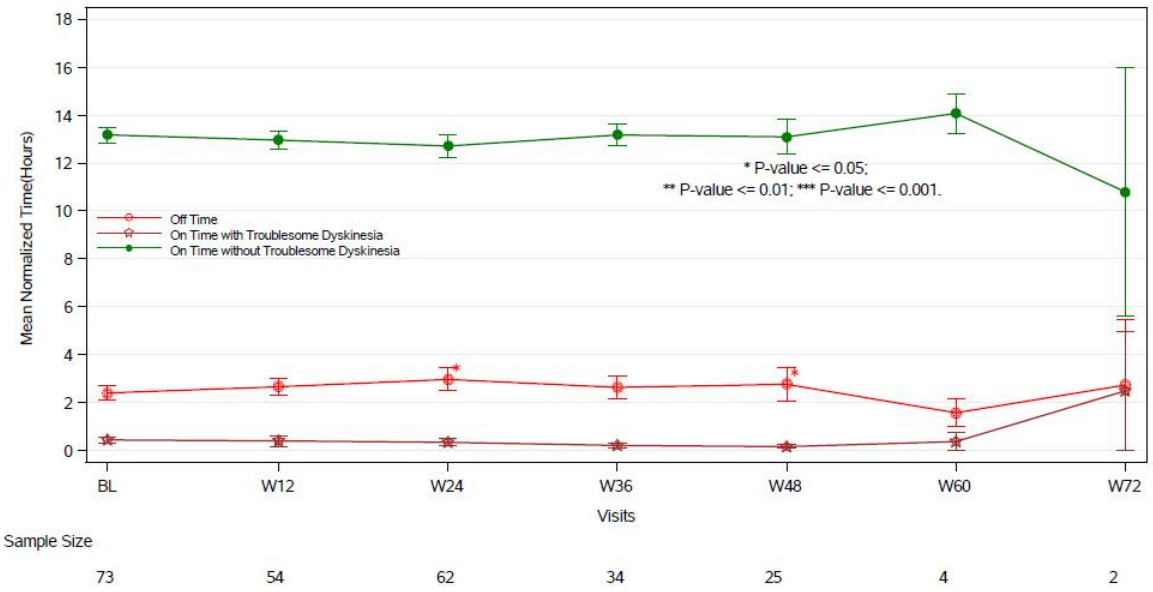
朝の無動状態を呈する被験者の割合は，投与 36 週にわたってベースライン（すなわち親試験である M15-741 試験の最終評価）と比較して減少した。なお，覚醒時にジスキネジアを伴わない「オン」状態を呈する被験者の割合は，すべての評価時点において 50%以上を維持していた（図 2.7.3-9）。

更新時

標準化した 1 日あたりの平均「オフ」時間，標準化した 1 日あたりの日常生活に支障のないジスキネジアを伴う平均「オン」時間及び標準化した 1 日あたりの日常生活に支障のあるジスキネジアを伴う平均「オン」時間の M15-737 試験のベースライン（すなわち親試験である M15-741 試験の最終評価）からの変化量は小さく，M15-741 試験で ABBV-951 を 12 ヵ月間投与した後も投与 72 週にわたって効果が維持されていた（図 2.7.3-10 及び表 2.7.3.6-20）。

朝の無動状態を呈する被験者の割合は，投与 36 週にわたってベースライン（すなわち親試験である M15-741 試験の最終評価）と比較して減少した。なお，覚醒時にジスキネジアを伴わない「オン」状態を呈する被験者の割合は，すべての評価時点において 50%以上を維持していた（図 2.7.3-11）。

図 2.7.3-8. PD 日誌に基づく，標準化した 1 日あたりの平均「オフ」時間及び「オン」時間の推移（FAS）：M15-737 試験



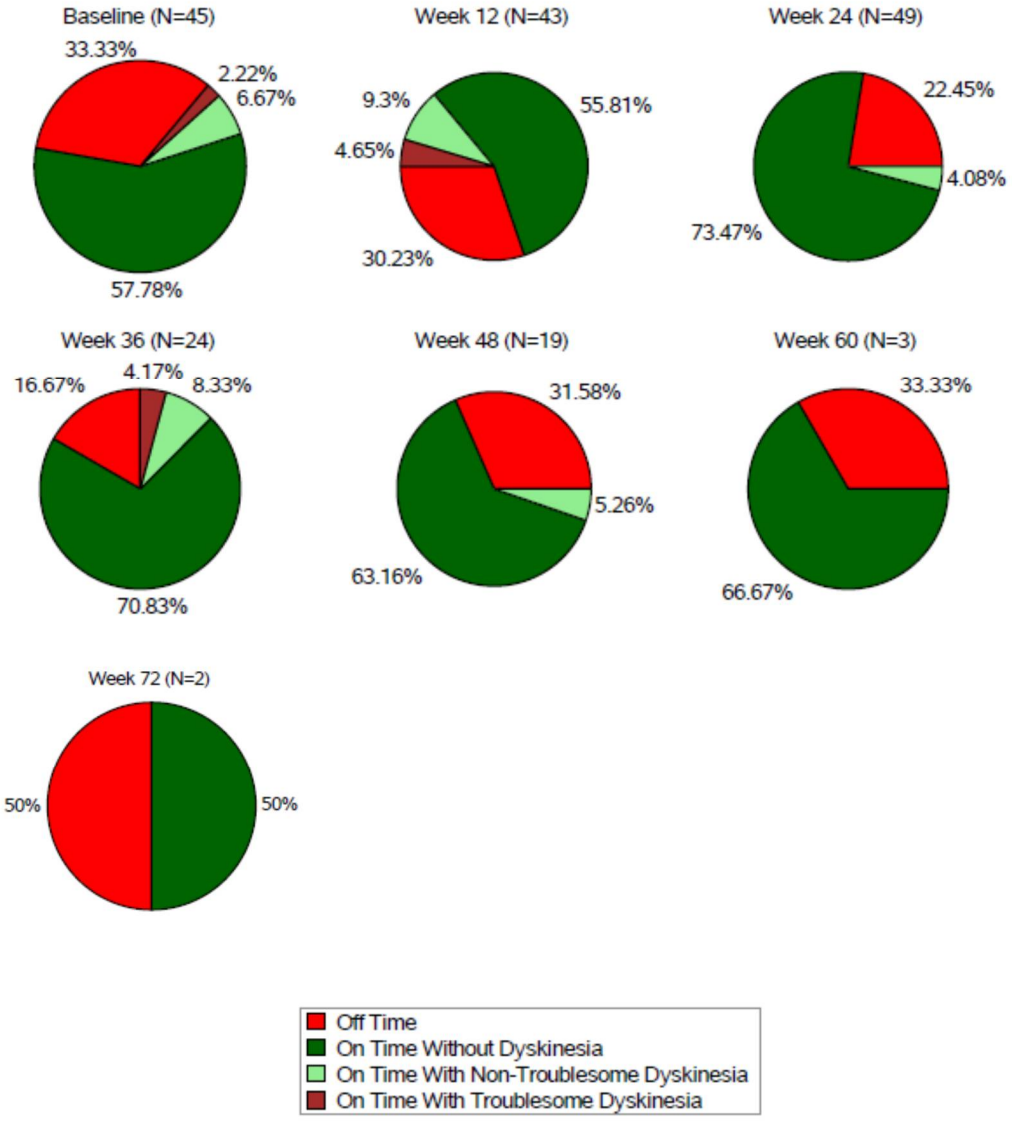
BL = Baseline; FAS = Full Analysis Set; PD = Parkinson's disease; W = Week

Notes: "On" time without troublesome dyskinesia is the sum of "On" time without dyskinesia and "On" time with non-troublesome dyskinesia.

Baseline value for efficacy variables was collected from the last assessment in parent Study M15-741.

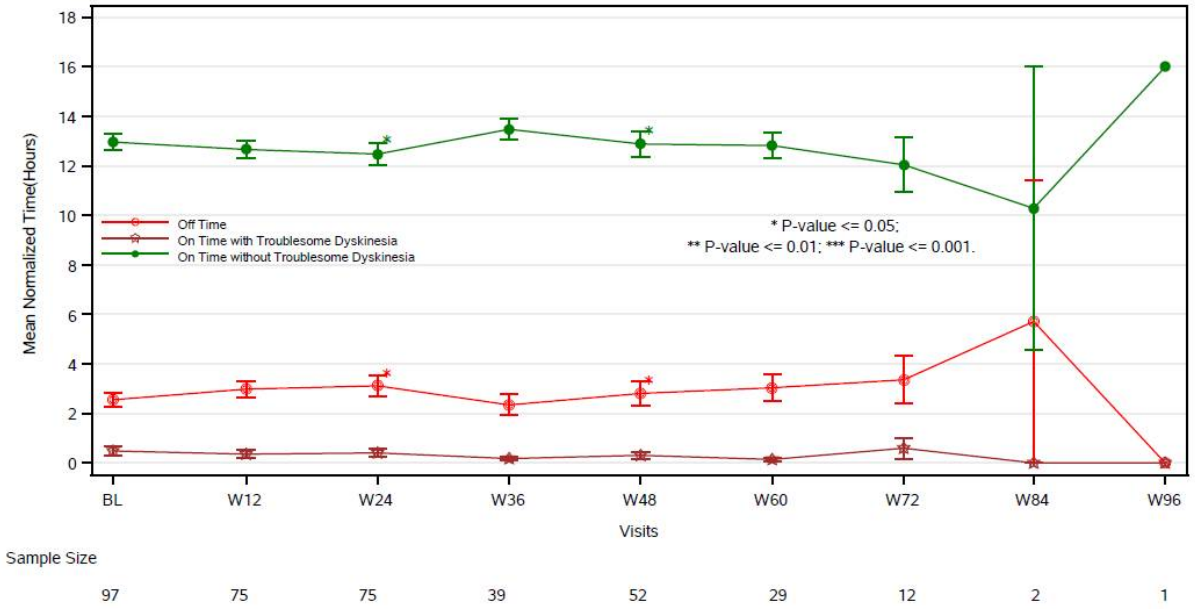
Cross References：M15-737 試験 CSR Figure 14.2　6.1

図 2.7.3-9. PD 日誌に基づく，早朝覚醒時状態の分布（FAS）：M15-737 試験



FAS = Full Analysis Set, PD = Parkinson's disease
Cross References：M15-737 試験 CSR Figure 14.2__6.3

図 2.7.3-10. PD 日誌に基づく，標準化した 1 日あたりの平均「オフ」時間及び「オン」時間の推移（FAS）：M15-737 試験（更新時）



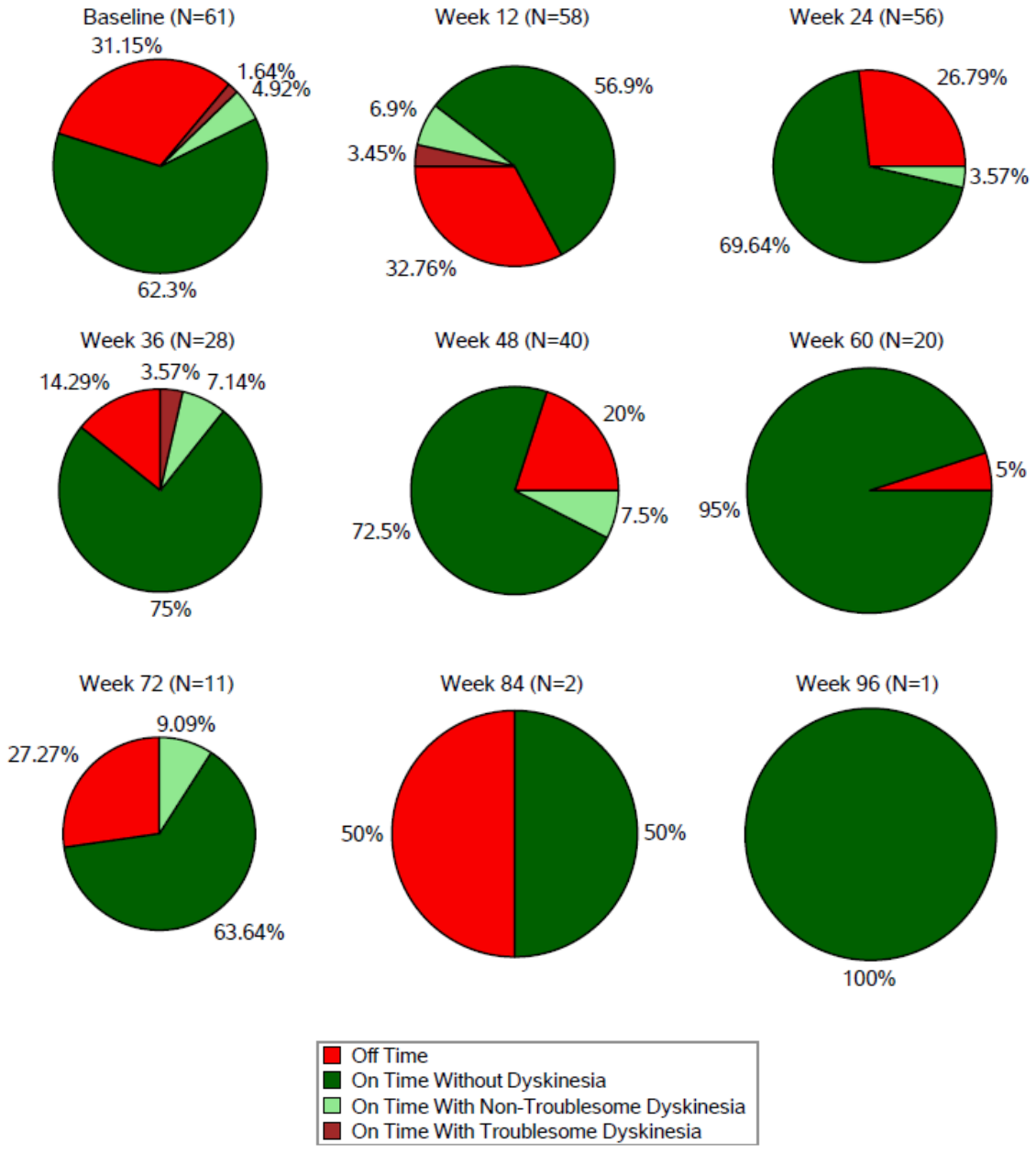
BL = Baseline; FAS = Full Analysis Set; PD = Parkinson's disease; W = Week

Notes: "On" time without troublesome dyskinesia is the sum of "On" time without dyskinesia and "On" time with non-troublesome dyskinesia.

Baseline value for efficacy variables was collected from the last assessment in parent Study M15-741.

Cross References：M15-737 試験 CSR update Figure 14.2__6.1

図 2.7.3-11.　　PD 日誌に基づく，早朝覚醒時状態の分布（FAS）：M15-737 試験（更新時）



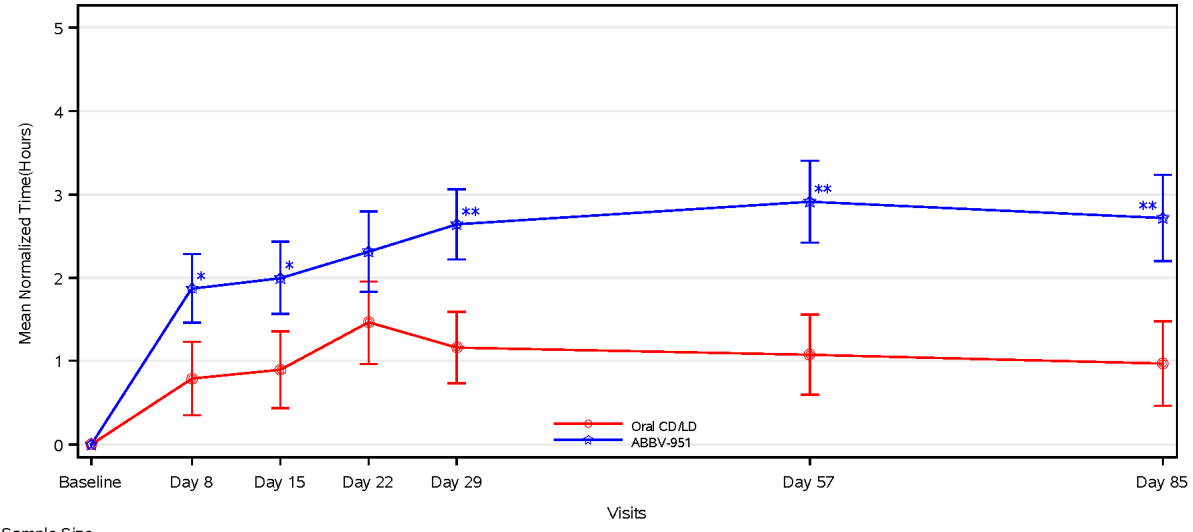
FAS = Full Analysis Set, PD = Parkinson's disease
Cross References：M15-737 試験 CSR update Figure 14.2　6.3

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2.7.3.3.2.1.3 M15-736 試験

主要評価項目である標準化した 1 日あたりの日常生活に支障のあるジスキネジアを伴わない平均「オン」時間のベースラインから投与 12 週時までの変化量は，CD/LD 経口投与群と比較して ABBV-951 投与群で統計学的に有意な改善（$P < 0.01$）を示した（表 2.7.3.6-4）。この改善は，ベースライン後の最初の評価時点である投与 8 日目から認められ，投与 12 週時（投与 85 日目）の二重盲検投与期間終了時まで持続した。CD/LD 経口投与群と比較した ABBV-951 投与群の改善は，投与 22 日目を除くすべての評価時点で nominal $P < 0.05$ であった（図 2.7.3-12）。また，主な副次評価項目（第 1 順位）である標準化した 1 日あたりの平均「オフ」時間のベースラインから投与 12 週時までの変化量も，CD/LD 経口投与群と比較して ABBV-951 投与群で統計学的に有意な改善（$P < 0.01$）を示した（表 2.7.3.6-4）。CD/LD 経口投与群と比較した ABBV-951 投与群の改善は，投与 22 日目を除くすべての評価時点で nominal $P < 0.05$ であった（図 2.7.3-13）。その他の評価項目（第 4 順位）である標準化した 1 日あたりのジスキネジアを伴わない平均「オン」時間のベースラインから投与 12 週時までの変化量は，CD/LD 経口投与群と比較して ABBV-951 投与群で高い改善が認められた（nominal $P < 0.01$）（図 2.7.3-14 及び表 2.7.3.6-4）。主な副次評価項目（第 3 順位）である投与 12 週時における朝の無動では，CD/LD 経口投与群と比較して ABBV-951 投与群で高い改善が認められた（nominal $P < 0.001$）（表 2.7.3.6-5）。ABBV-951 投与群では，朝の無動状態を呈する被験者の割合がベースライン時から著しく減少し，ABBV-951 投与後にジスキネジアを伴わない「オン」状態で覚醒したと報告した被験者の割合が大多数であった（図 2.7.3-15）。この改善は，ベースライン後の最初の評価時点である投与 8 日目に認められ，投与 85 日目（投与 12 週時）まで持続した。

図 2.7.3-12. PD 日誌に基づく，標準化した 1 日あたりの日常生活に支障のあるジスキネジアを伴わない平均「オン」時間のベースラインからの変化量の推移（FAS）：M15-736 試験



Sample Size							
Oral CD/LD	67	65	63	39	62	62	62
ABBV-951	73	70	66	39	54	47	47

CD/LD = carbidopa/levodopa

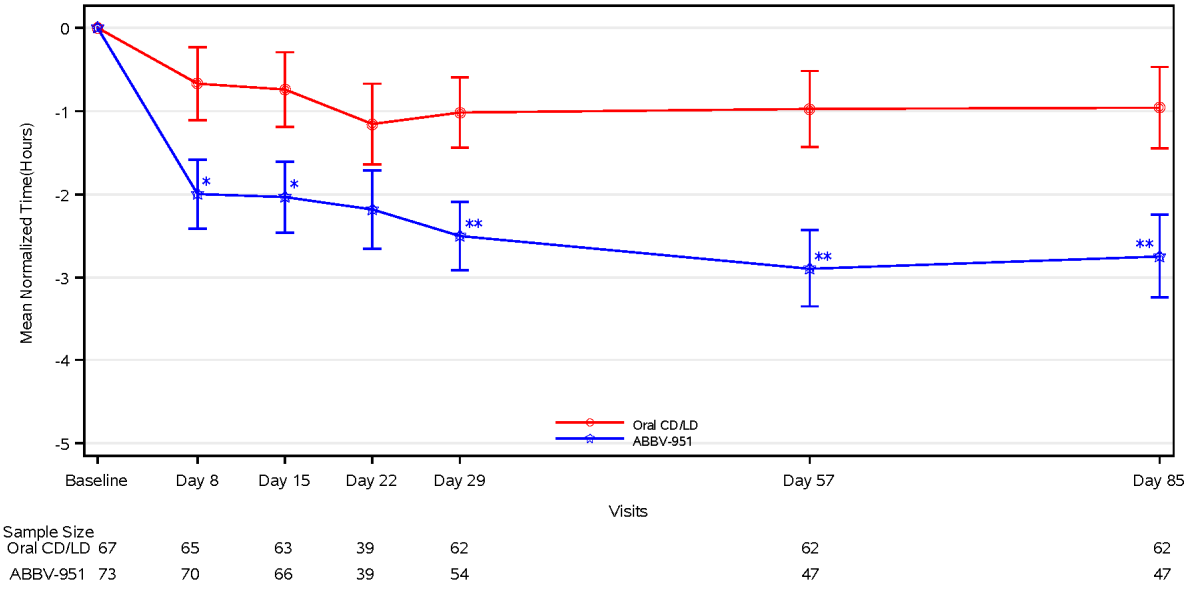
Note: Day 22 was an optional visit.

*P <= 0.05, **P <= 0.01, ***P <= 0.001, P-value reflects treatment difference between groups

Cross References：M15-736 試験 CSR Figure 14.2__12.1

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図 2.7.3-13. PD 日誌に基づく，標準化した 1 日あたりの平均「オフ」時間のベースラインからの変化量の推移（FAS）：M15-736 試験



Sample Size							
Oral CD/LD	67	65	63	39	62	62	62
ABBV-951	73	70	66	39	54	47	47

CD/LD = carbidopa/levodopa

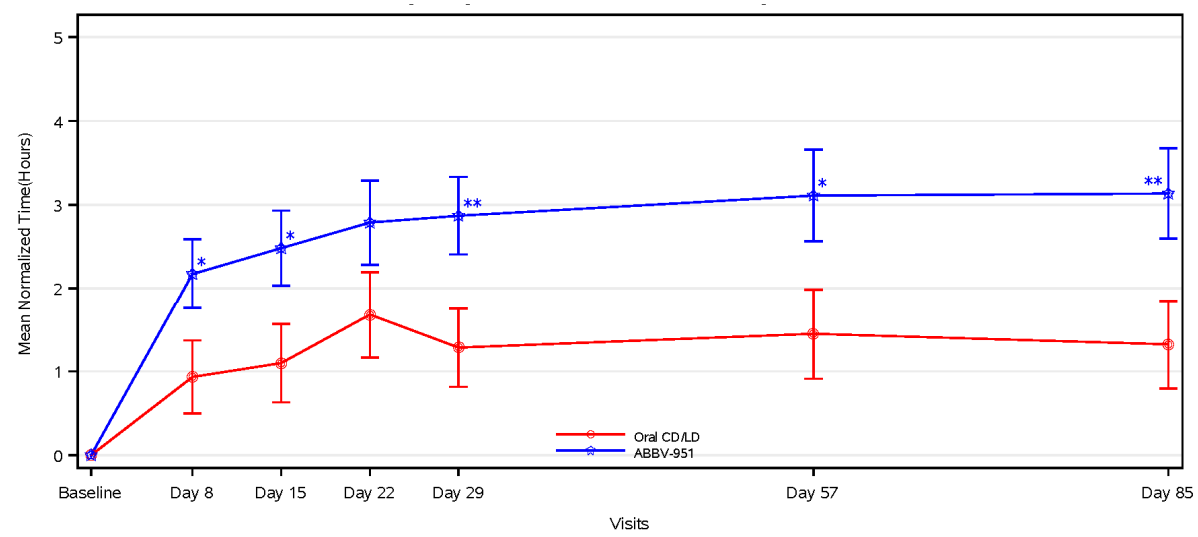
Note: Day 22 was an optional visit.

*P <= 0.05, **P <= 0.01, ***P <= 0.001, P-value reflects treatment difference between groups

Cross References：M15-736 試験 CSR Figure 14.2__12.1

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図 2.7.3-14.　PD 日誌に基づく，標準化した 1 日あたりのジスキネジアを伴わない平均「オン」時間のベースラインからの変化量の推移（FAS）：M15-736 試験



Sample Size							
Oral CD/LD	67	65	63	39	62	62	62
ABBV-951	73	70	66	39	54	47	47

CD/LD = carbidopa/levodopa

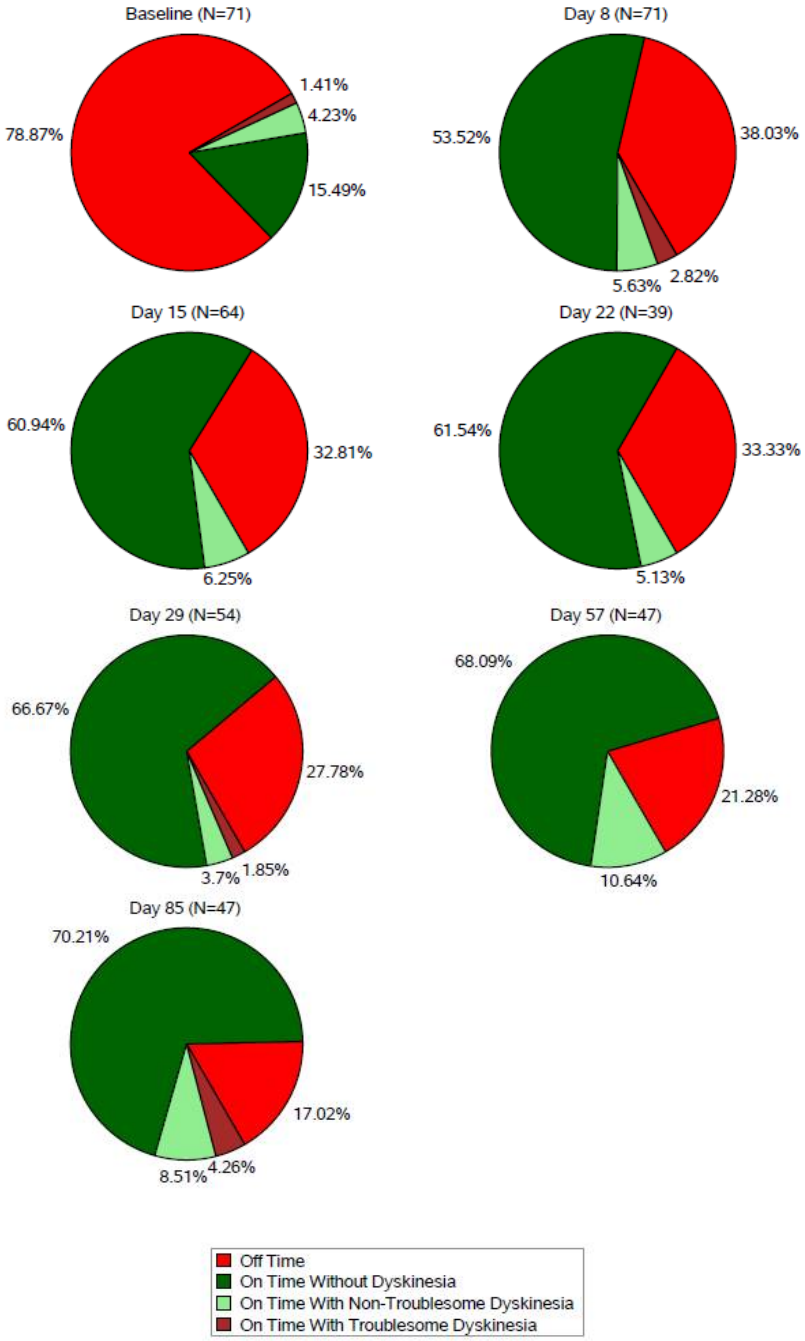
Note: Day 22 was an optional visit.

*P <= 0.05, **P <= 0.01, ***P <= 0.001, P-value reflects treatment difference between groups

Cross References：M15-736 試験 CSR Figure 14.2__12.1

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図 2.7.3-15. PD 日誌に基づく，早朝覚醒時状態の分布（FAS）：M15-736 試験（ABBV-0951 投与群）



FAS = Full Analysis Set, PD = Parkinson's disease

Cross References：M15-736 試験 CSR Figure 14.2__12.4

2.7.3.3.2.2 MDS-UPDRS

2.7.3.3.2.2.1 M15-741 試験

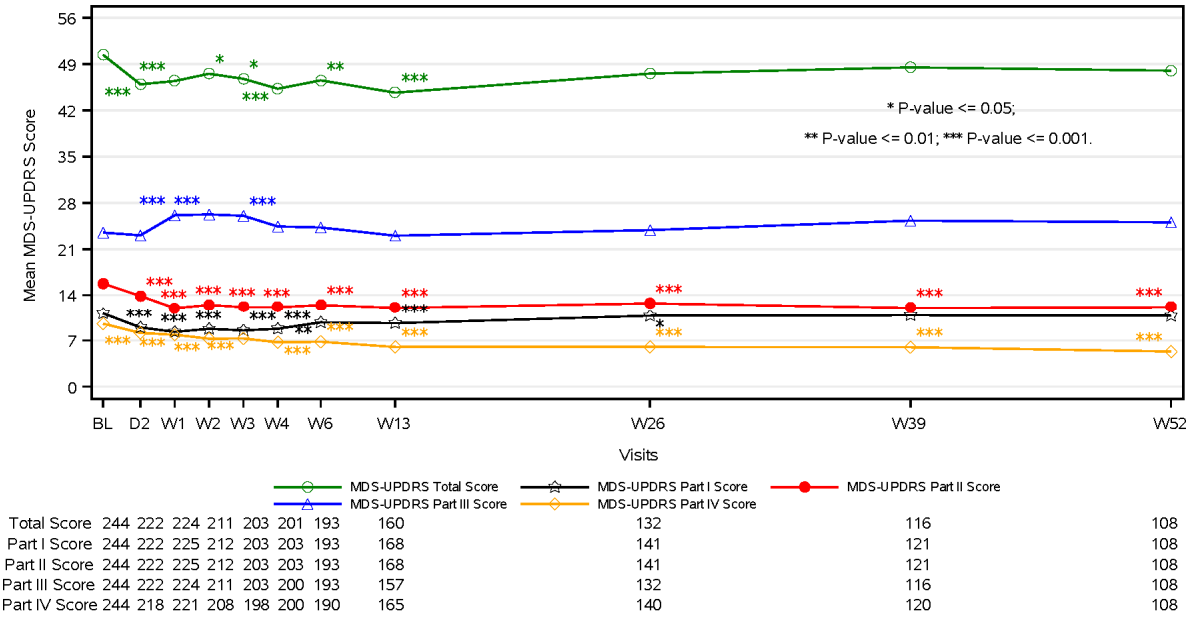
申請時

MDS-UPDRS Part II による M-EDL スコアは，ベースラインと比較してすべての評価時点において改善した（nominal $P < 0.001$，図 2.7.3-16 及び表 2.7.3.6-6）。MDS-UPDRS Part IV の運動合併症スコアも同様に，すべての評価時点において改善が認められた（nominal $P < 0.001$）。これらの改善は投与開始後早期（投与 2 日目）からみられた（表 2.7.3.6-6）。

更新時

MDS-UPDRS Part II による M-EDL スコアは，ベースラインと比較してすべての評価時点において改善した（nominal $P < 0.001$，図 2.7.3-17 及び表 2.7.3.6-21）。MDS-UPDRS Part IV の運動合併症スコアも同様に，すべての評価時点において改善が認められた（nominal $P < 0.001$）。これらの改善は投与開始後早期（投与 2 日目）からみられた（表 2.7.3.6-21）。

図 2.7.3-16. MDS-UPDRS スコアの推移（FAS）：M15-741 試験



Total Score	244	222	224	211	203	201	193	160	132	116	108
Part I Score	244	222	225	212	203	203	193	168	141	121	108
Part II Score	244	222	225	212	203	203	193	168	141	121	108
Part III Score	244	222	224	211	203	200	193	157	132	116	108
Part IV Score	244	218	221	208	198	200	190	165	140	120	108

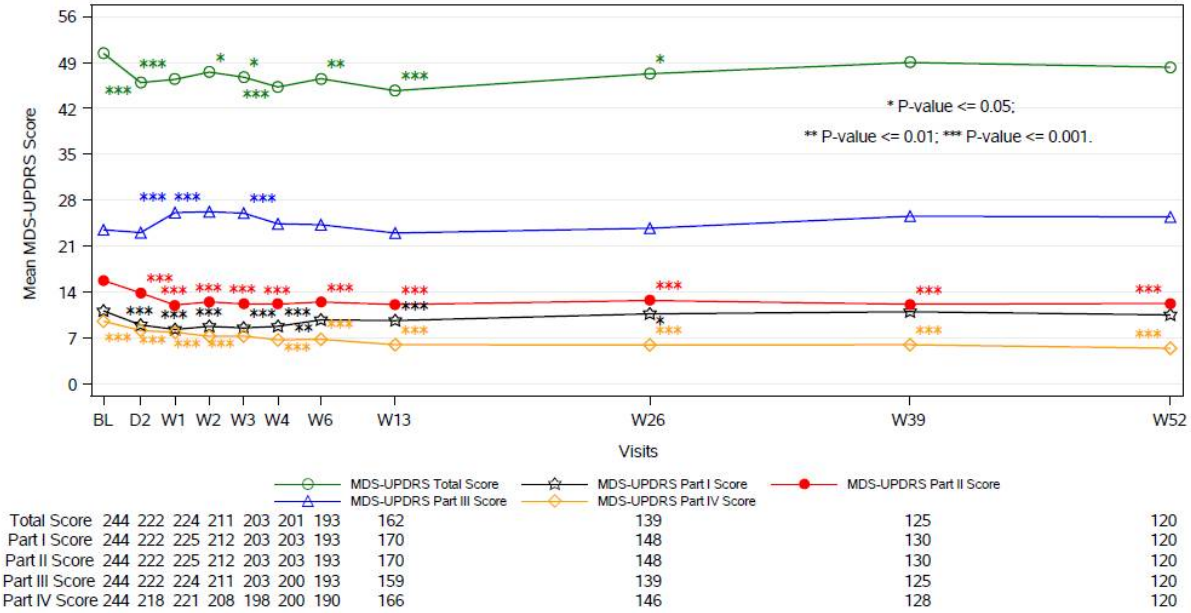
BL = Baseline; D = Day; FAS = Full Analysis Set; MDS-UPDRS = Movement Disorder Society-Unified Parkinson's Disease Rating Scale; W = Week

Note: Sample sizes are shown beneath the figure.

Cross References：M15-741 試験 CSR Figure 14.2__8

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図 2.7.3-17.　　MDS-UPDRS スコアの推移（FAS）：M15-741 試験（更新時）



Total Score	244	222	224	211	203	201	193	162	139	125	120
Part I Score	244	222	225	212	203	203	193	170	148	130	120
Part II Score	244	222	225	212	203	203	193	170	148	130	120
Part III Score	244	222	224	211	203	200	193	159	139	125	120
Part IV Score	244	218	221	208	198	200	190	166	146	128	120

BL = Baseline; D = Day; FAS = Full Analysis Set; MDS-UPDRS = Movement Disorder Society-Unified Parkinson's Disease Rating Scale; W = Week

Note: Sample sizes are shown beneath the figure.

Cross References：M15-741 試験 CSR update Figure 14.2__8

2.7.3.3.2.2.2　　M15-737 試験

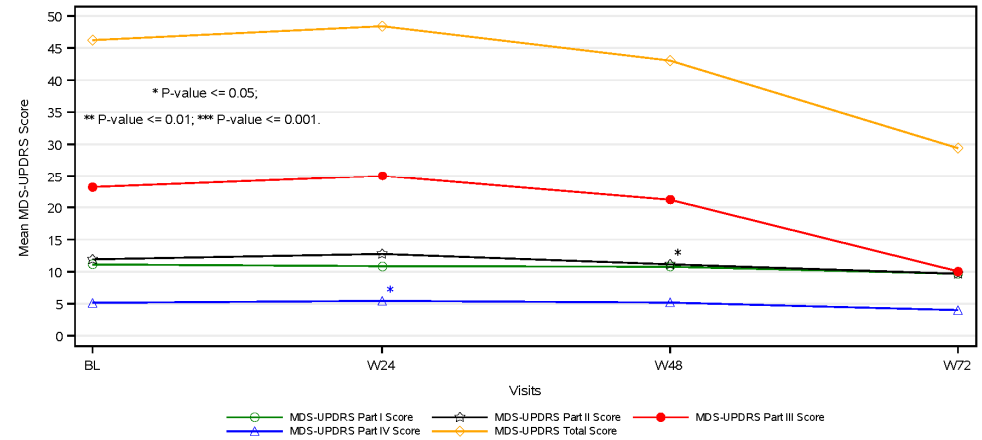
申請時

ベースラインから投与 48 週時までの MDS-UPDRS スコアはおおむね同様であり，M15-741 試験で ABBV-951 を 12 ヵ月間投与した後の治療効果が維持された（図 2.7.3-18 及び表 2.7.3.6-7）。

更新時

ベースラインから投与 72 週時までの MDS-UPDRS スコアはおおむね同様であり，M15-741 試験で ABBV-951 を 12 ヵ月間投与した後の治療効果が維持された（図 2.7.3-19 及び表 2.7.3.6-22）。

図 2.7.3-18. MDS-UPDRS スコアの推移（FAS）：M15-737 試験



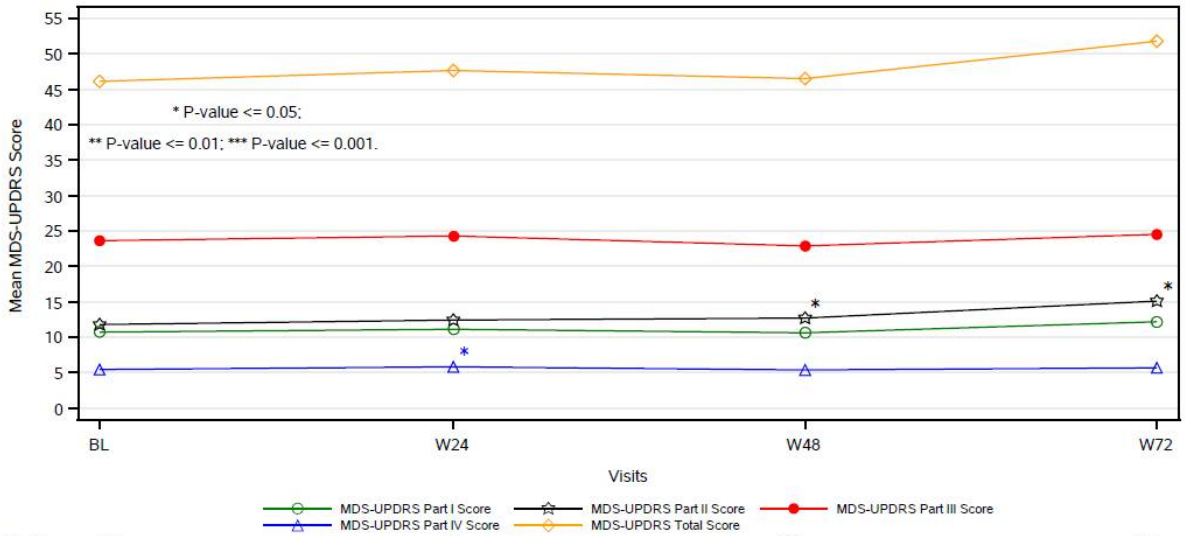
Total Score	81	69	24	3
Part I Score	81	73	29	3
Part II Score	81	73	29	3
Part III Score	81	69	24	3
Part IV Score	81	73	29	3

BL = Baseline; FAS = Full Analysis Set; MDS-UPDRS = Movement Disorder Society-Unified Parkinson's Disease Rating Scale; W = Week

Note: Sample sizes are shown beneath the figure.

Cross References：M15-737 試験 CSR Figure 14.2__7

図 2.7.3-19. MDS-UPDRS スコアの推移（FAS）：M15-737 試験（更新時）



Total Score	106	79	57	12
Part I Score	106	83	64	12
Part II Score	106	83	64	12
Part III Score	106	79	56	12
Part IV Score	106	83	63	12

BL = Baseline; FAS = Full Analysis Set; MDS-UPDRS = Movement Disorder Society-Unified Parkinson's Disease Rating Scale; W = Week

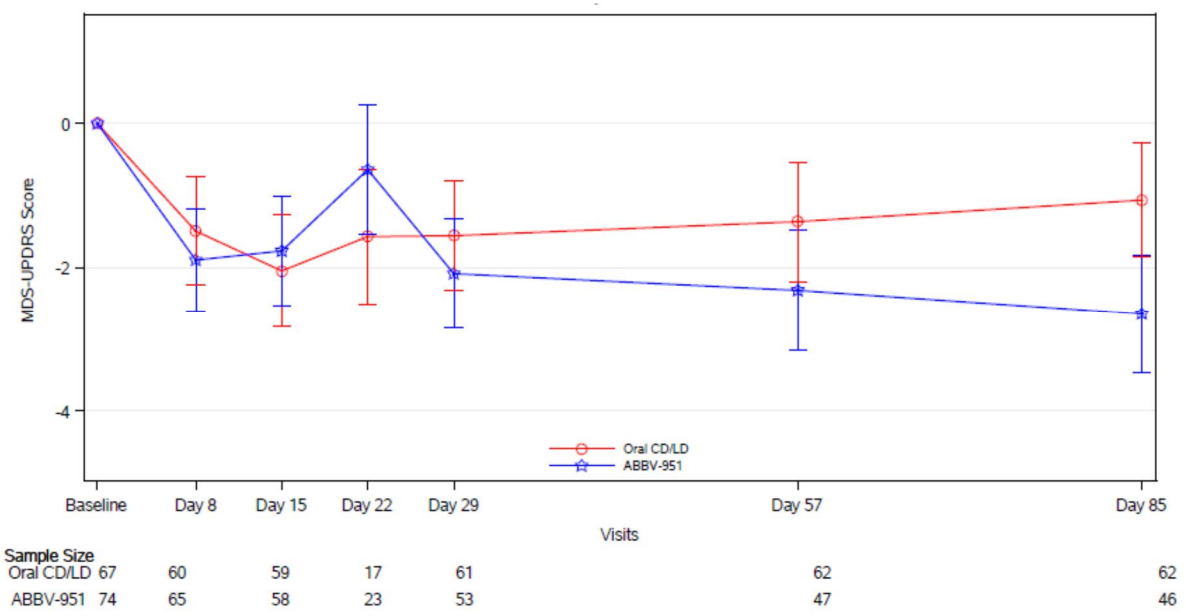
Note: Sample sizes are shown beneath the figure.

Cross References：M15-737 試験 CSR update Figure 14.2__7

2.7.3.3.2.2.3 M15-736 試験

主な副次評価項目（第 2 順位）である MDS-UPDRS Part II による M-EDL スコアのベースラインから投与 12 週時までの変化量は，CD/LD 経口投与群と ABBV-951 投与群で統計学的有意差は認められなかった（図 2.7.3-20 及び表 2.7.3.6-8）。

図 2.7.3-20. MDS-UPDRS Part II スコアのベースラインからの変化量の推移（FAS）：M15-736 試験



CD/LD = carbidopa/levodopa; D = Day; FAS = Full Analysis Set; MDS-UPDRS = Movement Disorder Society-Unified Parkinson's Disease Rating Scale

Note: Day 22 was an optional visit.

*P<=0.05, **P<=0.01, ***P<=0.001, P-value reflects treatment difference between groups

Cross References：M15-736 試験 CSR Figure 14.2__12.5

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2.7.3.3.2.3 PDSS-2

2.7.3.3.2.3.1 M15-741 試験

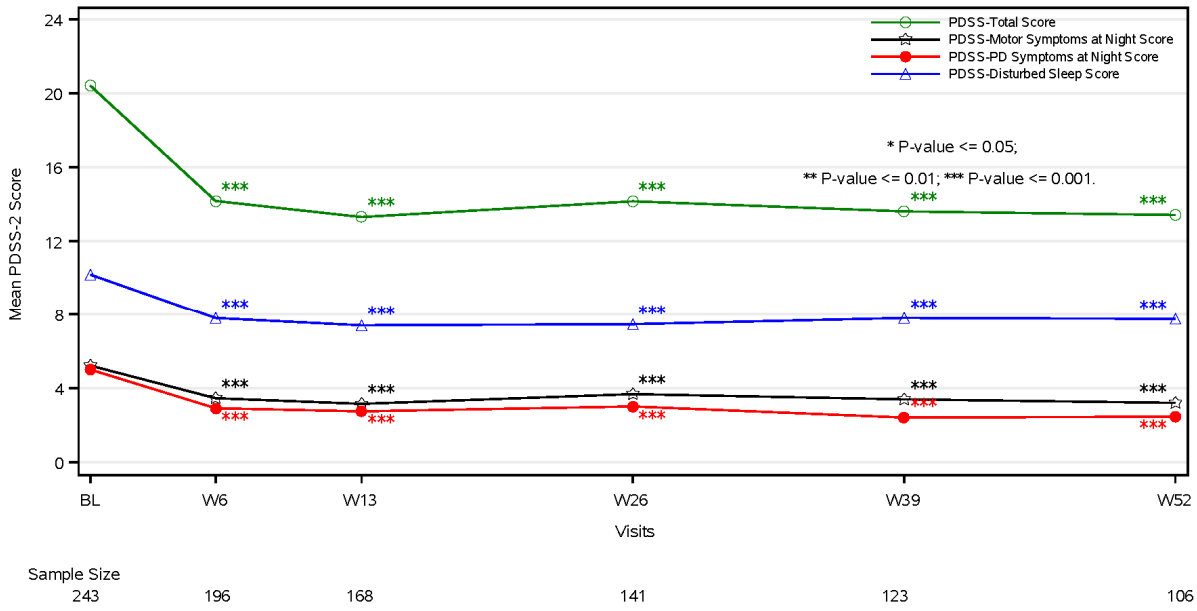
申請時

PDSS-2 合計スコア，夜間 PD スコア，夜間運動症状スコア及び睡眠中断スコアは，すべての評価時点においてベースラインから改善した（nominal $P < 0.01$）（図 2.7.3-21 及び表 2.7.3.6-9）。

更新時

PDSS-2 合計スコア，夜間 PD スコア，夜間運動症状スコア及び睡眠中断スコアは，すべての評価時点においてベースラインから改善した（nominal $P < 0.01$）（図 2.7.3-22 及び表 2.7.3.6-23）。

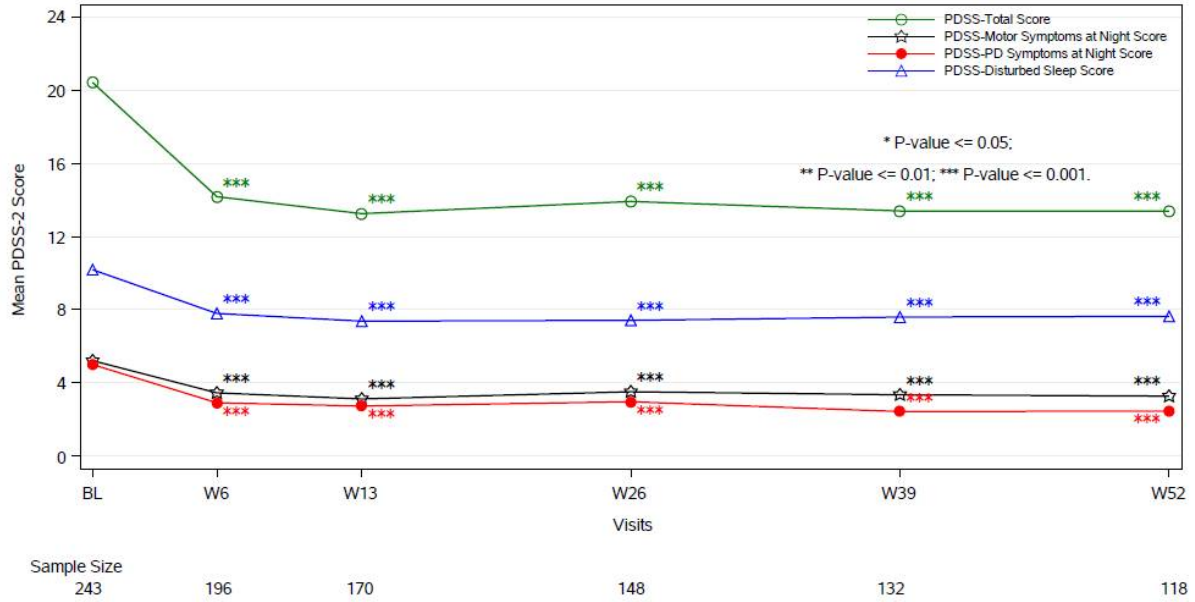
図 2.7.3-21. PDSS-2 スコアの推移（FAS）：M15-741 試験



BL = Baseline; FAS = Full Analysis Set; PDSS = Parkinson's disease sleep scale; W = Week
Cross References：M15-741 試験 CSR Figure 14.2__9

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図 2.7.3-22.　　PDSS-2 スコアの推移（FAS）：M15-741 試験（更新時）



BL = Baseline; FAS = Full Analysis Set; PDSS = Parkinson's disease sleep scale; W = Week
Cross References：M15-741 試験 CSR update Figure 14.2__9

2.7.3.3.2.3.2　　M15-736 試験

その他の副次評価項目（第 5 順位）である PDSS-2 合計スコアのベースラインから最終来院日までの変化量は，CD/LD 経口投与群と比較して ABBV-951 投与群で高い改善が認められた（nominal $P < 0.001$）。また，夜間運動症状スコア及び睡眠中断スコアのベースラインからの変化量は，CD/LD 経口投与群と比較して ABBV-951 投与群で高い改善を示した（nominal $P < 0.001$）（表 2.7.3.6-10）。

2.7.3.3.2.4　　生活の質

2.7.3.3.2.4.1　　M15-741 試験

申請時

PDQ-39 要約指標による PD 及び健康に関連した生活の質，すなわち運動能力，日常生活動作，恥辱感及び身体的苦痛の各スコアは，ベースラインと比較して改善した（nominal $P < 0.05$）。EQ-5D-5L 要約指標及び VAS による結果も同様であった（M15-741 試験 CSR Table 14.2__4 及び Table 14.2__5）。

更新時

PDQ-39 要約指標による PD 及び健康に関連した生活の質，すなわち運動能力，日常生活動作，恥辱感及び身体的苦痛の各スコアは，ベースラインと比較して改善した（nominal $P < 0.05$）。EQ-5D-5L 要約指標及び VAS による結果も同様であった（M15-741 試験 CSR update Table 14.2__4 及び Table 14.2__5)。

2.7.3.3.2.4.2 M15-737 試験

申請時

PDQ-39 要約指標及び EQ-5D-5L 要約指標は，ベースラインから投与後 48 週時までスコアの変化はみられず，M15-741 試験で ABBV-951 を 12 ヵ月間投与した後の治療効果が維持された（M15-737 試験 CSR Table 14.2__3 及び Table 14.2__4)。

更新時

PDQ-39 要約指標及び EQ-5D-5L 要約指標は，ベースラインから投与後 72 週時まで安定しており，M15-741 試験で ABBV-951 を 12 ヵ月間投与した後の治療効果が維持された（M15-737 試験 CSR update Table 14.2__3 及び Table 14.2__4)。

2.7.3.3.2.4.3 M15-736 試験

その他の副次評価項目（第 6 順位）である PDQ-39 要約指標のベースラインから最終来院日までの変化量は，CD/LD 経口投与群と比較して ABBV-951 投与群で高い改善が認められた（nominal $P < 0.05$）。また，運動能力及び恥辱感の PDQ-39 ドメインスコアのベースラインからの変化量は，CD/LD 経口投与群と比較して ABBV-951 投与群で高い改善を示した（nominal $P < 0.05$）（M15-736 試験 CSR Table 14.2__6）。

その他の副次評価項目（第 7 順位）である EQ-5D-5L 要約指標のベースラインから最終来院日までの変化量は，CD/LD 経口投与群と ABBV-951 投与群で差は認められなかった。EQ-5D-5L VAS のベースラインからの変化量は，CD/LD 経口投与群と比較して ABBV-951 投与群で高い改善を示した（nominal $P < 0.05$）（M15-736 試験 CSR Table 14.2__7）。

2.7.3.3.2.5 認知機能

申請時

M15-737 試験において，ベースラインから投与 48 週時までの MMSE 合計スコアの変化量に差は認められなかった。これは ABBV-951 の作用機序から考えられる予想の範囲内であった（M15-737 試験 CSR Table 14.2__5)。

更新時

M15-737 試験において，ベースラインから投与 72 週時までの MMSE 合計スコアの変化量に差は認められなかった。これは ABBV-951 の作用機序から考えられる予想の範囲内であった（M15-737 試験 CSR update Table 14.2__5)。

2.7.3.3.3 部分集団における結果の比較

2.7.3.3.3.1 日本人部分集団及び全体集団の結果の一貫性

2.7.3.3.3.1.1 試験対象集団

2.7.3.3.3.1.1.1 M15-741 試験

申請時

M15-741 試験の日本人被験者の内訳，人口統計学的特性及びベースライン特性を以下に示す。

本試験には 27 例の日本人が登録され，日本人部分集団の FAS は 27 例であった。

治験薬の投与を完了した被験者は 11 例（40.7%），治験薬投与継続中は 1 例（3.7%），治験薬投与中止は 15 例（55.6%）であった。治験薬の投与を中止した主な理由で最も多かったのは有害事象並びに同意の撤回であり，各 6 例（22.2%）であった（表 2.7.3-15，全体集団については表 2.7.3-5）。

Sample 1（18 例）では，投与開始後 12 週間において治験薬の投与を中止した被験者は 9 例（50.0%），治験薬投与継続中は 9 例（50.0%）であった。一方，Sample 2（9 例）では，投与開始後 12 週間において治験薬の投与を中止した被験者は 1 例（11.1%），治験薬投与継続中は 8 例（88.9%）であった（表 2.7.3-16，全体集団については表 2.7.3-6）。

安全性解析対象集団では，年齢の平均値が 63.3 歳（範囲：46～83 歳），65 歳以上の割合が 44.4%，体重の平均値が 56.23 kg（範囲：34.1～82.5 kg），女性が 51.9%であった。いくつかの項目で偏りが認められたものの，日本人部分集団と全体集団の被験者背景はおおむね同様であった（表 2.7.3-17，全体集団については表 2.7.3-11）。日本人部分集団の Sample 1 と Sample 2 では，Sample 2 で 65 歳未満の割合が高い以外は，両 Sample の被験者背景はおおむね同様であった。

更新時

M15-741 試験の日本人被験者の内訳，人口統計学的特性及びベースライン特性を以下に示す。

本試験には 27 例の日本人が登録され，日本人部分集団の FAS は 27 例であった。

治験薬の投与を完了した被験者は 12 例（44.4%），治験薬投与継続中は 0 例，治験薬投与中止は 15 例（55.6%）であった。治験薬の投与を中止した主な理由で最も多かったのは有害事象及び同意の撤回であり，各 6 例（22.2%）であった（表 2.7.3-18，全体集団については表 2.7.3-7）。

投与開始後 12 週時点の被験者の治験薬投与状況は申請時と同一であった（M15-741 試験 CSR update Table 14.1__1.1.2.J，全体集団については M15-741 試験 CSR update Table 14.1__1.1.2）。

安全性解析対象集団の人口統計学特性は，申請時と同一であった（M15-741 試験 CSR update Table 14.1__2.2.J）。

表 2.7.3-15. 被験者の内訳（All Enrolled Subjects，日本人部分集団）：M15-741 試験

	Number (%) of Subjects
	Total (N=27)
Total subjects enrolled	27 (100)
Full analysis set	27 (100)
Safety analysis set	27 (100)
ABBV-951 ongoing	1 (3.7)
ABBV-951 completed	11 (40.7)
ABBV-951 prematurely discontinued	15 (55.6)
Primary reasons for prematurely discontinued [a]	
Adverse event	6 (22.2)
Infusion site related non infection reactions	2 (7.4)
Hallucinations/psychosis	2 (7.4)
Withdrew consent	6 (22.2)
Lost to follow-up	0
Lack of efficacy	2 (7.4)
Difficulty with drug delivery system	0
Other	1 (3.7)

a. One subject can be only counted once.

Cross References：M15-741 試験 CSR Japan Study Data Table 14.1　1.1.1.J

表 2.7.3-16. 治験薬投与開始後 12 週間の登録時期別の被験者の内訳（All Enrolled Subjects, 日本人部分集団）：M15-741 試験

	Number (%) of Subjects		
	Sample 1 (N=18)	Sample 2 (N=9)	Total (N=27)
ABBV-951 ongoing	9 (50.0)	8 (88.9)	17 (63.0)
ABBV-951 prematurely discontinued	9 (50.0)	1 (11.1)	10 (37.0)
Primary reasons for prematurely discontinued [a]			
Adverse event	4 (22.2)	0	4 (14.8)
Infusion site related non infection reactions	2 (11.1)	0	2 (7.4)
Hallucinations/psychosis	1 (5.6)	0	1 (3.7)
Withdrew consent	3 (16.7)	1 (11.1)	4 (14.8)
Lost to follow-up	0	0	0
Lack of efficacy	2 (11.1)	0	2 (7.4)
Difficulty with drug delivery system	0	0	0
Other	0	0	0

Sample 1 = subjects enrolled before [redacted] 20[redacted], Sample 2 = subjects enrolled on or after [redacted] 20[redacted]

a. One subject can be only counted once.

Cross References：M15-741 試験 CSR Japan Study Data Table 14.1__1.1.2.J

表 2.7.3-17. 人口統計学的特性及びその他のベースラインの特性（安全性解析対象集団，日本人部分集団）：M15-741 試験

		Sample 1 (N=18)	Sample 2 (N=9)	Total (N=27)
Age, years	Mean (SD)	65.1 (9.17)	59.7 (7.81)	63.3 (8.97)
	Median (min, max)	66.5 (46, 83)	61.0 (47, 72)	62.0 (46, 83)
Age category, n (%)	< 65 years	8 (44.4)	7 (77.8)	15 (55.6)
	≥ 65 years	10 (55.6)	2 (22.2)	12 (44.4)
Weight, kg	Mean (SD)	56.51 (15.283)	55.68 (13.183)	56.23 (14.365)
	Median (min, max)	54.65 (34.1, 82.5)	62.30 (38.9, 71.4)	58.00 (34.1, 82.5)
Geographic region, n (%)	Japan	18 (100)	9 (100)	27 (100)
Sex, n (%)	Female	10 (55.6)	4 (44.4)	14 (51.9)
	Male	8 (44.4)	5 (55.6)	13 (48.1)
Ethnicity, n (%)	Hispanic or Latino	0	0	0
	Not Hispanic or Latino	18 (100)	9 (100)	27 (100)
Race, n (%)	White	0	0	0
	Black or African American	0	0	0
	Asian	18 (100)	9 (100)	27 (100)
	American Indian or Alaska Native	0	0	0
	Native Hawaiian or Other Pacific Islander	0	0	0
	Multiple	0	0	0

Sample 1 = subjects enrolled before [redacted] 20[redacted], Sample 2 = subjects enrolled on or after [redacted] 20[redacted]
SD = standard deviation
Cross References：M15-741 試験 CSR Japan Study Data Table 14.1__2.1.J 及び Table 14.1__2.2.J

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表 2.7.3-18.　被験者の内訳（All Enrolled Subjects，日本人部分集団）：M15-741 試験（更新時）

	Number (%) of Subjects
	Total (N = 27)
Total subjects enrolled	27 (100)
Full analysis set	27 (100)
Safety analysis set	27 (100)
ABBV-951 ongoing	0
ABBV-951 completed	12 (44.4)
ABBV-951 prematurely discontinued	15 (55.6)
Primary reasons for prematurely discontinued [a]	
Adverse event	6 (22.2)
Infusion site related non infection reactions	2 (7.4)
Hallucinations / psychosis	2 (7.4)
Withdrew consent	6 (22.2)
Lost to follow-up	0
Lack of efficacy	2 (7.4)
Difficulty with drug delivery system	0
Other	1 (3.7)

a.　One subject can be only counted once.

Cross References：M15-741 試験 CSR update Table 14.1　1.1.1.J

2.7.3.3.3.1.1.2　M15-737 試験

申請時

M15-737 試験の日本人被験者の内訳，人口統計学的特性及びベースライン特性を表 2.7.3-19，表 2.7.3-20 に示す。

本試験には M15-741 試験を完了した 11 例の日本人が登録され，日本人部分集団の FAS は 7 例であった。

治験薬の投与を完了した被験者はおらず，治験薬投与継続中は 10 例（90.9%），治験薬投与中止は 1 例（9.1%）であり，治験薬の投与を中止した主な理由は有害事象であった。

安全性解析対象集団では，年齢の平均値が 61.0 歳（範囲：47～72 歳），65 歳以上の割合が 36.4%，体重の平均値が 61.45 kg（範囲：38.9～82.5 kg），女性が 36.4%であった。65 歳以上の割合及び体重の平均値は全体集団と比較して日本人被験者で低かったものの，他の項目についてはおおむね同様であった（表 2.7.3-20，全体集団については表 2.7.3-12）。

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更新時

M15-737 試験の日本人被験者の内訳，人口統計学的特性及びベースライン特性を表 2.7.3-21，表 2.7.3-22 に示す。

本試験には M15-741 試験を完了した 12 例の日本人が登録され，日本人部分集団の FAS は 11 例であった。

治験薬の投与を完了した被験者はおらず，治験薬投与継続中は 11 例（91.7%），治験薬投与中止は 1 例（8.3%）であり，治験薬の投与を中止した主な理由は有害事象であった。

安全性解析対象集団では，年齢の平均値が 61.1 歳（範囲：47～72 歳），65 歳以上の割合が 33.3%，体重の平均値が 61.52 kg（範囲：38.9～82.5 kg），女性が 33.3%であった。65 歳以上の割合及び体重の平均値は全体集団と比較して日本人被験者で低かったものの，他の項目についてはおおむね同様であった（表 2.7.3-22，全体集団については表 2.7.3-13）。

表 2.7.3-19. 被験者の内訳（All Enrolled Subjects，日本人部分集団）：M15-737 試験

	Number (%) of Subjects
	Total (N=11)
Total subjects enrolled	11 (100)
Full analysis set	7 (63.6)
Safety analysis set	11 (100)
ABBV-951 ongoing	10 (90.9)
ABBV-951 completed	0
ABBV-951 prematurely discontinued	1 (9.1)
Primary reasons for prematurely discontinued [a]	
Adverse event	1 (9.1)
Infusion site related infections	0
Infusion site related non infection reactions	0
Polyneuropathy	0
Weight loss	0
Hallucinations/psychosis	0
Somnolence	0
Falls and associated injuries	0
Withdrew consent	0
Lost to follow-up	0
Lack of efficacy	0
Difficulty with drug delivery system	0
Other	0

a. One subject can be only counted once.

Cross References：M15-737 試験 CSR Japan Study Data Table 14.1__1.1.J

表 2.7.3-20. 人口統計学的特性及びその他のベースラインの特性（安全性解析対象集団，日本人部分集団）：M15-737 試験

		Total (N=11)
Age, years	Mean (SD)	61.0 (8.76)
	Median (min, max)	61.0 (47, 72)
Age category, n (%)	< 65 years	7 (63.6)
	≥ 65 years	4 (36.4)
Weight, kg	Mean (SD)	61.45 (16.305)
	Median (min, max)	66.90 (38.9, 82.5)
Geographic region, n (%)	Japan	11 (100)
Sex, n (%)	Female	4 (36.4)
	Male	7 (63.6)
Ethnicity, n (%)	Hispanic or Latino	0
	Not Hispanic or Latino	11 (100)
Race, n (%)	White	0
	Black or African American	0
	Asian	11 (100)
	American Indian or Alaska Native	0
	Native Hawaiian or Other Pacific Islander	0

SD = standard deviation
Cross References：M15-737 試験 CSR Japan Study Data Table 14.1__2.J

表 2.7.3-21.　被験者の内訳（All Enrolled Subjects，日本人部分集団）：M15-737 試験（更新時）

	Number (%) of Subjects
	Total (N = 12)
Total subjects enrolled	12 (100)
Full analysis set	11 (91.7)
Safety analysis set	12 (100)
ABBV-951 ongoing	11 (91.7)
ABBV-951 completed	0
ABBV-951 prematurely discontinued	1 (8.3)
Primary reasons for prematurely discontinued [a]	
Adverse event	1 (8.3)
Infusion site related infections	0
Infusion site related non infection reactions	0
Polyneuropathy	0
Weight loss	0
Hallucinations / psychosis	0
Somnolence	0
Falls and associated injuries	0
Withdrew consent	0
Lost to follow-up	0
Lack of efficacy	0
Difficulty with drug delivery system	0
Other	0

a.　One subject can be only counted once.

Cross References：M15-737 試験 CSR update Table 14.1__1.1.J

表 2.7.3-22. 人口統計学的特性及びその他のベースラインの特性（安全性解析対象集団，日本人部分集団）：M15-737 試験（更新時）

		Total (N = 12)
Age, years	Mean (SD)	61.1 (8.36)
	Median (min, max)	61.5 (47, 72)
Age category, n (%)	< 65 years	8 (66.7)
	≥ 65 years	4 (33.3)
Weight, kg	Mean (SD)	61.52 (15.548)
	Median (min, max)	66.05 (38.9, 82.5)
Geographic region, n (%)	Japan	12 (100)
Sex, n (%)	Female	4 (33.3)
	Male	8 (66.7)
Ethnicity, n (%)	Hispanic or Latino	0
	Not Hispanic or Latino	12 (100)
Race, n (%)	White	0
	Black or African American	0
	Asian	12 (100)
	American Indian or Alaska Native	0
	Native Hawaiian or Other Pacific Islander	0

SD = standard deviation
Cross References：M15-737 試験 CSR update Table 14.1__2.J

2.7.3.3.3.1.2 評価項目

2.7.3.3.3.1.2.1 パーキンソン病日誌

2.7.3.3.3.1.2.1.1 M15-741 試験

申請時

日本人部分集団を対象とした解析結果を以下に示す。全体集団の結果については 2.7.3.3.2.1.1 項に示す。

標準化した 1 日あたりの日常生活に支障のあるジスキネジアを伴わない平均「オン」時間（ジスキネジアを伴わない平均「オン」時間と日常生活に支障のないジスキネジアを伴う平均「オン」時間の合計）は，投与 1 週時（nominal $P < 0.05$），6 週時（nominal $P < 0.05$），39 週時（nominal $P < 0.01$）及び 52 週時（nominal $P < 0.01$）にベースラインと比較して改善が認められた。標準化した 1 日あたりの平均「オフ」時間は，投与 1 週時（nominal $P < 0.05$），39 週時（nominal $P < 0.05$）及び 52 週時（nominal $P < 0.05$）にベースラインと比較して改善が認められ

た。標準化した 1 日あたりの日常生活に支障のあるジスキネジアを伴わない平均「オン」時間は，ベースラインと比較して投与 26 週時に 1.25 時間，52 週時に 3.26 時間増加し，標準化した 1 日あたりの平均「オフ」時間は，投与 26 週時に 0.89 時間，投与 52 週時に 2.92 時間減少した。標準化した 1 日あたりのジスキネジアを伴わない平均「オン」時間は，ベースラインと比較して投与 26 週時に 2.40 時間，投与 52 週時に 4.49 時間増加した（図 2.7.3-23 及び表 2.7.3.6-11）。

また，登録時期別（Sample 1 及び Sample 2）でも，標準化した 1 日あたりの日常生活に支障のあるジスキネジアを伴わない平均「オン」時間及び標準化した 1 日あたりのジスキネジアを伴わない平均「オン」時間は増加する傾向，標準化した 1 日あたりの平均「オフ」時間及び標準化した 1 日あたりの日常生活に支障のあるジスキネジアを伴う平均「オン」時間は減少する傾向が認められた（表 2.7.3.6-12）。

朝の無動状態を呈する被験者の割合は，ベースラインと比較して著しく減少した。朝の無動状態を呈する被験者の割合は，ベースラインの 93.3%に対して投与 1 週時には 29.4%であった。また，覚醒時にジスキネジアを伴わない「オン」状態を呈する被験者の割合は，ベースラインの 0%に対して，投与 1 週時には 41.2%であった。これらの改善は，投与 52 週時まで持続した（M15-741 試験 CSR Japan Study Data Table 14.2__1.5.J）。

日本人被験者数が限られていたこと，評価時点によっては更に少数例での評価となったことなどの限界はあるが，日本人被験者の傾向として，「オン」時間が増加，「オフ」時間が減少し，全体集団と同様の有効性が認められたと考えた。

更新時

日本人部分集団を対象とした解析結果を以下に示す。全体集団の結果については 2.7.3.3.2.1.1 項に示す。

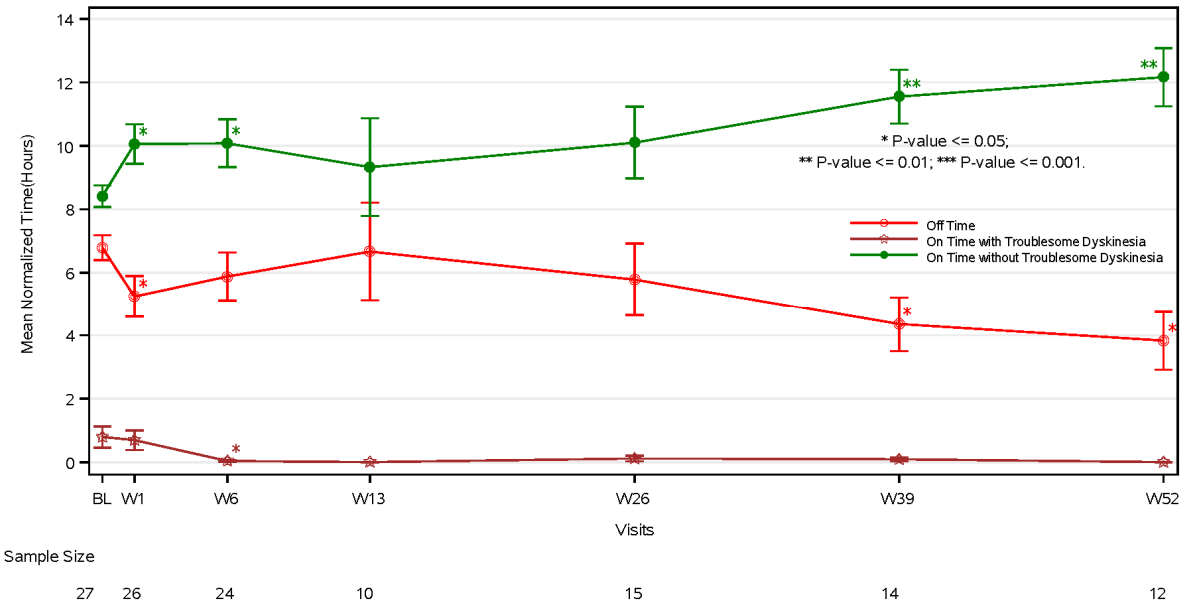
標準化した 1 日あたりの日常生活に支障のあるジスキネジアを伴わない平均「オン」時間（ジスキネジアを伴わない平均「オン」時間と日常生活に支障のないジスキネジアを伴う平均「オン」時間の合計）は，投与 1 週時（nominal $P < 0.05$），6 週時（nominal $P < 0.05$），39 週時（nominal $P < 0.01$）及び 52 週時（nominal $P < 0.01$）にベースラインと比較して改善が認められた。標準化した 1 日あたりの平均「オフ」時間は，投与 1 週時（nominal $P < 0.05$），39 週時（nominal $P < 0.05$）及び 52 週時（nominal $P < 0.05$）にベースラインと比較して改善が認められた。標準化した 1 日あたりの日常生活に支障のあるジスキネジアを伴わない平均「オン」時間は，ベースラインと比較して投与 26 週時に 1.25 時間，52 週時に 2.74 時間増加し，標準化した 1 日あたりの平均「オフ」時間は，投与 26 週時に 0.89 時間，投与 52 週時に 2.41 時間減少した。標準化した 1 日あたりのジスキネジアを伴わない平均「オン」時間は，ベースラインと比較して投与 26 週時に 2.40 時間，投与 52 週時に 4.22 時間増加した（図 2.7.3-24 及び表 2.7.3.6-24）。

また，登録時期別（Sample 1 及び Sample 2）でも，標準化した 1 日あたりの日常生活に支障のあるジスキネジアを伴わない平均「オン」時間及び標準化した 1 日あたりのジスキネジアを伴わない平均「オン」時間は増加する傾向，標準化した 1 日あたりの平均「オフ」時間及び標準化した 1 日あたりの日常生活に支障のあるジスキネジアを伴う平均「オン」時間は減少する傾向が認められた（表 2.7.3.6-25）。

朝の無動状態を呈する被験者の割合は，ベースラインと比較して著しく減少した。朝の無動状態を呈する被験者の割合は，ベースラインの 93.3%に対して投与 1 週時には 29.4%であった。また，覚醒時にジスキネジアを伴わない「オン」状態を呈する被験者の割合は，ベースラインの 0%に対して，投与 1 週時には 41.2%であった。これらの改善は，投与 52 週時まで持続した（M15-741 試験 CSR update Table 14.2__1.5.J）。

日本人被験者数が限られていたこと，評価時点によっては更に少数例での評価となったことなどの限界はあるが，日本人被験者の傾向として，「オン」時間が増加，「オフ」時間が減少し，全体集団と同様の有効性が認められたと考えた。

図 2.7.3-23. PD 日誌に基づく，標準化した 1 日あたりの平均「オフ」時間及び「オン」時間の推移（FAS，日本人部分集団）：M15-741 試験



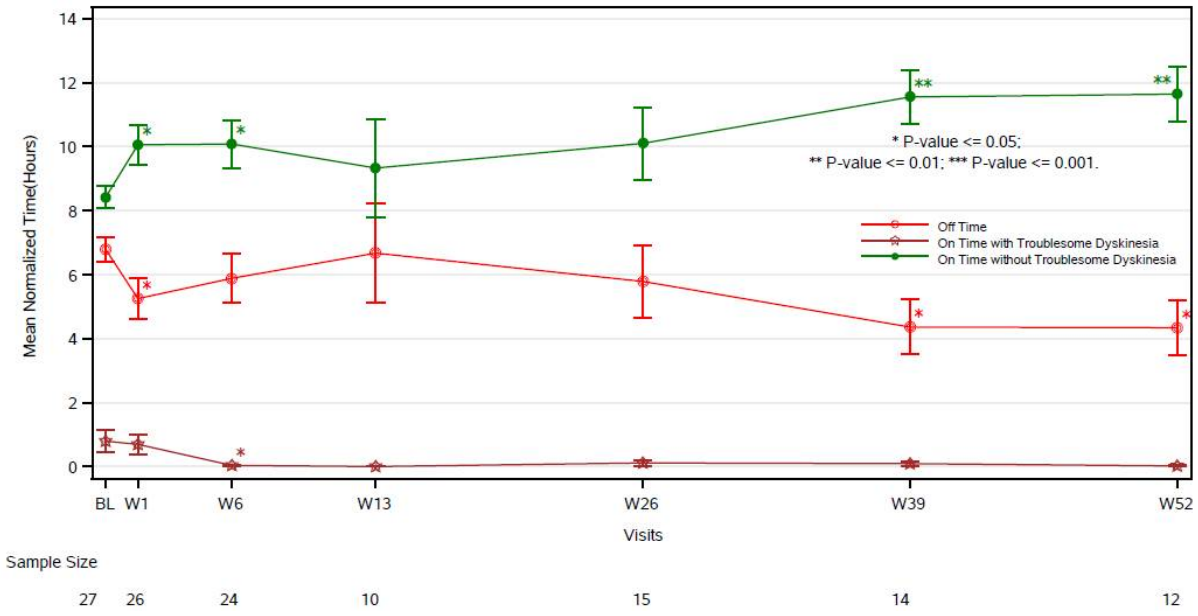
BL = Baseline; FAS = Full Analysis Set; PD = Parkinson's disease; W = Week

Notes: "On" time without troublesome dyskinesia is the sum of "On" time without dyskinesia and "On" time with non-troublesome dyskinesia.

Cross References：M15-741 試験 CSR Japan Study Data Figure 14.2__7.1.J

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図 2.7.3-24.　PD 日誌に基づく，標準化した 1 日あたりの平均「オフ」時間及び「オン」時間の推移（FAS，日本人部分集団）：M15-741 試験（更新時）



BL = Baseline; FAS = Full Analysis Set; PD = Parkinson's disease; W = Week

Notes: "On" time without troublesome dyskinesia is the sum of "On" time without dyskinesia and "On" time with non-troublesome dyskinesia.

Cross References：M15-741 試験 CSR update Figure 14.2__7.1.J

2.7.3.3.3.1.2.1.2　M15-737 試験

申請時

日本人部分集団を対象とした解析結果を以下に示す。全体集団の結果については 2.7.3.3.2.1.2 項に示す。

標準化した 1 日あたりの平均「オフ」時間，標準化した 1 日あたりの日常生活に支障のないジスキネジアを伴う平均「オン」時間及び標準化した 1 日あたりの日常生活に支障のあるジスキネジアを伴う平均「オン」時間の M15-737 試験のベースライン（すなわち親試験である M15-741 試験の最終評価）からの変化量は小さく，M15-741 試験で ABBV-951 を 12 ヵ月間投与した効果とおおむね同様であった（図 2.7.3-25 及び表 2.7.3.6-13）。

朝の無動状態を呈する被験者の割合は，投与 36 週にわたってベースライン（すなわち親試験である M15-741 試験の最終評価）と比較して減少した（M15-737 試験 CSR Japan Study Data Table 14.2__1.4.J）。

日本人被験者数が限られていたこと，評価時点によっては更に少数例での評価となったことなどの限界はあるが，日本人被験者の傾向として，ベースラインからの効果の低下はみられず，全体集団と同様の有効性が認められたと考えた。

更新時

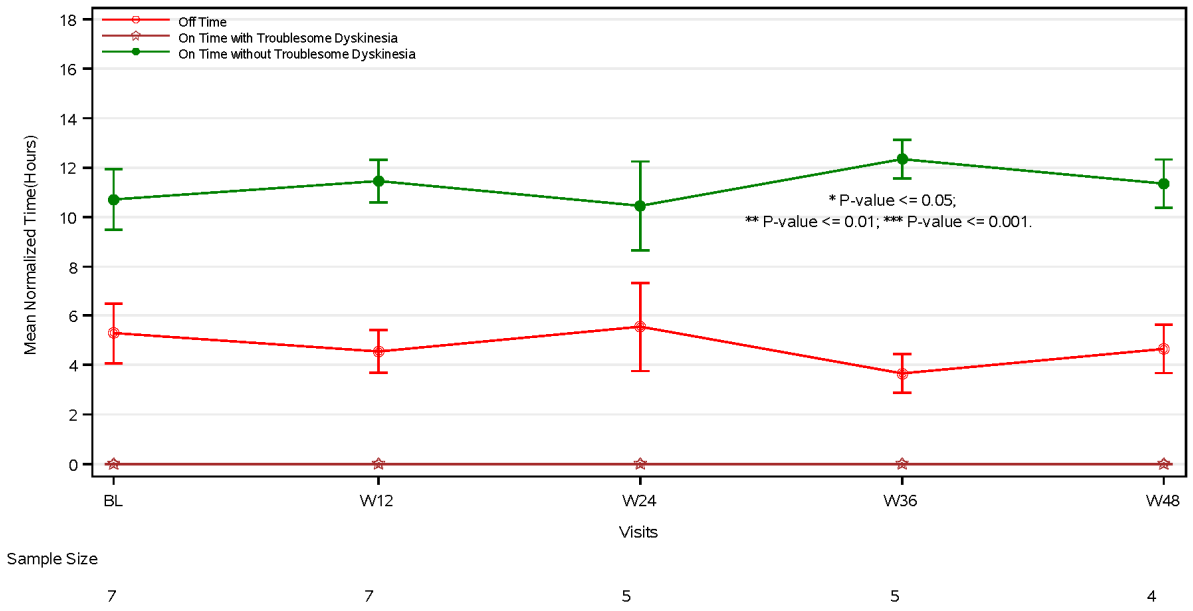
日本人部分集団を対象とした解析結果を以下に示す。全体集団の結果については 2.7.3.3.2.1.2 項に示す。

標準化した 1 日あたりの平均「オフ」時間，標準化した 1 日あたりの日常生活に支障のないジスキネジアを伴う平均「オン」時間及び標準化した 1 日あたりの日常生活に支障のあるジスキネジアを伴う平均「オン」時間の M15-737 試験のベースライン（すなわち親試験である M15-741 試験の最終評価）からの変化量は小さく，M15-741 試験で ABBV-951 を 12 ヵ月間投与した効果とおおむね同様であった（図 2.7.3-26 及び表 2.7.3.6-26）。

朝の無動状態を呈する被験者の割合は，投与 60 週にわたってベースライン（すなわち親試験である M15-741 試験の最終評価）と比較して減少した（M15-737 試験 CSR update Table 14.2__1.4.J）。

日本人被験者数が限られていたこと，評価時点によっては更に少数例での評価となったことなどの限界はあるが，日本人被験者の傾向として，ベースラインからの効果の低下はみられず，全体集団と同様の有効性が認められたと考えた。

図 2.7.3-25. PD 日誌に基づく，標準化した 1 日あたりの平均「オフ」時間及び「オン」時間の推移（FAS，日本人部分集団）：M15-737 試験



BL = Baseline; FAS = Full Analysis Set; PD = Parkinson's disease; W = Week

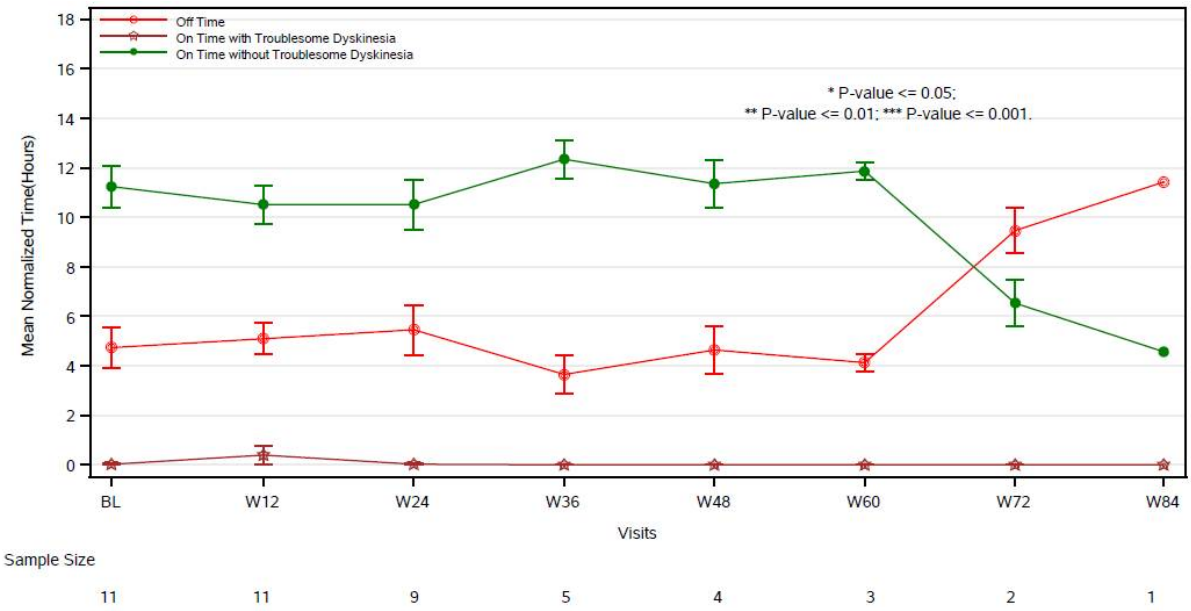
Notes: "On" time without troublesome dyskinesia is the sum of "On" time without dyskinesia and "On" time with non-troublesome dyskinesia.

Baseline value for efficacy variables was collected from the last assessment in parent Study M15-741.

Cross References：M15-737 試験 CSR Japan Study Data Figure 14.2__6.1.J

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図 2.7.3-26.　PD 日誌に基づく，標準化した 1 日あたりの平均「オフ」時間及び「オン」時間の推移（FAS，日本人部分集団）：M15-737 試験（更新時）



BL = Baseline; FAS = Full Analysis Set; PD = Parkinson's disease; W = Week

Notes: "On" time without troublesome dyskinesia is the sum of "On" time without dyskinesia and "On" time with non-troublesome dyskinesia.

Baseline value for efficacy variables was collected from the last assessment in parent Study M15-741.

Cross References：M15-737 試験 CSR update Figure 14.2__6.1.J

2.7.3.3.3.1.2.2　MDS-UPDRS

2.7.3.3.3.1.2.2.1　M15-741 試験

申請時

日本人部分集団を対象とした解析結果を以下に示す。全体集団の結果については 2.7.3.3.2.2.1 項に示す。

MDS-UPDRS Part II による M-EDL スコアは，すべての評価時点においてベースラインと比較して数値的に改善しており，投与 2 日目（nominal $P < 0.01$）及び投与 1 週時（nominal $P < 0.05$）ではベースラインと比較して改善が認められた（図 2.7.3-27 及び表 2.7.3.6-14）。MDS-UPDRS Part IV の運動合併症スコアは，投与 3 週時を除くすべての評価時点においてベースラインと比較して数値的に改善しており，投与 2 日目（nominal $P < 0.01$）及び投与 2 週時（nominal $P < 0.05$）ではベースラインと比較して改善が認められた（表 2.7.3.6-14）。

日本人被験者数が限られていたこと，評価時点によっては更に少数例での評価となったことなどの限界があり，また，評価時点によっては改善が認められなかったスコアがあったものの，

日本人被験者の傾向として，M-EDL スコア及び運動合併症スコアはいずれもベースラインから改善傾向を認め，全体集団と同様の有効性が認められたと考えた。

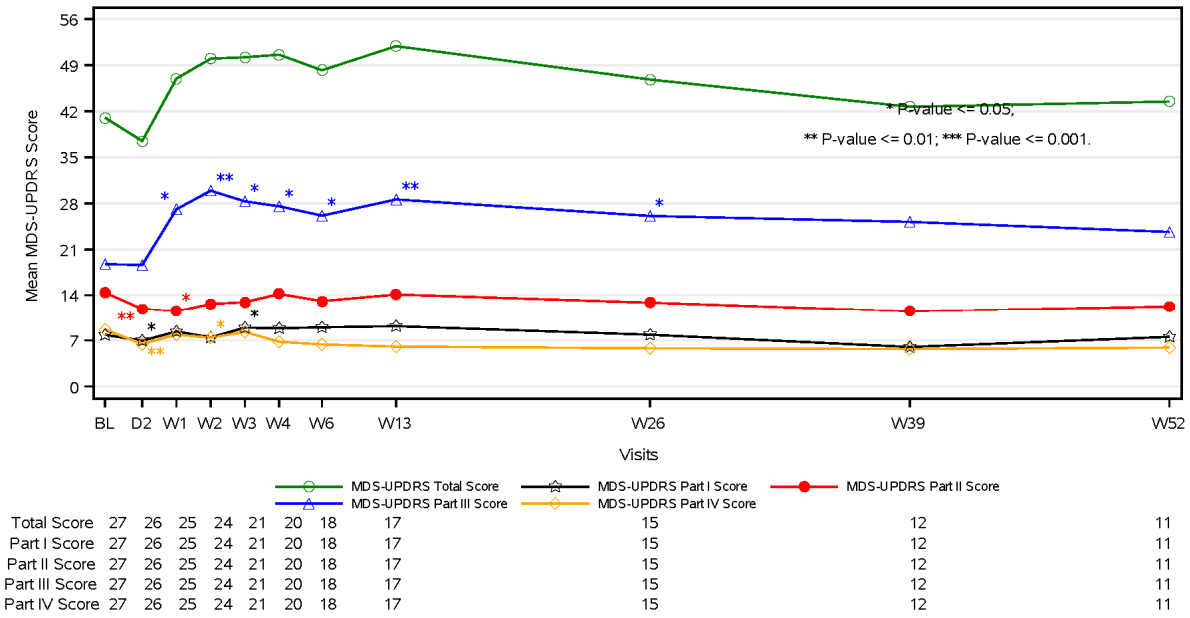
更新時

日本人部分集団を対象とした解析結果を以下に示す。全体集団の結果については 2.7.3.3.2.2.1 項に示す。

MDS-UPDRS Part II による M-EDL スコアは，すべての評価時点においてベースラインと比較して数値的に改善しており，投与 2 日目（nominal $P < 0.01$）及び投与 1 週時（nominal $P < 0.05$）ではベースラインと比較して改善が認められた（図 2.7.3-28 及び表 2.7.3.6-27）。MDS-UPDRS Part IV の運動合併症スコアは，投与 3 週時を除くすべての評価時点においてベースラインと比較して数値的に改善しており，投与 2 日目（nominal $P < 0.01$）及び投与 2 週時（nominal $P < 0.05$）ではベースラインと比較して改善が認められた（表 2.7.3.6-27）。

日本人被験者数が限られていたこと，評価時点によっては更に少数例での評価となったことなどの限界があり，また，評価時点によっては改善が認められなかったスコアがあったものの，日本人被験者の傾向として，M-EDL スコア及び運動合併症スコアはいずれもベースラインから改善傾向を認め，全体集団と同様の有効性が認められたと考えた。

図 2.7.3-27.　　MDS-UPDRS スコアの推移（FAS，日本人部分集団）：M15-741 試験



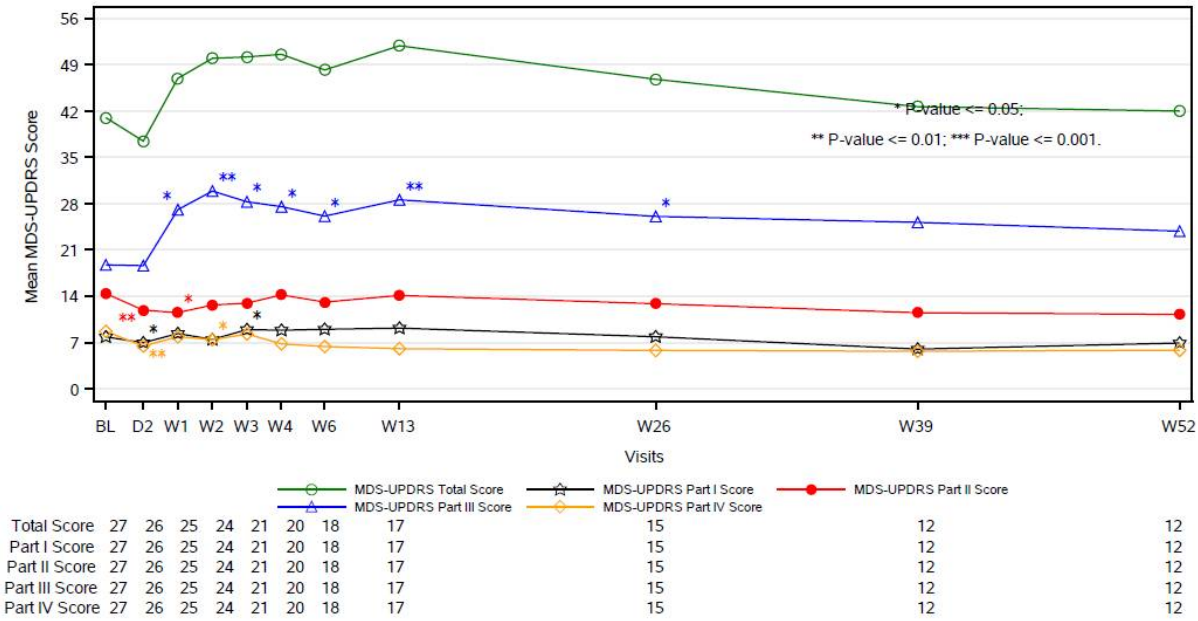
BL = Baseline; D = Day; FAS = Full Analysis Set; MDS-UPDRS = Movement Disorder Society-Unified Parkinson's Disease Rating Scale; W = Week

Note: Sample sizes are shown beneath the figure.

Cross References：M15-741 試験 CSR Japan Study Data Figure 14.2　8.J

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図 2.7.3-28.　　MDS-UPDRS スコアの推移（FAS，日本人部分集団）：M15-741 試験（更新時）



BL = Baseline; D = Day; FAS = Full Analysis Set; MDS-UPDRS = Movement Disorder Society-Unified Parkinson's Disease Rating Scale; W = Week

Note: Sample sizes are shown beneath the figure.

Cross References：M15-741 試験 CSR update Figure 14.2__8.J

2.7.3.3.3.1.2.2.2　M15-737 試験

申請時

日本人部分集団を対象とした解析結果を以下に示す。全体集団の結果については 2.7.3.3.2.2.2 項に示す。

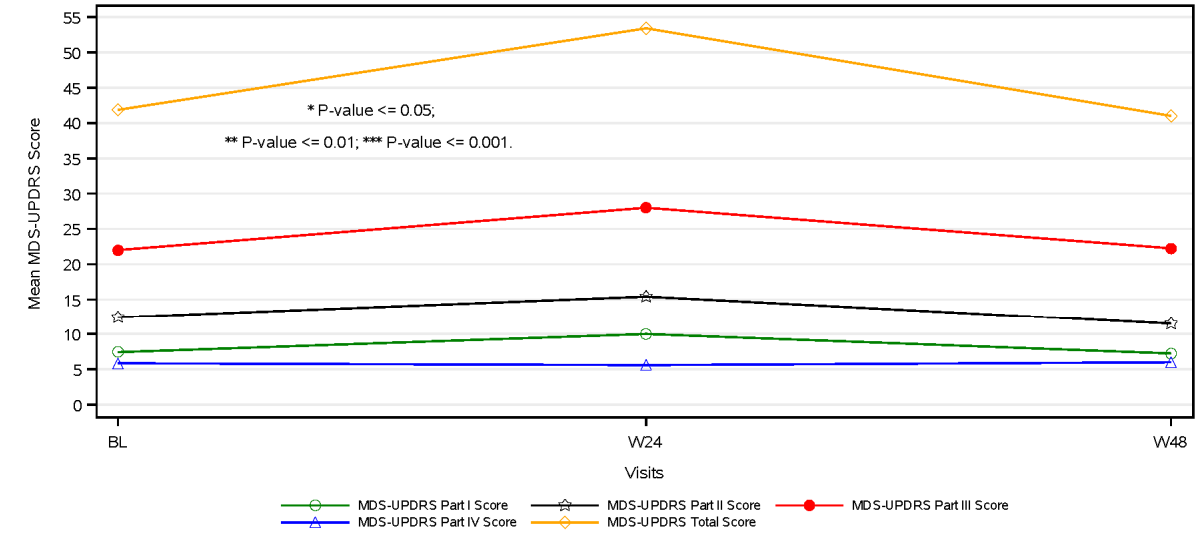
日本人被験者数は少ないものの，ベースラインから投与 48 週時までの MDS-UPDRS スコアは，全体集団とおおむね同様の推移を示した。これは，M15-741 試験で ABBV-951 を 12 ヵ月間投与したときのスコアとも同様であった（図 2.7.3-29 及び表 2.7.3.6-15）。

更新時

日本人部分集団を対象とした解析結果を以下に示す。全体集団の結果については 2.7.3.3.2.2.2 項に示す。

日本人被験者数は少ないものの，ベースラインから投与 72 週時までの MDS-UPDRS スコアは，全体集団とおおむね同様の推移を示した。これは，M15-741 試験で ABBV-951 を 12 ヵ月間投与したときのスコアとも同様であった（図 2.7.3-30 及び表 2.7.3.6-28）。

図 2.7.3-29.　　MDS-UPDRS スコアの推移（FAS，日本人部分集団）：M15-737 試験



Total Score	7	5	4
Part I Score	7	5	4
Part II Score	7	5	4
Part III Score	7	5	4
Part IV Score	7	5	4

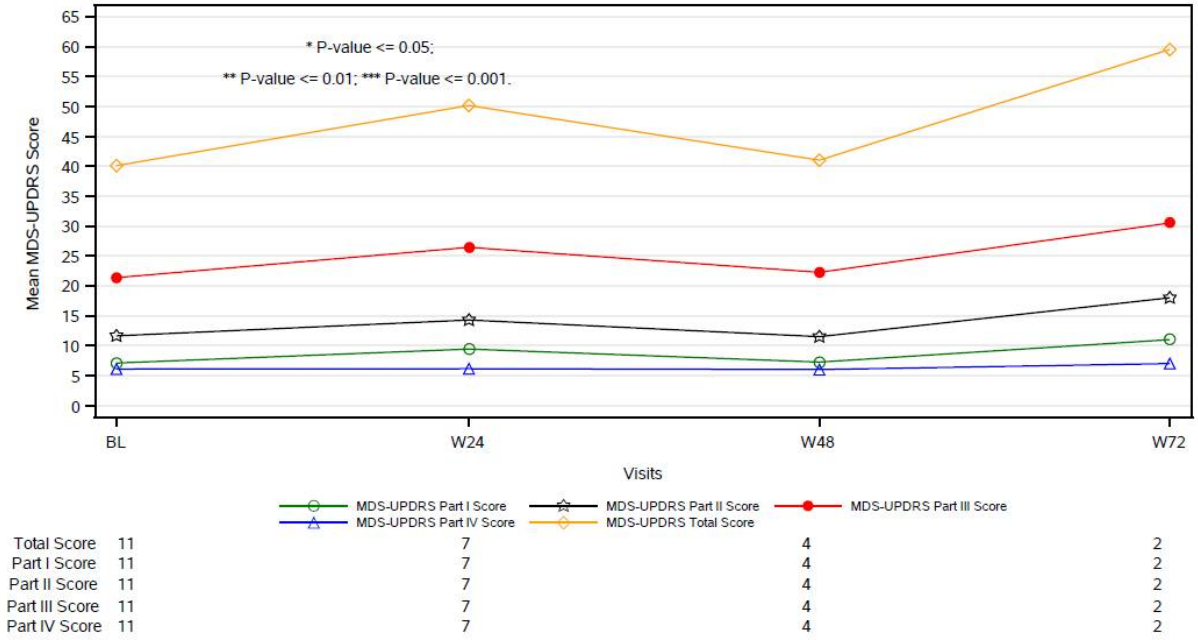
BL = Baseline; FAS = Full Analysis Set; MDS-UPDRS = Movement Disorder Society-Unified Parkinson's Disease Rating Scale; W = Week

Note: Sample sizes are shown beneath the figure.

Cross References：M15-737 試験 CSR Japan Study Data Figure 14.2__7.J

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図 2.7.3-30.　　MDS-UPDRS スコアの推移（FAS，日本人部分集団）：M15-737 試験（更新時）



BL = Baseline; FAS = Full Analysis Set; MDS-UPDRS = Movement Disorder Society-Unified Parkinson's Disease Rating Scale; W = Week

Note: Sample sizes are shown beneath the figure.

Cross References：M15-737 試験 CSR update Figure 14.2__7.J

2.7.3.3.3.1.2.3　　PDSS-2

申請時

日本人部分集団を対象とした解析結果（M15-741 試験）を以下に示す。全体集団の結果については 2.7.3.3.2.3.1 項に示す。

M15-741 試験において，PDSS-2 合計スコア，夜間 PD スコア，夜間運動症状スコア及び睡眠中断スコアの変化に，一定の傾向は認められなかった（表 2.7.3.6-16）。

日本人被験者数が限られていたこと，評価時点によっては更に少数例での評価となったことなどの限界はあるが，日本人被験者の傾向として，全体集団で認められたベースラインからの改善は認められなかった。

更新時

日本人部分集団を対象とした解析結果（M15-741 試験）を以下に示す。全体集団の結果については 2.7.3.3.2.3.1 項に示す。

M15-741 試験において，PDSS-2 合計スコア，夜間 PD スコア，夜間運動症状スコア及び睡眠中断スコアの変化に，一定の傾向は認められなかった（表 2.7.3.6-29）。

日本人被験者数が限られていたこと，評価時点によっては更に少数例での評価となったことなどの限界はあるが，日本人被験者の傾向として，全体集団で認められたベースラインからの改善は認められなかった。

2.7.3.3.3.1.2.4 生活の質

2.7.3.3.3.1.2.4.1 M15-741 試験

申請時

日本人部分集団を対象とした解析結果を以下に示す。全体集団の結果については 2.7.3.3.2.4.1 項に示す。

PDQ-39 要約指標による PD 及び健康に関連した生活の質のうち，恥辱感及び身体的苦痛の各スコアのベースラインからの変化量に数値的な改善傾向がみられた。EQ-5D-5L 要約指標及び VAS は，投与 52 週にわたって，おおむねベースラインからの改善が認められた（M15-741 試験 CSR Japan Study Data Table 14.2__4.J 及び Table 14.2__5.J)。

日本人被験者数が限られていたこと，評価時点によっては更に少数例での評価となったことなどの限界はあるが，日本人被験者の傾向として，PDQ-39 要約指標による PD 及び健康に関連した生活の質（恥辱感及び身体的苦痛の各スコア），並びに EQ-5D-5L 要約指標及び VAS については，全体集団と同様の有効性が認められたと考えた。

更新時

日本人部分集団を対象とした解析結果を以下に示す。全体集団の結果については 2.7.3.3.2.4.1 項に示す。

PDQ-39 要約指標による PD 及び健康に関連した生活の質のうち，恥辱感及び身体的苦痛の各スコアのベースラインからの変化量に数値的な改善傾向がみられた。EQ-5D-5L 要約指標及び VAS は，投与 52 週にわたって，おおむねベースラインからの改善が認められた（M15-741 試験 CSR update Table 14.2__4.J 及び Table 14.2__5.J)。

日本人被験者数が限られていたこと，評価時点によっては更に少数例での評価となったことなどの限界はあるが，日本人被験者の傾向として，PDQ-39 要約指標による PD 及び健康に関連した生活の質（恥辱感及び身体的苦痛の各スコア），並びに EQ-5D-5L 要約指標及び VAS については，全体集団と同様の有効性が認められたと考えた。

2.7.3.3.3.1.2.4.2 M15-737 試験

申請時

日本人部分集団を対象とした解析結果を以下に示す。全体集団の結果については 2.7.3.3.2.4.2 項に示す。

ABBV-951 を投与継続したとき，PDQ-39 要約指標及び EQ-5D-5L 要約指標の投与後 48 週時までスコアの変化はみられなかった（M15-737 試験 CSR Japan Study Data Table 14.2__3.J 及び Table 14.2__4.J)。

日本人被験者数が限られていたこと，評価時点によっては更に少数例での評価となったことなどの限界はあるが，日本人被験者の傾向として，PDQ-39 及び EQ-5D-5L のベースラインからの変化量に一定の傾向はなく，全体集団と同様の有効性が認められたと考えた。

更新時

日本人部分集団を対象とした解析結果を以下に示す。全体集団の結果については 2.7.3.3.2.4.2 項に示す。

ABBV-951 を投与継続したとき，PDQ-39 要約指標及び EQ-5D-5L 要約指標は、ベースラインから投与後 72 週時まで安定していた（M15-737 試験 CSR update Table 14.2__3.J 及び Table 14.2__4.J)。

日本人被験者数が限られていたこと，評価時点によっては更に少数例での評価となったことなどの限界はあるが，日本人被験者の傾向として，PDQ-39 及び EQ-5D-5L のベースラインからの変化量に一定の傾向はなく，全体集団と同様の有効性が認められたと考えた。

2.7.3.3.3.1.2.5　　認知機能

申請時

日本人部分集団を対象とした解析結果（M15-737 試験）を以下に示す。全体集団の結果については 2.7.3.3.2.5 項に示す。

M15-737 試験において，ベースラインから投与 48 週時までの MMSE 合計スコアの変化量に差は認められなかった（表 2.7.3.6-17）。

日本人被験者数が限られていたこと，評価時点によっては更に少数例での評価となったことなどの限界はあるが，日本人被験者の傾向として，ベースラインから投与 48 週時までの MMSE 合計スコアの変化はみられず，全体集団と同様の有効性が認められたと考えた。

更新時

日本人部分集団を対象とした解析結果（M15-737 試験）を以下に示す。全体集団の結果については 2.7.3.3.2.5 項に示す。

M15-737 試験において，ベースラインから投与 72 週時までの MMSE 合計スコアの変化量に差は認められなかった（表 2.7.3.6-30）。

日本人被験者数が限られていたこと，評価時点によっては更に少数例での評価となったことなどの限界はあるが，日本人被験者の傾向として，ベースラインから投与 72 週時までの MMSE 合計スコアの変化はみられず，全体集団と同様の有効性が認められたと考えた。

2.7.3.3.3.2 部分集団解析

2.7.3.3.3.2.1 M15-741 試験

2.7.3.1.4.1 項において定義された部分集団解析の結果，有効性解析の結果とおおむね一致していた（表 2.7.3.6-11）。ただし，白人を除く人種及び日本を含むいくつかの地域の被験者数は少なく，解析実施要件を満たしていない。

更新時データも申請時データと同様の結果であった（表 2.7.3.6-24）。

2.7.3.3.3.2.2 M15-737 試験

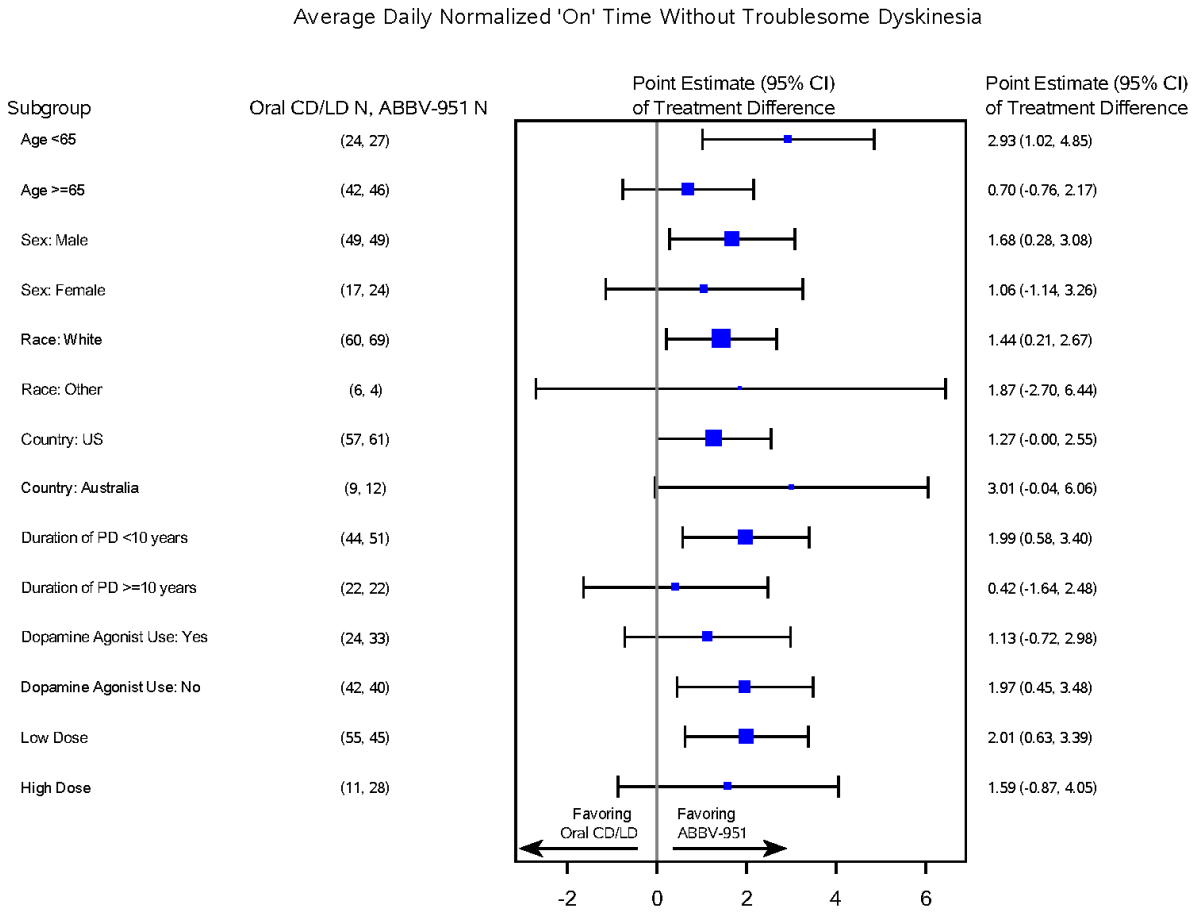
2.7.3.1.4.2 項において定義された部分集団解析の結果，各部分集団の有効性解析の結果に対する影響は認められなかった（表 2.7.3.6-13）。

更新時データも申請時データと同様の結果であった（表 2.7.3.6-26）。

2.7.3.3.3.2.3 M15-736 試験

2.7.3.1.4.3 項において定義された部分集団解析の結果，性別，人種，実施国，PD 罹病期間，ドパミンアゴニストの併用及び LD の用量（低用量又は高用量）について，主要有効性評価項目に対する投与群と部分集団との交互作用は認められなかった。各部分集団の差異については，おおむね，主要有効性解析の結果との矛盾はみられなかった（図 2.7.3-31，M15-736 試験 CSR Table 14.2　9.1）。

図 2.7.3-31. PD 日誌に基づく，標準化した 1 日あたりの日常生活に支障のあるジスキネジアを伴わない平均「オン」時間の部分集団別解析（FAS）：M15-736 試験



CD/LD = carbidopa/levodopa; CI = confidence interval; FAS = Full Analysis Set; PD = Parkinson's disease; US = United States

Cross References：M15-736 試験 CSR Figure 14.2__12.6

2.7.3.4 推奨用法・用量に関する臨床情報の解析

2.7.3.4.1 第 III 相試験の ABBV-951 の用法・用量の設定

M15-741 試験及び M15-736 試験における各被験者の ABBV-951 の開始用量は，被験者が使用していた経口 LD 含有製剤の 1 日 LD 等価量，COMT 阻害薬併用の有無，ホスレボドパ及び LD の分子量の差，ABBV-951 とレボドパ・カルビドパ水和物配合経腸用液の LD のバイオアベイラビリティの差，ABBV-951 製剤濃度及び被験者の覚醒時間を考慮して設定した（2.7.2.3.5 項）。M15-737 試験の開始用量は，親試験である M15-741 試験の最終日の用法・用量と同様とした。

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M15-741 試験及び M15-737 試験では，最適な治療効果が得られるよう，治験責任医師の判断により試験期間中どの時点でも被験者ごとに ABBV-951 の用量調節及び追加投与を可能とした。M15-736 試験では，二重盲検期の CSCI 最適化期中では ABBV-951 の用量調節を可能としたが，維持期では用量調節を不可とした（ただし，PD 症状によって緊急的対応が必要となった場合は，CD/LD IR 製剤の使用を可能とした）。

ABBV-951 の持続注入速度は，M15-741 試験及び M15-737 試験で 0.17～1.04 mL/時間（LD 換算量として約 29～177 mg/時間），M15-736 試験で 0.15～1.04 mL/時間（LD 換算量として約 25～177 mg/時間）の範囲内で設定することとし，いずれの試験でもホスレボドパ 6000 mg/24 時間（LD 換算量として 4260 mg/24 時間）を超える投与はいかなる状況下でも許容しないこととした。負荷投与は，被験者が ABBV-951 治療開始前の朝最初の LD 投与量に可能な限り近い LD（換算）量となるように，M15-741 試験及び M15-737 試験では経口 CD/LD IR 製剤を，M15-736 試験ではポンプを用いて ABBV-951 を投与した。追加投与は，M15-741 試験及び M15-737 試験で 1 回あたり 0.11～0.3 mL（LD 換算量として約 20～50 mg）の ABBV-951 を投与できることとし，M15-736 試験では追加投与は行わないこととした。

経口 LD 含有製剤から ABBV-951 への変換及び最適化は，M15-741 試験で平均 3.5 回の来院（申請時及び更新時），M15-736 試験で平均 2.4 回の来院で達成された。

ABBV-951 の 1 日あたりの LD 換算平均投与量は，M15-741 試験で約 305～3838 mg（申請時及び更新時），M15-737 試験で約 702～3889 mg（申請時）及び 715～3968 mg（更新時），M15-736 試験で約 686～3888 mg であった。日本人被験者の ABBV-951 の 1 日あたりの LD 換算平均投与量は，M15-741 試験で約 669～1951 mg（申請時及び更新時），M15-737 試験で約 865～2286 mg（申請時）及び 715～2305 mg（更新時）であった。

2.7.3.4.2 推奨用法・用量の設定根拠

2.7.3.4.1 項に示した方法で ABBV-951 の開始用量を設定し，最適な治療効果が得られるように調節した用法・用量で M15-741 試験，M15-737 試験及び M15-736 試験を実施した結果，進行期 PD における下記の運動症状の改善が認められた。

- 日常生活に支障があるジスキネジアを伴わない「オン」時間の延長
- 「オフ」時間の減少
- ジスキネジアを伴わない「オン」時間の延長
- 日常生活に支障があるジスキネジアを伴う「オン」時間の減少
- 日常生活に支障があるジスキネジアを伴わない「オン」時間延長の維持，「オフ」時間減少の維持

更に，ABBV-951 により PD と関係した朝の無動の減少，睡眠症状の改善，生活の質の改善，及び健康アウトカムの測定可能な改善が示された。

M15-741 試験及び M15-737 試験において，日本人被験者数が限られていたことから限界はあるものの，日本人部分集団の有効性は全体集団とおおむね同様であった。

上記を総合的に勘案し，用法・用量（案）を設定した。

2.7.3.5 効果の持続，耐薬性

LD の薬物動態や作用機序を考慮すると，ABBV-951 投与中止後の効果の持続は期待できない。ABBV-951 の CSCI により，被験者ごとに調節された治療域内で血漿中濃度が安定して維持され（2.7.2 項），耐薬性は認められなかった。

参考文献

該当なし

2.7.3.6 付録

表2.7.3.6-1　PD日誌に基づく，標準化した1日あたりの平均「オフ」時間及び「オン」時間の要約（FAS）：M15-741試験

[redacted]20[redacted] 10:12 <[redacted]>
ABBV-951
STUDY M15-741 - SECOND INTERIM (CUTOFF [redacted]20[redacted])
R&D/20/1632 - CLINICAL/STATISTICAL

TABLE 14.2__1.1

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary
(FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Average Daily Normalized 'Off' Time									
BASELINE	236		5.90 (2.24)	5.9	0.0, 12.6				
Low Dose	127		5.68 (2.19)	5.8	0.0, 10.3				
High Dose	109		6.16 (2.28)	6.4	0.0, 12.6				
WEEK 1	225	5.91	3.97 (3.43)	3.1	0.0, 16.0	-1.94 (3.68)	-2.2	-10.2, 10.4	<=0.001***
Low Dose	121	5.73	3.69 (3.19)	2.9	0.0, 13.8	-2.04 (3.49)	-2.2	-10.2, 5.9	<=0.001***
High Dose	104	6.12	4.29 (3.67)	3.6	0.0, 16.0	-1.83 (3.89)	-2.1	-8.9, 10.4	<=0.001***
WEEK 6	205	5.94	3.55 (3.26)	3.1	0.0, 16.0	-2.39 (3.60)	-2.9	-10.6, 9.9	<=0.001***
Low Dose	111	5.73	3.32 (3.33)	3.1	0.0, 16.0	-2.41 (3.65)	-2.9	-10.2, 9.9	<=0.001***
High Dose	94	6.19	3.82 (3.16)	3.1	0.0, 12.5	-2.37 (3.57)	-2.9	-10.6, 6.8	<=0.001***
WEEK 13	115	5.54	3.12 (3.47)	1.8	0.0, 13.4	-2.42 (3.69)	-3.2	-9.9, 8.1	<=0.001***
Low Dose	64	5.41	2.88 (3.53)	1.6	0.0, 13.4	-2.52 (3.80)	-3.3	-9.9, 8.1	<=0.001***
High Dose	51	5.71	3.42 (3.40)	2.1	0.0, 10.7	-2.29 (3.57)	-2.4	-9.2, 6.3	<=0.001***
WEEK 26	127	5.92	2.65 (3.02)	1.5	0.0, 14.3	-3.27 (3.24)	-3.2	-10.6, 7.1	<=0.001***
Low Dose	66	5.73	2.46 (3.17)	0.9	0.0, 14.3	-3.27 (3.36)	-3.8	-10.2, 7.1	<=0.001***
High Dose	61	6.13	2.86 (2.86)	1.8	0.0, 9.8	-3.28 (3.14)	-2.8	-10.6, 5.5	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours
(i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.1

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary
(FAS)

Parameter Time Point Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Average Daily Normalized 'Off' Time (Cont.)									
WEEK 39	111	5.84	2.71 (2.80)	2.0	0.0, 13.3	-3.13 (3.18)	-3.1	-9.9, 9.6	<=0.001***
Low Dose	63	5.65	2.69 (2.94)	2.0	0.0, 13.3	-2.97 (3.36)	-2.9	-9.9, 9.6	<=0.001***
High Dose	48	6.09	2.74 (2.62)	2.4	0.0, 7.3	-3.34 (2.94)	-3.4	-9.2, 4.0	<=0.001***
WEEK 52	96	5.90	2.51 (2.92)	1.3	0.0, 11.5	-3.39 (3.08)	-3.5	-11.2, 5.9	<=0.001***
Low Dose	51	5.86	2.53 (2.83)	2.3	0.0, 10.9	-3.33 (3.07)	-3.5	-10.2, 5.9	<=0.001***
High Dose	45	5.94	2.48 (3.04)	0.8	0.0, 11.5	-3.46 (3.14)	-3.5	-11.2, 2.8	<=0.001***
Average Daily Normalized 'On' Time Without Dyskinesia									
BASELINE	236		6.51 (3.35)	6.6	0.0, 15.4				
Low Dose	127		6.35 (3.47)	6.4	0.0, 15.4				
High Dose	109		6.70 (3.22)	6.7	0.0, 13.8				
WEEK 1	225	6.48	8.43 (4.52)	8.3	0.0, 16.0	1.94 (4.09)	1.6	-8.9, 12.0	<=0.001***
Low Dose	121	6.21	7.99 (4.53)	8.3	0.0, 16.0	1.78 (3.93)	1.6	-8.9, 10.7	<=0.001***
High Dose	104	6.80	8.94 (4.47)	9.0	0.0, 16.0	2.14 (4.27)	1.9	-8.1, 12.0	<=0.001***
WEEK 6	205	6.54	9.92 (4.48)	10.6	0.0, 16.0	3.38 (4.39)	3.5	-9.1, 13.8	<=0.001***
Low Dose	111	6.37	9.86 (4.55)	10.5	0.0, 16.0	3.49 (4.50)	3.9	-9.1, 13.8	<=0.001***
High Dose	94	6.74	9.99 (4.43)	10.7	0.0, 16.0	3.25 (4.28)	3.2	-6.7, 12.0	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.1

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary
(FAS)

Parameter Time Point Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 13	115	6.67	10.79 (4.60)	11.3	0.0, 16.0	4.12 (4.35)	4.3	-9.0, 15.2	<=0.001***
Low Dose	64	6.66	10.66 (4.93)	12.4	0.0, 16.0	4.01 (4.41)	4.0	-9.0, 15.2	<=0.001***
High Dose	51	6.68	10.94 (4.19)	10.9	0.9, 16.0	4.25 (4.30)	4.3	-6.3, 14.1	<=0.001***
WEEK 26	127	6.89	11.20 (4.33)	12.5	0.0, 16.0	4.31 (4.47)	4.7	-11.0, 14.1	<=0.001***
Low Dose	66	6.88	11.59 (4.20)	12.8	0.0, 16.0	4.72 (3.97)	5.3	-10.1, 11.5	<=0.001***
High Dose	61	6.90	10.78 (4.47)	11.8	0.0, 16.0	3.88 (4.95)	4.6	-11.0, 14.1	<=0.001***
WEEK 39	111	7.03	11.08 (4.17)	11.3	0.0, 16.0	4.05 (4.09)	4.1	-10.6, 13.5	<=0.001***
Low Dose	63	6.88	11.14 (4.35)	11.8	0.3, 16.0	4.25 (4.25)	4.9	-10.6, 11.4	<=0.001***
High Dose	48	7.22	11.00 (3.97)	11.3	0.0, 16.0	3.79 (3.91)	3.2	-2.9, 13.5	<=0.001***
WEEK 52	96	7.03	10.81 (4.71)	11.8	0.0, 16.0	3.78 (4.29)	4.1	-12.0, 13.8	<=0.001***
Low Dose	51	6.83	11.30 (4.42)	12.4	0.0, 16.0	4.47 (3.89)	4.8	-6.5, 11.3	<=0.001***
High Dose	45	7.26	10.26 (5.00)	11.2	0.0, 16.0	3.01 (4.62)	2.4	-12.0, 13.8	<=0.001***
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia									
BASELINE	236		2.63 (2.55)	2.4	0.0, 12.2				
Low Dose	127		2.69 (2.39)	2.6	0.0, 10.3				
High Dose	109		2.55 (2.73)	1.9	0.0, 12.2				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.1

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary
(FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 1	225	2.66	2.61 (3.16)	1.5	0.0, 14.9	-0.05 (3.04)	0.0	-8.5, 13.6	0.8070
Low Dose	121	2.77	3.04 (3.28)	2.2	0.0, 14.9	0.27 (3.29)	0.0	-8.5, 13.6	0.3612
High Dose	104	2.54	2.12 (2.95)	0.7	0.0, 12.8	-0.43 (2.68)	0.0	-8.2, 8.8	0.1075
WEEK 6	205	2.67	2.09 (3.29)	0.5	0.0, 15.4	-0.58 (3.01)	-0.3	-7.8, 11.6	0.0064**
Low Dose	111	2.75	2.23 (3.17)	0.8	0.0, 15.4	-0.51 (3.05)	-0.2	-7.6, 11.6	0.0785
High Dose	94	2.58	1.93 (3.43)	0.0	0.0, 14.6	-0.66 (2.97)	-0.3	-7.8, 9.6	0.0352*
WEEK 13	115	2.97	1.77 (3.30)	0.0	0.0, 16.0	-1.20 (3.49)	-1.0	-12.2, 13.2	<=0.001***
Low Dose	64	2.94	2.06 (3.70)	0.2	0.0, 16.0	-0.87 (3.59)	-1.1	-8.0, 13.2	0.0560
High Dose	51	3.01	1.40 (2.70)	0.0	0.0, 14.4	-1.61 (3.37)	-0.8	-12.2, 7.2	0.0013**
WEEK 26	127	2.48	1.82 (2.96)	0.3	0.0, 15.2	-0.66 (3.30)	-0.1	-12.2, 12.0	0.0256*
Low Dose	66	2.60	1.63 (2.42)	0.7	0.0, 12.1	-0.97 (2.82)	-0.6	-6.8, 5.4	0.0069**
High Dose	61	2.35	2.02 (3.46)	0.0	0.0, 15.2	-0.33 (3.74)	0.0	-12.2, 12.0	0.4957
WEEK 39	111	2.47	1.89 (3.32)	0.0	0.0, 16.0	-0.59 (3.26)	0.0	-7.8, 15.4	0.0603
Low Dose	63	2.69	1.93 (3.35)	0.0	0.0, 15.4	-0.76 (3.48)	-0.2	-7.8, 15.4	0.0873
High Dose	48	2.19	1.83 (3.31)	0.0	0.0, 16.0	-0.36 (2.96)	0.0	-7.8, 6.1	0.4070

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.1

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary
(FAS)

Parameter Time Point Dose Category	N	Baseline Mean	Visit Mean (SD)	Visit Median	Visit Min, Max	Change from Baseline Mean (SD)	Change from Baseline Median	Change from Baseline Min, Max	Change from Baseline P-Value &
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 52	96	2.49	2.28 (3.96)	0.2	0.0, 16.0	-0.21 (3.37)	0.0	-7.3, 12.9	0.5489
Low Dose	51	2.65	1.95 (3.64)	0.2	0.0, 16.0	-0.70 (3.28)	-0.4	-6.8, 9.2	0.1346
High Dose	45	2.31	2.66 (4.31)	0.5	0.0, 16.0	0.35 (3.41)	0.0	-7.3, 12.9	0.4932
Average Daily Normalized 'On' Time With Troublesome Dyskinesia									
BASELINE	236		0.96 (1.73)	0.0	0.0, 10.5				
Low Dose	127		1.27 (2.02)	0.0	0.0, 10.5				
High Dose	109		0.59 (1.20)	0.0	0.0, 5.3				
WEEK 1	225	0.94	0.99 (2.09)	0.0	0.0, 11.7	0.05 (1.89)	0.0	-6.0, 10.5	0.6962
Low Dose	121	1.29	1.28 (2.35)	0.0	0.0, 11.7	-0.01 (2.09)	0.0	-6.0, 10.5	0.9647
High Dose	104	0.53	0.65 (1.68)	0.0	0.0, 9.8	0.12 (1.65)	0.0	-4.9, 7.0	0.4714
WEEK 6	205	0.85	0.44 (1.30)	0.0	0.0, 9.0	-0.41 (1.60)	0.0	-9.2, 6.9	<=0.001***
Low Dose	111	1.15	0.59 (1.59)	0.0	0.0, 9.0	-0.56 (1.94)	0.0	-9.2, 6.9	0.0030**
High Dose	94	0.49	0.26 (0.81)	0.0	0.0, 4.4	-0.23 (1.06)	0.0	-4.9, 4.4	0.0402*
WEEK 13	115	0.82	0.33 (1.12)	0.0	0.0, 8.0	-0.50 (1.45)	0.0	-7.2, 6.0	<=0.001***
Low Dose	64	1.00	0.39 (1.32)	0.0	0.0, 8.0	-0.61 (1.71)	0.0	-7.2, 6.0	0.0056**
High Dose	51	0.60	0.25 (0.81)	0.0	0.0, 3.7	-0.36 (1.04)	0.0	-4.9, 2.6	0.0178*

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.1

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary
(FAS)

Parameter Time Point Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Average Daily Normalized 'On' Time With Troublesome Dyskinesia (Cont.)									
WEEK 26	127	0.71	0.33 (1.40)	0.0	0.0, 12.1	-0.38 (1.71)	0.0	-5.1, 8.8	0.0128*
Low Dose	66	0.79	0.31 (1.56)	0.0	0.0, 12.1	-0.48 (1.68)	0.0	-5.1, 7.2	0.0233*
High Dose	61	0.62	0.34 (1.22)	0.0	0.0, 8.8	-0.28 (1.75)	0.0	-4.9, 8.8	0.2200
WEEK 39	111	0.66	0.32 (1.04)	0.0	0.0, 8.1	-0.34 (1.36)	0.0	-5.1, 7.3	0.0107*
Low Dose	63	0.77	0.25 (0.75)	0.0	0.0, 3.8	-0.53 (1.08)	0.0	-5.1, 0.8	<=0.001***
High Dose	48	0.51	0.42 (1.33)	0.0	0.0, 8.1	-0.08 (1.63)	0.0	-5.0, 7.3	0.7201
WEEK 52	96	0.59	0.40 (1.10)	0.0	0.0, 6.3	-0.19 (1.50)	0.0	-5.0, 6.3	0.2214
Low Dose	51	0.66	0.22 (0.66)	0.0	0.0, 3.3	-0.44 (1.18)	0.0	-3.4, 3.3	0.0104*
High Dose	45	0.50	0.60 (1.43)	0.0	0.0, 6.3	0.10 (1.76)	0.0	-5.0, 6.3	0.7075
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia									
BASELINE	236		9.14 (2.50)	9.4	0.3, 16.0				
Low Dose	127		9.05 (2.67)	9.7	0.3, 16.0				
High Dose	109		9.25 (2.30)	9.4	2.6, 16.0				
WEEK 1	225	9.15	11.04 (3.68)	11.2	0.0, 16.0	1.89 (3.77)	1.8	-10.4, 11.3	<=0.001***
Low Dose	121	8.98	11.03 (3.64)	11.2	1.6, 16.0	2.05 (3.53)	2.2	-5.9, 11.3	<=0.001***
High Dose	104	9.35	11.06 (3.75)	11.5	0.0, 16.0	1.71 (4.05)	1.6	-10.4, 8.9	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.1

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary
(FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia (Cont.)									
WEEK 6	205	9.21	12.01 (3.36)	12.4	0.0, 16.0	2.80 (3.59)	3.2	-9.9, 10.6	<=0.001***
Low Dose	111	9.12	12.09 (3.52)	12.6	0.0, 16.0	2.97 (3.58)	3.3	-9.9, 10.5	<=0.001***
High Dose	94	9.32	11.92 (3.18)	12.3	3.5, 16.0	2.60 (3.60)	3.2	-6.8, 10.6	<=0.001***
WEEK 13	115	9.64	12.55 (3.61)	13.9	2.6, 16.0	2.92 (3.47)	3.3	-6.3, 9.9	<=0.001***
Low Dose	64	9.59	12.73 (3.72)	14.2	2.6, 16.0	3.14 (3.31)	3.7	-5.0, 9.9	<=0.001***
High Dose	51	9.69	12.33 (3.50)	13.5	5.3, 16.0	2.64 (3.67)	3.0	-6.3, 9.2	<=0.001***
WEEK 26	127	9.36	13.02 (3.24)	14.3	1.5, 16.0	3.65 (3.53)	3.9	-5.5, 12.5	<=0.001***
Low Dose	66	9.47	13.22 (3.52)	14.9	1.5, 16.0	3.75 (3.74)	4.0	-5.5, 12.5	<=0.001***
High Dose	61	9.25	12.80 (2.92)	13.8	6.2, 16.0	3.55 (3.31)	2.9	-5.5, 10.6	<=0.001***
WEEK 39	111	9.50	12.97 (3.04)	13.5	2.4, 16.0	3.46 (3.36)	3.3	-9.2, 9.9	<=0.001***
Low Dose	63	9.57	13.07 (2.99)	13.5	2.7, 16.0	3.49 (3.39)	3.1	-9.1, 9.9	<=0.001***
High Dose	48	9.40	12.83 (3.14)	13.2	2.4, 16.0	3.43 (3.34)	3.4	-9.2, 9.7	<=0.001***
WEEK 52	96	9.52	13.09 (3.01)	13.7	4.5, 16.0	3.58 (3.03)	3.5	-5.4, 11.2	<=0.001***
Low Dose	51	9.47	13.24 (2.82)	13.6	5.1, 16.0	3.77 (2.99)	3.5	-5.4, 10.2	<=0.001***
High Dose	45	9.56	12.92 (3.24)	14.2	4.5, 16.0	3.36 (3.10)	3.4	-2.8, 11.2	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

表2.7.3.6-2　PD日誌に基づく，標準化した1日あたりの平均「オフ」時間及び「オン」時間の登録時期別の要約（FAS）：M15-741試験

[redacted]20[redacted] 10:12 <[redacted]>
ABBV-951
STUDY M15-741 - SECOND INTERIM (CUTOFF [redacted]20[redacted])
R&D/20/1632 - CLINICAL/STATISTICAL

TABLE 14.2__1.7

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Enrollment Sample
(FAS)

Parameter / Time Point / Sample Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Average Daily Normalized 'Off' Time									
BASELINE	236		5.90 (2.24)	5.9	0.0, 12.6				
Sample 1	150		5.82 (2.36)	5.9	0.0, 12.6				
Sample 2	86		6.04 (2.03)	5.9	0.6, 10.3				
WEEK 1	225	5.91	3.97 (3.43)	3.1	0.0, 16.0	-1.94 (3.68)	-2.2	-10.2, 10.4	<=0.001***
Sample 1	143	5.81	4.33 (3.34)	3.9	0.0, 16.0	-1.48 (3.57)	-1.5	-9.7, 8.0	<=0.001***
Sample 2	82	6.09	3.34 (3.50)	2.2	0.0, 14.8	-2.75 (3.75)	-3.4	-10.2, 10.4	<=0.001***
WEEK 6	205	5.94	3.55 (3.26)	3.1	0.0, 16.0	-2.39 (3.60)	-2.9	-10.6, 9.9	<=0.001***
Sample 1	129	5.89	3.70 (3.23)	3.2	0.0, 14.9	-2.19 (3.51)	-2.6	-10.6, 8.1	<=0.001***
Sample 2	76	6.02	3.29 (3.31)	3.0	0.0, 16.0	-2.73 (3.76)	-3.6	-10.2, 9.9	<=0.001***
WEEK 13	115	5.54	3.12 (3.47)	1.8	0.0, 13.4	-2.42 (3.69)	-3.2	-9.9, 8.1	<=0.001***
Sample 1	75	5.33	2.83 (3.14)	1.7	0.0, 10.7	-2.50 (3.44)	-2.7	-9.9, 8.1	<=0.001***
Sample 2	40	5.93	3.68 (4.00)	1.9	0.0, 13.4	-2.26 (4.15)	-3.3	-9.3, 7.8	0.0014**
WEEK 26	127	5.92	2.65 (3.02)	1.5	0.0, 14.3	-3.27 (3.24)	-3.2	-10.6, 7.1	<=0.001***
Sample 1	77	5.79	2.53 (2.60)	1.6	0.0, 8.9	-3.26 (2.77)	-2.9	-10.6, 4.4	<=0.001***
Sample 2	50	6.13	2.84 (3.60)	1.2	0.0, 14.3	-3.29 (3.89)	-4.0	-10.2, 7.1	<=0.001***

Note: Sample 1 contains subjects who were enrolled prior to [redacted]20[redacted].
Sample 2 contains subjects who were enrolled on or after [redacted]20[redacted].
Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.7

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Enrollment Sample
(FAS)

Parameter / Time Point / Sample Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Average Daily Normalized 'Off' Time (Cont.)									
WEEK 39	111	5.84	2.71 (2.80)	2.0	0.0, 13.3	-3.13 (3.18)	-3.1	-9.9, 9.6	<=0.001***
Sample 1	70	5.69	2.51 (2.69)	1.9	0.0, 13.3	-3.18 (3.13)	-3.1	-9.9, 9.6	<=0.001***
Sample 2	41	6.10	3.05 (2.96)	2.3	0.0, 12.3	-3.04 (3.28)	-3.1	-9.8, 6.4	<=0.001***
WEEK 52	96	5.90	2.51 (2.92)	1.3	0.0, 11.5	-3.39 (3.08)	-3.5	-11.2, 5.9	<=0.001***
Sample 1	66	5.68	2.13 (2.45)	1.0	0.0, 8.8	-3.55 (2.82)	-3.5	-11.2, 3.1	<=0.001***
Sample 2	30	6.37	3.34 (3.65)	2.8	0.0, 11.5	-3.03 (3.62)	-3.7	-10.2, 5.9	<=0.001***
Average Daily Normalized 'On' Time Without Dyskinesia									
BASELINE	236		6.51 (3.35)	6.6	0.0, 15.4				
Sample 1	150		6.66 (3.29)	6.6	0.0, 15.4				
Sample 2	86		6.26 (3.47)	6.5	0.0, 12.6				
WEEK 1	225	6.48	8.43 (4.52)	8.3	0.0, 16.0	1.94 (4.09)	1.6	-8.9, 12.0	<=0.001***
Sample 1	143	6.60	8.18 (4.27)	8.1	0.0, 16.0	1.58 (3.52)	1.3	-8.2, 8.7	<=0.001***
Sample 2	82	6.29	8.87 (4.92)	8.9	0.0, 16.0	2.58 (4.88)	2.3	-8.9, 12.0	<=0.001***
WEEK 6	205	6.54	9.92 (4.48)	10.6	0.0, 16.0	3.38 (4.39)	3.5	-9.1, 13.8	<=0.001***
Sample 1	129	6.71	9.86 (4.54)	10.6	0.0, 16.0	3.14 (4.37)	3.3	-9.1, 13.8	<=0.001***
Sample 2	76	6.25	10.03 (4.42)	10.5	0.0, 16.0	3.78 (4.42)	4.0	-7.5, 12.0	<=0.001***

Note: Sample 1 contains subjects who were enrolled prior to [redacted]20[redacted].
Sample 2 contains subjects who were enrolled on or after [redacted]20[redacted].
Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.7

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Enrollment Sample
(FAS)

Parameter / Time Point / Sample Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 13	115	6.67	10.79 (4.60)	11.3	0.0, 16.0	4.12 (4.35)	4.3	-9.0, 15.2	<=0.001***
Sample 1	75	6.67	10.76 (4.54)	11.1	0.0, 16.0	4.09 (4.11)	4.3	-6.5, 11.2	<=0.001***
Sample 2	40	6.66	10.84 (4.76)	12.8	0.0, 16.0	4.17 (4.81)	4.0	-9.0, 15.2	<=0.001***
WEEK 26	127	6.89	11.20 (4.33)	12.5	0.0, 16.0	4.31 (4.47)	4.7	-11.0, 14.1	<=0.001***
Sample 1	77	7.12	11.45 (3.96)	12.8	0.0, 16.0	4.33 (4.24)	4.6	-9.6, 12.7	<=0.001***
Sample 2	50	6.53	10.82 (4.88)	11.9	0.0, 16.0	4.29 (4.85)	4.8	-11.0, 14.1	<=0.001***
WEEK 39	111	7.03	11.08 (4.17)	11.3	0.0, 16.0	4.05 (4.09)	4.1	-10.6, 13.5	<=0.001***
Sample 1	70	7.21	11.38 (4.14)	11.8	0.3, 16.0	4.17 (3.98)	4.2	-6.4, 13.5	<=0.001***
Sample 2	41	6.72	10.56 (4.23)	11.0	0.0, 16.0	3.85 (4.32)	4.1	-10.6, 12.4	<=0.001***
WEEK 52	96	7.03	10.81 (4.71)	11.8	0.0, 16.0	3.78 (4.29)	4.1	-12.0, 13.8	<=0.001***
Sample 1	66	6.90	10.64 (4.83)	11.5	0.0, 16.0	3.74 (4.55)	4.3	-12.0, 13.8	<=0.001***
Sample 2	30	7.30	11.19 (4.47)	12.2	0.0, 16.0	3.88 (3.73)	3.2	-2.8, 10.1	<=0.001***
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia									
BASELINE	236		2.63 (2.55)	2.4	0.0, 12.2				
Sample 1	150		2.71 (2.55)	2.6	0.0, 10.3				
Sample 2	86		2.49 (2.56)	1.9	0.0, 12.2				

Note: Sample 1 contains subjects who were enrolled prior to [redacted]20[redacted].
Sample 2 contains subjects who were enrolled on or after [redacted]20[redacted].
Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.7

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Enrollment Sample
(FAS)

Parameter / Time Point / Sample Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 1	225	2.66	2.61 (3.16)	1.5	0.0, 14.9	-0.05 (3.04)	0.0	-8.5, 13.6	0.8070
Sample 1	143	2.77	2.57 (2.98)	1.5	0.0, 14.9	-0.20 (2.64)	0.0	-6.9, 8.8	0.3663
Sample 2	82	2.47	2.68 (3.46)	1.1	0.0, 13.6	0.21 (3.64)	0.0	-8.5, 13.6	0.5974
WEEK 6	205	2.67	2.09 (3.29)	0.5	0.0, 15.4	-0.58 (3.01)	-0.3	-7.8, 11.6	0.0064**
Sample 1	129	2.71	2.11 (3.34)	0.5	0.0, 15.4	-0.61 (3.10)	-0.3	-7.8, 11.6	0.0276*
Sample 2	76	2.60	2.07 (3.21)	0.5	0.0, 14.6	-0.53 (2.87)	-0.4	-7.6, 7.5	0.1119
WEEK 13	115	2.97	1.77 (3.30)	0.0	0.0, 16.0	-1.20 (3.49)	-1.0	-12.2, 13.2	<=0.001***
Sample 1	75	3.17	2.05 (3.51)	0.2	0.0, 16.0	-1.12 (3.48)	-1.2	-7.1, 13.2	0.0069**
Sample 2	40	2.59	1.24 (2.81)	0.0	0.0, 14.4	-1.35 (3.55)	-0.3	-12.2, 7.2	0.0207*
WEEK 26	127	2.48	1.82 (2.96)	0.3	0.0, 15.2	-0.66 (3.30)	-0.1	-12.2, 12.0	0.0256*
Sample 1	77	2.57	1.69 (2.92)	0.0	0.0, 15.2	-0.88 (3.29)	-0.1	-7.4, 12.0	0.0211*
Sample 2	50	2.33	2.01 (3.03)	0.7	0.0, 14.9	-0.32 (3.30)	0.0	-12.2, 7.8	0.5002
WEEK 39	111	2.47	1.89 (3.32)	0.0	0.0, 16.0	-0.59 (3.26)	0.0	-7.8, 15.4	0.0603
Sample 1	70	2.53	1.70 (2.89)	0.0	0.0, 13.2	-0.83 (3.02)	-0.2	-7.8, 6.1	0.0248*
Sample 2	41	2.37	2.20 (3.96)	0.0	0.0, 16.0	-0.17 (3.63)	0.0	-7.8, 15.4	0.7605

Note: Sample 1 contains subjects who were enrolled prior to [redacted]20[redacted].
Sample 2 contains subjects who were enrolled on or after [redacted]20[redacted].
Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.7

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Enrollment Sample
(FAS)

Parameter / Time Point / Sample Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 52	96	2.49	2.28 (3.96)	0.2	0.0, 16.0	-0.21 (3.37)	0.0	-7.3, 12.9	0.5489
Sample 1	66	2.78	2.71 (4.24)	0.5	0.0, 16.0	-0.07 (3.79)	0.0	-7.3, 12.9	0.8829
Sample 2	30	1.85	1.34 (3.13)	0.0	0.0, 16.0	-0.51 (2.18)	0.0	-4.9, 4.6	0.2110
Average Daily Normalized 'On' Time With Troublesome Dyskinesia									
BASELINE	236		0.96 (1.73)	0.0	0.0, 10.5				
Sample 1	150		0.81 (1.57)	0.0	0.0, 10.5				
Sample 2	86		1.21 (1.95)	0.0	0.0, 9.2				
WEEK 1	225	0.94	0.99 (2.09)	0.0	0.0, 11.7	0.05 (1.89)	0.0	-6.0, 10.5	0.6962
Sample 1	143	0.82	0.92 (1.97)	0.0	0.0, 10.5	0.10 (1.96)	0.0	-6.0, 10.5	0.5414
Sample 2	82	1.15	1.11 (2.28)	0.0	0.0, 11.7	-0.04 (1.79)	0.0	-4.9, 6.1	0.8432
WEEK 6	205	0.85	0.44 (1.30)	0.0	0.0, 9.0	-0.41 (1.60)	0.0	-9.2, 6.9	<=0.001***
Sample 1	129	0.68	0.34 (1.23)	0.0	0.0, 9.0	-0.34 (1.36)	0.0	-7.2, 5.3	0.0051**
Sample 2	76	1.13	0.61 (1.41)	0.0	0.0, 6.9	-0.52 (1.95)	0.0	-9.2, 6.9	0.0233*
WEEK 13	115	0.82	0.33 (1.12)	0.0	0.0, 8.0	-0.50 (1.45)	0.0	-7.2, 6.0	<=0.001***
Sample 1	75	0.83	0.37 (1.20)	0.0	0.0, 8.0	-0.46 (1.60)	0.0	-7.2, 6.0	0.0139*
Sample 2	40	0.81	0.25 (0.96)	0.0	0.0, 5.5	-0.56 (1.13)	0.0	-4.9, 1.3	0.0033**

Note: Sample 1 contains subjects who were enrolled prior to [redacted]20[redacted].
Sample 2 contains subjects who were enrolled on or after [redacted]20[redacted].
Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.7

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Enrollment Sample
(FAS)

Parameter / Time Point / Sample Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Average Daily Normalized 'On' Time With Troublesome Dyskinesia (Cont.)									
WEEK 26	127	0.71	0.33 (1.40)	0.0	0.0, 12.1	-0.38 (1.71)	0.0	-5.1, 8.8	0.0128*
Sample 1	77	0.52	0.33 (1.17)	0.0	0.0, 8.8	-0.19 (1.52)	0.0	-4.0, 8.8	0.2824
Sample 2	50	1.01	0.33 (1.72)	0.0	0.0, 12.1	-0.68 (1.94)	0.0	-5.1, 7.2	0.0162*
WEEK 39	111	0.66	0.32 (1.04)	0.0	0.0, 8.1	-0.34 (1.36)	0.0	-5.1, 7.3	0.0107*
Sample 1	70	0.57	0.41 (1.21)	0.0	0.0, 8.1	-0.16 (1.43)	0.0	-5.0, 7.3	0.3453
Sample 2	41	0.81	0.18 (0.65)	0.0	0.0, 3.5	-0.63 (1.20)	0.0	-5.1, 0.2	0.0016**
WEEK 52	96	0.59	0.40 (1.10)	0.0	0.0, 6.3	-0.19 (1.50)	0.0	-5.0, 6.3	0.2214
Sample 1	66	0.63	0.52 (1.29)	0.0	0.0, 6.3	-0.12 (1.69)	0.0	-5.0, 6.3	0.5789
Sample 2	30	0.48	0.13 (0.36)	0.0	0.0, 1.5	-0.35 (0.96)	0.0	-3.4, 1.1	0.0580
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia									
BASELINE	236		9.14 (2.50)	9.4	0.3, 16.0				
Sample 1	150		9.37 (2.29)	9.5	3.4, 16.0				
Sample 2	86		8.75 (2.81)	9.1	0.3, 14.5				
WEEK 1	225	9.15	11.04 (3.68)	11.2	0.0, 16.0	1.89 (3.77)	1.8	-10.4, 11.3	<=0.001***
Sample 1	143	9.37	10.75 (3.43)	10.6	0.0, 16.0	1.38 (3.51)	1.3	-8.0, 9.7	<=0.001***
Sample 2	82	8.76	11.55 (4.05)	12.6	1.2, 16.0	2.79 (4.07)	3.2	-10.4, 11.3	<=0.001***

Note: Sample 1 contains subjects who were enrolled prior to [redacted]20[redacted].
Sample 2 contains subjects who were enrolled on or after [redacted]20[redacted].
Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.7

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Enrollment Sample
(FAS)

Parameter / Time Point / Sample Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia (Cont.)									
WEEK 6	205	9.21	12.01 (3.36)	12.4	0.0, 16.0	2.80 (3.59)	3.2	-9.9, 10.6	<=0.001***
Sample 1	129	9.43	11.96 (3.28)	12.3	1.1, 16.0	2.54 (3.27)	2.9	-6.7, 10.6	<=0.001***
Sample 2	76	8.85	12.10 (3.53)	12.6	0.0, 16.0	3.25 (4.05)	4.0	-9.9, 10.5	<=0.001***
WEEK 13	115	9.64	12.55 (3.61)	13.9	2.6, 16.0	2.92 (3.47)	3.3	-6.3, 9.9	<=0.001***
Sample 1	75	9.84	12.81 (3.38)	14.1	5.3, 16.0	2.97 (3.13)	3.3	-6.3, 9.9	<=0.001***
Sample 2	40	9.26	12.07 (4.01)	13.6	2.6, 16.0	2.82 (4.07)	3.8	-5.0, 9.3	<=0.001***
WEEK 26	127	9.36	13.02 (3.24)	14.3	1.5, 16.0	3.65 (3.53)	3.9	-5.5, 12.5	<=0.001***
Sample 1	77	9.69	13.14 (2.71)	14.0	7.1, 16.0	3.45 (2.81)	3.0	-2.7, 10.6	<=0.001***
Sample 2	50	8.86	12.83 (3.95)	14.6	1.5, 16.0	3.97 (4.43)	4.6	-5.5, 12.5	<=0.001***
WEEK 39	111	9.50	12.97 (3.04)	13.5	2.4, 16.0	3.46 (3.36)	3.3	-9.2, 9.9	<=0.001***
Sample 1	70	9.74	13.08 (3.08)	13.5	2.4, 16.0	3.34 (3.37)	3.2	-9.2, 9.9	<=0.001***
Sample 2	41	9.09	12.76 (3.00)	12.8	3.7, 16.0	3.67 (3.36)	3.4	-5.9, 9.8	<=0.001***
WEEK 52	96	9.52	13.09 (3.01)	13.7	4.5, 16.0	3.58 (3.03)	3.5	-5.4, 11.2	<=0.001***
Sample 1	66	9.68	13.35 (2.61)	14.0	7.2, 16.0	3.67 (2.81)	3.5	-3.1, 11.2	<=0.001***
Sample 2	30	9.15	12.53 (3.74)	13.2	4.5, 16.0	3.37 (3.52)	3.6	-5.4, 10.2	<=0.001***

Note: Sample 1 contains subjects who were enrolled prior to [redacted]20[redacted].
Sample 2 contains subjects who were enrolled on or after [redacted]20[redacted].
Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

表2.7.3.6-3　PD日誌に基づく，標準化した1日あたりの平均「オフ」時間及び「オン」時間の要約（FAS）：M15-737試験

[redacted]20[redacted] 07:19 <[redacted]>
ABBV-951
STUDY M15-737 - SECOND INTERIM (CUTOFF [redacted]20[redacted])
R&D/20/1639 - CLINICAL/STATISTICAL

TABLE 14.2__1.1

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary
(FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Average Daily Normalized 'Off' Time									
BASELINE	73		2.39 (2.68)	1.2	0.0, 10.1				
Low Dose	30		3.01 (2.66)	2.6	0.0, 10.1				
High Dose	43		1.96 (2.64)	0.5	0.0, 8.8				
WEEK 12	54	2.64	2.65 (2.51)	2.3	0.0, 7.6	0.01 (2.17)	0.0	-6.4, 6.8	0.9641
Low Dose	25	2.98	2.49 (2.27)	2.5	0.0, 7.3	-0.49 (1.80)	0.0	-4.2, 2.8	0.1884
High Dose	29	2.35	2.79 (2.72)	2.1	0.0, 7.6	0.44 (2.40)	0.0	-6.4, 6.8	0.3277
WEEK 24	62	2.12	2.96 (3.74)	1.8	0.0, 16.0	0.84 (2.78)	0.0	-5.7, 13.3	0.0208*
Low Dose	25	2.59	3.16 (4.23)	1.3	0.0, 16.0	0.57 (3.58)	0.0	-5.7, 13.3	0.4340
High Dose	37	1.81	2.83 (3.43)	2.3	0.0, 13.4	1.02 (2.11)	0.0	-3.3, 6.2	0.0058**
WEEK 36	34	2.54	2.63 (2.70)	2.0	0.0, 12.1	0.09 (2.04)	0.0	-5.5, 5.6	0.8007
Low Dose	17	2.93	3.14 (3.26)	2.3	0.0, 12.1	0.21 (2.09)	0.3	-5.5, 5.6	0.6847
High Dose	17	2.14	2.11 (1.96)	1.7	0.0, 6.1	-0.03 (2.06)	0.0	-3.9, 3.9	0.9517

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours
(i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.1

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary
(FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Average Daily Normalized 'Off' Time (Cont.)									
WEEK 48	25	1.80	2.76 (3.60)	1.1	0.0, 14.3	0.95 (2.29)	0.0	-3.0, 6.1	0.0477*
Low Dose	10	1.41	1.16 (1.49)	0.4	0.0, 4.2	-0.26 (1.21)	-0.0	-3.0, 1.6	0.5191
High Dose	15	2.06	3.82 (4.21)	2.8	0.0, 14.3	1.76 (2.51)	0.4	-1.0, 6.1	0.0166*
WEEK 60	4	0.26	1.57 (1.15)	1.9	0.0, 2.4	1.31 (1.07)	1.4	0.0, 2.4	0.0928
Low Dose	2	0.27	1.21 (1.71)	1.2	0.0, 2.4	0.95 (1.34)	0.9	0.0, 1.9	0.5000
High Dose	2	0.25	1.92 (0.72)	1.9	1.4, 2.4	1.67 (1.07)	1.7	0.9, 2.4	0.2710
WEEK 72	2	0.00	2.73 (3.85)	2.7	0.0, 5.5	2.73 (3.85)	2.7	0.0, 5.5	0.5000
Low Dose	1	0.00	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	1	0.00	5.45 (N/A)	5.5	5.5, 5.5	5.45 (N/A)	5.5	5.5, 5.5	
Average Daily Normalized 'On' Time Without Dyskinesia									
BASELINE	73		10.32 (4.99)	11.2	0.0, 16.0				
Low Dose	30		11.05 (4.22)	11.7	1.3, 16.0				
High Dose	43		9.80 (5.45)	10.0	0.0, 16.0				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.1

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary
(FAS)

Parameter Time Point Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 12	54	10.32	11.08 (4.63)	11.9	0.0, 16.0	0.75 (3.51)	0.2	-9.6, 14.2	0.1205
Low Dose	25	11.31	12.05 (4.06)	13.3	1.0, 16.0	0.75 (3.93)	0.0	-6.6, 14.2	0.3513
High Dose	29	9.47	10.23 (4.99)	10.7	0.0, 16.0	0.76 (3.18)	0.3	-9.6, 9.0	0.2084
WEEK 24	62	10.84	11.09 (4.64)	11.9	0.0, 16.0	0.26 (4.45)	0.0	-13.3, 14.2	0.6529
Low Dose	25	11.46	11.58 (4.91)	13.6	0.0, 16.0	0.12 (4.91)	0.0	-13.3, 14.2	0.9026
High Dose	37	10.42	10.76 (4.48)	10.6	0.0, 16.0	0.35 (4.18)	0.0	-9.2, 13.7	0.6177
WEEK 36	34	10.89	10.88 (4.76)	11.9	0.0, 16.0	-0.00 (4.71)	0.0	-11.2, 14.2	0.9977
Low Dose	17	11.41	11.55 (4.61)	13.3	1.3, 16.0	0.14 (4.44)	-0.3	-5.9, 14.2	0.8972
High Dose	17	10.36	10.21 (4.95)	11.9	0.0, 16.0	-0.15 (5.09)	0.2	-11.2, 14.0	0.9073
WEEK 48	25	11.07	11.40 (4.61)	12.4	1.4, 16.0	0.34 (4.40)	0.0	-5.6, 13.7	0.7059
Low Dose	10	11.48	12.80 (4.75)	15.3	1.8, 16.0	1.32 (5.62)	0.0	-5.1, 13.7	0.4762
High Dose	15	10.79	10.47 (4.43)	10.7	1.4, 16.0	-0.32 (3.41)	0.0	-5.6, 7.9	0.7209

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.1

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary
(FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 60	4	8.29	12.15 (4.14)	13.1	6.3, 16.0	3.86 (2.72)	4.6	0.0, 6.3	0.0655
Low Dose	2	12.32	14.79 (1.71)	14.8	13.6, 16.0	2.46 (3.48)	2.5	0.0, 4.9	0.5000
High Dose	2	4.25	9.50 (4.53)	9.5	6.3, 12.7	5.25 (1.48)	5.3	4.2, 6.3	0.1254
WEEK 72	2	13.65	8.71 (10.30)	8.7	1.4, 16.0	-4.93 (6.98)	-4.9	-9.9, 0.0	0.5000
Low Dose	1	16.00	16.00 (N/A)	16.0	16.0, 16.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	1	11.29	1.43 (N/A)	1.4	1.4, 1.4	-9.87 (N/A)	-9.9	-9.9, -9.9	
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia									
BASELINE	73		2.86 (4.60)	0.5	0.0, 16.0				
Low Dose	30		1.66 (3.20)	0.0	0.0, 12.0				
High Dose	43		3.69 (5.24)	0.8	0.0, 16.0				
WEEK 12	54	2.61	1.88 (3.80)	0.0	0.0, 16.0	-0.73 (3.94)	0.0	-15.8, 7.4	0.1806
Low Dose	25	1.40	1.43 (3.22)	0.0	0.0, 12.4	0.03 (3.21)	0.0	-11.6, 7.4	0.9614
High Dose	29	3.65	2.27 (4.26)	0.0	0.0, 16.0	-1.38 (4.43)	0.0	-15.8, 6.7	0.1039

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.1

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary
(FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 24	62	2.57	1.62 (3.16)	0.0	0.0, 16.0	-0.95 (4.06)	0.0	-16.0, 6.1	0.0702
Low Dose	25	1.70	1.18 (2.69)	0.0	0.0, 12.4	-0.52 (3.79)	0.0	-12.0, 5.7	0.5004
High Dose	37	3.15	1.91 (3.44)	0.0	0.0, 16.0	-1.24 (4.26)	0.0	-16.0, 6.1	0.0846
WEEK 36	34	2.27	2.29 (4.23)	0.1	0.0, 16.0	0.02 (4.10)	0.0	-12.9, 11.2	0.9767
Low Dose	17	1.48	1.21 (2.74)	0.0	0.0, 11.1	-0.28 (3.14)	0.0	-11.6, 4.4	0.7229
High Dose	17	3.05	3.37 (5.19)	0.2	0.0, 16.0	0.32 (4.96)	0.0	-12.9, 11.2	0.7959
WEEK 48	25	2.71	1.69 (2.95)	0.2	0.0, 11.9	-1.02 (4.31)	0.0	-12.8, 5.2	0.2477
Low Dose	10	2.51	1.95 (3.94)	0.0	0.0, 11.9	-0.56 (4.32)	0.0	-11.1, 5.2	0.6893
High Dose	15	2.85	1.52 (2.20)	0.3	0.0, 6.4	-1.33 (4.42)	0.0	-12.8, 4.9	0.2654
WEEK 60	4	5.06	1.93 (2.74)	0.9	0.0, 5.8	-3.14 (5.09)	-1.8	-10.2, 1.1	0.3056
Low Dose	2	1.75	0.00 (0.00)	0.0	0.0, 0.0	-1.75 (2.48)	-1.8	-3.5, 0.0	0.5000
High Dose	2	8.38	3.85 (2.78)	3.9	1.9, 5.8	-4.52 (8.00)	-4.5	-10.2, 1.1	0.5705

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.1

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary
(FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 72	2	2.35	2.08 (2.94)	2.1	0.0, 4.2	-0.27 (0.39)	-0.3	-0.5, 0.0	0.5000
Low Dose	1	0.00	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	1	4.71	4.16 (N/A)	4.2	4.2, 4.2	-0.55 (N/A)	-0.5	-0.5, -0.5	
Average Daily Normalized 'On' Time With Troublesome Dyskinesia									
BASELINE	73		0.43 (1.18)	0.0	0.0, 6.3				
Low Dose	30		0.27 (0.79)	0.0	0.0, 3.3				
High Dose	43		0.55 (1.38)	0.0	0.0, 6.3				
WEEK 12	54	0.43	0.39 (1.66)	0.0	0.0, 11.0	-0.04 (1.92)	0.0	-5.3, 11.0	0.8799
Low Dose	25	0.32	0.03 (0.13)	0.0	0.0, 0.7	-0.29 (0.88)	0.0	-3.3, 0.7	0.1107
High Dose	29	0.53	0.71 (2.24)	0.0	0.0, 11.0	0.18 (2.50)	0.0	-5.3, 11.0	0.7043
WEEK 24	62	0.47	0.33 (1.14)	0.0	0.0, 7.2	-0.14 (1.19)	0.0	-5.3, 4.3	0.3522
Low Dose	25	0.25	0.08 (0.24)	0.0	0.0, 0.9	-0.17 (0.89)	0.0	-3.3, 0.9	0.3423
High Dose	37	0.62	0.50 (1.45)	0.0	0.0, 7.2	-0.12 (1.37)	0.0	-5.3, 4.3	0.5934

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.1

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary
(FAS)

Parameter Time Point Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Average Daily Normalized 'On' Time With Troublesome Dyskinesia (Cont.)									
WEEK 36	34	0.31	0.20 (0.60)	0.0	0.0, 2.8	-0.11 (1.11)	0.0	-5.3, 1.8	0.5768
Low Dose	17	0.17	0.10 (0.31)	0.0	0.0, 1.2	-0.08 (0.74)	0.0	-2.7, 1.2	0.6799
High Dose	17	0.45	0.31 (0.79)	0.0	0.0, 2.8	-0.14 (1.42)	0.0	-5.3, 1.8	0.6895
WEEK 48	25	0.42	0.15 (0.35)	0.0	0.0, 1.6	-0.27 (0.98)	0.0	-3.3, 0.7	0.1821
Low Dose	10	0.60	0.10 (0.23)	0.0	0.0, 0.7	-0.50 (1.34)	0.0	-3.3, 0.7	0.2668
High Dose	15	0.31	0.19 (0.42)	0.0	0.0, 1.6	-0.12 (0.66)	0.0	-2.5, 0.4	0.5089
WEEK 60	4	2.39	0.36 (0.73)	0.0	0.0, 1.5	-2.03 (3.45)	-1.7	-6.3, 1.5	0.3247
Low Dose	2	1.66	0.00 (0.00)	0.0	0.0, 0.0	-1.66 (2.34)	-1.7	-3.3, 0.0	0.5000
High Dose	2	3.13	0.73 (1.03)	0.7	0.0, 1.5	-2.40 (5.45)	-2.4	-6.3, 1.5	0.6456
WEEK 72	2	0.00	2.48 (3.51)	2.5	0.0, 5.0	2.48 (3.51)	2.5	0.0, 5.0	0.5000
Low Dose	1	0.00	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	1	0.00	4.96 (N/A)	5.0	5.0, 5.0	4.96 (N/A)	5.0	5.0, 5.0	

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.1

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary
(FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia									
BASELINE	73		13.17 (2.78)	13.7	5.9, 16.0				
Low Dose	30		12.72 (2.62)	13.3	5.9, 16.0				
High Dose	43		13.49 (2.88)	14.9	7.2, 16.0				
WEEK 12	54	12.93	12.96 (2.83)	13.5	5.0, 16.0	0.03 (2.87)	0.0	-11.0, 6.4	0.9464
Low Dose	25	12.70	13.48 (2.25)	13.5	8.8, 16.0	0.78 (1.96)	0.0	-2.8, 4.4	0.0586
High Dose	29	13.12	12.50 (3.23)	13.7	5.0, 16.0	-0.62 (3.37)	0.0	-11.0, 6.4	0.3284
WEEK 24	62	13.40	12.71 (3.87)	13.7	0.0, 16.0	-0.69 (2.98)	-0.0	-13.3, 5.7	0.0711
Low Dose	25	13.16	12.76 (4.27)	14.7	0.0, 16.0	-0.40 (3.78)	0.0	-13.3, 5.7	0.6038
High Dose	37	13.57	12.67 (3.64)	13.7	2.6, 16.0	-0.90 (2.32)	-0.6	-6.2, 3.3	0.0247*
WEEK 36	34	13.15	13.17 (2.70)	14.0	3.9, 16.0	0.02 (2.25)	0.0	-5.6, 5.5	0.9624
Low Dose	17	12.89	12.76 (3.31)	13.8	3.9, 16.0	-0.13 (2.26)	0.0	-5.6, 5.5	0.8106
High Dose	17	13.41	13.58 (1.93)	14.0	9.9, 16.0	0.17 (2.29)	0.0	-3.9, 4.3	0.7635

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.1

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary
(FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia (Cont.)									
WEEK 48	25	13.78	13.09 (3.61)	14.2	1.7, 16.0	-0.68 (2.48)	-0.2	-6.1, 3.8	0.1804
Low Dose	10	13.99	14.75 (1.67)	15.6	11.1, 16.0	0.76 (1.90)	0.0	-2.3, 3.8	0.2400
High Dose	15	13.64	11.99 (4.16)	13.2	1.7, 16.0	-1.65 (2.40)	-0.4	-6.1, 1.0	0.0187*
WEEK 60	4	13.35	14.07 (1.64)	14.1	12.1, 16.0	0.72 (3.81)	0.7	-3.9, 5.3	0.7302
Low Dose	2	14.08	14.79 (1.71)	14.8	13.6, 16.0	0.71 (1.01)	0.7	0.0, 1.4	0.5000
High Dose	2	12.63	13.35 (1.74)	13.4	12.1, 14.6	0.73 (6.52)	0.7	-3.9, 5.3	0.9000
WEEK 72	2	16.00	10.79 (7.36)	10.8	5.6, 16.0	-5.21 (7.36)	-5.2	-10.4, 0.0	0.5000
Low Dose	1	16.00	16.00 (N/A)	16.0	16.0, 16.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	1	16.00	5.59 (N/A)	5.6	5.6, 5.6	-10.41 (N/A)	-10.4	-10.4, -10.4	

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

表2.7.3.6-4　PD日誌に基づく，標準化した1日あたりの平均「オフ」時間及び「オン」時間の要約（FAS）：M15-736試験

[redacted]20[redacted] 19:31 <[redacted]>
ABBV-951
STUDY M15-736
R&D/20/1640 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 5

TABLE 14.2__2.1

Repeated-Measure Analysis of Change from Baseline to Post-Baseline Visits in Normalized Time (Hours) Assessed by PD Diary
(Full Analysis Set)

Status / Visit / Treatment	N	Summary Statistics: Mean (SD)	Min	Max	Model-Based Statistics@: LS Mean (SE)	Within Group P-Value	Treatment Difference between Groups: LS Mean of Difference (SE)	95% CI	Two-Sided P-Value
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia									
Baseline									
Oral CD/LD	67	9.49 (2.62)	0.0	13.5					
ABBV-951	73	9.20 (2.42)	0.0	13.3					
Change to Day 8									
Oral CD/LD	65	0.62 (2.51)	-4.9	7.7	0.79 (0.44)	0.0746			
ABBV-951	70	1.90 (3.55)	-8.0	10.3	1.87 (0.42)	<=0.001***	1.08 (0.52)	(0.05, 2.12)	0.0393*
Change to Day 15									
Oral CD/LD	63	0.72 (2.38)	-3.7	8.1	0.89 (0.46)	0.0528			
ABBV-951	66	1.94 (3.98)	-8.1	11.3	2.00 (0.44)	<=0.001***	1.11 (0.55)	(0.01, 2.20)	0.0474*
Change to Day 22									
Oral CD/LD	39	1.63 (2.91)	-3.1	8.1	1.46 (0.50)	0.0039**			
ABBV-951	39	1.92 (4.09)	-7.0	11.3	2.32 (0.48)	<=0.001***	0.86 (0.62)	(-0.37, 2.09)	0.1712
Change to Day 29									
Oral CD/LD	62	0.94 (2.48)	-4.9	8.1	1.16 (0.42)	0.0073**			
ABBV-951	54	2.77 (3.46)	-5.7	9.3	2.64 (0.42)	<=0.001***	1.49 (0.51)	(0.47, 2.50)	0.0044**
Change to Day 57									
Oral CD/LD	62	0.96 (3.10)	-7.0	8.1	1.07 (0.48)	0.0269*			
ABBV-951	47	3.76 (3.86)	-6.5	15.7	2.91 (0.49)	<=0.001***	1.84 (0.61)	(0.63, 3.06)	0.0032**
Change to Day 85									
Oral CD/LD	62	0.85 (3.46)	-10.0	8.4	0.97 (0.50)	0.0574			
ABBV-951	47	3.36 (3.62)	-6.7	11.1	2.72 (0.52)	<=0.001***	1.75 (0.65)	(0.46, 3.05)	0.0083**

Note: @ The repeated measures model: change = treatment country visit baseline treatment*visit treatment*baseline.
The unstructured variance-covariance structure is used.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 2.1

Repeated-Measure Analysis of Change from Baseline to Post-Baseline Visits in Normalized Time (Hours) Assessed by PD Diary
(Full Analysis Set)

Status / Visit / Treatment	N	Summary Statistics: Mean (SD)	Min	Max	Model-Based Statistics@: LS Mean (SE)	Within Group P-Value	Treatment Difference between Groups: LS Mean of Difference (SE)	95% CI	Two-Sided P-Value
Average Daily Normalized 'Off' Time									
Baseline									
Oral CD/LD	67	5.91 (1.88)	2.5	10.3					
ABBV-951	73	6.34 (2.27)	2.7	14.0					
Change to Day 8									
Oral CD/LD	65	-0.59 (2.41)	-6.4	5.1	-0.67 (0.44)	0.1295			
ABBV-951	70	-2.17 (3.70)	-13.0	8.0	-2.00 (0.41)	<=0.001***	-1.32 (0.52)	(-2.36, -0.29)	0.0124*
Change to Day 15									
Oral CD/LD	63	-0.66 (2.43)	-6.5	3.7	-0.74 (0.45)	0.1004			
ABBV-951	66	-2.08 (3.86)	-11.3	9.1	-2.03 (0.43)	<=0.001***	-1.29 (0.54)	(-2.36, -0.23)	0.0177*
Change to Day 22									
Oral CD/LD	39	-1.35 (2.92)	-6.5	3.6	-1.15 (0.48)	0.0186*			
ABBV-951	39	-1.82 (3.95)	-11.3	7.0	-2.18 (0.47)	<=0.001***	-1.03 (0.60)	(-2.22, 0.17)	0.0909
Change to Day 29									
Oral CD/LD	62	-0.89 (2.58)	-6.4	3.9	-1.02 (0.42)	0.0167*			
ABBV-951	54	-2.69 (3.25)	-9.3	5.7	-2.50 (0.41)	<=0.001***	-1.48 (0.51)	(-2.48, -0.48)	0.0039**
Change to Day 57									
Oral CD/LD	62	-0.95 (2.88)	-6.5	5.9	-0.97 (0.46)	0.0347*			
ABBV-951	47	-3.79 (3.63)	-12.7	6.3	-2.89 (0.46)	<=0.001***	-1.92 (0.58)	(-3.06, -0.78)	0.0011**
Change to Day 85									
Oral CD/LD	62	-0.93 (3.31)	-8.4	10.0	-0.96 (0.49)	0.0518			
ABBV-951	47	-3.41 (3.76)	-12.3	6.7	-2.75 (0.50)	<=0.001***	-1.79 (0.63)	(-3.03, -0.54)	0.0054**

Note: @ The repeated measures model: change = treatment country visit baseline treatment*visit treatment*baseline.
The unstructured variance-covariance structure is used.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 2.1

Repeated-Measure Analysis of Change from Baseline to Post-Baseline Visits in Normalized Time (Hours) Assessed by PD Diary
(Full Analysis Set)

Status / Visit / Treatment	N	Summary Statistics: Mean (SD)	Min	Max	Model-Based Statistics@: LS Mean (SE)	Within Group P-Value	Treatment Difference between Groups: LS Mean of Difference (SE)	95% CI	Two-Sided P-Value
Average Daily Normalized 'On' Time Without Dyskinesia									
Baseline									
Oral CD/LD	67	7.47 (3.72)	0.0	13.5					
ABBV-951	73	7.23 (3.14)	0.0	13.2					
Change to Day 8									
Oral CD/LD	65	0.74 (2.36)	-5.4	5.7	0.93 (0.44)	0.0344*			
ABBV-951	70	2.13 (3.43)	-8.0	9.4	2.17 (0.41)	<=0.001***	1.24 (0.51)	(0.22, 2.25)	0.0170*
Change to Day 15									
Oral CD/LD	63	0.90 (2.76)	-4.6	11.7	1.10 (0.47)	0.0203*			
ABBV-951	66	2.33 (3.74)	-5.0	13.0	2.48 (0.45)	<=0.001***	1.38 (0.57)	(0.27, 2.50)	0.0157*
Change to Day 22									
Oral CD/LD	39	1.84 (3.13)	-3.4	11.7	1.68 (0.52)	0.0014**			
ABBV-951	39	2.28 (4.01)	-7.0	13.0	2.79 (0.50)	<=0.001***	1.11 (0.65)	(-0.17, 2.39)	0.0889
Change to Day 29									
Oral CD/LD	62	1.03 (2.72)	-5.1	11.7	1.29 (0.47)	0.0068**			
ABBV-951	54	2.98 (3.77)	-6.2	13.0	2.87 (0.46)	<=0.001***	1.58 (0.58)	(0.44, 2.73)	0.0069**
Change to Day 57									
Oral CD/LD	62	1.30 (3.50)	-6.4	11.7	1.45 (0.54)	0.0078**			
ABBV-951	47	4.07 (4.02)	-6.5	14.0	3.11 (0.55)	<=0.001***	1.66 (0.70)	(0.28, 3.04)	0.0188*
Change to Day 85									
Oral CD/LD	62	1.15 (3.63)	-10.4	11.7	1.32 (0.53)	0.0130*			
ABBV-951	47	3.96 (3.77)	-4.3	14.0	3.13 (0.54)	<=0.001***	1.81 (0.68)	(0.46, 3.16)	0.0091**

Note: @ The repeated measures model: change = treatment country visit baseline treatment*visit treatment*baseline.
The unstructured variance-covariance structure is used.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 2.1

Repeated-Measure Analysis of Change from Baseline to Post-Baseline Visits in Normalized Time (Hours) Assessed by PD Diary
(Full Analysis Set)

Status / Visit / Treatment	N	Summary Statistics: Mean (SD)	Min	Max	Model-Based Statistics@: LS Mean (SE)	Within Group P-Value	Treatment Difference between Groups: LS Mean of Difference (SE)	95% CI	Two-Sided P-Value
Average Daily Normalized 'On' Time With Non-troublesome Dyskinesia									
Baseline									
Oral CD/LD	67	2.02 (2.75)	0.0	9.8					
ABBV-951	73	1.97 (2.46)	0.0	9.7					
Change to Day 8									
Oral CD/LD	65	-0.12 (1.49)	-3.6	6.2	-0.13 (0.25)	0.5998			
ABBV-951	70	-0.22 (2.17)	-5.4	8.6	-0.23 (0.24)	0.3415	-0.09 (0.31)	(-0.70, 0.51)	0.7569
Change to Day 15									
Oral CD/LD	63	-0.18 (1.50)	-5.8	4.2	-0.20 (0.25)	0.4224			
ABBV-951	66	-0.39 (2.29)	-6.9	6.6	-0.45 (0.24)	0.0645	-0.24 (0.31)	(-0.85, 0.36)	0.4250
Change to Day 22									
Oral CD/LD	39	-0.21 (1.85)	-8.0	3.4	-0.23 (0.27)	0.3835			
ABBV-951	39	-0.37 (1.87)	-4.6	4.7	-0.40 (0.26)	0.1217	-0.17 (0.33)	(-0.82, 0.49)	0.6168
Change to Day 29									
Oral CD/LD	62	-0.09 (1.62)	-8.0	4.9	-0.13 (0.30)	0.6613			
ABBV-951	54	-0.22 (2.95)	-6.9	7.2	-0.27 (0.30)	0.3727	-0.14 (0.39)	(-0.91, 0.63)	0.7249
Change to Day 57									
Oral CD/LD	62	-0.34 (2.15)	-8.0	7.2	-0.38 (0.32)	0.2287			
ABBV-951	47	-0.32 (3.09)	-7.2	9.6	-0.29 (0.33)	0.3808	0.09 (0.43)	(-0.76, 0.94)	0.8343
Change to Day 85									
Oral CD/LD	62	-0.30 (1.88)	-8.0	6.1	-0.36 (0.28)	0.2109			
ABBV-951	47	-0.59 (2.46)	-6.9	6.4	-0.41 (0.29)	0.1660	-0.05 (0.37)	(-0.79, 0.69)	0.8864

Note: @ The repeated measures model: change = treatment country visit baseline treatment*visit treatment*baseline.
The unstructured variance-covariance structure is used.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 2.1

Repeated-Measure Analysis of Change from Baseline to Post-Baseline Visits in Normalized Time (Hours) Assessed by PD Diary
(Full Analysis Set)

Status / Visit / Treatment	N	Summary Statistics: Mean (SD)	Min	Max	Model-Based Statistics@: LS Mean (SE)	Within Group P-Value	Treatment Difference between Groups: LS Mean of Difference (SE)	95% CI	Two-Sided P-Value
Average Daily Normalized 'On' Time With Troublesome Dyskinesia									
Baseline									
Oral CD/LD	67	0.60 (1.46)	0.0	6.7					
ABBV-951	73	0.46 (0.86)	0.0	4.6					
Change to Day 8									
Oral CD/LD	65	-0.03 (0.61)	-2.2	1.7	-0.13 (0.14)	0.3673			
ABBV-951	70	0.27 (1.41)	-1.8	8.0	0.16 (0.14)	0.2453	0.29 (0.19)	(-0.08, 0.66)	0.1243
Change to Day 15									
Oral CD/LD	63	-0.06 (0.74)	-3.1	2.2	-0.16 (0.14)	0.2338			
ABBV-951	66	0.14 (1.23)	-1.9	5.9	0.08 (0.13)	0.5430	0.24 (0.18)	(-0.11, 0.59)	0.1737
Change to Day 22									
Oral CD/LD	39	-0.28 (0.59)	-2.0	0.5	-0.31 (0.10)	0.0027**			
ABBV-951	39	-0.10 (0.77)	-3.0	2.3	-0.16 (0.10)	0.1129	0.15 (0.13)	(-0.10, 0.41)	0.2294
Change to Day 29									
Oral CD/LD	62	-0.05 (0.98)	-3.9	3.2	-0.15 (0.12)	0.2123			
ABBV-951	54	-0.08 (0.80)	-2.2	3.2	-0.12 (0.12)	0.3236	0.03 (0.16)	(-0.29, 0.35)	0.8507
Change to Day 57									
Oral CD/LD	62	-0.01 (1.07)	-2.7	6.2	-0.11 (0.15)	0.4519			
ABBV-951	47	0.04 (1.07)	-3.0	4.4	0.07 (0.15)	0.6620	0.18 (0.20)	(-0.22, 0.58)	0.3798
Change to Day 85									
Oral CD/LD	62	0.08 (1.13)	-2.2	6.4	-0.02 (0.16)	0.9232			
ABBV-951	47	0.05 (1.06)	-1.7	5.8	-0.03 (0.17)	0.8554	-0.02 (0.23)	(-0.46, 0.43)	0.9424

Note: @ The repeated measures model: change = treatment country visit baseline treatment*visit treatment*baseline.
The unstructured variance-covariance structure is used.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

表2.7.3.6-5　朝の無動（FAS）：M15-736試験

[redacted]20[redacted] 19:30 <[redacted]>
ABBV-951
STUDY M15-736
R&D/20/1640 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 1

TABLE 14.2 4.2

Repeated-Measure Analysis of Early Morning 'Off' Status at Post-Baseline Visits
(Full Analysis Set)

			Model-Based Statistics@		
	Summary Statistics		Odds Ratio between Groups		
Visit Treatment	N	n (%)	LS Mean of Odds Ratio (SE)	95% CI	Two-Sided P-Value
Baseline					
Oral CD/LD	67	51 (76.1)			
ABBV-951	71	56 (78.9)			
Day 8					
Oral CD/LD	64	37 (57.8)			
ABBV-951	71	27 (38.0)	0.41 (0.36)	(0.20, 0.85)	0.0168*
Day 15					
Oral CD/LD	62	38 (61.3)			
ABBV-951	64	21 (32.8)	0.28 (0.38)	(0.13, 0.59)	<=0.001***
Day 22					
Oral CD/LD	38	22 (57.9)			
ABBV-951	39	13 (33.3)	0.34 (0.46)	(0.14, 0.85)	0.0210*
Day 29					
Oral CD/LD	61	39 (63.9)			
ABBV-951	54	15 (27.8)	0.24 (0.41)	(0.11, 0.53)	<=0.001***
Day 57					
Oral CD/LD	61	39 (63.9)			
ABBV-951	47	10 (21.3)	0.17 (0.45)	(0.07, 0.40)	<=0.001***
Day 85					
Oral CD/LD	60	38 (63.3)			
ABBV-951	47	8 (17.0)	0.12 (0.49)	(0.04, 0.31)	<=0.001***

Note: @ The generalized linear mixed model: status = treatment country visit baseline treatment*visit.
The unstructured variance-covariance structure is used.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

表2.7.3.6-6　MDS-UPDRSスコア（FAS）：M15-741試験

[redacted]20[redacted] 10:12 <[redacted]>
ABBV-951
STUDY M15-741 - SECOND INTERIM (CUTOFF [redacted]20[redacted])
R&D/20/1632 - CLINICAL/STATISTICAL

TABLE 14.2__2.1

Change from Baseline to Each Planned Visit in Parkinson's Disease Symptoms as Assessed
by The Movement Disorder Society-Unified Parkinson's Disease Rating Scale Score by Part and Total
(FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
MDS-UPDRS Total Score of Parts I-III									
BASELINE	244		50.4 (18.89)	50.0	13, 117				
Low dose	132		49.9 (19.55)	46.5	13, 117				
High dose	112		51.0 (18.15)	51.0	14, 109				
DAY 2	222	51.0	45.9 (20.28)	44.0	4, 100	-5.0 (12.19)	-4.0	-42, 38	<=0.001***
Low dose	121	49.9	43.9 (18.94)	42.0	5, 100	-6.0 (11.67)	-4.0	-42, 28	<=0.001***
High dose	101	52.2	48.3 (21.62)	46.0	4, 100	-3.9 (12.76)	-4.0	-36, 38	0.0028**
WEEK 1	224	50.4	46.4 (22.58)	43.0	3, 114	-4.0 (16.62)	-4.0	-45, 68	<=0.001***
Low dose	119	49.6	45.2 (21.66)	42.0	3, 109	-4.3 (15.85)	-3.0	-45, 68	0.0034**
High dose	105	51.4	47.8 (23.61)	43.0	10, 114	-3.6 (17.53)	-6.0	-41, 51	0.0378*
WEEK 2	211	50.2	47.5 (23.46)	44.0	2, 114	-2.6 (18.19)	-5.0	-39, 60	0.0367*
Low dose	118	50.0	48.6 (23.95)	44.0	2, 111	-1.4 (18.47)	-5.5	-35, 60	0.4011
High dose	93	50.4	46.2 (22.88)	44.0	6, 114	-4.2 (17.81)	-5.0	-39, 49	0.0268*
WEEK 3	203	49.9	46.8 (22.87)	45.0	1, 135	-3.2 (18.50)	-4.0	-50, 94	0.0156*
Low dose	108	49.2	47.2 (23.93)	43.0	1, 135	-2.0 (18.01)	-3.0	-39, 94	0.2531
High dose	95	50.7	46.2 (21.73)	45.0	7, 104	-4.5 (19.06)	-5.0	-50, 58	0.0234*
WEEK 4	201	49.8	45.3 (22.94)	41.0	5, 107	-4.5 (18.42)	-6.0	-53, 63	<=0.001***
Low dose	109	48.9	47.2 (24.53)	40.0	5, 107	-1.7 (19.35)	-4.0	-43, 63	0.3699
High dose	92	50.9	42.9 (20.80)	41.0	6, 106	-7.9 (16.73)	-8.0	-53, 34	<=0.001***

&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 2.1

Change from Baseline to Each Planned Visit in Parkinson's Disease Symptoms as Assessed
by The Movement Disorder Society-Unified Parkinson's Disease Rating Scale Score by Part and Total
(FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
MDS-UPDRS Total Score of Parts I-III									
WEEK 6	193	50.2	46.5 (22.63)	43.0	3, 118	-3.7 (19.60)	-6.0	-59, 75	0.0099**
Low dose	105	49.5	48.4 (25.11)	43.0	5, 118	-1.0 (21.92)	-5.0	-39, 75	0.6282
High dose	88	51.1	44.2 (19.14)	43.0	3, 93	-6.8 (15.98)	-6.0	-59, 44	<=0.001***
WEEK 13	160	50.0	44.7 (22.70)	39.0	10, 141	-5.3 (20.07)	-6.0	-58, 66	<=0.001***
Low dose	90	48.7	45.6 (24.05)	41.0	11, 141	-3.1 (21.32)	-5.0	-51, 66	0.1653
High dose	70	51.6	43.5 (20.96)	39.0	10, 103	-8.1 (18.09)	-8.0	-58, 34	<=0.001***
WEEK 26	132	50.5	47.6 (21.88)	45.0	7, 122	-3.0 (17.51)	-2.0	-55, 39	0.0525
Low dose	71	48.8	46.7 (24.12)	43.0	7, 122	-2.0 (17.03)	-2.0	-40, 39	0.3157
High dose	61	52.6	48.5 (19.09)	48.0	11, 95	-4.1 (18.14)	-2.0	-55, 24	0.0842
WEEK 39	116	49.9	48.5 (24.04)	45.5	11, 132	-1.4 (20.55)	-2.5	-58, 60	0.4680
Low dose	68	48.3	46.5 (24.84)	43.5	15, 132	-1.8 (19.39)	-3.0	-42, 60	0.4372
High dose	48	52.1	51.4 (22.80)	49.0	11, 98	-0.8 (22.29)	2.0	-58, 55	0.8157
WEEK 52	108	49.9	48.0 (23.94)	47.0	6, 117	-1.9 (19.74)	-2.5	-50, 47	0.3222
Low dose	60	47.8	46.9 (24.03)	44.0	8, 117	-0.9 (19.84)	-1.5	-50, 47	0.7314
High dose	48	52.5	49.4 (24.02)	47.0	6, 105	-3.1 (19.75)	-3.0	-49, 47	0.2754

&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 2.1

Change from Baseline to Each Planned Visit in Parkinson's Disease Symptoms as Assessed
by The Movement Disorder Society-Unified Parkinson's Disease Rating Scale Score by Part and Total
(FAS)

Parameter Time Point Dose Category	N	Baseline Mean	Visit Mean (SD)	Visit Median	Visit Min, Max	Change from Baseline Mean (SD)	Change from Baseline Median	Change from Baseline Min, Max	Change from Baseline P-Value &
MDS-UPDRS Part I Score									
BASELINE	244		11.1 (6.39)	10.0	0, 37				
Low dose	132		11.0 (6.66)	10.0	0, 31				
High dose	112		11.3 (6.09)	10.0	1, 37				
DAY 2	222	11.2	9.0 (5.86)	8.0	0, 32	-2.3 (4.00)	-1.0	-16, 6	<=0.001***
Low dose	121	11.1	8.5 (5.91)	7.0	0, 32	-2.6 (4.27)	-2.0	-16, 6	<=0.001***
High dose	101	11.4	9.6 (5.76)	9.0	0, 27	-1.9 (3.62)	-1.0	-14, 6	<=0.001***
WEEK 1	225	11.3	8.3 (5.73)	7.0	0, 32	-3.0 (5.62)	-3.0	-29, 18	<=0.001***
Low dose	120	11.2	8.5 (6.05)	7.0	0, 30	-2.6 (5.74)	-2.0	-18, 18	<=0.001***
High dose	105	11.5	8.0 (5.34)	7.0	0, 32	-3.4 (5.48)	-3.0	-29, 11	<=0.001***
WEEK 2	212	11.1	8.8 (5.71)	8.0	0, 27	-2.3 (5.20)	-2.0	-18, 11	<=0.001***
Low dose	118	10.9	8.6 (5.85)	8.0	0, 27	-2.3 (5.42)	-2.0	-18, 11	<=0.001***
High dose	94	11.2	9.0 (5.54)	8.0	0, 26	-2.2 (4.95)	-2.0	-15, 8	<=0.001***
WEEK 3	203	11.1	8.5 (5.58)	7.0	0, 31	-2.6 (5.77)	-2.0	-22, 10	<=0.001***
Low dose	108	11.2	8.9 (6.18)	7.5	0, 31	-2.3 (5.63)	-2.0	-16, 10	<=0.001***
High dose	95	11.1	8.1 (4.82)	7.0	0, 23	-2.9 (5.94)	-2.0	-22, 9	<=0.001***
WEEK 4	203	11.1	8.8 (5.81)	8.0	0, 36	-2.3 (5.88)	-2.0	-21, 27	<=0.001***
Low dose	110	11.0	9.3 (6.71)	8.0	0, 36	-1.7 (6.24)	-2.0	-16, 27	0.0058**
High dose	93	11.2	8.1 (4.47)	8.0	0, 22	-3.1 (5.37)	-2.0	-21, 9	<=0.001***

&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 2.1

Change from Baseline to Each Planned Visit in Parkinson's Disease Symptoms as Assessed by The Movement Disorder Society-Unified Parkinson's Disease Rating Scale Score by Part and Total (FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
MDS-UPDRS Part I Score									
WEEK 6	193	11.1	9.8 (6.42)	9.0	0, 39	-1.4 (6.21)	-2.0	-17, 30	0.0026**
Low dose	105	11.3	10.3 (7.20)	9.0	1, 39	-1.0 (7.07)	-2.0	-17, 30	0.1580
High dose	88	10.9	9.1 (5.30)	9.0	0, 23	-1.8 (5.00)	-2.0	-16, 15	<=0.001***
WEEK 13	168	11.4	9.6 (5.81)	8.0	0, 30	-1.7 (5.72)	-2.0	-18, 16	<=0.001***
Low dose	92	11.3	9.5 (5.74)	8.0	0, 30	-1.8 (5.83)	-2.0	-18, 14	0.0045**
High dose	76	11.5	9.8 (5.92)	8.0	1, 28	-1.7 (5.62)	-2.0	-15, 16	0.0103*
WEEK 26	141	11.8	10.8 (6.27)	10.0	1, 29	-1.0 (5.44)	-1.0	-21, 15	0.0331*
Low dose	75	11.3	10.1 (6.09)	9.0	1, 25	-1.1 (4.92)	-1.0	-12, 15	0.0473*
High dose	66	12.3	11.5 (6.43)	11.0	1, 29	-0.8 (6.01)	0.0	-21, 9	0.2814
WEEK 39	121	11.3	10.9 (6.42)	10.0	0, 26	-0.5 (5.82)	-1.0	-14, 14	0.3754
Low dose	68	11.0	10.2 (6.48)	9.0	0, 26	-0.8 (5.64)	-1.0	-14, 14	0.2676
High dose	53	11.8	11.7 (6.30)	11.0	2, 25	-0.1 (6.08)	-1.0	-12, 13	0.9105
WEEK 52	108	11.4	10.8 (5.96)	10.5	2, 27	-0.6 (5.91)	-1.0	-17, 14	0.2775
Low dose	60	10.9	10.6 (5.51)	10.5	2, 27	-0.2 (5.40)	-0.5	-13, 11	0.7392
High dose	48	12.1	11.0 (6.54)	10.5	2, 25	-1.1 (6.51)	-1.0	-17, 14	0.2457

&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 2.1

Change from Baseline to Each Planned Visit in Parkinson's Disease Symptoms as Assessed by The Movement Disorder Society-Unified Parkinson's Disease Rating Scale Score by Part and Total (FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
MDS-UPDRS Part II Score									
BASELINE	244		15.8 (7.38)	15.0	1, 37				
Low dose	132		15.2 (7.48)	14.5	1, 36				
High dose	112		16.4 (7.23)	16.0	2, 37				
DAY 2	222	15.9	13.9 (7.62)	13.0	0, 35	-2.1 (4.47)	-1.0	-19, 12	<=0.001***
Low dose	121	15.1	12.4 (7.12)	11.0	0, 31	-2.7 (4.54)	-1.0	-15, 6	<=0.001***
High dose	101	16.9	15.6 (7.86)	15.0	0, 35	-1.3 (4.26)	-1.0	-19, 12	0.0038**
WEEK 1	225	15.8	12.0 (7.32)	11.0	0, 34	-3.8 (5.39)	-4.0	-18, 14	<=0.001***
Low dose	120	15.0	11.4 (7.16)	10.0	0, 30	-3.7 (4.94)	-3.0	-17, 8	<=0.001***
High dose	105	16.7	12.8 (7.46)	12.0	1, 34	-3.9 (5.88)	-4.0	-18, 14	<=0.001***
WEEK 2	212	15.8	12.5 (7.69)	11.0	0, 37	-3.3 (6.26)	-4.0	-19, 18	<=0.001***
Low dose	118	15.4	12.1 (7.67)	11.0	0, 33	-3.3 (6.03)	-3.5	-19, 16	<=0.001***
High dose	94	16.4	13.1 (7.73)	12.0	0, 37	-3.4 (6.56)	-4.0	-18, 18	<=0.001***
WEEK 3	203	15.9	12.2 (7.47)	12.0	0, 37	-3.7 (6.21)	-3.0	-23, 12	<=0.001***
Low dose	108	15.2	11.7 (7.74)	11.0	0, 37	-3.5 (5.81)	-3.0	-19, 12	<=0.001***
High dose	95	16.6	12.8 (7.15)	12.0	0, 34	-3.8 (6.66)	-2.0	-23, 12	<=0.001***
WEEK 4	203	15.8	12.2 (6.92)	11.0	0, 31	-3.7 (5.98)	-4.0	-29, 12	<=0.001***
Low dose	110	15.2	12.5 (7.40)	11.5	0, 31	-2.7 (5.47)	-3.0	-14, 12	<=0.001***
High dose	93	16.6	11.8 (6.33)	11.0	1, 28	-4.9 (6.36)	-4.0	-29, 7	<=0.001***

&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 2.1

Change from Baseline to Each Planned Visit in Parkinson's Disease Symptoms as Assessed
by The Movement Disorder Society-Unified Parkinson's Disease Rating Scale Score by Part and Total
(FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
MDS-UPDRS Part II Score									
WEEK 6	193	15.8	12.5 (7.42)	12.0	0, 32	-3.3 (6.41)	-3.0	-22, 17	<=0.001***
Low dose	105	15.1	12.6 (8.00)	12.0	0, 32	-2.5 (6.56)	-3.0	-16, 17	<=0.001***
High dose	88	16.5	12.3 (6.72)	12.0	0, 31	-4.2 (6.12)	-3.0	-22, 10	<=0.001***
WEEK 13	168	15.7	12.1 (7.07)	11.0	0, 35	-3.6 (6.52)	-3.0	-24, 15	<=0.001***
Low dose	92	15.0	11.9 (7.42)	11.0	0, 35	-3.1 (6.44)	-3.0	-19, 15	<=0.001***
High dose	76	16.6	12.3 (6.67)	11.0	2, 31	-4.3 (6.60)	-3.0	-24, 7	<=0.001***
WEEK 26	141	15.9	12.8 (7.54)	12.0	0, 38	-3.1 (6.69)	-3.0	-21, 21	<=0.001***
Low dose	75	14.6	12.3 (7.85)	10.0	0, 38	-2.3 (6.17)	-3.0	-15, 21	0.0016**
High dose	66	17.2	13.3 (7.21)	14.0	0, 33	-4.0 (7.19)	-3.0	-21, 10	<=0.001***
WEEK 39	121	15.1	12.1 (7.44)	11.0	0, 36	-3.1 (6.73)	-2.0	-21, 19	<=0.001***
Low dose	68	14.2	11.8 (8.00)	11.0	1, 36	-2.4 (6.36)	-3.0	-16, 19	0.0025**
High dose	53	16.3	12.5 (6.70)	12.0	0, 27	-3.9 (7.16)	-2.0	-21, 8	<=0.001***
WEEK 52	108	15.0	12.2 (7.50)	11.0	1, 35	-2.8 (7.35)	-3.0	-19, 18	<=0.001***
Low dose	60	13.6	12.2 (7.90)	10.5	1, 35	-1.5 (7.12)	-1.0	-14, 18	0.1120
High dose	48	16.6	12.2 (7.05)	12.0	1, 29	-4.4 (7.36)	-4.0	-19, 13	<=0.001***

&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 2.1

Change from Baseline to Each Planned Visit in Parkinson's Disease Symptoms as Assessed
by The Movement Disorder Society-Unified Parkinson's Disease Rating Scale Score by Part and Total
(FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
MDS-UPDRS Part III Score									
BASELINE	244		23.5 (11.47)	23.0	2, 63				
Low dose	132		23.7 (11.85)	22.0	2, 63				
High dose	112		23.2 (11.05)	23.0	3, 55				
DAY 2	222	23.8	23.1 (12.96)	21.0	1, 66	-0.7 (8.78)	-1.0	-24, 30	0.2315
Low dose	121	23.7	23.0 (12.25)	21.0	1, 66	-0.6 (8.43)	-1.0	-24, 30	0.4080
High dose	101	23.9	23.1 (13.83)	21.0	1, 59	-0.8 (9.23)	-1.0	-20, 28	0.3904
WEEK 1	224	23.3	26.1 (14.93)	25.0	0, 76	2.8 (11.31)	1.0	-36, 67	<=0.001***
Low dose	119	23.4	25.4 (14.19)	24.0	0, 76	1.9 (11.53)	1.0	-36, 67	0.0719
High dose	105	23.2	27.0 (15.76)	26.0	1, 70	3.7 (11.04)	2.0	-17, 37	<=0.001***
WEEK 2	211	23.3	26.2 (14.91)	23.0	0, 77	2.9 (12.18)	2.0	-29, 68	<=0.001***
Low dose	118	23.7	27.9 (15.17)	24.0	0, 77	4.2 (12.98)	2.5	-29, 68	<=0.001***
High dose	93	22.8	24.1 (14.38)	23.0	1, 68	1.3 (10.94)	0.0	-24, 35	0.2401
WEEK 3	203	22.9	26.0 (14.64)	24.0	0, 84	3.1 (12.02)	2.0	-24, 75	<=0.001***
Low dose	108	22.9	26.7 (14.66)	24.0	0, 84	3.8 (11.94)	2.0	-20, 75	0.0013**
High dose	95	23.0	25.3 (14.67)	24.0	3, 66	2.3 (12.13)	1.0	-24, 40	0.0707
WEEK 4	200	23.0	24.4 (15.00)	22.0	0, 80	1.5 (12.05)	0.0	-36, 53	0.0891
Low dose	108	22.7	25.5 (15.35)	22.5	0, 80	2.8 (12.80)	1.0	-23, 53	0.0251*
High dose	92	23.2	23.1 (14.55)	21.0	1, 75	-0.1 (10.97)	0.0	-36, 48	0.9170

&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 2.1

Change from Baseline to Each Planned Visit in Parkinson's Disease Symptoms as Assessed by The Movement Disorder Society-Unified Parkinson's Disease Rating Scale Score by Part and Total (FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
MDS-UPDRS Part III Score									
WEEK 6	193	23.3	24.3 (14.12)	23.0	0, 74	0.9 (12.07)	0.0	-36, 60	0.2764
Low dose	105	23.0	25.5 (15.53)	23.0	0, 74	2.4 (13.69)	0.0	-36, 60	0.0719
High dose	88	23.6	22.8 (12.16)	22.5	0, 55	-0.8 (9.57)	0.0	-31, 28	0.4242
WEEK 13	157	23.0	23.0 (14.56)	22.0	0, 82	0.1 (13.07)	0.0	-47, 37	0.9612
Low dose	88	22.6	24.1 (14.69)	23.5	0, 82	1.5 (13.84)	2.0	-38, 37	0.3240
High dose	69	23.4	21.7 (14.39)	20.0	0, 60	-1.8 (11.86)	-1.0	-47, 33	0.2241
WEEK 26	132	23.0	23.9 (14.86)	22.5	0, 83	0.9 (12.36)	0.0	-34, 39	0.4268
Low dose	71	23.3	24.6 (16.54)	22.0	0, 83	1.4 (12.93)	-1.0	-34, 39	0.3762
High dose	61	22.7	23.0 (12.70)	23.0	0, 59	0.3 (11.76)	0.0	-30, 27	0.8601
WEEK 39	116	23.4	25.3 (15.48)	23.0	1, 76	1.9 (13.28)	0.0	-28, 47	0.1330
Low dose	68	23.1	24.5 (16.10)	22.0	4, 76	1.4 (12.96)	0.0	-28, 47	0.3924
High dose	48	23.8	26.4 (14.64)	25.0	1, 63	2.6 (13.83)	1.5	-28, 40	0.2003
WEEK 52	108	23.5	25.0 (15.78)	22.0	1, 66	1.5 (12.78)	1.0	-35, 42	0.2195
Low dose	60	23.3	24.1 (16.16)	21.0	1, 66	0.8 (12.17)	0.5	-35, 32	0.5978
High dose	48	23.9	26.2 (15.37)	26.0	2, 62	2.4 (13.58)	2.5	-26, 42	0.2316

&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 2.1

Change from Baseline to Each Planned Visit in Parkinson's Disease Symptoms as Assessed
by The Movement Disorder Society-Unified Parkinson's Disease Rating Scale Score by Part and Total
(FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
MDS-UPDRS Part IV Score									
BASELINE	244		9.5 (3.17)	9.0	0, 20				
Low dose	132		9.6 (3.21)	9.0	0, 20				
High dose	112		9.5 (3.13)	9.0	1, 18				
DAY 2	218	9.6	8.2 (4.01)	8.0	0, 20	-1.5 (3.52)	-1.0	-12, 9	<=0.001***
Low dose	118	9.7	8.0 (4.07)	8.0	0, 20	-1.7 (3.56)	-1.0	-12, 9	<=0.001***
High dose	100	9.5	8.4 (3.94)	8.0	0, 19	-1.1 (3.46)	0.0	-11, 8	0.0018**
WEEK 1	221	9.6	7.9 (4.13)	8.0	0, 19	-1.7 (3.97)	-2.0	-17, 10	<=0.001***
Low dose	117	9.6	7.9 (4.12)	8.0	0, 18	-1.7 (3.86)	-2.0	-17, 9	<=0.001***
High dose	104	9.6	7.9 (4.17)	8.0	0, 19	-1.7 (4.11)	-2.0	-14, 10	<=0.001***
WEEK 2	208	9.7	7.3 (3.92)	7.0	0, 17	-2.4 (3.57)	-2.0	-13, 6	<=0.001***
Low dose	116	9.7	7.3 (4.01)	7.0	0, 17	-2.5 (3.57)	-2.0	-11, 6	<=0.001***
High dose	92	9.6	7.3 (3.83)	7.0	0, 16	-2.3 (3.58)	-2.0	-13, 6	<=0.001***
WEEK 3	198	9.5	7.3 (4.03)	7.0	0, 19	-2.2 (3.90)	-2.0	-15, 8	<=0.001***
Low dose	103	9.6	7.4 (4.35)	7.0	0, 19	-2.2 (4.09)	-3.0	-11, 8	<=0.001***
High dose	95	9.5	7.2 (3.67)	7.0	0, 16	-2.3 (3.72)	-2.0	-15, 5	<=0.001***
WEEK 4	200	9.5	6.7 (4.17)	7.0	0, 21	-2.8 (3.73)	-3.0	-15, 7	<=0.001***
Low dose	107	9.6	6.6 (4.50)	7.0	0, 21	-3.0 (3.69)	-3.0	-14, 5	<=0.001***
High dose	93	9.5	6.8 (3.78)	7.0	0, 16	-2.7 (3.78)	-3.0	-15, 7	<=0.001***

&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 2.1

Change from Baseline to Each Planned Visit in Parkinson's Disease Symptoms as Assessed
by The Movement Disorder Society-Unified Parkinson's Disease Rating Scale Score by Part and Total
(FAS)

Parameter Time Point Dose Category	N	Baseline Mean	Visit Mean (SD)	Visit Median	Visit Min, Max	Change from Baseline Mean (SD)	Change from Baseline Median	Change from Baseline Min, Max	P-Value &
MDS-UPDRS Part IV Score									
WEEK 6	190	9.5	6.8 (4.05)	7.0	0, 17	-2.7 (3.61)	-3.0	-15, 5	<=0.001***
Low dose	102	9.5	7.0 (4.13)	7.0	0, 17	-2.5 (3.37)	-3.0	-9, 5	<=0.001***
High dose	88	9.4	6.6 (3.97)	6.0	0, 17	-2.9 (3.88)	-3.0	-15, 5	<=0.001***
WEEK 13	165	9.5	6.0 (3.85)	6.0	0, 15	-3.5 (3.75)	-3.0	-15, 10	<=0.001***
Low dose	89	9.3	5.6 (3.88)	6.0	0, 15	-3.7 (3.48)	-4.0	-12, 10	<=0.001***
High dose	76	9.7	6.5 (3.78)	6.0	0, 14	-3.2 (4.06)	-3.0	-15, 6	<=0.001***
WEEK 26	140	9.5	6.0 (3.92)	6.0	0, 16	-3.5 (3.81)	-3.0	-15, 6	<=0.001***
Low dose	74	9.4	5.9 (3.90)	6.0	0, 16	-3.5 (3.46)	-3.0	-14, 5	<=0.001***
High dose	66	9.7	6.2 (3.96)	6.0	0, 14	-3.5 (4.20)	-3.0	-15, 6	<=0.001***
WEEK 39	120	9.3	6.0 (4.04)	6.0	0, 17	-3.3 (4.12)	-3.0	-15, 6	<=0.001***
Low dose	68	9.4	6.0 (4.01)	6.0	0, 17	-3.4 (4.09)	-3.0	-14, 6	<=0.001***
High dose	52	9.2	5.9 (4.12)	6.0	0, 17	-3.3 (4.20)	-2.5	-15, 5	<=0.001***
WEEK 52	108	9.2	5.3 (4.06)	5.0	0, 21	-3.9 (4.47)	-4.0	-17, 13	<=0.001***
Low dose	60	9.4	5.3 (3.63)	5.5	0, 16	-4.1 (3.94)	-4.0	-17, 6	<=0.001***
High dose	48	9.0	5.4 (4.59)	5.0	0, 21	-3.6 (5.08)	-3.0	-15, 13	<=0.001***

&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

表2.7.3.6-7　MDS-UPDRSスコア（FAS）：M15-737試験

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ABBV-951
STUDY M15-737 - SECOND INTERIM (CUTOFF [redacted]20[redacted])
R&D/20/1639 - CLINICAL/STATISTICAL

TABLE 14.2__2.1

Change from Baseline to Each Planned Visit in Parkinson's Disease Symptoms as Assessed
by The Movement Disorder Society-Unified Parkinson's Disease Rating Scale Score by Part and Total
(FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
MDS-UPDRS Part I Score									
BASELINE	81		11.1 (6.25)	11.0	2, 27				
Low dose	33		11.2 (6.28)	11.0	2, 27				
High dose	48		11.1 (6.31)	11.0	2, 25				
WEEK 24	73	10.5	10.8 (6.17)	10.0	0, 26	0.4 (4.33)	1.0	-11, 12	0.4680
Low dose	28	10.5	10.7 (6.52)	11.5	0, 26	0.2 (4.36)	0.5	-8, 8	0.8299
High dose	45	10.5	11.0 (6.01)	10.0	1, 23	0.5 (4.36)	1.0	-11, 12	0.4562
WEEK 48	29	10.3	10.8 (5.08)	10.0	4, 23	0.5 (3.85)	1.0	-9, 8	0.5052
Low dose	11	9.5	9.9 (5.80)	8.0	4, 23	0.4 (3.41)	1.0	-6, 8	0.7312
High dose	18	10.7	11.3 (4.68)	10.5	4, 20	0.6 (4.19)	1.0	-9, 8	0.5811
WEEK 72	3	6.7	9.7 (9.07)	6.0	3, 20	3.0 (5.20)	0.0	0, 9	0.4226
Low dose	1	6.0	6.0 (N/A)	6.0	6, 6	0.0 (N/A)	0.0	0, 0	
High dose	2	7.0	11.5 (12.02)	11.5	3, 20	4.5 (6.36)	4.5	0, 9	0.5000
MDS-UPDRS Part II Score									
BASELINE	81		11.9 (7.18)	12.0	1, 29				
Low dose	33		11.4 (8.02)	10.0	1, 26				
High dose	48		12.3 (6.60)	12.0	1, 29				
WEEK 24	73	11.9	12.8 (8.17)	12.0	0, 38	0.9 (4.41)	0.0	-9, 15	0.0889
Low dose	28	11.1	11.6 (8.44)	10.0	0, 32	0.5 (4.95)	0.5	-9, 11	0.5972
High dose	45	12.3	13.4 (8.02)	13.0	2, 38	1.1 (4.08)	0.0	-7, 15	0.0692

&: P-value is obtained from two-sided paired-sample t-test.
N/A = Not Applicable.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 2.1

Change from Baseline to Each Planned Visit in Parkinson's Disease Symptoms as Assessed by The Movement Disorder Society-Unified Parkinson's Disease Rating Scale Score by Part and Total (FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
MDS-UPDRS Part II Score									
WEEK 48	29	9.4	11.1 (6.39)	11.0	1, 25	1.8 (4.43)	1.0	-4, 14	0.0414*
Low dose	11	5.5	7.0 (4.10)	6.0	1, 15	1.5 (3.93)	2.0	-4, 9	0.2218
High dose	18	11.8	13.7 (6.29)	13.5	3, 25	1.9 (4.81)	1.0	-4, 14	0.1142
WEEK 72	3	8.3	9.7 (9.81)	4.0	4, 21	1.3 (1.53)	1.0	0, 3	0.2697
Low dose	1	4.0	4.0 (N/A)	4.0	4, 4	0.0 (N/A)	0.0	0, 0	
High dose	2	10.5	12.5 (12.02)	12.5	4, 21	2.0 (1.41)	2.0	1, 3	0.2952
MDS-UPDRS Part III Score									
BASELINE	81		23.2 (13.89)	21.0	1, 62				
Low dose	33		20.5 (13.51)	19.0	1, 58				
High dose	48		25.1 (13.99)	23.0	2, 62				
WEEK 24	69	23.5	25.0 (16.31)	24.0	0, 92	1.5 (9.73)	1.0	-21, 40	0.2048
Low dose	27	19.0	23.3 (14.65)	23.0	0, 58	4.2 (7.35)	3.0	-6, 22	0.0061**
High dose	42	26.3	26.1 (17.37)	24.5	0, 92	-0.3 (10.71)	-0.5	-21, 40	0.8798
WEEK 48	24	21.1	21.2 (13.92)	22.0	0, 45	0.1 (8.48)	0.0	-16, 16	0.9620
Low dose	9	16.0	20.2 (14.32)	17.0	0, 40	4.2 (8.61)	3.0	-9, 16	0.1796
High dose	15	24.2	21.8 (14.14)	23.0	2, 45	-2.4 (7.63)	-1.0	-16, 13	0.2434
WEEK 72	3	7.7	10.0 (13.05)	4.1	1, 25	2.4 (4.51)	2.1	-2, 7	0.4576
Low dose	1	3.0	1.0 (N/A)	1.0	1, 1	-2.0 (N/A)	-2.0	-2, -2	
High dose	2	10.0	14.6 (14.76)	14.6	4, 25	4.6 (3.45)	4.6	2, 7	0.3124

&: P-value is obtained from two-sided paired-sample t-test.
N/A = Not Applicable.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 2.1

Change from Baseline to Each Planned Visit in Parkinson's Disease Symptoms as Assessed by The Movement Disorder Society-Unified Parkinson's Disease Rating Scale Score by Part and Total (FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
MDS-UPDRS Part IV Score									
BASELINE	81		5.1 (3.91)	5.0	0, 17				
Low dose	33		5.3 (4.03)	5.0	0, 16				
High dose	48		5.0 (3.86)	4.5	0, 17				
WEEK 24	73	4.6	5.4 (3.95)	6.0	0, 18	0.8 (3.26)	0.0	-10, 14	0.0410*
Low dose	28	4.4	4.7 (3.45)	5.0	0, 13	0.3 (1.60)	0.0	-3, 4	0.4160
High dose	45	4.8	5.9 (4.20)	6.0	0, 18	1.1 (3.94)	0.0	-10, 14	0.0601
WEEK 48	29	4.6	5.2 (3.96)	5.0	0, 13	0.6 (3.66)	0.0	-11, 8	0.3957
Low dose	11	4.1	4.8 (4.35)	5.0	0, 12	0.7 (3.32)	0.0	-3, 8	0.4841
High dose	18	4.9	5.4 (3.82)	5.5	0, 13	0.5 (3.94)	1.0	-11, 6	0.5977
WEEK 72	3	2.7	4.0 (1.00)	4.0	3, 5	1.3 (0.58)	1.0	1, 2	0.0572
Low dose	1	2.0	3.0 (N/A)	3.0	3, 3	1.0 (N/A)	1.0	1, 1	
High dose	2	3.0	4.5 (0.71)	4.5	4, 5	1.5 (0.71)	1.5	1, 2	0.2048
MDS-UPDRS Total Score of Parts I-III									
BASELINE	81		46.2 (22.33)	45.0	6, 105				
Low dose	33		43.1 (22.55)	38.0	8, 94				
High dose	48		48.4 (22.15)	47.0	6, 105				
WEEK 24	69	45.7	48.4 (26.98)	46.0	1, 148	2.7 (13.68)	2.0	-24, 64	0.1098
Low dose	27	40.1	45.2 (25.09)	39.0	1, 105	5.0 (11.23)	6.0	-12, 39	0.0283*
High dose	42	49.3	50.5 (28.23)	46.5	7, 148	1.2 (14.98)	0.5	-24, 64	0.6197

&: P-value is obtained from two-sided paired-sample t-test.
N/A = Not Applicable.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 2.1

Change from Baseline to Each Planned Visit in Parkinson's Disease Symptoms as Assessed
by The Movement Disorder Society-Unified Parkinson's Disease Rating Scale Score by Part and Total
(FAS)

Parameter Time Point Dose Category	N	Baseline Mean	Visit Mean (SD)	Visit Median	Visit Min, Max	Change from Baseline Mean (SD)	Change from Baseline Median	Change from Baseline Min, Max	P-Value &
MDS-UPDRS Total Score of Parts I-III									
WEEK 48	24	41.1	43.0 (20.51)	42.5	11, 77	1.9 (11.40)	3.0	-23, 21	0.4187
Low dose	9	31.4	37.3 (20.61)	40.0	11, 72	5.9 (11.20)	4.0	-12, 20	0.1532
High dose	15	46.9	46.5 (20.37)	49.0	13, 77	-0.5 (11.21)	1.0	-23, 21	0.8742
WEEK 72	3	22.7	29.4 (31.70)	11.2	11, 66	6.7 (9.59)	5.2	-2, 17	0.3483
Low dose	1	13.0	11.0 (N/A)	11.0	11, 11	-2.0 (N/A)	-2.0	-2, -2	
High dose	2	27.5	38.6 (38.76)	38.6	11, 66	11.1 (8.35)	11.1	5, 17	0.3114

&: P-value is obtained from two-sided paired-sample t-test.
N/A = Not Applicable.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

表2.7.3.6-8　MDS-UPDRSスコア（FAS）：M15-736試験

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ABBV-951
STUDY M15-736
R&D/20/1640 - CLINICAL/STATISTICAL

TABLE 14.2__3

Repeated-Measure Analysis of Change from Baseline to Post-Baseline Visits in MDS-UPDRS Scores
(Full Analysis Set)

Status / Visit / Treatment	N	Summary Statistics: Mean (SD)	Min	Max	Model-Based Statistics@: LS Mean (SE)	Within Group P-Value	Treatment Difference between Groups: LS Mean of Difference (SE)	95% CI	Two-Sided P-Value
Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Total Score of Part I-III									
Baseline									
Oral CD/LD	67	50.88 (19.84)	16.0	106.0					
ABBV-951	74	55.84 (22.24)	18.0	118.0					
Change to Day 2									
Oral CD/LD	65	-3.96 (11.21)	-29.0	29.0	-4.94 (1.82)	0.0076**			
ABBV-951	73	-5.75 (14.27)	-42.0	34.0	-5.76 (1.71)	0.0010**	-0.82 (2.13)	(-5.04, 3.40)	0.7026
Change to Day 8									
Oral CD/LD	60	-6.46 (12.46)	-38.0	25.0	-6.81 (2.14)	0.0019**			
ABBV-951	64	-5.22 (18.66)	-65.0	52.0	-4.93 (2.05)	0.0175*	1.88 (2.65)	(-3.37, 7.13)	0.4797
Change to Day 15									
Oral CD/LD	59	-7.78 (16.94)	-49.0	28.0	-8.31 (2.45)	<=0.001***			
ABBV-951	58	-3.44 (19.24)	-39.0	56.0	-4.09 (2.38)	0.0877	4.22 (3.14)	(-2.00, 10.44)	0.1815

Note: @ The repeated measures model: change = treatment country visit baseline treatment*visit treatment*baseline.
The unstructured variance-covariance structure is used.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 3

Repeated-Measure Analysis of Change from Baseline to Post-Baseline Visits in MDS-UPDRS Scores
(Full Analysis Set)

Status / Visit / Treatment	N	Summary Statistics: Mean (SD)	Min	Max	Model-Based Statistics@: LS Mean (SE)	Within Group P-Value	Treatment Difference between Groups: LS Mean of Difference (SE)	95% CI	Two-Sided P-Value
Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Total Score of Part I-III									
Change to Day 22									
Oral CD/LD	17	-11.17 (12.57)	-39.0	6.0	-9.54 (2.99)	0.0018**			
ABBV-951	23	0.33 (22.96)	-70.5	50.0	-2.17 (2.75)	0.4311	7.36 (3.85)	(-0.24, 14.97)	0.0575
Change to Day 29									
Oral CD/LD	59	-6.12 (15.56)	-47.0	48.0	-7.67 (2.24)	<=0.001***			
ABBV-951	53	-5.12 (16.91)	-52.0	38.0	-3.93 (2.22)	0.0790	3.74 (2.87)	(-1.93, 9.41)	0.1943
Change to Day 57									
Oral CD/LD	60	-5.99 (15.48)	-47.0	25.6	-7.35 (2.32)	0.0019**			
ABBV-951	45	-9.59 (18.32)	-62.0	34.0	-5.65 (2.35)	0.0174*	1.70 (3.03)	(-4.29, 7.69)	0.5757
Change to Day 85									
Oral CD/LD	62	-5.40 (16.38)	-57.0	30.0	-6.52 (2.36)	0.0066**			
ABBV-951	46	-11.08 (19.02)	-75.0	23.3	-8.12 (2.48)	0.0014**	-1.60 (3.16)	(-7.86, 4.65)	0.6132

Note: @ The repeated measures model: change = treatment country visit baseline treatment*visit treatment*baseline.
The unstructured variance-covariance structure is used.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 3

Repeated-Measure Analysis of Change from Baseline to Post-Baseline Visits in MDS-UPDRS Scores
(Full Analysis Set)

Status / Visit / Treatment	N	Summary Statistics: Mean (SD)	Min	Max	Model-Based Statistics@: LS Mean (SE)	Within Group P-Value	Treatment Difference between Groups: LS Mean of Difference (SE)	95% CI	Two-Sided P-Value
Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part I Score									
Baseline									
Oral CD/LD	67	9.37 (5.18)	1.0	24.0					
ABBV-951	74	11.35 (6.37)	0.0	31.0					
Change to Day 2									
Oral CD/LD	65	-1.09 (4.40)	-18.0	9.0	-1.68 (0.59)	0.0050**			
ABBV-951	73	-1.63 (5.25)	-24.0	12.0	-1.09 (0.55)	0.0498*	0.59 (0.69)	(-0.77, 1.95)	0.3918
Change to Day 8									
Oral CD/LD	60	-1.13 (5.84)	-18.0	14.0	-1.31 (0.68)	0.0580			
ABBV-951	65	-2.55 (5.61)	-24.0	8.0	-2.02 (0.65)	0.0023**	-0.72 (0.84)	(-2.38, 0.95)	0.3965
Change to Day 15									
Oral CD/LD	59	-1.58 (5.47)	-17.0	9.0	-1.87 (0.72)	0.0108*			
ABBV-951	58	-0.98 (5.35)	-11.0	19.0	-0.84 (0.70)	0.2357	1.03 (0.92)	(-0.78, 2.84)	0.2623

Note: @ The repeated measures model: change = treatment country visit baseline treatment*visit treatment*baseline.
The unstructured variance-covariance structure is used.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 3

Repeated-Measure Analysis of Change from Baseline to Post-Baseline Visits in MDS-UPDRS Scores
(Full Analysis Set)

Status / Visit / Treatment	N	Summary Statistics: Mean (SD)	Min	Max	Model-Based Statistics@: LS Mean (SE)	Within Group P-Value	Treatment Difference between Groups: LS Mean of Difference (SE)	95% CI	Two-Sided P-Value
Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part I Score									
Change to Day 22									
Oral CD/LD	17	-4.24 (4.56)	-17.0	2.0	-2.23 (0.85)	0.0096**			
ABBV-951	23	-1.30 (7.70)	-26.0	10.0	-0.06 (0.79)	0.9392	2.17 (1.08)	(0.03, 4.30)	0.0473*
Change to Day 29									
Oral CD/LD	61	-1.23 (5.55)	-19.0	11.0	-1.60 (0.70)	0.0248*			
ABBV-951	53	-1.18 (5.53)	-25.0	7.0	-0.32 (0.70)	0.6437	1.27 (0.90)	(-0.51, 3.05)	0.1593
Change to Day 57									
Oral CD/LD	62	-0.98 (5.79)	-15.0	18.0	-1.58 (0.75)	0.0363*			
ABBV-951	47	-2.19 (5.94)	-25.0	12.0	-0.83 (0.77)	0.2806	0.75 (0.99)	(-1.20, 2.70)	0.4472
Change to Day 85									
Oral CD/LD	62	-0.82 (5.91)	-16.0	14.0	-1.22 (0.75)	0.1029			
ABBV-951	46	-2.63 (6.93)	-26.0	12.0	-1.22 (0.77)	0.1156	0.00 (0.99)	(-1.95, 1.95)	>0.999

Note: @ The repeated measures model: change = treatment country visit baseline treatment*visit treatment*baseline.
The unstructured variance-covariance structure is used.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 3

Repeated-Measure Analysis of Change from Baseline to Post-Baseline Visits in MDS-UPDRS Scores
(Full Analysis Set)

Status / Visit / Treatment	N	Summary Statistics: Mean (SD)	Min	Max	Model-Based Statistics@: LS Mean (SE)	Within Group P-Value	Treatment Difference between Groups: LS Mean of Difference (SE)	95% CI	Two-Sided P-Value
Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part II Score									
Baseline									
Oral CD/LD	67	13.27 (6.37)	0.0	30.0					
ABBV-951	74	15.31 (6.93)	3.0	33.0					
Change to Day 2									
Oral CD/LD	65	-0.66 (3.92)	-9.0	10.0	-1.16 (0.61)	0.0587			
ABBV-951	73	-1.14 (4.56)	-16.0	10.0	-1.30 (0.57)	0.0251*	-0.14 (0.71)	(-1.54, 1.27)	0.8457
Change to Day 8									
Oral CD/LD	60	-1.15 (4.58)	-11.0	12.0	-1.49 (0.75)	0.0490*			
ABBV-951	65	-1.48 (6.19)	-22.0	14.0	-1.89 (0.72)	0.0093**	-0.40 (0.94)	(-2.26, 1.45)	0.6684
Change to Day 15									
Oral CD/LD	59	-1.49 (5.17)	-15.0	10.0	-2.04 (0.78)	0.0100*			
ABBV-951	58	-1.76 (6.14)	-16.0	18.0	-1.77 (0.76)	0.0213*	0.28 (0.99)	(-1.69, 2.24)	0.7814

Note: @ The repeated measures model: change = treatment country visit baseline treatment*visit treatment*baseline.
The unstructured variance-covariance structure is used.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 3

Repeated-Measure Analysis of Change from Baseline to Post-Baseline Visits in MDS-UPDRS Scores
(Full Analysis Set)

Status / Visit / Treatment	N	Summary Statistics: Mean (SD)	Min	Max	Model-Based Statistics@: LS Mean (SE)	Within Group P-Value	Treatment Difference between Groups: LS Mean of Difference (SE)	95% CI	Two-Sided P-Value
Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part II Score									
Change to Day 22									
Oral CD/LD	17	-3.29 (4.50)	-10.0	3.0	-1.57 (0.94)	0.0970			
ABBV-951	23	0.78 (7.24)	-14.0	13.0	-0.64 (0.89)	0.4754	0.93 (1.22)	(-1.48, 3.34)	0.4468
Change to Day 29									
Oral CD/LD	61	-0.97 (4.60)	-12.0	12.0	-1.55 (0.76)	0.0440*			
ABBV-951	53	-2.32 (6.44)	-22.0	11.0	-2.08 (0.76)	0.0070**	-0.53 (0.98)	(-2.47, 1.42)	0.5929
Change to Day 57									
Oral CD/LD	62	-0.77 (5.53)	-17.0	12.0	-1.36 (0.83)	0.1030			
ABBV-951	47	-3.36 (6.72)	-21.0	11.0	-2.32 (0.84)	0.0069**	-0.95 (1.09)	(-3.12, 1.21)	0.3844
Change to Day 85									
Oral CD/LD	62	-0.48 (4.91)	-12.0	14.0	-1.06 (0.79)	0.1809			
ABBV-951	46	-3.76 (6.98)	-21.0	7.0	-2.65 (0.82)	0.0015**	-1.58 (1.05)	(-3.65, 0.48)	0.1318

Note: @ The repeated measures model: change = treatment country visit baseline treatment*visit treatment*baseline.
The unstructured variance-covariance structure is used.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 3

Repeated-Measure Analysis of Change from Baseline to Post-Baseline Visits in MDS-UPDRS Scores
(Full Analysis Set)

Status / Visit / Treatment	N	Summary Statistics: Mean (SD)	Min	Max	Model-Based Statistics@: LS Mean (SE)	Within Group P-Value	Treatment Difference between Groups: LS Mean of Difference (SE)	95% CI	Two-Sided P-Value
Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part III Score									
Baseline									
Oral CD/LD	67	28.23 (13.76)	3.0	66.0					
ABBV-951	73	29.47 (14.97)	6.0	78.0					
Change to Day 2									
Oral CD/LD	65	-2.22 (8.97)	-27.0	23.0	-2.43 (1.36)	0.0757			
ABBV-951	71	-3.18 (10.72)	-29.0	22.0	-3.29 (1.30)	0.0126*	-0.86 (1.61)	(-4.04, 2.33)	0.5955
Change to Day 8									
Oral CD/LD	59	-4.01 (9.03)	-31.0	12.0	-4.48 (1.47)	0.0029**			
ABBV-951	61	-1.38 (12.46)	-29.0	37.0	-1.21 (1.43)	0.3990	3.26 (1.80)	(-0.31, 6.83)	0.0728
Change to Day 15									
Oral CD/LD	59	-4.69 (11.25)	-34.0	22.0	-4.75 (1.59)	0.0033**			
ABBV-951	57	-0.79 (12.71)	-27.0	39.0	-1.11 (1.57)	0.4801	3.64 (2.00)	(-0.32, 7.60)	0.0711

Note: @ The repeated measures model: change = treatment country visit baseline treatment*visit treatment*baseline.
The unstructured variance-covariance structure is used.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 3

Repeated-Measure Analysis of Change from Baseline to Post-Baseline Visits in MDS-UPDRS Scores
(Full Analysis Set)

Status / Visit / Treatment	Summary Statistics: N	Mean (SD)	Min	Max	Model-Based Statistics@: LS Mean (SE)	Within Group P-Value	Treatment Difference between Groups: LS Mean of Difference (SE)	95% CI	Two-Sided P-Value
Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part III Score									
Change to Day 22									
Oral CD/LD	17	-3.57 (10.19)	-26.0	12.0	-5.70 (2.20)	0.0105*			
ABBV-951	23	0.85 (13.43)	-30.5	32.0	-0.75 (1.99)	0.7066	4.95 (2.80)	(-0.59, 10.49)	0.0793
Change to Day 29									
Oral CD/LD	58	-4.03 (11.20)	-32.0	29.0	-4.68 (1.54)	0.0029**			
ABBV-951	52	-1.65 (11.28)	-24.0	31.0	-1.38 (1.55)	0.3733	3.30 (1.95)	(-0.56, 7.15)	0.0933
Change to Day 57									
Oral CD/LD	58	-4.08 (9.54)	-24.0	17.4	-4.53 (1.47)	0.0025**			
ABBV-951	45	-4.00 (11.63)	-28.0	29.0	-3.30 (1.51)	0.0302*	1.23 (1.86)	(-2.44, 4.90)	0.5090
Change to Day 85									
Oral CD/LD	62	-4.07 (11.34)	-36.0	31.7	-4.57 (1.51)	0.0029**			
ABBV-951	45	-4.77 (10.97)	-33.0	19.0	-4.25 (1.63)	0.0102*	0.32 (1.99)	(-3.62, 4.26)	0.8731

Note: @ The repeated measures model: change = treatment country visit baseline treatment*visit treatment*baseline.
The unstructured variance-covariance structure is used.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 3

Repeated-Measure Analysis of Change from Baseline to Post-Baseline Visits in MDS-UPDRS Scores
(Full Analysis Set)

Status / Visit / Treatment	N	Summary Statistics: Mean (SD)	Min	Max	Model-Based Statistics@: LS Mean (SE)	Within Group P-Value	Treatment Difference between Groups: LS Mean of Difference (SE)	95% CI	Two-Sided P-Value
Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part IV Score									
Baseline									
Oral CD/LD	67	7.73 (3.14)	0.0	16.0					
ABBV-951	74	8.91 (3.33)	3.0	18.0					
Change to Day 2									
Oral CD/LD	65	0.23 (2.44)	-5.0	9.0	0.23 (0.39)	0.5521			
ABBV-951	73	-0.34 (3.23)	-13.0	9.0	-0.04 (0.37)	0.9095	-0.28 (0.48)	(-1.22, 0.67)	0.5651
Change to Day 8									
Oral CD/LD	60	0.03 (2.36)	-6.0	10.0	-0.02 (0.43)	0.9666			
ABBV-951	65	-1.85 (3.91)	-16.0	7.0	-1.41 (0.41)	<=0.001***	-1.40 (0.53)	(-2.45, -0.34)	0.0100**
Change to Day 15									
Oral CD/LD	59	-0.32 (2.60)	-6.0	8.0	-0.46 (0.40)	0.2573			
ABBV-951	58	-1.74 (3.14)	-11.0	3.0	-1.33 (0.40)	0.0011**	-0.87 (0.51)	(-1.88, 0.14)	0.0911

Note: @ The repeated measures model: change = treatment country visit baseline treatment*visit treatment*baseline.
The unstructured variance-covariance structure is used.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 3

Repeated-Measure Analysis of Change from Baseline to Post-Baseline Visits in MDS-UPDRS Scores
(Full Analysis Set)

Status / Visit / Treatment	N	Mean (SD)	Min	Max	LS Mean (SE)	Within Group P-Value	LS Mean of Difference (SE)	95% CI	Two-Sided P-Value
		Summary Statistics			Model-Based Statistics@		Treatment Difference between Groups		
Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part IV Score									
Change to Day 22									
Oral CD/LD	17	-0.24 (2.49)	-5.0	4.0	-0.45 (0.60)	0.4566			
ABBV-951	23	-1.43 (3.41)	-12.0	2.0	-1.69 (0.56)	0.0029**	-1.24 (0.78)	(-2.78, 0.30)	0.1128
Change to Day 29									
Oral CD/LD	61	-0.34 (2.33)	-8.0	5.0	-0.44 (0.42)	0.2968			
ABBV-951	52	-2.06 (3.86)	-12.0	3.0	-1.28 (0.44)	0.0039**	-0.84 (0.56)	(-1.94, 0.26)	0.1329
Change to Day 57									
Oral CD/LD	62	-0.35 (2.88)	-8.0	5.0	-0.41 (0.47)	0.3897			
ABBV-951	45	-3.33 (4.38)	-16.0	4.0	-2.62 (0.51)	<=0.001***	-2.21 (0.65)	(-3.49, -0.93)	<=0.001***
Change to Day 85									
Oral CD/LD	62	0.13 (2.53)	-6.0	7.0	0.08 (0.43)	0.8489			
ABBV-951	46	-2.83 (3.90)	-13.0	4.0	-2.14 (0.46)	<=0.001***	-2.22 (0.58)	(-3.36, -1.08)	<=0.001***

Note: @ The repeated measures model: change = treatment country visit baseline treatment*visit treatment*baseline.
The unstructured variance-covariance structure is used.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 3

Repeated-Measure Analysis of Change from Baseline to Post-Baseline Visits in MDS-UPDRS Scores
(Full Analysis Set)

Status / Visit / Treatment	N	Mean (SD)	Min	Max	LS Mean (SE)	Within Group P-Value	LS Mean of Difference (SE)	95% CI	Two-Sided P-Value
		Summary Statistics			Model-Based Statistics@		Treatment Difference between Groups		
Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Hoehn and Yahr Stage									
Baseline									
Oral CD/LD	67	2.22 (0.73)	0.0	5.0					
ABBV-951	74	2.20 (0.68)	1.0	4.0					
Change to Day 2									
Oral CD/LD	65	-0.11 (0.59)	-2.0	1.0	-0.06 (0.08)	0.4787			
ABBV-951	73	-0.05 (0.62)	-3.0	1.0	-0.04 (0.08)	0.6124	0.02 (0.10)	(-0.18, 0.22)	0.8481
Change to Day 8									
Oral CD/LD	60	-0.13 (0.47)	-2.0	1.0	-0.11 (0.08)	0.1969			
ABBV-951	64	-0.13 (0.68)	-3.0	2.0	-0.09 (0.08)	0.2608	0.02 (0.10)	(-0.18, 0.22)	0.8615
Change to Day 15									
Oral CD/LD	59	-0.12 (0.59)	-2.0	1.0	-0.13 (0.09)	0.1553			
ABBV-951	58	-0.09 (0.71)	-3.0	1.0	-0.10 (0.09)	0.2663	0.03 (0.11)	(-0.19, 0.25)	0.7860

Note: @ The repeated measures model: change = treatment country visit baseline treatment*visit treatment*baseline.
The unstructured variance-covariance structure is used.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 3

Repeated-Measure Analysis of Change from Baseline to Post-Baseline Visits in MDS-UPDRS Scores
(Full Analysis Set)

Status / Visit / Treatment	N	Mean (SD)	Min	Max	LS Mean (SE)	Within Group P-Value	LS Mean of Difference (SE)	95% CI	Two-Sided P-Value
	Summary Statistics				Model-Based Statistics@		Treatment Difference between Groups		
Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Hoehn and Yahr Stage									
Change to Day 22									
Oral CD/LD	17	-0.18 (0.39)	-1.0	0.0	-0.21 (0.10)	0.0387*			
ABBV-951	23	0.22 (0.67)	-1.0	2.0	0.14 (0.10)	0.1432	0.35 (0.13)	(0.10, 0.60)	0.0070**
Change to Day 29									
Oral CD/LD	58	-0.10 (0.61)	-2.0	1.0	-0.09 (0.09)	0.2680			
ABBV-951	53	-0.11 (0.58)	-1.0	1.0	-0.04 (0.09)	0.6422	0.06 (0.11)	(-0.16, 0.27)	0.6065
Change to Day 57									
Oral CD/LD	59	-0.15 (0.66)	-2.0	1.0	-0.13 (0.09)	0.1619			
ABBV-951	45	-0.18 (0.58)	-1.0	1.0	-0.01 (0.09)	0.8804	0.11 (0.11)	(-0.12, 0.34)	0.3322
Change to Day 85									
Oral CD/LD	62	-0.11 (0.66)	-2.0	2.0	-0.09 (0.09)	0.3148			
ABBV-951	45	-0.04 (0.67)	-1.0	1.0	0.06 (0.10)	0.5374	0.15 (0.12)	(-0.09, 0.39)	0.2130

Note: @ The repeated measures model: change = treatment country visit baseline treatment*visit treatment*baseline.
The unstructured variance-covariance structure is used.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

表2.7.3.6-9　PDSS-2スコア（FAS）：M15-741試験

[redacted]20[redacted] 10:12 <[redacted]>
ABBV-951
STUDY M15-741 - SECOND INTERIM (CUTOFF [redacted]20[redacted])
R&D/20/1632 - CLINICAL/STATISTICAL

TABLE 14.2__3

Change from Baseline to Each Planned Visit in Sleep Symptoms as Assessed
by The Parkinson's Disease Sleep Scale - 2
(FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
PDSS-2 Total Score									
BASELINE	243		20.4 (9.64)	19.0	0.0, 56.0				
Low dose	132		19.6 (9.41)	18.0	2.0, 56.0				
High dose	111		21.3 (9.87)	20.0	0.0, 47.0				
WEEK 6	196	20.2	14.2 (8.54)	12.5	0.0, 45.0	-6.1 (10.31)	-6.0	-50.0, 27.0	<=0.001***
Low dose	106	19.8	14.8 (8.84)	13.0	1.0, 45.0	-5.0 (11.35)	-4.0	-50.0, 27.0	<=0.001***
High dose	90	20.7	13.5 (8.15)	12.0	0.0, 43.0	-7.3 (8.85)	-7.0	-27.0, 14.0	<=0.001***
WEEK 13	168	20.7	13.3 (8.40)	11.5	0.0, 45.0	-7.4 (9.95)	-6.0	-48.0, 21.0	<=0.001***
Low dose	92	19.8	13.0 (8.74)	9.5	0.0, 45.0	-6.7 (10.71)	-6.0	-48.0, 17.0	<=0.001***
High dose	76	21.8	13.6 (8.02)	13.0	2.0, 43.0	-8.2 (8.94)	-8.0	-27.0, 21.0	<=0.001***
WEEK 26	141	20.6	14.2 (9.26)	12.0	0.0, 51.0	-6.5 (11.20)	-7.0	-48.0, 40.0	<=0.001***
Low dose	75	19.3	14.5 (9.76)	11.0	1.0, 51.0	-4.8 (13.15)	-6.0	-48.0, 40.0	0.0025**
High dose	66	22.1	13.7 (8.72)	12.0	0.0, 35.0	-8.4 (8.13)	-8.0	-34.0, 10.0	<=0.001***
WEEK 39	123	20.2	13.6 (8.47)	12.0	1.0, 53.0	-6.6 (10.52)	-6.0	-53.0, 18.0	<=0.001***
Low dose	69	19.6	13.1 (7.73)	12.0	2.0, 43.0	-6.4 (11.28)	-5.0	-53.0, 18.0	<=0.001***
High dose	54	21.0	14.2 (9.37)	12.0	1.0, 53.0	-6.8 (9.54)	-7.0	-30.0, 16.0	<=0.001***
WEEK 52	106	20.3	13.4 (8.58)	12.0	0.0, 47.0	-6.8 (10.58)	-7.5	-53.0, 21.0	<=0.001***
Low dose	59	19.5	13.3 (8.02)	12.0	2.0, 44.0	-6.2 (12.51)	-7.0	-53.0, 21.0	<=0.001***
High dose	47	21.2	13.6 (9.32)	12.0	0.0, 47.0	-7.6 (7.58)	-8.0	-23.0, 7.0	<=0.001***

&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 3

Change from Baseline to Each Planned Visit in Sleep Symptoms as Assessed
by The Parkinson's Disease Sleep Scale - 2
(FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
PDSS-2 Motor Symptoms at Night Score									
BASELINE	243		5.2 (4.10)	5.0	0.0, 20.0				
Low dose	132		5.1 (4.06)	4.5	0.0, 20.0				
High dose	111		5.3 (4.16)	5.0	0.0, 16.0				
WEEK 6	196	5.2	3.5 (3.59)	2.0	0.0, 15.0	-1.7 (4.61)	-2.0	-19.0, 12.0	<=0.001***
Low dose	106	5.2	3.7 (3.63)	3.0	0.0, 14.0	-1.5 (4.95)	-1.0	-19.0, 12.0	0.0025**
High dose	90	5.1	3.1 (3.53)	2.0	0.0, 15.0	-2.0 (4.18)	-2.0	-11.0, 10.0	<=0.001***
WEEK 13	168	5.4	3.2 (3.48)	2.0	0.0, 16.0	-2.3 (4.40)	-2.0	-19.0, 11.0	<=0.001***
Low dose	92	5.3	3.1 (3.64)	2.0	0.0, 16.0	-2.2 (4.56)	-2.0	-19.0, 9.0	<=0.001***
High dose	76	5.7	3.3 (3.31)	2.0	0.0, 15.0	-2.4 (4.22)	-2.5	-13.0, 11.0	<=0.001***
WEEK 26	141	5.4	3.7 (3.96)	2.0	0.0, 20.0	-1.7 (5.10)	-2.0	-20.0, 20.0	<=0.001***
Low dose	75	5.0	3.9 (4.22)	2.0	0.0, 20.0	-1.1 (6.00)	-2.0	-20.0, 20.0	0.1191
High dose	66	5.7	3.4 (3.66)	2.0	0.0, 16.0	-2.3 (3.77)	-2.0	-12.0, 11.0	<=0.001***
WEEK 39	123	5.2	3.4 (3.74)	2.0	0.0, 20.0	-1.8 (4.60)	-1.0	-18.0, 12.0	<=0.001***
Low dose	69	5.1	3.3 (3.55)	2.0	0.0, 16.0	-1.8 (4.78)	-1.0	-18.0, 12.0	0.0023**
High dose	54	5.4	3.6 (4.00)	2.5	0.0, 20.0	-1.8 (4.41)	-1.0	-12.0, 12.0	0.0042**
WEEK 52	106	5.2	3.2 (3.64)	2.0	0.0, 16.0	-2.0 (4.76)	-2.0	-19.0, 14.0	<=0.001***
Low dose	59	5.1	3.2 (3.56)	2.0	0.0, 14.0	-1.9 (5.64)	-2.0	-19.0, 14.0	0.0123*
High dose	47	5.3	3.2 (3.77)	2.0	0.0, 16.0	-2.1 (3.42)	-2.0	-13.0, 6.0	<=0.001***

&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 3

Change from Baseline to Each Planned Visit in Sleep Symptoms as Assessed
by The Parkinson's Disease Sleep Scale - 2
(FAS)

Parameter Time Point Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
PDSS-2 PD Symptoms at Night Score									
BASELINE	243		5.0 (3.99)	4.0	0.0, 20.0				
Low dose	132		4.7 (3.88)	4.0	0.0, 20.0				
High dose	111		5.4 (4.11)	5.0	0.0, 16.0				
WEEK 6	196	4.9	2.9 (3.41)	2.0	0.0, 18.0	-2.0 (3.81)	-2.0	-19.0, 12.0	<=0.001***
Low dose	106	4.8	2.9 (3.59)	2.0	0.0, 18.0	-1.8 (4.04)	-1.5	-19.0, 12.0	<=0.001***
High dose	90	5.2	2.9 (3.21)	2.0	0.0, 15.0	-2.3 (3.51)	-2.0	-12.0, 5.0	<=0.001***
WEEK 13	168	4.9	2.8 (3.19)	2.0	0.0, 18.0	-2.2 (3.99)	-2.0	-16.0, 11.0	<=0.001***
Low dose	92	4.7	2.7 (3.25)	2.0	0.0, 18.0	-1.9 (4.01)	-2.0	-16.0, 10.0	<=0.001***
High dose	76	5.3	2.8 (3.14)	2.0	0.0, 16.0	-2.5 (3.98)	-2.0	-11.0, 11.0	<=0.001***
WEEK 26	141	5.0	3.0 (3.68)	2.0	0.0, 19.0	-2.0 (4.32)	-2.0	-16.0, 17.0	<=0.001***
Low dose	75	4.6	3.3 (4.02)	2.0	0.0, 19.0	-1.3 (4.71)	-1.0	-16.0, 17.0	0.0227*
High dose	66	5.5	2.7 (3.24)	1.0	0.0, 12.0	-2.8 (3.68)	-3.0	-14.0, 5.0	<=0.001***
WEEK 39	123	4.7	2.4 (3.19)	1.0	0.0, 20.0	-2.3 (4.06)	-2.0	-19.0, 8.0	<=0.001***
Low dose	69	4.5	2.3 (2.86)	1.0	0.0, 13.0	-2.2 (4.42)	-2.0	-19.0, 7.0	<=0.001***
High dose	54	5.0	2.6 (3.58)	1.0	0.0, 20.0	-2.4 (3.57)	-2.0	-12.0, 8.0	<=0.001***
WEEK 52	106	4.8	2.5 (3.12)	2.0	0.0, 15.0	-2.3 (4.21)	-2.0	-19.0, 14.0	<=0.001***
Low dose	59	4.4	2.5 (3.15)	2.0	0.0, 15.0	-1.9 (4.64)	-2.0	-19.0, 14.0	0.0026**
High dose	47	5.3	2.4 (3.11)	1.0	0.0, 14.0	-2.9 (3.58)	-3.0	-12.0, 5.0	<=0.001***

&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 3

Change from Baseline to Each Planned Visit in Sleep Symptoms as Assessed
by The Parkinson's Disease Sleep Scale - 2
(FAS)

Parameter Time Point Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
PDSS-2 Disturbed Sleep Score									
BASELINE	243		10.2 (3.71)	10.0	0.0, 19.0				
Low dose	132		9.8 (3.66)	10.0	1.0, 19.0				
High dose	111		10.6 (3.73)	11.0	0.0, 19.0				
WEEK 6	196	10.1	7.8 (3.63)	8.0	0.0, 19.0	-2.3 (4.56)	-2.0	-12.0, 17.0	<=0.001***
Low dose	106	9.8	8.1 (3.75)	8.0	1.0, 19.0	-1.7 (4.78)	-2.0	-12.0, 17.0	<=0.001***
High dose	90	10.4	7.4 (3.47)	8.0	0.0, 16.0	-3.0 (4.20)	-2.0	-11.0, 8.0	<=0.001***
WEEK 13	168	10.3	7.4 (4.03)	7.0	0.0, 20.0	-2.9 (4.53)	-3.0	-13.0, 11.0	<=0.001***
Low dose	92	9.8	7.3 (4.00)	7.0	0.0, 17.0	-2.6 (4.63)	-2.0	-13.0, 11.0	<=0.001***
High dose	76	10.9	7.6 (4.09)	8.0	0.0, 20.0	-3.3 (4.42)	-3.0	-13.0, 6.0	<=0.001***
WEEK 26	141	10.3	7.5 (3.65)	7.0	0.0, 17.0	-2.8 (4.39)	-2.0	-14.0, 10.0	<=0.001***
Low dose	75	9.7	7.3 (3.35)	7.0	1.0, 14.0	-2.4 (4.48)	-2.0	-12.0, 10.0	<=0.001***
High dose	66	10.9	7.7 (3.97)	7.0	0.0, 17.0	-3.3 (4.28)	-3.0	-14.0, 7.0	<=0.001***
WEEK 39	123	10.3	7.8 (3.59)	8.0	0.0, 16.0	-2.5 (4.53)	-2.0	-16.0, 7.0	<=0.001***
Low dose	69	10.0	7.6 (3.58)	7.0	0.0, 16.0	-2.4 (4.60)	-2.0	-16.0, 7.0	<=0.001***
High dose	54	10.7	8.1 (3.62)	8.0	1.0, 15.0	-2.6 (4.50)	-2.0	-13.0, 5.0	<=0.001***
WEEK 52	106	10.3	7.7 (3.86)	8.0	0.0, 17.0	-2.5 (4.62)	-3.0	-15.0, 10.0	<=0.001***
Low dose	59	10.0	7.5 (3.69)	7.0	0.0, 15.0	-2.4 (4.72)	-3.0	-15.0, 10.0	<=0.001***
High dose	47	10.6	8.0 (4.08)	8.0	0.0, 17.0	-2.6 (4.54)	-3.0	-11.0, 7.0	<=0.001***

&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

表2.7.3.6-10　PDSS-2スコア（FAS）：M15-736試験

[redacted]20[redacted] 19:30 <[redacted]>
ABBV-951
STUDY M15-736
R&D/20/1640 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 4

TABLE 14.2__5

ANCOVA of Change from Baseline to Final Visit in PDSS-2 Scores
(Full Analysis Set)

Status / Visit / Treatment	Summary Statistics: N	Mean (SD)	Min	Max	Within Group P-Value#	Model-Based Statistics@: LS Mean (SE)	Treatment Difference between Groups: LS Mean of Difference (SE)	95% CI	Two-Sided P-Value
Parkinson's Disease Sleep Scale-2 (PDSS-2) Total Score									
Baseline									
Oral CD/LD	59	18.71 (8.77)	2.0	47.0					
ABBV-951	44	21.70 (9.04)	7.0	42.0					
Final									
Oral CD/LD	59	17.07 (8.29)	4.0	38.0					
ABBV-951	44	13.36 (8.27)	0.0	36.0					
Change to final									
Oral CD/LD	59	-1.64 (6.22)	-12.0	19.0	0.0469*	-2.52 (1.12)			
ABBV-951	44	-8.34 (8.86)	-40.0	3.0	<=0.001***	-7.92 (1.18)	-5.40 (1.32)	(-8.03, -2.78)	<=0.001***

Note: @ ANCOVA model including effects for treatment, country and baseline.
From one-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 5

ANCOVA of Change from Baseline to Final Visit in PDSS-2 Scores
(Full Analysis Set)

Status / Visit / Treatment	N	Summary Statistics: Mean (SD)	Min	Max	Within Group P-Value#	Model-Based Statistics@: LS Mean (SE)	Treatment Difference between Groups: LS Mean of Difference (SE)	95% CI	Two-Sided P-Value
Parkinson's Disease Sleep Scale-2 (PDSS-2) Moto Symptoms at Night Domain Score									
Baseline									
Oral CD/LD	59	5.19 (4.05)	0.0	18.0					
ABBV-951	44	6.00 (3.92)	0.0	16.0					
Final									
Oral CD/LD	59	4.42 (3.85)	0.0	17.0					
ABBV-951	44	2.91 (2.95)	0.0	12.0					
Change to final									
Oral CD/LD	59	-0.76 (3.15)	-7.0	8.0	0.0683	-0.96 (0.46)			
ABBV-951	44	-3.09 (3.18)	-12.0	1.0	<=0.001***	-2.93 (0.48)	-1.97 (0.54)	(-3.04, -0.90)	<=0.001***

Note: @ ANCOVA model including effects for treatment, country and baseline.
From one-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 5

ANCOVA of Change from Baseline to Final Visit in PDSS-2 Scores
(Full Analysis Set)

Status / Visit / Treatment	N	Summary Statistics: Mean (SD)	Min	Max	Within Group P-Value#	Model-Based Statistics@: LS Mean (SE)	Treatment Difference between Groups: LS Mean of Difference (SE)	95% CI	Two-Sided P-Value
Parkinson's Disease Sleep Scale-2 (PDSS-2) PD Symptoms at Night Domain Score									
Baseline									
Oral CD/LD	59	3.83 (2.90)	0.0	12.0					
ABBV-951	44	4.70 (3.24)	0.0	12.0					
Final									
Oral CD/LD	59	3.19 (2.94)	0.0	14.0					
ABBV-951	44	2.86 (2.79)	0.0	11.0					
Change to final									
Oral CD/LD	59	-0.64 (2.20)	-4.0	7.0	0.0280*	-0.96 (0.40)			
ABBV-951	44	-1.84 (3.32)	-12.0	5.0	<=0.001***	-1.74 (0.43)	-0.78 (0.48)	(-1.73, 0.16)	0.1039

Note: @ ANCOVA model including effects for treatment, country and baseline.
From one-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 5

ANCOVA of Change from Baseline to Final Visit in PDSS-2 Scores
(Full Analysis Set)

Status / Visit / Treatment	N	Mean (SD)	Min	Max	Within Group P-Value#	LS Mean (SE)	LS Mean of Difference (SE)	95% CI	Two-Sided P-Value
		Summary Statistics				Model-Based Statistics@	Treatment Difference between Groups		
Parkinson's Disease Sleep Scale-2 (PDSS-2) Disturbed Sleep Domain Score									
Baseline									
Oral CD/LD	59	9.69 (3.98)	1.0	19.0					
ABBV-951	44	11.00 (4.02)	3.0	20.0					
Final									
Oral CD/LD	59	9.46 (4.11)	2.0	18.0					
ABBV-951	44	7.59 (4.00)	0.0	17.0					
Change to final									
Oral CD/LD	59	-0.24 (3.03)	-6.0	9.0	0.5499	-0.61 (0.57)			
ABBV-951	44	-3.41 (4.40)	-16.0	5.0	<=0.001***	-3.24 (0.60)	-2.62 (0.67)	(-3.96, -1.29)	<=0.001***

Note: @ ANCOVA model including effects for treatment, country and baseline.
From one-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

表2.7.3.6-11　PD日誌に基づく，標準化した1日あたりの平均「オフ」時間及び「オン」時間の要約（FAS，部分集団別）：M15-741試験

[redacted]20[redacted] 10:12 <[redacted]>
ABBV-951
STUDY M15-741 - SECOND INTERIM (CUTOFF [redacted]20[redacted])
R&D/20/1632 - CLINICAL/STATISTICAL

TABLE 14.2__1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Gender:Female									
Average Daily Normalized 'Off' Time									
BASELINE	95		5.99 (2.28)	6.1	0.0, 10.3				
Low Dose	64		6.02 (2.32)	6.2	0.0, 10.3				
High Dose	31		5.93 (2.23)	5.7	1.5, 9.5				
WEEK 1	92	5.96	4.44 (3.75)	3.8	0.0, 14.8	-1.52 (4.10)	-1.7	-10.2, 10.4	<=0.001***
Low Dose	62	6.03	3.83 (3.54)	2.9	0.0, 13.8	-2.20 (3.89)	-2.3	-10.2, 5.9	<=0.001***
High Dose	30	5.82	5.71 (3.91)	5.5	0.0, 14.8	-0.11 (4.24)	-0.3	-7.5, 10.4	0.8888
WEEK 6	83	5.90	4.20 (3.40)	3.8	0.0, 14.9	-1.70 (3.91)	-2.0	-10.2, 8.1	<=0.001***
Low Dose	55	5.87	3.67 (3.34)	3.3	0.0, 14.9	-2.21 (3.75)	-2.7	-10.2, 8.1	<=0.001***
High Dose	28	5.96	5.25 (3.34)	5.2	0.0, 12.5	-0.71 (4.09)	-1.1	-7.5, 6.8	0.3659
WEEK 13	45	5.68	3.38 (3.34)	2.0	0.0, 12.1	-2.30 (4.20)	-3.3	-9.9, 8.1	<=0.001***
Low Dose	32	5.68	3.06 (3.39)	1.6	0.0, 12.1	-2.62 (4.31)	-3.3	-9.9, 8.1	0.0017**
High Dose	13	5.68	4.15 (3.20)	4.2	0.0, 10.3	-1.53 (3.99)	-2.4	-7.5, 6.3	0.1930

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours
(i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Gender:Female (Cont.)									
Average Daily Normalized 'Off' Time (Cont.)									
WEEK 26	49	6.08	2.17 (2.62)	1.0	0.0, 9.8	-3.91 (3.29)	-4.0	-10.2, 5.5	<=0.001***
Low Dose	33	5.98	1.65 (2.14)	0.8	0.0, 7.9	-4.33 (2.96)	-4.0	-10.2, 2.7	<=0.001***
High Dose	16	6.30	3.26 (3.22)	2.2	0.0, 9.8	-3.04 (3.83)	-3.4	-9.2, 5.5	0.0062**
WEEK 39	46	6.01	2.51 (2.23)	1.8	0.0, 7.3	-3.50 (3.17)	-2.8	-9.9, 2.9	<=0.001***
Low Dose	33	5.92	2.09 (1.96)	1.7	0.0, 6.2	-3.83 (2.87)	-3.1	-9.9, 1.1	<=0.001***
High Dose	13	6.24	3.58 (2.59)	4.2	0.0, 7.3	-2.66 (3.82)	-2.3	-9.2, 2.9	0.0274*
WEEK 52	34	6.29	1.92 (2.29)	1.0	0.0, 8.8	-4.37 (3.01)	-4.3	-10.2, 3.1	<=0.001***
Low Dose	26	6.43	2.09 (2.50)	1.0	0.0, 8.8	-4.34 (3.05)	-4.2	-10.2, 3.1	<=0.001***
High Dose	8	5.83	1.37 (1.35)	0.9	0.0, 3.6	-4.46 (3.06)	-4.5	-8.6, -0.3	0.0044**
Average Daily Normalized 'On' Time Without Dyskinesia									
BASELINE	95		6.26 (3.20)	6.5	0.0, 14.0				
Low Dose	64		5.95 (3.11)	5.8	0.0, 14.0				
High Dose	31		6.90 (3.32)	6.9	0.9, 12.0				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Gender:Female (Cont.)									
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 1	92	6.17	8.03 (4.47)	7.8	0.0, 16.0	1.86 (4.29)	1.9	-8.9, 10.4	<=0.001***
Low Dose	62	5.82	7.75 (4.68)	7.3	0.0, 16.0	1.93 (4.17)	1.9	-8.9, 10.4	<=0.001***
High Dose	30	6.89	8.61 (4.01)	8.2	0.5, 16.0	1.72 (4.59)	1.9	-8.1, 8.7	0.0497*
WEEK 6	83	6.31	9.75 (4.05)	9.9	0.0, 16.0	3.45 (4.32)	4.1	-8.3, 12.7	<=0.001***
Low Dose	55	6.00	9.91 (4.20)	10.2	0.0, 16.0	3.91 (4.11)	4.3	-8.3, 12.7	<=0.001***
High Dose	28	6.91	9.45 (3.80)	9.8	2.4, 16.0	2.54 (4.65)	2.7	-6.7, 9.5	0.0074**
WEEK 13	45	6.64	11.16 (4.42)	13.1	0.0, 16.0	4.52 (4.27)	5.6	-9.0, 11.0	<=0.001***
Low Dose	32	6.43	11.35 (4.66)	13.2	0.0, 16.0	4.92 (4.17)	5.6	-9.0, 11.0	<=0.001***
High Dose	13	7.17	10.69 (3.88)	10.6	3.8, 16.0	3.52 (4.53)	4.3	-6.3, 9.5	0.0159*
WEEK 26	49	6.53	12.08 (3.59)	13.1	0.6, 16.0	5.55 (4.34)	6.4	-11.0, 11.5	<=0.001***
Low Dose	33	6.50	12.98 (2.60)	13.5	7.5, 16.0	6.48 (2.92)	6.6	-1.2, 11.5	<=0.001***
High Dose	16	6.58	10.23 (4.63)	9.9	0.6, 16.0	3.65 (6.03)	5.2	-11.0, 9.5	0.0286*
WEEK 39	46	6.60	11.58 (3.73)	11.8	1.2, 16.0	4.98 (3.97)	5.4	-5.0, 12.4	<=0.001***
Low Dose	33	6.38	11.82 (3.65)	12.4	5.0, 16.0	5.45 (3.73)	5.9	-5.0, 11.4	<=0.001***
High Dose	13	7.15	10.96 (3.99)	11.8	1.2, 16.0	3.81 (4.46)	3.0	-2.9, 12.4	0.0096**

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Gender:Female (Cont.)									
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 52	34	6.82	11.77 (4.64)	13.2	0.0, 16.0	4.94 (4.83)	6.0	-12.0, 11.3	<=0.001***
Low Dose	26	6.14	11.90 (4.51)	13.2	1.3, 16.0	5.76 (4.00)	6.6	-6.5, 11.3	<=0.001***
High Dose	8	9.04	11.33 (5.35)	13.1	0.0, 16.0	2.29 (6.52)	2.5	-12.0, 9.5	0.3534
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia									
BASELINE	95		2.52 (2.11)	2.6	0.0, 8.5				
Low Dose	64		2.55 (2.18)	2.6	0.0, 8.5				
High Dose	31		2.44 (1.98)	2.4	0.0, 7.6				
WEEK 1	92	2.59	2.45 (3.11)	1.1	0.0, 13.6	-0.15 (3.39)	-0.3	-8.5, 13.6	0.6809
Low Dose	62	2.63	3.01 (3.35)	2.2	0.0, 13.6	0.38 (3.77)	0.0	-8.5, 13.6	0.4338
High Dose	30	2.52	1.29 (2.15)	0.4	0.0, 8.1	-1.23 (2.09)	-0.7	-5.1, 5.0	0.0032**
WEEK 6	83	2.60	1.58 (2.67)	0.5	0.0, 15.4	-1.02 (2.73)	-0.8	-7.6, 11.6	0.0010**
Low Dose	55	2.67	1.90 (2.99)	0.8	0.0, 15.4	-0.76 (2.90)	-0.8	-7.6, 11.6	0.0562
High Dose	28	2.48	0.95 (1.80)	0.0	0.0, 6.2	-1.53 (2.33)	-0.8	-7.6, 4.0	0.0018**

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Gender:Female (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 13	45	2.79	1.10 (2.41)	0.0	0.0, 14.0	-1.70 (2.65)	-2.0	-6.5, 7.9	<=0.001***
Low Dose	32	2.79	1.18 (2.60)	0.0	0.0, 14.0	-1.61 (2.83)	-1.6	-6.5, 7.9	0.0031**
High Dose	13	2.81	0.90 (1.93)	0.0	0.0, 6.4	-1.92 (2.22)	-2.0	-5.3, 1.9	0.0091**
WEEK 26	49	2.61	1.60 (2.65)	0.0	0.0, 15.2	-1.00 (3.30)	-1.0	-6.7, 12.0	0.0386*
Low Dose	33	2.69	1.32 (1.74)	0.2	0.0, 7.3	-1.38 (2.86)	-1.0	-6.7, 4.3	0.0093**
High Dose	16	2.43	2.20 (3.94)	0.0	0.0, 15.2	-0.23 (4.06)	-1.0	-5.3, 12.0	0.8255
WEEK 39	46	2.72	1.50 (2.41)	0.0	0.0, 7.7	-1.23 (2.98)	-0.7	-7.8, 6.1	0.0077**
Low Dose	33	2.85	1.79 (2.60)	0.0	0.0, 7.7	-1.06 (3.00)	0.0	-7.8, 5.0	0.0505
High Dose	13	2.41	0.76 (1.69)	0.0	0.0, 6.1	-1.65 (3.03)	-2.0	-6.4, 6.1	0.0731
WEEK 52	34	2.23	1.94 (3.68)	0.1	0.0, 12.9	-0.29 (3.94)	-0.2	-6.7, 12.9	0.6747
Low Dose	26	2.59	1.78 (3.42)	0.1	0.0, 12.0	-0.81 (3.55)	-0.2	-6.7, 9.2	0.2535
High Dose	8	1.06	2.49 (4.64)	0.3	0.0, 12.9	1.43 (4.87)	-0.2	-2.0, 12.9	0.4350

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Gender:Female (Cont.)									
Average Daily Normalized 'On' Time With Troublesome Dyskinesia									
BASELINE	95		1.24 (2.06)	0.0	0.0, 10.5				
Low Dose	64		1.48 (2.30)	0.0	0.0, 10.5				
High Dose	31		0.74 (1.33)	0.0	0.0, 5.3				
WEEK 1	92	1.28	1.08 (2.15)	0.0	0.0, 10.5	-0.20 (1.99)	0.0	-6.0, 10.5	0.3434
Low Dose	62	1.52	1.41 (2.49)	0.2	0.0, 10.5	-0.11 (2.25)	0.0	-6.0, 10.5	0.7022
High Dose	30	0.77	0.39 (0.89)	0.0	0.0, 4.2	-0.38 (1.33)	0.0	-4.9, 3.4	0.1286
WEEK 6	83	1.19	0.46 (1.30)	0.0	0.0, 5.8	-0.72 (1.79)	0.0	-9.2, 4.1	<=0.001***
Low Dose	55	1.46	0.52 (1.43)	0.0	0.0, 5.8	-0.94 (2.10)	0.0	-9.2, 4.1	0.0016**
High Dose	28	0.66	0.35 (1.01)	0.0	0.0, 4.3	-0.30 (0.82)	0.0	-2.5, 1.4	0.0583
WEEK 13	45	0.88	0.36 (1.37)	0.0	0.0, 8.0	-0.52 (1.90)	0.0	-7.2, 6.0	0.0735
Low Dose	32	1.10	0.41 (1.53)	0.0	0.0, 8.0	-0.70 (2.14)	0.0	-7.2, 6.0	0.0757
High Dose	13	0.34	0.26 (0.93)	0.0	0.0, 3.4	-0.08 (1.02)	0.0	-2.2, 2.6	0.7786

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Gender:Female (Cont.)									
Average Daily Normalized 'On' Time With Troublesome Dyskinesia (Cont.)									
WEEK 26	49	0.78	0.14 (0.46)	0.0	0.0, 2.4	-0.64 (1.41)	0.0	-5.1, 1.6	0.0026**
Low Dose	33	0.82	0.06 (0.23)	0.0	0.0, 1.3	-0.77 (1.39)	0.0	-5.1, 1.3	0.0033**
High Dose	16	0.69	0.31 (0.73)	0.0	0.0, 2.4	-0.38 (1.46)	0.0	-4.9, 1.6	0.3172
WEEK 39	46	0.67	0.41 (1.41)	0.0	0.0, 8.1	-0.26 (1.50)	0.0	-5.1, 7.3	0.2502
Low Dose	33	0.86	0.30 (0.93)	0.0	0.0, 3.8	-0.56 (1.11)	0.0	-5.1, 0.5	0.0069**
High Dose	13	0.19	0.69 (2.24)	0.0	0.0, 8.1	0.50 (2.08)	0.0	-0.5, 7.3	0.4012
WEEK 52	34	0.66	0.37 (1.17)	0.0	0.0, 6.3	-0.29 (1.57)	0.0	-3.0, 6.3	0.2924
Low Dose	26	0.84	0.24 (0.62)	0.0	0.0, 2.7	-0.61 (1.19)	0.0	-3.0, 1.8	0.0155*
High Dose	8	0.06	0.81 (2.20)	0.0	0.0, 6.3	0.75 (2.23)	0.0	-0.5, 6.3	0.3757
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia									
BASELINE	95		8.78 (2.72)	8.9	0.3, 15.0				
Low Dose	64		8.51 (2.70)	8.8	0.3, 15.0				
High Dose	31		9.33 (2.70)	9.8	2.6, 14.5				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit Mean (SD)	Visit Median	Visit Min, Max	Change from Baseline Mean (SD)	Change from Baseline Median	Change from Baseline Min, Max	P-Value &
Gender:Female (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia (Cont.)									
WEEK 1	92	8.76	10.48 (3.82)	10.5	1.2, 16.0	1.71 (4.08)	1.5	-10.4, 11.3	<=0.001***
Low Dose	62	8.45	10.76 (3.81)	11.0	2.2, 16.0	2.31 (3.68)	2.1	-5.9, 11.3	<=0.001***
High Dose	30	9.41	9.90 (3.84)	9.9	1.2, 16.0	0.49 (4.64)	0.8	-10.4, 8.3	0.5679
WEEK 6	83	8.91	11.34 (3.49)	11.7	1.1, 16.0	2.43 (3.99)	2.8	-6.8, 10.5	<=0.001***
Low Dose	55	8.67	11.81 (3.50)	12.3	1.1, 16.0	3.15 (3.69)	3.0	-5.7, 10.5	<=0.001***
High Dose	28	9.38	10.40 (3.35)	10.2	3.5, 16.0	1.02 (4.26)	1.2	-6.8, 8.4	0.2180
WEEK 13	45	9.44	12.26 (3.63)	14.0	3.9, 16.0	2.82 (3.88)	3.5	-6.3, 9.9	<=0.001***
Low Dose	32	9.22	12.53 (3.73)	14.4	3.9, 16.0	3.32 (3.63)	3.6	-5.0, 9.9	<=0.001***
High Dose	13	9.98	11.59 (3.43)	11.8	5.7, 16.0	1.61 (4.33)	2.4	-6.3, 7.5	0.2057
WEEK 26	49	9.14	13.69 (2.65)	14.8	6.2, 16.0	4.55 (3.82)	4.7	-5.5, 12.5	<=0.001***
Low Dose	33	9.20	14.30 (2.19)	15.2	8.1, 16.0	5.10 (3.46)	5.2	-2.7, 12.5	<=0.001***
High Dose	16	9.01	12.43 (3.11)	12.9	6.2, 16.0	3.42 (4.36)	4.1	-5.5, 10.2	0.0067**
WEEK 39	46	9.32	13.08 (2.77)	13.9	2.4, 16.0	3.76 (3.77)	3.1	-9.2, 9.9	<=0.001***
Low Dose	33	9.22	13.61 (2.04)	14.0	9.8, 16.0	4.39 (3.04)	3.3	-1.1, 9.9	<=0.001***
High Dose	13	9.57	11.73 (3.85)	11.8	2.4, 16.0	2.16 (4.97)	2.1	-9.2, 9.7	0.1434

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Gender:Female (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia (Cont.)									
WEEK 52	34	9.05	13.71 (2.48)	14.8	7.2, 16.0	4.66 (3.03)	4.7	-3.1, 10.2	<=0.001***
Low Dose	26	8.73	13.67 (2.58)	14.8	7.2, 16.0	4.95 (3.12)	4.9	-3.1, 10.2	<=0.001***
High Dose	8	10.11	13.82 (2.27)	14.4	9.3, 16.0	3.72 (2.69)	3.3	0.3, 7.5	0.0058**
Gender:Male									
Average Daily Normalized 'Off' Time									
BASELINE	141		5.85 (2.22)	5.8	0.0, 12.6				
Low Dose	63		5.34 (2.01)	5.4	0.0, 10.0				
High Dose	78		6.26 (2.31)	6.4	0.0, 12.6				
WEEK 1	133	5.88	3.64 (3.16)	2.7	0.0, 16.0	-2.24 (3.34)	-2.7	-9.7, 8.0	<=0.001***
Low Dose	59	5.42	3.54 (2.81)	2.8	0.0, 11.2	-1.88 (3.05)	-2.2	-9.7, 5.6	<=0.001***
High Dose	74	6.24	3.72 (3.43)	2.7	0.0, 16.0	-2.53 (3.54)	-3.4	-8.9, 8.0	<=0.001***
WEEK 6	122	5.97	3.10 (3.09)	2.5	0.0, 16.0	-2.86 (3.32)	-3.4	-10.6, 9.9	<=0.001***
Low Dose	56	5.59	2.98 (3.33)	2.3	0.0, 16.0	-2.62 (3.57)	-3.4	-8.6, 9.9	<=0.001***
High Dose	66	6.29	3.21 (2.90)	2.7	0.0, 11.3	-3.07 (3.09)	-3.3	-10.6, 5.6	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Gender:Male (Cont.)									
Average Daily Normalized 'Off' Time (Cont.)									
WEEK 13	70	5.45	2.96 (3.56)	1.8	0.0, 13.4	-2.49 (3.34)	-3.2	-9.2, 7.8	<=0.001***
Low Dose	32	5.13	2.71 (3.70)	1.2	0.0, 13.4	-2.43 (3.29)	-3.4	-6.6, 7.8	<=0.001***
High Dose	38	5.72	3.17 (3.47)	1.8	0.0, 10.7	-2.55 (3.43)	-2.7	-9.2, 5.2	<=0.001***
WEEK 26	78	5.82	2.95 (3.23)	1.8	0.0, 14.3	-2.87 (3.17)	-2.8	-10.6, 7.1	<=0.001***
Low Dose	33	5.49	3.28 (3.81)	1.7	0.0, 14.3	-2.20 (3.43)	-2.8	-6.6, 7.1	<=0.001***
High Dose	45	6.07	2.71 (2.75)	1.8	0.0, 8.9	-3.36 (2.91)	-2.8	-10.6, 4.4	<=0.001***
WEEK 39	65	5.72	2.85 (3.14)	2.5	0.0, 13.3	-2.87 (3.18)	-3.3	-8.1, 9.6	<=0.001***
Low Dose	30	5.36	3.34 (3.66)	3.0	0.0, 13.3	-2.02 (3.65)	-2.8	-7.1, 9.6	0.0051**
High Dose	35	6.03	2.43 (2.60)	1.3	0.0, 7.2	-3.60 (2.55)	-3.6	-8.1, 4.0	<=0.001***
WEEK 52	62	5.68	2.83 (3.18)	1.9	0.0, 11.5	-2.85 (3.01)	-2.9	-11.2, 5.9	<=0.001***
Low Dose	25	5.28	3.00 (3.11)	2.5	0.0, 10.9	-2.28 (2.76)	-2.6	-5.9, 5.9	<=0.001***
High Dose	37	5.96	2.72 (3.26)	0.7	0.0, 11.5	-3.24 (3.15)	-3.4	-11.2, 2.8	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Gender:Male (Cont.)									
Average Daily Normalized 'On' Time Without Dyskinesia									
BASELINE	141		6.68 (3.45)	6.7	0.0, 15.4				
Low Dose	63		6.76 (3.77)	7.5	0.0, 15.4				
High Dose	78		6.62 (3.20)	6.6	0.0, 13.8				
WEEK 1	133	6.70	8.70 (4.55)	8.9	0.0, 16.0	2.00 (3.96)	1.2	-6.1, 12.0	<=0.001***
Low Dose	59	6.62	8.24 (4.40)	8.6	0.0, 16.0	1.62 (3.70)	1.0	-6.0, 10.7	0.0014**
High Dose	74	6.77	9.08 (4.66)	9.1	0.0, 16.0	2.31 (4.16)	1.8	-6.1, 12.0	<=0.001***
WEEK 6	122	6.70	10.03 (4.77)	11.4	0.0, 16.0	3.33 (4.45)	3.0	-9.1, 13.8	<=0.001***
Low Dose	56	6.74	9.81 (4.90)	11.3	0.0, 16.0	3.07 (4.85)	2.9	-9.1, 13.8	<=0.001***
High Dose	66	6.67	10.22 (4.68)	11.6	0.0, 16.0	3.55 (4.11)	3.4	-6.4, 12.0	<=0.001***
WEEK 13	70	6.68	10.54 (4.73)	10.8	0.0, 16.0	3.86 (4.41)	3.6	-6.5, 15.2	<=0.001***
Low Dose	32	6.88	9.98 (5.17)	10.1	0.0, 16.0	3.09 (4.53)	2.5	-6.5, 15.2	<=0.001***
High Dose	38	6.52	11.02 (4.34)	11.1	0.9, 16.0	4.50 (4.26)	4.5	-4.7, 14.1	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Gender:Male (Cont.)									
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 26	78	7.11	10.65 (4.68)	11.3	0.0, 16.0	3.54 (4.40)	4.0	-10.1, 14.1	<=0.001***
Low Dose	33	7.25	10.21 (5.01)	10.6	0.0, 16.0	2.95 (4.12)	3.5	-10.1, 11.2	<=0.001***
High Dose	45	7.01	10.97 (4.44)	12.5	0.0, 16.0	3.96 (4.58)	4.6	-9.6, 14.1	<=0.001***
WEEK 39	65	7.33	10.72 (4.46)	11.3	0.0, 16.0	3.39 (4.08)	3.1	-10.6, 13.5	<=0.001***
Low Dose	30	7.44	10.38 (4.97)	11.3	0.3, 16.0	2.94 (4.46)	3.0	-10.6, 11.2	0.0011**
High Dose	35	7.24	11.02 (4.02)	11.3	0.0, 16.0	3.78 (3.75)	3.3	-2.5, 13.5	<=0.001***
WEEK 52	62	7.14	10.29 (4.70)	11.2	0.0, 16.0	3.15 (3.85)	3.0	-3.1, 13.8	<=0.001***
Low Dose	25	7.54	10.67 (4.33)	12.0	0.0, 16.0	3.13 (3.35)	3.4	-2.9, 8.1	<=0.001***
High Dose	37	6.87	10.03 (4.97)	10.0	0.0, 16.0	3.16 (4.20)	2.4	-3.1, 13.8	<=0.001***
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia									
BASELINE	141		2.70 (2.82)	2.1	0.0, 12.2				
Low Dose	63		2.83 (2.60)	2.7	0.0, 10.3				
High Dose	78		2.60 (2.99)	1.4	0.0, 12.2				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Gender:Male (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 1	133	2.71	2.73 (3.20)	1.5	0.0, 14.9	0.02 (2.78)	0.0	-8.2, 8.8	0.9435
Low Dose	59	2.91	3.07 (3.22)	2.4	0.0, 14.9	0.17 (2.73)	0.0	-5.3, 8.6	0.6419
High Dose	74	2.55	2.45 (3.17)	1.0	0.0, 12.8	-0.10 (2.83)	0.0	-8.2, 8.8	0.7582
WEEK 6	122	2.72	2.44 (3.62)	0.5	0.0, 14.6	-0.28 (3.16)	0.0	-7.8, 9.6	0.3320
Low Dose	56	2.82	2.55 (3.34)	0.9	0.0, 12.2	-0.27 (3.20)	0.0	-6.8, 9.6	0.5296
High Dose	66	2.63	2.34 (3.86)	0.1	0.0, 14.6	-0.29 (3.15)	-0.1	-7.8, 9.6	0.4642
WEEK 13	70	3.08	2.20 (3.71)	0.0	0.0, 16.0	-0.88 (3.93)	-0.6	-12.2, 13.2	0.0649
Low Dose	32	3.09	2.95 (4.40)	0.5	0.0, 16.0	-0.14 (4.12)	-0.5	-8.0, 13.2	0.8499
High Dose	38	3.07	1.57 (2.92)	0.0	0.0, 14.4	-1.51 (3.70)	-0.7	-12.2, 7.2	0.0165*
WEEK 26	78	2.39	1.95 (3.14)	0.6	0.0, 14.9	-0.45 (3.29)	0.0	-12.2, 7.8	0.2364
Low Dose	33	2.50	1.94 (2.94)	0.7	0.0, 12.1	-0.56 (2.75)	0.0	-6.8, 5.4	0.2550
High Dose	45	2.32	1.96 (3.32)	0.0	0.0, 14.9	-0.36 (3.67)	0.0	-12.2, 7.8	0.5091
WEEK 39	65	2.30	2.16 (3.83)	0.0	0.0, 16.0	-0.13 (3.39)	0.0	-7.8, 15.4	0.7507
Low Dose	30	2.52	2.09 (4.05)	0.0	0.0, 15.4	-0.43 (3.97)	-0.4	-6.8, 15.4	0.5550
High Dose	35	2.10	2.23 (3.68)	0.0	0.0, 16.0	0.12 (2.83)	0.0	-7.8, 5.8	0.8006

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Gender:Male (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 52	62	2.63	2.47 (4.13)	0.3	0.0, 16.0	-0.16 (3.05)	0.0	-7.3, 7.5	0.6742
Low Dose	25	2.71	2.13 (3.92)	0.3	0.0, 16.0	-0.58 (3.06)	-0.4	-6.8, 6.0	0.3511
High Dose	37	2.58	2.70 (4.30)	0.5	0.0, 16.0	0.12 (3.05)	0.0	-7.3, 7.5	0.8138
Average Daily Normalized 'On' Time With Troublesome Dyskinesia									
BASELINE	141		0.77 (1.44)	0.0	0.0, 8.8				
Low Dose	63		1.07 (1.69)	0.2	0.0, 8.8				
High Dose	78		0.52 (1.16)	0.0	0.0, 5.0				
WEEK 1	133	0.71	0.93 (2.05)	0.0	0.0, 11.7	0.22 (1.81)	0.0	-5.7, 7.9	0.1624
Low Dose	59	1.05	1.14 (2.20)	0.0	0.0, 11.7	0.10 (1.92)	0.0	-5.7, 7.9	0.6962
High Dose	74	0.44	0.75 (1.91)	0.0	0.0, 9.8	0.32 (1.72)	0.0	-3.7, 7.0	0.1167
WEEK 6	122	0.61	0.42 (1.31)	0.0	0.0, 9.0	-0.19 (1.43)	0.0	-4.9, 6.9	0.1425
Low Dose	56	0.85	0.66 (1.75)	0.0	0.0, 9.0	-0.19 (1.71)	0.0	-3.4, 6.9	0.4157
High Dose	66	0.41	0.22 (0.71)	0.0	0.0, 4.4	-0.19 (1.15)	0.0	-4.9, 4.4	0.1753

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Gender:Male (Cont.)									
Average Daily Normalized 'On' Time With Troublesome Dyskinesia (Cont.)									
WEEK 13	70	0.79	0.30 (0.93)	0.0	0.0, 5.5	-0.49 (1.08)	0.0	-4.9, 1.7	<=0.001***
Low Dose	32	0.90	0.37 (1.09)	0.0	0.0, 5.5	-0.53 (1.14)	0.0	-3.4, 1.7	0.0135*
High Dose	38	0.69	0.24 (0.77)	0.0	0.0, 3.7	-0.45 (1.04)	0.0	-4.9, 0.9	0.0113*
WEEK 26	78	0.67	0.45 (1.75)	0.0	0.0, 12.1	-0.22 (1.86)	0.0	-4.9, 8.8	0.2978
Low Dose	33	0.76	0.57 (2.19)	0.0	0.0, 12.1	-0.19 (1.90)	0.0	-3.6, 7.2	0.5637
High Dose	45	0.60	0.36 (1.36)	0.0	0.0, 8.8	-0.24 (1.85)	0.0	-4.9, 8.8	0.3869
WEEK 39	65	0.65	0.26 (0.68)	0.0	0.0, 2.9	-0.39 (1.26)	0.0	-5.0, 2.7	0.0151*
Low Dose	30	0.68	0.19 (0.50)	0.0	0.0, 2.4	-0.49 (1.07)	0.0	-3.6, 0.8	0.0178*
High Dose	35	0.63	0.32 (0.80)	0.0	0.0, 2.9	-0.30 (1.41)	0.0	-5.0, 2.7	0.2120
WEEK 52	62	0.55	0.41 (1.07)	0.0	0.0, 5.3	-0.13 (1.46)	0.0	-5.0, 5.3	0.4774
Low Dose	25	0.47	0.21 (0.72)	0.0	0.0, 3.3	-0.27 (1.17)	0.0	-3.4, 3.3	0.2639
High Dose	37	0.59	0.55 (1.24)	0.0	0.0, 5.3	-0.04 (1.64)	0.0	-5.0, 5.3	0.8793

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Gender:Male (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia									
BASELINE	141		9.39 (2.33)	9.6	3.1, 16.0				
Low Dose	63		9.59 (2.54)	10.1	3.1, 16.0				
High Dose	78		9.22 (2.14)	9.3	3.4, 16.0				
WEEK 1	133	9.41	11.43 (3.55)	11.7	0.0, 16.0	2.02 (3.56)	2.5	-8.0, 9.7	<=0.001***
Low Dose	59	9.53	11.31 (3.46)	11.2	1.6, 16.0	1.78 (3.39)	2.2	-5.6, 9.7	<=0.001***
High Dose	74	9.32	11.53 (3.63)	11.9	0.0, 16.0	2.21 (3.70)	2.6	-8.0, 8.9	<=0.001***
WEEK 6	122	9.42	12.47 (3.21)	13.0	0.0, 16.0	3.05 (3.27)	3.5	-9.9, 10.6	<=0.001***
Low Dose	56	9.56	12.37 (3.56)	12.9	0.0, 16.0	2.80 (3.50)	3.7	-9.9, 9.2	<=0.001***
High Dose	66	9.30	12.57 (2.90)	13.1	4.7, 16.0	3.27 (3.07)	3.5	-2.6, 10.6	<=0.001***
WEEK 13	70	9.76	12.74 (3.61)	13.8	2.6, 16.0	2.98 (3.21)	3.2	-5.2, 9.2	<=0.001***
Low Dose	32	9.97	12.93 (3.76)	13.9	2.6, 16.0	2.96 (3.00)	3.7	-4.9, 7.2	<=0.001***
High Dose	38	9.59	12.59 (3.53)	13.7	5.3, 16.0	3.00 (3.41)	3.1	-5.2, 9.2	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Gender:Male (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia (Cont.)									
WEEK 26	78	9.51	12.60 (3.52)	14.0	1.5, 16.0	3.09 (3.24)	2.9	-5.5, 10.6	<=0.001***
Low Dose	33	9.75	12.15 (4.25)	13.3	1.5, 16.0	2.40 (3.57)	2.9	-5.5, 9.4	<=0.001***
High Dose	45	9.33	12.93 (2.87)	14.0	7.1, 16.0	3.60 (2.91)	2.9	-2.5, 10.6	<=0.001***
WEEK 39	65	9.63	12.89 (3.24)	13.1	2.7, 16.0	3.26 (3.05)	3.4	-9.1, 9.4	<=0.001***
Low Dose	30	9.96	12.47 (3.71)	12.7	2.7, 16.0	2.51 (3.53)	2.9	-9.1, 9.4	<=0.001***
High Dose	35	9.34	13.24 (2.78)	13.8	6.6, 16.0	3.90 (2.43)	3.8	-1.3, 8.9	<=0.001***
WEEK 52	62	9.77	12.76 (3.24)	13.5	4.5, 16.0	2.99 (2.89)	3.0	-5.4, 11.2	<=0.001***
Low Dose	25	10.25	12.80 (3.03)	13.4	5.1, 16.0	2.55 (2.33)	2.9	-5.4, 5.9	<=0.001***
High Dose	37	9.45	12.73 (3.41)	14.2	4.5, 16.0	3.28 (3.21)	3.4	-2.8, 11.2	<=0.001***
Race:WHITE									
Average Daily Normalized 'Off' Time									
BASELINE	199		5.75 (2.25)	5.8	0.0, 12.6				
Low Dose	98		5.46 (2.16)	5.6	0.0, 10.2				
High Dose	101		6.04 (2.30)	6.1	0.0, 12.6				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:WHITE (Cont.)									
Average Daily Normalized 'Off' Time (Cont.)									
WEEK 1	190	5.76	3.86 (3.46)	2.9	0.0, 16.0	-1.91 (3.68)	-2.1	-10.2, 10.4	<=0.001***
Low Dose	93	5.53	3.45 (3.17)	2.7	0.0, 11.2	-2.08 (3.45)	-2.4	-10.2, 5.9	<=0.001***
High Dose	97	5.99	4.24 (3.70)	3.1	0.0, 16.0	-1.75 (3.90)	-2.0	-8.9, 10.4	<=0.001***
WEEK 6	173	5.82	3.25 (3.08)	2.9	0.0, 16.0	-2.57 (3.52)	-2.9	-10.6, 9.9	<=0.001***
Low Dose	86	5.59	2.93 (3.16)	2.6	0.0, 16.0	-2.66 (3.54)	-2.9	-10.2, 9.9	<=0.001***
High Dose	87	6.05	3.57 (2.98)	3.0	0.0, 10.7	-2.48 (3.51)	-2.9	-10.6, 6.8	<=0.001***
WEEK 13	100	5.47	2.73 (3.12)	1.7	0.0, 12.6	-2.75 (3.43)	-3.2	-9.9, 7.8	<=0.001***
Low Dose	51	5.31	2.22 (2.81)	1.1	0.0, 12.6	-3.09 (3.26)	-3.4	-9.9, 7.8	<=0.001***
High Dose	49	5.65	3.26 (3.37)	2.0	0.0, 10.7	-2.39 (3.60)	-3.2	-9.2, 6.3	<=0.001***
WEEK 26	108	5.83	2.20 (2.52)	1.2	0.0, 9.8	-3.62 (2.90)	-3.9	-10.6, 5.5	<=0.001***
Low Dose	51	5.63	1.66 (2.14)	0.7	0.0, 7.4	-3.97 (2.59)	-4.0	-10.2, 3.3	<=0.001***
High Dose	57	6.00	2.69 (2.75)	1.7	0.0, 9.8	-3.32 (3.14)	-2.9	-10.6, 5.5	<=0.001***
WEEK 39	92	5.68	2.33 (2.46)	1.7	0.0, 11.4	-3.35 (2.84)	-3.1	-9.9, 6.4	<=0.001***
Low Dose	48	5.47	2.06 (2.32)	1.4	0.0, 11.4	-3.41 (2.80)	-3.1	-9.9, 6.4	<=0.001***
High Dose	44	5.91	2.63 (2.60)	2.0	0.0, 7.3	-3.29 (2.92)	-3.4	-9.2, 4.0	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:WHITE (Cont.)									
Average Daily Normalized 'Off' Time (Cont.)									
WEEK 52	81	5.69	2.27 (2.84)	0.9	0.0, 11.5	-3.43 (3.05)	-3.7	-11.2, 5.9	<=0.001***
Low Dose	40	5.65	2.25 (2.69)	1.2	0.0, 10.9	-3.40 (2.97)	-3.7	-10.2, 5.9	<=0.001***
High Dose	41	5.74	2.29 (3.02)	0.7	0.0, 11.5	-3.45 (3.17)	-3.7	-11.2, 2.8	<=0.001***
Average Daily Normalized 'On' Time Without Dyskinesia									
BASELINE	199		6.63 (3.42)	6.7	0.0, 15.4				
Low Dose	98		6.52 (3.59)	6.6	0.0, 15.4				
High Dose	101		6.74 (3.27)	6.7	0.0, 13.8				
WEEK 1	190	6.61	8.80 (4.52)	8.8	0.0, 16.0	2.19 (4.09)	1.9	-8.8, 12.0	<=0.001***
Low Dose	93	6.37	8.61 (4.59)	8.6	0.0, 16.0	2.24 (3.85)	1.9	-8.8, 10.7	<=0.001***
High Dose	97	6.83	8.98 (4.47)	9.0	0.0, 16.0	2.14 (4.34)	2.1	-8.1, 12.0	<=0.001***
WEEK 6	173	6.62	10.28 (4.42)	11.2	0.0, 16.0	3.67 (4.16)	3.9	-8.3, 12.7	<=0.001***
Low Dose	86	6.46	10.22 (4.60)	10.9	0.0, 16.0	3.75 (4.20)	4.0	-8.3, 12.7	<=0.001***
High Dose	87	6.77	10.34 (4.25)	11.2	0.0, 16.0	3.58 (4.14)	3.5	-6.7, 12.0	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:WHITE (Cont.)									
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 13	100	6.79	11.39 (4.25)	12.5	0.0, 16.0	4.60 (4.09)	4.8	-6.3, 15.2	<=0.001***
Low Dose	51	6.86	11.63 (4.39)	13.2	0.0, 16.0	4.77 (3.90)	4.9	-3.9, 15.2	<=0.001***
High Dose	49	6.72	11.14 (4.13)	11.3	0.9, 16.0	4.42 (4.30)	4.7	-6.3, 14.1	<=0.001***
WEEK 26	108	7.03	11.65 (4.05)	13.0	0.0, 16.0	4.62 (4.39)	5.1	-11.0, 14.1	<=0.001***
Low Dose	51	7.15	12.51 (3.37)	13.4	0.5, 16.0	5.36 (3.41)	5.4	-2.4, 11.5	<=0.001***
High Dose	57	6.92	10.89 (4.47)	12.0	0.0, 16.0	3.96 (5.05)	4.6	-11.0, 14.1	<=0.001***
WEEK 39	92	7.28	11.46 (4.06)	11.8	0.0, 16.0	4.18 (4.16)	4.1	-10.6, 13.5	<=0.001***
Low Dose	48	7.27	11.77 (4.19)	12.6	0.6, 16.0	4.50 (4.34)	5.0	-10.6, 11.4	<=0.001***
High Dose	44	7.28	11.11 (3.95)	11.3	0.0, 16.0	3.83 (3.99)	3.3	-2.9, 13.5	<=0.001***
WEEK 52	81	7.24	10.92 (4.82)	12.4	0.0, 16.0	3.68 (4.52)	4.3	-12.0, 13.8	<=0.001***
Low Dose	40	7.15	11.51 (4.54)	13.2	0.0, 16.0	4.36 (4.23)	4.8	-6.5, 11.3	<=0.001***
High Dose	41	7.33	10.35 (5.06)	11.3	0.0, 16.0	3.02 (4.74)	2.5	-12.0, 13.8	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Race:WHITE (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia									
BASELINE	199		2.64 (2.52)	2.4	0.0, 12.2				
Low Dose	98		2.64 (2.31)	2.6	0.0, 10.3				
High Dose	101		2.64 (2.71)	2.0	0.0, 12.2				
WEEK 1	190	2.67	2.37 (2.90)	1.1	0.0, 13.6	-0.29 (2.89)	0.0	-8.5, 13.6	0.1648
Low Dose	93	2.71	2.67 (2.96)	2.0	0.0, 13.6	-0.04 (3.06)	0.0	-8.5, 13.6	0.9055
High Dose	97	2.63	2.09 (2.83)	0.7	0.0, 11.9	-0.54 (2.71)	0.0	-8.2, 8.8	0.0541
WEEK 6	173	2.69	2.03 (3.21)	0.5	0.0, 15.4	-0.66 (2.85)	-0.4	-7.8, 11.6	0.0026**
Low Dose	86	2.71	2.26 (3.18)	1.0	0.0, 15.4	-0.45 (2.89)	-0.3	-7.6, 11.6	0.1497
High Dose	87	2.68	1.81 (3.25)	0.0	0.0, 14.6	-0.87 (2.82)	-0.6	-7.8, 7.5	0.0051**
WEEK 13	100	2.98	1.55 (2.98)	0.0	0.0, 15.5	-1.43 (3.24)	-1.1	-12.2, 7.9	<=0.001***
Low Dose	51	2.88	1.69 (3.22)	0.0	0.0, 15.5	-1.19 (3.07)	-1.2	-8.0, 7.9	0.0080**
High Dose	49	3.08	1.40 (2.74)	0.0	0.0, 14.4	-1.68 (3.42)	-0.9	-12.2, 7.2	0.0012**

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Race:WHITE (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 26	108	2.41	1.80 (2.97)	0.6	0.0, 15.2	-0.61 (3.38)	-0.1	-12.2, 12.0	0.0614
Low Dose	51	2.35	1.47 (2.13)	0.7	0.0, 10.8	-0.88 (2.75)	-0.6	-6.8, 5.4	0.0265*
High Dose	57	2.47	2.09 (3.55)	0.0	0.0, 15.2	-0.38 (3.86)	-0.1	-12.2, 12.0	0.4642
WEEK 39	92	2.42	1.90 (3.35)	0.0	0.0, 16.0	-0.53 (3.28)	-0.1	-7.8, 15.4	0.1278
Low Dose	48	2.51	1.95 (3.32)	0.1	0.0, 15.4	-0.56 (3.52)	-0.1	-7.8, 15.4	0.2767
High Dose	44	2.33	1.84 (3.42)	0.0	0.0, 16.0	-0.49 (3.04)	-0.1	-7.8, 6.1	0.2915
WEEK 52	81	2.52	2.39 (4.21)	0.2	0.0, 16.0	-0.14 (3.51)	0.0	-7.3, 12.9	0.7270
Low Dose	40	2.57	2.00 (3.95)	0.1	0.0, 16.0	-0.57 (3.44)	-0.4	-6.8, 9.2	0.2981
High Dose	41	2.47	2.76 (4.47)	0.5	0.0, 16.0	0.29 (3.56)	0.0	-7.3, 12.9	0.6043
Average Daily Normalized 'On' Time With Troublesome Dyskinesia									
BASELINE	199		0.97 (1.73)	0.0	0.0, 10.5				
Low Dose	98		1.38 (2.08)	0.2	0.0, 10.5				
High Dose	101		0.58 (1.21)	0.0	0.0, 5.3				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Race:WHITE (Cont.)									
Average Daily Normalized 'On' Time With Troublesome Dyskinesia (Cont.)									
WEEK 1	190	0.96	0.97 (2.05)	0.0	0.0, 11.7	0.01 (1.78)	0.0	-5.7, 10.5	0.9551
Low Dose	93	1.39	1.26 (2.31)	0.0	0.0, 11.7	-0.13 (1.86)	0.0	-5.7, 10.5	0.5025
High Dose	97	0.55	0.69 (1.73)	0.0	0.0, 9.8	0.14 (1.70)	0.0	-4.9, 7.0	0.4237
WEEK 6	173	0.87	0.44 (1.28)	0.0	0.0, 9.0	-0.43 (1.48)	0.0	-9.2, 5.3	<=0.001***
Low Dose	86	1.23	0.60 (1.60)	0.0	0.0, 9.0	-0.64 (1.77)	0.0	-9.2, 5.3	0.0012**
High Dose	87	0.51	0.28 (0.84)	0.0	0.0, 4.4	-0.23 (1.09)	0.0	-4.9, 4.4	0.0564
WEEK 13	100	0.76	0.33 (1.16)	0.0	0.0, 8.0	-0.42 (1.29)	0.0	-5.2, 6.0	0.0014**
Low Dose	51	0.95	0.46 (1.46)	0.0	0.0, 8.0	-0.49 (1.49)	0.0	-5.2, 6.0	0.0223*
High Dose	49	0.55	0.20 (0.73)	0.0	0.0, 3.7	-0.35 (1.06)	0.0	-4.9, 2.6	0.0229*
WEEK 26	108	0.73	0.35 (1.51)	0.0	0.0, 12.1	-0.38 (1.79)	0.0	-5.1, 8.8	0.0288*
Low Dose	51	0.87	0.36 (1.77)	0.0	0.0, 12.1	-0.51 (1.80)	0.0	-5.1, 7.2	0.0473*
High Dose	57	0.60	0.34 (1.25)	0.0	0.0, 8.8	-0.27 (1.80)	0.0	-4.9, 8.8	0.2684
WEEK 39	92	0.62	0.32 (1.08)	0.0	0.0, 8.1	-0.30 (1.43)	0.0	-5.1, 7.3	0.0464*
Low Dose	48	0.76	0.23 (0.71)	0.0	0.0, 3.8	-0.53 (1.12)	0.0	-5.1, 0.8	0.0019**
High Dose	44	0.47	0.42 (1.37)	0.0	0.0, 8.1	-0.05 (1.69)	0.0	-5.0, 7.3	0.8444

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:WHITE (Cont.)									
Average Daily Normalized 'On' Time With Troublesome Dyskinesia (Cont.)									
WEEK 52	81	0.54	0.43 (1.16)	0.0	0.0, 6.3	-0.12 (1.55)	0.0	-5.0, 6.3	0.4928
Low Dose	40	0.63	0.25 (0.71)	0.0	0.0, 3.3	-0.38 (1.17)	0.0	-2.7, 3.3	0.0435*
High Dose	41	0.46	0.60 (1.46)	0.0	0.0, 6.3	0.14 (1.83)	0.0	-5.0, 6.3	0.6255
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia									
BASELINE	199		9.27 (2.55)	9.6	0.3, 16.0				
Low Dose	98		9.16 (2.77)	9.8	0.3, 16.0				
High Dose	101		9.38 (2.33)	9.5	2.6, 16.0				
WEEK 1	190	9.27	11.17 (3.73)	11.7	0.0, 16.0	1.90 (3.81)	2.0	-10.4, 11.3	<=0.001***
Low Dose	93	9.08	11.29 (3.69)	12.0	1.6, 16.0	2.21 (3.52)	2.6	-5.9, 11.3	<=0.001***
High Dose	97	9.46	11.06 (3.78)	11.7	0.0, 16.0	1.61 (4.07)	1.5	-10.4, 8.9	<=0.001***
WEEK 6	173	9.31	12.31 (3.23)	12.8	0.0, 16.0	3.00 (3.54)	3.3	-9.9, 10.6	<=0.001***
Low Dose	86	9.17	12.47 (3.43)	12.8	0.0, 16.0	3.30 (3.49)	3.3	-9.9, 10.5	<=0.001***
High Dose	87	9.45	12.15 (3.04)	12.6	5.1, 16.0	2.71 (3.57)	3.3	-6.8, 10.6	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:WHITE (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia (Cont.)									
WEEK 13	100	9.77	12.94 (3.31)	14.1	3.4, 16.0	3.17 (3.40)	3.4	-6.3, 9.9	<=0.001***
Low Dose	51	9.74	13.32 (3.19)	14.5	3.4, 16.0	3.58 (3.05)	4.0	-4.9, 9.9	<=0.001***
High Dose	49	9.80	12.54 (3.41)	13.6	5.3, 16.0	2.74 (3.71)	3.2	-6.3, 9.2	<=0.001***
WEEK 26	108	9.44	13.45 (2.84)	14.4	1.5, 16.0	4.01 (3.35)	4.0	-5.5, 12.5	<=0.001***
Low Dose	51	9.50	13.98 (2.83)	15.2	1.5, 16.0	4.48 (3.33)	4.4	-4.5, 12.5	<=0.001***
High Dose	57	9.39	12.98 (2.79)	14.0	6.2, 16.0	3.58 (3.33)	3.0	-5.5, 10.6	<=0.001***
WEEK 39	92	9.70	13.35 (2.82)	14.1	2.4, 16.0	3.65 (3.16)	3.3	-9.2, 9.9	<=0.001***
Low Dose	48	9.78	13.72 (2.46)	14.3	4.6, 16.0	3.94 (2.94)	3.1	-5.9, 9.9	<=0.001***
High Dose	44	9.61	12.95 (3.14)	13.6	2.4, 16.0	3.34 (3.39)	3.4	-9.2, 9.7	<=0.001***
WEEK 52	81	9.76	13.31 (2.94)	14.0	4.5, 16.0	3.54 (3.06)	3.4	-5.4, 11.2	<=0.001***
Low Dose	40	9.72	13.51 (2.65)	13.8	5.1, 16.0	3.79 (2.99)	3.5	-5.4, 10.2	<=0.001***
High Dose	41	9.80	13.11 (3.21)	14.6	4.5, 16.0	3.31 (3.15)	3.4	-2.8, 11.2	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Race:ASIAN									
Average Daily Normalized 'Off' Time									
BASELINE	34		6.68 (2.04)	6.8	0.0, 10.3				
Low Dose	27		6.45 (2.13)	6.6	0.0, 10.3				
High Dose	7		7.60 (1.44)	8.1	5.7, 9.6				
WEEK 1	32	6.70	4.78 (3.25)	4.7	0.0, 13.8	-1.92 (3.79)	-2.2	-9.7, 4.7	0.0074**
Low Dose	26	6.43	4.72 (3.18)	4.6	0.0, 13.8	-1.71 (3.75)	-2.0	-9.7, 4.7	0.0283*
High Dose	6	7.89	5.05 (3.84)	5.1	0.0, 10.9	-2.83 (4.22)	-3.9	-8.3, 2.8	0.1613
WEEK 6	29	6.56	5.41 (3.69)	4.3	0.0, 13.4	-1.15 (3.98)	-2.7	-7.5, 6.8	0.1319
Low Dose	23	6.21	5.00 (3.55)	3.8	0.0, 13.4	-1.21 (3.90)	-2.4	-7.5, 6.2	0.1520
High Dose	6	7.89	6.96 (4.16)	5.8	1.6, 12.5	-0.92 (4.67)	-3.1	-5.4, 6.8	0.6493
WEEK 13	13	5.95	5.96 (4.52)	6.2	0.0, 13.4	0.01 (4.89)	0.3	-7.0, 8.1	0.9927
Low Dose	12	5.96	5.94 (4.72)	5.0	0.0, 13.4	-0.01 (5.10)	-0.3	-7.0, 8.1	0.9930
High Dose	1	5.87	6.20 (N/A)	6.2	6.2, 6.2	0.32 (N/A)	0.3	0.3, 0.3	

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Race:ASIAN (Cont.)									
Average Daily Normalized 'Off' Time (Cont.)									
WEEK 26	18	6.63	5.50 (4.17)	5.4	0.0, 14.3	-1.13 (4.40)	-0.7	-8.1, 7.1	0.2919
Low Dose	14	6.25	5.56 (4.41)	5.4	0.0, 14.3	-0.69 (4.62)	-0.4	-7.8, 7.1	0.5870
High Dose	4	7.98	5.31 (3.81)	6.2	0.0, 8.9	-2.67 (3.64)	-1.1	-8.1, -0.4	0.2388
WEEK 39	18	6.78	4.08 (2.97)	4.2	0.0, 12.3	-2.70 (3.48)	-1.7	-8.1, 5.1	0.0043**
Low Dose	14	6.44	4.09 (3.09)	4.2	0.0, 12.3	-2.35 (3.51)	-1.6	-8.1, 5.1	0.0266*
High Dose	4	7.98	4.03 (2.93)	4.6	0.0, 6.8	-3.95 (3.53)	-3.6	-8.1, -0.6	0.1110
WEEK 52	15	7.00	3.80 (3.06)	3.7	0.0, 10.1	-3.20 (3.35)	-3.5	-8.7, 4.1	0.0024**
Low Dose	11	6.64	3.57 (3.20)	3.0	0.0, 10.1	-3.07 (3.54)	-3.5	-8.7, 4.1	0.0165*
High Dose	4	7.98	4.41 (2.99)	5.6	0.0, 6.4	-3.57 (3.23)	-2.7	-8.1, -0.7	0.1143
Average Daily Normalized 'On' Time Without Dyskinesia									
BASELINE	34		5.67 (2.94)	5.8	0.0, 11.8				
Low Dose	27		5.61 (3.03)	5.1	0.0, 11.8				
High Dose	7		5.91 (2.79)	6.5	0.5, 8.4				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:ASIAN (Cont.)									
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 1	32	5.62	6.34 (4.03)	6.8	0.3, 16.0	0.72 (3.85)	0.7	-8.9, 10.2	0.2970
Low Dose	26	5.48	5.96 (3.81)	6.4	0.3, 14.9	0.48 (3.90)	0.6	-8.9, 10.2	0.5371
High Dose	6	6.22	8.00 (4.92)	8.0	1.2, 16.0	1.78 (3.78)	1.0	-2.8, 8.3	0.3018
WEEK 6	29	5.95	8.38 (4.29)	8.6	0.0, 14.4	2.43 (4.98)	3.5	-6.4, 13.8	0.0137*
Low Dose	23	5.88	9.25 (3.81)	9.3	2.1, 14.4	3.37 (4.78)	3.9	-6.1, 13.8	0.0027**
High Dose	6	6.22	5.06 (4.74)	3.1	0.0, 11.2	-1.16 (4.33)	-1.0	-6.4, 3.5	0.5391
WEEK 13	13	5.47	6.53 (5.28)	5.9	0.0, 14.7	1.06 (5.15)	1.1	-9.0, 9.6	0.4744
Low Dose	12	5.59	6.72 (5.47)	6.1	0.0, 14.7	1.13 (5.38)	1.4	-9.0, 9.6	0.4812
High Dose	1	4.05	4.20 (N/A)	4.2	4.2, 4.2	0.15 (N/A)	0.1	0.1, 0.1	
WEEK 26	18	5.90	8.42 (5.13)	7.8	0.0, 16.0	2.52 (4.76)	2.3	-10.1, 9.5	0.0385*
Low Dose	14	5.73	8.18 (5.36)	7.8	0.0, 16.0	2.45 (5.16)	3.2	-10.1, 9.5	0.0986
High Dose	4	6.50	9.24 (4.80)	7.9	5.1, 16.0	2.74 (3.60)	1.2	0.4, 8.1	0.2257
WEEK 39	18	5.64	9.62 (4.13)	10.3	0.3, 16.0	3.98 (3.01)	4.7	-1.9, 8.1	<=0.001***
Low Dose	14	5.39	9.56 (4.16)	10.5	0.3, 16.0	4.17 (3.02)	4.9	-1.9, 8.0	<=0.001***
High Dose	4	6.50	9.82 (4.67)	9.3	4.7, 16.0	3.32 (3.35)	2.3	0.6, 8.1	0.1414

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Race:ASIAN (Cont.)									
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 52	15	5.88	10.23 (4.16)	10.7	4.0, 16.0	4.35 (2.77)	3.1	-0.1, 8.7	<=0.001***
Low Dose	11	5.66	10.53 (4.06)	11.0	4.2, 16.0	4.87 (2.41)	4.8	1.9, 8.7	<=0.001***
High Dose	4	6.50	9.42 (4.99)	8.8	4.0, 16.0	2.91 (3.57)	1.8	-0.1, 8.1	0.2009
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia									
BASELINE	34		2.72 (2.80)	2.4	0.0, 8.5				
Low Dose	27		2.97 (2.73)	2.8	0.0, 8.0				
High Dose	7		1.75 (3.10)	0.3	0.0, 8.5				
WEEK 1	32	2.81	3.85 (4.13)	2.5	0.0, 14.9	1.04 (3.49)	0.1	-5.4, 13.2	0.1021
Low Dose	26	3.08	4.07 (4.00)	2.7	0.0, 14.9	0.99 (3.80)	0.1	-5.4, 13.2	0.1978
High Dose	6	1.63	2.90 (4.95)	1.0	0.0, 12.8	1.27 (1.81)	0.7	-0.4, 4.3	0.1459
WEEK 6	29	2.72	2.09 (3.35)	0.5	0.0, 12.3	-0.63 (3.34)	0.0	-6.7, 9.6	0.3169
Low Dose	23	3.01	1.60 (2.46)	0.5	0.0, 9.0	-1.41 (2.76)	0.0	-6.7, 4.4	0.0227*
High Dose	6	1.63	3.98 (5.53)	1.0	0.0, 12.3	2.35 (3.95)	0.8	-1.0, 9.6	0.2048

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:ASIAN (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 13	13	3.15	3.18 (4.95)	1.2	0.0, 16.0	0.03 (4.96)	0.0	-6.5, 13.2	0.9809
Low Dose	12	3.20	3.21 (5.17)	0.7	0.0, 16.0	0.01 (5.18)	-0.3	-6.5, 13.2	0.9947
High Dose	1	2.48	2.80 (N/A)	2.8	2.8, 2.8	0.32 (N/A)	0.3	0.3, 0.3	
WEEK 26	18	2.86	1.84 (3.04)	0.2	0.0, 12.1	-1.01 (2.90)	0.0	-6.7, 4.6	0.1559
Low Dose	14	3.50	2.09 (3.33)	0.2	0.0, 12.1	-1.41 (3.19)	-2.3	-6.7, 4.6	0.1218
High Dose	4	0.62	0.99 (1.76)	0.2	0.0, 3.6	0.37 (0.54)	0.2	0.0, 1.1	0.2625
WEEK 39	18	2.73	1.95 (3.32)	0.0	0.0, 13.2	-0.78 (3.26)	0.0	-6.7, 5.2	0.3235
Low Dose	14	3.33	2.01 (3.65)	0.0	0.0, 13.2	-1.32 (3.48)	-0.9	-6.7, 5.2	0.1800
High Dose	4	0.62	1.72 (2.12)	1.3	0.0, 4.3	1.10 (1.30)	0.9	0.0, 2.5	0.1889
WEEK 52	15	2.31	1.72 (2.20)	0.3	0.0, 6.7	-0.59 (2.55)	0.0	-6.7, 3.9	0.3890
Low Dose	11	2.92	1.77 (2.31)	0.3	0.0, 6.7	-1.16 (2.72)	0.0	-6.7, 3.9	0.1896
High Dose	4	0.62	1.60 (2.16)	0.9	0.0, 4.6	0.98 (1.13)	0.9	0.0, 2.1	0.1832

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:ASIAN (Cont.)									
Average Daily Normalized 'On' Time With Troublesome Dyskinesia									
BASELINE	34		0.93 (1.77)	0.0	0.0, 7.2				
Low Dose	27		0.98 (1.89)	0.0	0.0, 7.2				
High Dose	7		0.74 (1.31)	0.0	0.0, 3.6				
WEEK 1	32	0.87	1.03 (2.27)	0.0	0.0, 10.3	0.16 (2.39)	0.0	-6.0, 7.9	0.7122
Low Dose	26	1.01	1.26 (2.47)	0.1	0.0, 10.3	0.24 (2.65)	0.0	-6.0, 7.9	0.6420
High Dose	6	0.26	0.04 (0.10)	0.0	0.0, 0.3	-0.22 (0.35)	0.0	-0.8, 0.0	0.1861
WEEK 6	29	0.77	0.12 (0.52)	0.0	0.0, 2.7	-0.65 (1.69)	0.0	-7.2, 1.0	0.0473*
Low Dose	23	0.91	0.16 (0.58)	0.0	0.0, 2.7	-0.75 (1.88)	0.0	-7.2, 1.0	0.0684
High Dose	6	0.26	0.00 (0.00)	0.0	0.0, 0.0	-0.26 (0.41)	0.0	-0.8, 0.0	0.1748
WEEK 13	13	1.43	0.33 (0.85)	0.0	0.0, 2.8	-1.10 (2.39)	0.0	-7.2, 1.3	0.1220
Low Dose	12	1.25	0.13 (0.43)	0.0	0.0, 1.5	-1.13 (2.49)	0.0	-7.2, 1.3	0.1451
High Dose	1	3.59	2.81 (N/A)	2.8	2.8, 2.8	-0.79 (N/A)	-0.8	-0.8, -0.8	

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Race:ASIAN (Cont.)									
Average Daily Normalized 'On' Time With Troublesome Dyskinesia (Cont.)									
WEEK 26	18	0.61	0.23 (0.52)	0.0	0.0, 1.8	-0.37 (1.16)	0.0	-3.4, 1.3	0.1884
Low Dose	14	0.52	0.17 (0.38)	0.0	0.0, 1.3	-0.36 (1.25)	0.0	-3.4, 1.3	0.3082
High Dose	4	0.90	0.46 (0.92)	0.0	0.0, 1.8	-0.44 (0.87)	0.0	-1.7, 0.0	0.3910
WEEK 39	18	0.86	0.36 (0.89)	0.0	0.0, 3.5	-0.50 (0.99)	0.0	-3.0, 0.0	0.0481*
Low Dose	14	0.85	0.34 (0.93)	0.0	0.0, 3.5	-0.51 (1.04)	0.0	-3.0, 0.0	0.0918
High Dose	4	0.90	0.43 (0.86)	0.0	0.0, 1.7	-0.47 (0.94)	0.0	-1.9, 0.0	0.3910
WEEK 52	15	0.81	0.25 (0.68)	0.0	0.0, 2.3	-0.56 (1.14)	0.0	-3.4, 0.0	0.0758
Low Dose	11	0.78	0.13 (0.44)	0.0	0.0, 1.5	-0.65 (1.28)	0.0	-3.4, 0.0	0.1250
High Dose	4	0.90	0.57 (1.14)	0.0	0.0, 2.3	-0.33 (0.65)	0.0	-1.3, 0.0	0.3910
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia									
BASELINE	34		8.39 (2.10)	8.7	2.2, 11.8				
Low Dose	27		8.57 (2.26)	9.0	2.2, 11.8				
High Dose	7		7.66 (1.21)	7.7	6.4, 9.5				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:ASIAN (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia (Cont.)									
WEEK 1	32	8.43	10.19 (3.33)	10.2	2.2, 16.0	1.76 (3.75)	1.1	-4.0, 9.7	0.0123*
Low Dose	26	8.56	10.03 (3.27)	9.9	2.2, 16.0	1.47 (3.69)	1.0	-4.0, 9.7	0.0538
High Dose	6	7.85	10.90 (3.85)	10.8	5.1, 16.0	3.05 (4.08)	4.2	-2.8, 8.3	0.1261
WEEK 6	29	8.67	10.47 (3.78)	11.5	2.6, 16.0	1.80 (3.90)	3.1	-6.0, 7.5	0.0193*
Low Dose	23	8.88	10.84 (3.69)	12.2	2.6, 16.0	1.96 (3.88)	3.1	-5.7, 7.5	0.0242*
High Dose	6	7.85	9.04 (4.16)	10.2	3.5, 14.4	1.18 (4.29)	3.1	-6.0, 5.4	0.5288
WEEK 13	13	8.62	9.70 (4.53)	9.4	2.6, 16.0	1.09 (3.71)	0.5	-5.0, 7.0	0.3109
Low Dose	12	8.79	9.93 (4.66)	10.5	2.6, 16.0	1.14 (3.87)	0.8	-5.0, 7.0	0.3291
High Dose	1	6.53	7.00 (N/A)	7.0	7.0, 7.0	0.46 (N/A)	0.5	0.5, 0.5	
WEEK 26	18	8.76	10.26 (4.16)	10.0	1.7, 16.0	1.50 (4.02)	0.7	-5.5, 8.1	0.1315
Low Dose	14	9.23	10.27 (4.37)	10.5	1.7, 16.0	1.04 (4.18)	0.5	-5.5, 7.8	0.3678
High Dose	4	7.12	10.23 (3.94)	8.9	7.1, 16.0	3.11 (3.38)	1.8	0.7, 8.1	0.1633
WEEK 39	18	8.36	11.57 (2.90)	11.6	3.7, 16.0	3.20 (3.15)	2.6	-2.1, 9.1	<=0.001***
Low Dose	14	8.72	11.57 (2.92)	11.6	3.7, 16.0	2.86 (3.20)	2.3	-2.1, 9.1	0.0053**
High Dose	4	7.12	11.54 (3.28)	10.6	9.0, 16.0	4.42 (3.02)	4.0	1.5, 8.1	0.0614

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:ASIAN (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia (Cont.)									
WEEK 52	15	8.19	11.95 (3.27)	12.3	5.9, 16.0	3.76 (2.97)	3.5	-1.2, 8.7	<=0.001***
Low Dose	11	8.58	12.29 (3.33)	13.0	5.9, 16.0	3.71 (3.14)	3.5	-1.2, 8.7	0.0028**
High Dose	4	7.12	11.01 (3.37)	9.7	8.6, 16.0	3.89 (2.90)	2.8	1.9, 8.1	0.0745
Race:OTHER									
Average Daily Normalized 'Off' Time									
BASELINE	3		6.91 (2.75)	8.5	3.7, 8.5				
Low Dose	2		6.13 (3.39)	6.1	3.7, 8.5				
High Dose	1		8.46 (N/A)	8.5	8.5, 8.5				
WEEK 1	3	6.91	2.44 (2.29)	2.8	0.0, 4.5	-4.47 (1.12)	-3.9	-5.8, -3.7	0.0201*
Low Dose	2	6.13	1.39 (1.96)	1.4	0.0, 2.8	-4.74 (1.43)	-4.7	-5.8, -3.7	0.1335
High Dose	1	8.46	4.53 (N/A)	4.5	4.5, 4.5	-3.92 (N/A)	-3.9	-3.9, -3.9	
WEEK 6	3	6.91	2.71 (3.86)	1.0	0.0, 7.1	-4.19 (3.13)	-3.7	-7.5, -1.3	0.1460
Low Dose	2	6.13	0.50 (0.71)	0.5	0.0, 1.0	-5.63 (2.68)	-5.6	-7.5, -3.7	0.2070
High Dose	1	8.46	7.14 (N/A)	7.1	7.1, 7.1	-1.32 (N/A)	-1.3	-1.3, -1.3	

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:OTHER (Cont.)									
Average Daily Normalized 'Off' Time (Cont.)									
WEEK 13	2	6.10	4.24 (5.99)	4.2	0.0, 8.5	-1.86 (2.65)	-1.9	-3.7, 0.0	0.5035
Low Dose	1	3.73	0.00 (N/A)	0.0	0.0, 0.0	-3.73 (N/A)	-3.7	-3.7, -3.7	
High Dose	1	8.46	8.48 (N/A)	8.5	8.5, 8.5	0.02 (N/A)	0.0	0.0, 0.0	
WEEK 26	1	3.73	0.00 (N/A)	0.0	0.0, 0.0	-3.73 (N/A)	-3.7	-3.7, -3.7	
Low Dose	1	3.73	0.00 (N/A)	0.0	0.0, 0.0	-3.73 (N/A)	-3.7	-3.7, -3.7	
High Dose	0								
WEEK 39	1	3.73	13.33 (N/A)	13.3	13.3, 13.3	9.60 (N/A)	9.6	9.6, 9.6	
Low Dose	1	3.73	13.33 (N/A)	13.3	13.3, 13.3	9.60 (N/A)	9.6	9.6, 9.6	
High Dose	0								
Average Daily Normalized 'On' Time Without Dyskinesia									
BASELINE	3		8.03 (0.90)	7.5	7.5, 9.1				
Low Dose	2		8.27 (1.13)	8.3	7.5, 9.1				
High Dose	1		7.54 (N/A)	7.5	7.5, 7.5				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:OTHER (Cont.)									
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 1	3	8.03	7.25 (4.01)	6.8	3.5, 11.5	-0.78 (4.16)	-2.3	-4.0, 3.9	0.7761
Low Dose	2	8.27	5.14 (2.34)	5.1	3.5, 6.8	-3.13 (1.21)	-3.1	-4.0, -2.3	0.1695
High Dose	1	7.54	11.47 (N/A)	11.5	11.5, 11.5	3.92 (N/A)	3.9	3.9, 3.9	
WEEK 6	3	8.03	4.09 (4.47)	3.4	0.0, 8.9	-3.94 (5.20)	-4.1	-9.1, 1.3	0.3194
Low Dose	2	8.27	1.70 (2.40)	1.7	0.0, 3.4	-6.57 (3.53)	-6.6	-9.1, -4.1	0.2310
High Dose	1	7.54	8.86 (N/A)	8.9	8.9, 8.9	1.32 (N/A)	1.3	1.3, 1.3	
WEEK 13	2	8.30	8.15 (0.89)	8.1	7.5, 8.8	-0.16 (0.19)	-0.2	-0.3, -0.0	0.4548
Low Dose	1	9.07	8.77 (N/A)	8.8	8.8, 8.8	-0.29 (N/A)	-0.3	-0.3, -0.3	
High Dose	1	7.54	7.52 (N/A)	7.5	7.5, 7.5	-0.02 (N/A)	-0.0	-0.0, -0.0	
WEEK 26	1	9.07	12.58 (N/A)	12.6	12.6, 12.6	3.52 (N/A)	3.5	3.5, 3.5	
Low Dose	1	9.07	12.58 (N/A)	12.6	12.6, 12.6	3.52 (N/A)	3.5	3.5, 3.5	
High Dose	0								
WEEK 39	1	9.07	2.67 (N/A)	2.7	2.7, 2.7	-6.40 (N/A)	-6.4	-6.4, -6.4	
Low Dose	1	9.07	2.67 (N/A)	2.7	2.7, 2.7	-6.40 (N/A)	-6.4	-6.4, -6.4	
High Dose	0								

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:OTHER (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia									
BASELINE	3		0.89 (1.54)	0.0	0.0, 2.7				
Low Dose	2		1.33 (1.89)	1.3	0.0, 2.7				
High Dose	1		0.00 (N/A)	0.0	0.0, 0.0				
WEEK 1	3	0.89	4.58 (4.61)	4.5	0.0, 9.2	3.69 (3.35)	4.5	0.0, 6.5	0.1969
Low Dose	2	1.33	6.86 (3.32)	6.9	4.5, 9.2	5.53 (1.43)	5.5	4.5, 6.5	0.1154
High Dose	1	0.00	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
WEEK 6	3	0.89	5.65 (6.18)	4.7	0.0, 12.2	4.76 (4.79)	4.7	0.0, 9.6	0.2274
Low Dose	2	1.33	8.47 (5.33)	8.5	4.7, 12.2	7.14 (3.45)	7.1	4.7, 9.6	0.2097
High Dose	1	0.00	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
WEEK 13	2	1.33	3.61 (5.11)	3.6	0.0, 7.2	2.28 (3.22)	2.3	0.0, 4.6	0.5000
Low Dose	1	2.67	7.23 (N/A)	7.2	7.2, 7.2	4.56 (N/A)	4.6	4.6, 4.6	
High Dose	1	0.00	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:OTHER (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 26	1	2.67	3.42 (N/A)	3.4	3.4, 3.4	0.75 (N/A)	0.7	0.7, 0.7	
Low Dose	1	2.67	3.42 (N/A)	3.4	3.4, 3.4	0.75 (N/A)	0.7	0.7, 0.7	
High Dose	0								
WEEK 39	1	2.67	0.00 (N/A)	0.0	0.0, 0.0	-2.67 (N/A)	-2.7	-2.7, -2.7	
Low Dose	1	2.67	0.00 (N/A)	0.0	0.0, 0.0	-2.67 (N/A)	-2.7	-2.7, -2.7	
High Dose	0								
Average Daily Normalized 'On' Time With Troublesome Dyskinesia									
BASELINE	3		0.18 (0.31)	0.0	0.0, 0.5				
Low Dose	2		0.27 (0.38)	0.3	0.0, 0.5				
High Dose	1		0.00 (N/A)	0.0	0.0, 0.0				
WEEK 1	3	0.18	1.74 (3.02)	0.0	0.0, 5.2	1.56 (3.18)	0.0	-0.5, 5.2	0.4843
Low Dose	2	0.27	2.61 (3.69)	2.6	0.0, 5.2	2.35 (4.07)	2.3	-0.5, 5.2	0.5648
High Dose	1	0.00	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:OTHER (Cont.)									
Average Daily Normalized 'On' Time With Troublesome Dyskinesia (Cont.)									
WEEK 6	3	0.18	3.56 (3.46)	3.8	0.0, 6.9	3.38 (3.46)	3.2	0.0, 6.9	0.2326
Low Dose	2	0.27	5.33 (2.23)	5.3	3.8, 6.9	5.07 (2.60)	5.1	3.2, 6.9	0.2220
High Dose	1	0.00	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
WEEK 13	2	0.27	0.00 (0.00)	0.0	0.0, 0.0	-0.27 (0.38)	-0.3	-0.5, 0.0	0.5000
Low Dose	1	0.53	0.00 (N/A)	0.0	0.0, 0.0	-0.53 (N/A)	-0.5	-0.5, -0.5	
High Dose	1	0.00	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
WEEK 26	1	0.53	0.00 (N/A)	0.0	0.0, 0.0	-0.53 (N/A)	-0.5	-0.5, -0.5	
Low Dose	1	0.53	0.00 (N/A)	0.0	0.0, 0.0	-0.53 (N/A)	-0.5	-0.5, -0.5	
High Dose	0								
WEEK 39	1	0.53	0.00 (N/A)	0.0	0.0, 0.0	-0.53 (N/A)	-0.5	-0.5, -0.5	
Low Dose	1	0.53	0.00 (N/A)	0.0	0.0, 0.0	-0.53 (N/A)	-0.5	-0.5, -0.5	
High Dose	0								

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:OTHER (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia									
BASELINE	3		8.92 (2.44)	7.5	7.5, 11.7				
Low Dose	2		9.60 (3.01)	9.6	7.5, 11.7				
High Dose	1		7.54 (N/A)	7.5	7.5, 7.5				
WEEK 1	3	8.92	11.82 (4.01)	11.5	8.0, 16.0	2.91 (2.07)	3.9	0.5, 4.3	0.1351
Low Dose	2	9.60	12.00 (5.66)	12.0	8.0, 16.0	2.40 (2.64)	2.4	0.5, 4.3	0.4214
High Dose	1	7.54	11.47 (N/A)	11.5	11.5, 11.5	3.92 (N/A)	3.9	3.9, 3.9	
WEEK 6	3	8.92	9.73 (2.21)	8.9	8.1, 12.2	0.82 (0.44)	0.6	0.5, 1.3	0.0850
Low Dose	2	9.60	10.17 (2.93)	10.2	8.1, 12.2	0.56 (0.08)	0.6	0.5, 0.6	0.0631
High Dose	1	7.54	8.86 (N/A)	8.9	8.9, 8.9	1.32 (N/A)	1.3	1.3, 1.3	
WEEK 13	2	9.64	11.76 (5.99)	11.8	7.5, 16.0	2.12 (3.03)	2.1	-0.0, 4.3	0.5031
Low Dose	1	11.73	16.00 (N/A)	16.0	16.0, 16.0	4.27 (N/A)	4.3	4.3, 4.3	
High Dose	1	7.54	7.52 (N/A)	7.5	7.5, 7.5	-0.02 (N/A)	-0.0	-0.0, -0.0	

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:OTHER (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia (Cont.)									
WEEK 26	1	11.73	16.00 (N/A)	16.0	16.0, 16.0	4.27 (N/A)	4.3	4.3, 4.3	
Low Dose	1	11.73	16.00 (N/A)	16.0	16.0, 16.0	4.27 (N/A)	4.3	4.3, 4.3	
High Dose	0								
WEEK 39	1	11.73	2.67 (N/A)	2.7	2.7, 2.7	-9.07 (N/A)	-9.1	-9.1, -9.1	
Low Dose	1	11.73	2.67 (N/A)	2.7	2.7, 2.7	-9.07 (N/A)	-9.1	-9.1, -9.1	
High Dose	0								
Age category:< 65 years									
Average Daily Normalized 'Off' Time									
BASELINE	117		5.78 (2.19)	5.8	0.0, 10.3				
Low Dose	61		5.81 (2.06)	5.8	0.0, 10.3				
High Dose	56		5.74 (2.34)	5.8	0.0, 9.6				
WEEK 1	112	5.80	3.62 (3.29)	2.7	0.0, 14.8	-2.18 (3.35)	-2.4	-10.2, 5.9	<=0.001***
Low Dose	57	5.86	3.92 (3.22)	2.9	0.0, 13.8	-1.94 (3.12)	-1.9	-10.2, 5.2	<=0.001***
High Dose	55	5.74	3.31 (3.37)	2.1	0.0, 14.8	-2.42 (3.59)	-3.3	-8.9, 5.9	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Age category:< 65 years (Cont.)									
Average Daily Normalized 'Off' Time (Cont.)									
WEEK 6	99	5.79	3.06 (3.03)	2.6	0.0, 12.3	-2.73 (3.27)	-3.1	-10.2, 6.7	<=0.001***
Low Dose	52	5.84	3.21 (2.97)	3.1	0.0, 12.3	-2.63 (3.37)	-2.9	-10.2, 5.7	<=0.001***
High Dose	47	5.73	2.90 (3.12)	1.9	0.0, 10.7	-2.83 (3.19)	-3.3	-8.2, 6.7	<=0.001***
WEEK 13	57	5.48	3.09 (3.62)	1.7	0.0, 12.1	-2.39 (3.60)	-3.2	-9.9, 6.3	<=0.001***
Low Dose	29	5.83	2.65 (3.44)	1.5	0.0, 12.1	-3.18 (3.41)	-3.4	-9.9, 5.0	<=0.001***
High Dose	28	5.12	3.55 (3.81)	1.8	0.0, 10.7	-1.57 (3.67)	-1.5	-7.5, 6.3	0.0321*
WEEK 26	65	5.63	2.62 (2.95)	1.5	0.0, 11.2	-3.02 (3.21)	-3.2	-10.2, 5.5	<=0.001***
Low Dose	31	5.70	2.60 (3.20)	1.2	0.0, 11.2	-3.10 (3.52)	-3.8	-10.2, 5.5	<=0.001***
High Dose	34	5.57	2.63 (2.76)	1.6	0.0, 8.9	-2.94 (2.94)	-2.7	-9.2, 4.4	<=0.001***
WEEK 39	58	5.64	2.35 (2.56)	1.4	0.0, 11.4	-3.28 (2.94)	-3.1	-9.9, 6.4	<=0.001***
Low Dose	30	5.66	2.28 (2.57)	1.4	0.0, 11.4	-3.38 (3.24)	-2.8	-9.9, 6.4	<=0.001***
High Dose	28	5.61	2.43 (2.59)	1.4	0.0, 7.2	-3.19 (2.64)	-3.4	-9.2, 4.0	<=0.001***
WEEK 52	57	5.61	2.62 (3.22)	1.1	0.0, 11.5	-2.99 (3.16)	-3.5	-10.2, 5.9	<=0.001***
Low Dose	30	5.77	2.66 (3.24)	1.5	0.0, 10.9	-3.11 (3.55)	-3.5	-10.2, 5.9	<=0.001***
High Dose	27	5.43	2.58 (3.26)	0.7	0.0, 11.5	-2.85 (2.73)	-3.4	-7.5, 2.6	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Age category:< 65 years (Cont.)									
Average Daily Normalized 'On' Time Without Dyskinesia									
BASELINE	117		6.82 (3.42)	6.7	0.0, 15.4				
Low Dose	61		6.64 (3.49)	6.7	0.0, 15.4				
High Dose	56		7.01 (3.35)	6.7	0.0, 13.8				
WEEK 1	112	6.78	8.85 (4.57)	8.7	0.0, 16.0	2.07 (3.69)	1.7	-5.4, 12.0	<=0.001***
Low Dose	57	6.51	8.63 (4.42)	8.6	0.0, 16.0	2.13 (3.12)	2.0	-4.0, 10.2	<=0.001***
High Dose	55	7.06	9.07 (4.74)	9.1	0.0, 16.0	2.01 (4.23)	1.5	-5.4, 12.0	<=0.001***
WEEK 6	99	6.93	10.49 (4.57)	11.6	0.0, 16.0	3.56 (4.33)	4.0	-6.7, 12.7	<=0.001***
Low Dose	52	6.75	10.38 (4.45)	11.4	0.0, 16.0	3.63 (4.07)	4.0	-6.1, 12.7	<=0.001***
High Dose	47	7.14	10.62 (4.74)	12.8	0.0, 16.0	3.48 (4.63)	4.2	-6.7, 12.0	<=0.001***
WEEK 13	57	6.97	10.79 (4.81)	12.3	0.0, 16.0	3.82 (4.31)	3.7	-9.0, 14.1	<=0.001***
Low Dose	29	7.12	10.65 (5.27)	12.3	0.0, 16.0	3.53 (4.22)	3.7	-9.0, 9.9	<=0.001***
High Dose	28	6.81	10.94 (4.37)	11.9	2.7, 16.0	4.13 (4.45)	4.1	-6.3, 14.1	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Age category:< 65 years (Cont.)									
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 26	65	7.28	11.20 (4.51)	12.8	0.0, 16.0	3.92 (4.45)	4.5	-10.1, 14.1	<=0.001***
Low Dose	31	7.13	11.30 (4.95)	13.1	0.0, 16.0	4.17 (4.47)	4.7	-10.1, 11.0	<=0.001***
High Dose	34	7.42	11.11 (4.14)	12.2	0.0, 16.0	3.68 (4.49)	4.0	-9.6, 14.1	<=0.001***
WEEK 39	58	7.24	10.88 (4.59)	11.3	0.0, 16.0	3.64 (4.04)	3.2	-10.6, 12.4	<=0.001***
Low Dose	30	7.23	11.42 (4.75)	12.4	0.3, 16.0	4.19 (4.46)	4.7	-10.6, 10.9	<=0.001***
High Dose	28	7.25	10.29 (4.42)	11.0	0.0, 16.0	3.04 (3.52)	2.8	-2.8, 12.4	<=0.001***
WEEK 52	57	7.20	10.42 (5.25)	12.0	0.0, 16.0	3.21 (4.40)	3.4	-12.0, 11.3	<=0.001***
Low Dose	30	6.79	10.99 (4.89)	12.4	0.0, 16.0	4.20 (4.16)	4.3	-6.5, 11.3	<=0.001***
High Dose	27	7.66	9.77 (5.64)	9.6	0.0, 16.0	2.11 (4.48)	2.2	-12.0, 9.5	0.0214*
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia									
BASELINE	117		2.56 (2.71)	2.1	0.0, 12.2				
Low Dose	61		2.49 (2.48)	2.1	0.0, 10.3				
High Dose	56		2.64 (2.96)	2.2	0.0, 12.2				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Age category:< 65 years (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 1	112	2.61	2.59 (2.88)	1.7	0.0, 11.9	-0.02 (2.53)	0.0	-8.2, 8.8	0.9198
Low Dose	57	2.58	2.54 (2.72)	2.1	0.0, 10.7	-0.04 (2.30)	0.0	-5.3, 6.9	0.8870
High Dose	55	2.65	2.64 (3.07)	1.5	0.0, 11.9	-0.00 (2.77)	0.0	-8.2, 8.8	0.9913
WEEK 6	99	2.62	1.98 (3.13)	0.5	0.0, 13.9	-0.64 (2.74)	-0.4	-7.6, 9.6	0.0220*
Low Dose	52	2.56	1.86 (2.77)	0.6	0.0, 10.4	-0.70 (2.43)	-0.3	-5.1, 6.2	0.0431*
High Dose	47	2.67	2.10 (3.52)	0.0	0.0, 13.9	-0.58 (3.07)	-0.4	-7.6, 9.6	0.2049
WEEK 13	57	2.80	1.67 (2.77)	0.6	0.0, 15.5	-1.14 (3.06)	-0.5	-12.2, 5.2	0.0068**
Low Dose	29	2.27	2.20 (3.49)	1.0	0.0, 15.5	-0.08 (2.43)	0.0	-4.2, 5.2	0.8648
High Dose	28	3.35	1.12 (1.62)	0.0	0.0, 5.9	-2.24 (3.29)	-1.3	-12.2, 3.3	0.0013**
WEEK 26	65	2.46	1.69 (2.53)	0.7	0.0, 12.1	-0.77 (3.11)	-0.0	-12.2, 7.2	0.0493*
Low Dose	31	2.50	1.60 (2.44)	0.7	0.0, 12.1	-0.90 (2.58)	-0.6	-6.5, 4.6	0.0612
High Dose	34	2.43	1.77 (2.65)	0.4	0.0, 11.0	-0.66 (3.56)	-0.0	-12.2, 7.2	0.2905
WEEK 39	58	2.42	2.34 (3.82)	0.2	0.0, 16.0	-0.08 (3.32)	-0.2	-6.4, 15.4	0.8584
Low Dose	30	2.40	2.05 (3.80)	0.1	0.0, 15.4	-0.35 (3.78)	-0.6	-4.4, 15.4	0.6154
High Dose	28	2.44	2.65 (3.88)	0.7	0.0, 16.0	0.21 (2.80)	0.0	-6.4, 5.8	0.6896

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Age category:< 65 years (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 52	57	2.50	2.67 (4.51)	0.5	0.0, 16.0	0.17 (3.55)	0.0	-6.5, 12.9	0.7258
Low Dose	30	2.74	2.15 (4.01)	0.2	0.0, 16.0	-0.60 (3.31)	-0.5	-6.5, 9.2	0.3311
High Dose	27	2.24	3.25 (5.02)	0.7	0.0, 16.0	1.01 (3.68)	0.0	-4.9, 12.9	0.1646
Average Daily Normalized 'On' Time With Troublesome Dyskinesia									
BASELINE	117		0.85 (1.53)	0.0	0.0, 8.8				
Low Dose	61		1.06 (1.77)	0.0	0.0, 8.8				
High Dose	56		0.61 (1.18)	0.0	0.0, 5.0				
WEEK 1	112	0.81	0.94 (2.17)	0.0	0.0, 11.7	0.13 (1.88)	0.0	-5.7, 7.0	0.4566
Low Dose	57	1.05	0.91 (2.18)	0.0	0.0, 11.7	-0.14 (1.82)	0.0	-5.7, 5.8	0.5637
High Dose	55	0.56	0.97 (2.17)	0.0	0.0, 9.8	0.42 (1.91)	0.0	-2.9, 7.0	0.1130
WEEK 6	99	0.66	0.47 (1.37)	0.0	0.0, 9.0	-0.19 (1.38)	0.0	-4.1, 6.9	0.1716
Low Dose	52	0.84	0.54 (1.64)	0.0	0.0, 9.0	-0.30 (1.64)	0.0	-4.1, 6.9	0.1924
High Dose	47	0.46	0.39 (1.01)	0.0	0.0, 4.4	-0.07 (1.02)	0.0	-3.4, 4.4	0.6423

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Age category:< 65 years (Cont.)									
Average Daily Normalized 'On' Time With Troublesome Dyskinesia (Cont.)									
WEEK 13	57	0.75	0.45 (1.45)	0.0	0.0, 8.0	-0.30 (1.31)	0.0	-4.6, 6.0	0.0916
Low Dose	29	0.78	0.51 (1.77)	0.0	0.0, 8.0	-0.27 (1.60)	0.0	-4.6, 6.0	0.3720
High Dose	28	0.72	0.39 (1.05)	0.0	0.0, 3.7	-0.33 (0.94)	0.0	-3.4, 2.6	0.0777
WEEK 26	65	0.62	0.49 (1.88)	0.0	0.0, 12.1	-0.13 (1.78)	0.0	-4.0, 8.8	0.5670
Low Dose	31	0.67	0.50 (2.18)	0.0	0.0, 12.1	-0.17 (1.71)	0.0	-3.4, 7.2	0.5882
High Dose	34	0.58	0.49 (1.58)	0.0	0.0, 8.8	-0.09 (1.87)	0.0	-4.0, 8.8	0.7809
WEEK 39	58	0.71	0.43 (1.27)	0.0	0.0, 8.1	-0.27 (1.48)	0.0	-5.0, 7.3	0.1643
Low Dose	30	0.71	0.25 (0.76)	0.0	0.0, 3.5	-0.46 (0.79)	0.0	-2.8, 0.0	0.0031**
High Dose	28	0.70	0.63 (1.65)	0.0	0.0, 8.1	-0.07 (1.97)	0.0	-5.0, 7.3	0.8528
WEEK 52	57	0.68	0.29 (0.74)	0.0	0.0, 3.0	-0.39 (1.18)	0.0	-5.0, 1.8	0.0155*
Low Dose	30	0.69	0.20 (0.60)	0.0	0.0, 2.7	-0.49 (1.14)	0.0	-3.4, 1.8	0.0255*
High Dose	27	0.67	0.39 (0.87)	0.0	0.0, 3.0	-0.28 (1.23)	0.0	-5.0, 1.6	0.2531

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Age category:< 65 years (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia									
BASELINE	117		9.38 (2.48)	9.8	2.2, 16.0				
Low Dose	61		9.13 (2.63)	9.9	2.2, 16.0				
High Dose	56		9.65 (2.30)	9.6	4.8, 16.0				
WEEK 1	112	9.39	11.44 (3.65)	11.8	1.2, 16.0	2.04 (3.46)	2.0	-5.9, 8.9	<=0.001***
Low Dose	57	9.09	11.18 (3.62)	11.3	1.6, 16.0	2.08 (3.07)	1.9	-5.2, 8.3	<=0.001***
High Dose	55	9.71	11.71 (3.68)	12.0	1.2, 16.0	2.01 (3.86)	2.1	-5.9, 8.9	<=0.001***
WEEK 6	99	9.55	12.47 (3.22)	13.1	3.7, 16.0	2.92 (3.33)	3.5	-6.7, 9.9	<=0.001***
Low Dose	52	9.31	12.24 (3.24)	12.7	3.7, 16.0	2.93 (3.36)	3.6	-5.7, 9.9	<=0.001***
High Dose	47	9.81	12.71 (3.21)	13.5	5.1, 16.0	2.90 (3.33)	3.5	-6.7, 8.2	<=0.001***
WEEK 13	57	9.77	12.46 (3.86)	13.8	3.9, 16.0	2.69 (3.56)	2.9	-6.3, 9.9	<=0.001***
Low Dose	29	9.39	12.84 (3.83)	14.5	3.9, 16.0	3.45 (3.31)	3.3	-5.0, 9.9	<=0.001***
High Dose	28	10.16	12.06 (3.93)	13.6	5.3, 16.0	1.89 (3.69)	2.3	-6.3, 7.5	0.0115*

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Age category:< 65 years (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia (Cont.)									
WEEK 26	65	9.75	12.89 (3.40)	14.3	1.5, 16.0	3.14 (3.35)	3.1	-5.5, 10.2	<=0.001***
Low Dose	31	9.63	12.90 (3.88)	14.8	1.5, 16.0	3.27 (3.83)	4.0	-5.5, 10.2	<=0.001***
High Dose	34	9.86	12.88 (2.95)	13.9	7.1, 16.0	3.03 (2.91)	2.7	-2.5, 9.4	<=0.001***
WEEK 39	58	9.66	13.21 (3.01)	14.0	2.4, 16.0	3.56 (3.29)	3.3	-9.2, 9.9	<=0.001***
Low Dose	30	9.62	13.47 (2.69)	14.2	4.6, 16.0	3.84 (3.27)	3.0	-5.9, 9.9	<=0.001***
High Dose	28	9.69	12.94 (3.35)	13.9	2.4, 16.0	3.25 (3.36)	3.4	-9.2, 9.7	<=0.001***
WEEK 52	57	9.71	13.09 (3.33)	14.0	4.5, 16.0	3.38 (3.10)	3.4	-5.4, 10.2	<=0.001***
Low Dose	30	9.54	13.14 (3.23)	13.8	5.1, 16.0	3.60 (3.41)	3.3	-5.4, 10.2	<=0.001***
High Dose	27	9.90	13.03 (3.50)	14.9	4.5, 16.0	3.12 (2.76)	3.4	-2.3, 8.4	<=0.001***
Age category:>= 65 years									
Average Daily Normalized 'Off' Time									
BASELINE	119		6.03 (2.30)	6.1	0.0, 12.6				
Low Dose	66		5.56 (2.32)	5.9	0.0, 10.0				
High Dose	53		6.62 (2.15)	7.0	1.5, 12.6				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Age category:>= 65 years (Cont.)									
Average Daily Normalized 'Off' Time (Cont.)									
WEEK 1	113	6.02	4.31 (3.54)	3.8	0.0, 16.0	-1.71 (3.97)	-2.1	-9.7, 10.4	<=0.001***
Low Dose	64	5.62	3.49 (3.18)	2.6	0.0, 10.3	-2.13 (3.82)	-2.5	-9.7, 5.9	<=0.001***
High Dose	49	6.55	5.39 (3.73)	5.6	0.0, 16.0	-1.16 (4.15)	-1.4	-8.3, 10.4	0.0551
WEEK 6	106	6.08	4.00 (3.41)	3.7	0.0, 16.0	-2.08 (3.88)	-2.4	-10.6, 9.9	<=0.001***
Low Dose	59	5.63	3.41 (3.65)	2.9	0.0, 16.0	-2.22 (3.90)	-2.4	-8.2, 9.9	<=0.001***
High Dose	47	6.65	4.74 (2.95)	4.5	0.0, 12.5	-1.91 (3.88)	-2.4	-10.6, 6.8	0.0016**
WEEK 13	58	5.60	3.15 (3.34)	2.0	0.0, 13.4	-2.45 (3.80)	-3.2	-9.2, 8.1	<=0.001***
Low Dose	35	5.06	3.08 (3.63)	1.7	0.0, 13.4	-1.98 (4.07)	-2.7	-7.0, 8.1	0.0069**
High Dose	23	6.42	3.26 (2.91)	2.9	0.0, 9.3	-3.16 (3.30)	-3.2	-9.2, 4.0	<=0.001***
WEEK 26	62	6.23	2.69 (3.12)	1.5	0.0, 14.3	-3.54 (3.28)	-3.7	-10.6, 7.1	<=0.001***
Low Dose	35	5.76	2.35 (3.20)	0.8	0.0, 14.3	-3.41 (3.24)	-3.7	-7.8, 7.1	<=0.001***
High Dose	27	6.84	3.14 (3.02)	2.0	0.0, 9.8	-3.70 (3.39)	-2.9	-10.6, 5.5	<=0.001***
WEEK 39	53	6.06	3.10 (3.01)	2.7	0.0, 13.3	-2.96 (3.43)	-3.0	-9.1, 9.6	<=0.001***
Low Dose	33	5.65	3.05 (3.24)	2.0	0.0, 13.3	-2.59 (3.48)	-3.0	-7.5, 9.6	<=0.001***
High Dose	20	6.75	3.19 (2.66)	3.0	0.0, 7.3	-3.56 (3.36)	-3.1	-9.1, 2.9	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Age category:>= 65 years (Cont.)									
Average Daily Normalized 'Off' Time (Cont.)									
WEEK 52	39	6.32	2.34 (2.43)	1.9	0.0, 8.1	-3.98 (2.90)	-3.8	-11.2, 2.8	<=0.001***
Low Dose	21	5.99	2.35 (2.16)	2.6	0.0, 6.7	-3.64 (2.24)	-3.6	-8.7, 1.2	<=0.001***
High Dose	18	6.70	2.32 (2.76)	1.1	0.0, 8.1	-4.37 (3.55)	-4.3	-11.2, 2.8	<=0.001***
Average Daily Normalized 'On' Time Without Dyskinesia									
BASELINE	119		6.21 (3.27)	6.5	0.0, 14.0				
Low Dose	66		6.09 (3.44)	5.9	0.0, 14.0				
High Dose	53		6.37 (3.08)	6.7	0.0, 11.6				
WEEK 1	113	6.19	8.01 (4.45)	8.1	0.0, 16.0	1.82 (4.46)	1.6	-8.9, 10.7	<=0.001***
Low Dose	64	5.94	7.41 (4.59)	7.3	0.0, 16.0	1.46 (4.54)	1.3	-8.9, 10.7	0.0122*
High Dose	49	6.52	8.80 (4.18)	8.9	0.0, 16.0	2.28 (4.36)	3.0	-8.1, 8.7	<=0.001***
WEEK 6	106	6.18	9.39 (4.36)	10.0	0.0, 16.0	3.21 (4.46)	3.2	-9.1, 13.8	<=0.001***
Low Dose	59	6.04	9.41 (4.62)	10.2	0.0, 16.0	3.36 (4.87)	3.9	-9.1, 13.8	<=0.001***
High Dose	47	6.34	9.37 (4.06)	9.9	0.0, 16.0	3.03 (3.92)	2.9	-4.9, 10.6	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Age category:>= 65 years (Cont.)									
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 13	58	6.38	10.78 (4.43)	11.2	0.0, 16.0	4.40 (4.40)	4.8	-6.5, 15.2	<=0.001***
Low Dose	35	6.27	10.68 (4.71)	12.4	0.0, 16.0	4.41 (4.59)	4.8	-6.5, 15.2	<=0.001***
High Dose	23	6.53	10.93 (4.07)	10.6	0.9, 16.0	4.40 (4.21)	4.7	-4.7, 10.0	<=0.001***
WEEK 26	62	6.47	11.20 (4.18)	12.2	0.0, 16.0	4.73 (4.48)	5.3	-11.0, 12.7	<=0.001***
Low Dose	35	6.65	11.85 (3.46)	12.6	1.3, 16.0	5.20 (3.46)	5.4	-1.2, 11.5	<=0.001***
High Dose	27	6.23	10.36 (4.89)	10.7	0.0, 16.0	4.13 (5.55)	4.9	-11.0, 12.7	<=0.001***
WEEK 39	53	6.80	11.30 (3.70)	11.8	2.7, 16.0	4.51 (4.14)	4.9	-6.4, 13.5	<=0.001***
Low Dose	33	6.57	10.88 (4.01)	10.7	2.7, 16.0	4.31 (4.12)	4.9	-6.4, 11.4	<=0.001***
High Dose	20	7.17	11.99 (3.08)	11.8	6.6, 16.0	4.83 (4.27)	4.7	-2.9, 13.5	<=0.001***
WEEK 52	39	6.77	11.39 (3.77)	11.6	1.3, 16.0	4.62 (4.02)	4.8	-3.1, 13.8	<=0.001***
Low Dose	21	6.87	11.73 (3.74)	13.0	1.3, 16.0	4.85 (3.53)	5.1	-2.5, 9.1	<=0.001***
High Dose	18	6.65	11.00 (3.88)	11.2	1.3, 16.0	4.35 (4.61)	3.3	-3.1, 13.8	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Age category:>= 65 years (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia									
BASELINE	119		2.69 (2.40)	2.7	0.0, 8.9				
Low Dose	66		2.88 (2.32)	2.9	0.0, 8.5				
High Dose	53		2.46 (2.49)	1.9	0.0, 8.9				
WEEK 1	113	2.71	2.64 (3.42)	1.1	0.0, 14.9	-0.07 (3.48)	0.0	-8.5, 13.6	0.8200
Low Dose	64	2.93	3.49 (3.67)	2.6	0.0, 14.9	0.56 (3.98)	0.0	-8.5, 13.6	0.2661
High Dose	49	2.43	1.53 (2.73)	0.0	0.0, 12.8	-0.90 (2.52)	-0.2	-6.9, 8.1	0.0157*
WEEK 6	106	2.72	2.20 (3.44)	0.5	0.0, 15.4	-0.52 (3.25)	-0.2	-7.8, 11.6	0.1019
Low Dose	59	2.91	2.55 (3.48)	1.3	0.0, 15.4	-0.35 (3.52)	-0.1	-7.6, 11.6	0.4465
High Dose	47	2.49	1.76 (3.37)	0.0	0.0, 14.6	-0.74 (2.91)	-0.3	-7.8, 7.5	0.0896
WEEK 13	58	3.13	1.87 (3.77)	0.0	0.0, 16.0	-1.26 (3.90)	-1.4	-8.0, 13.2	0.0170*
Low Dose	35	3.49	1.95 (3.91)	0.0	0.0, 16.0	-1.53 (4.24)	-2.2	-8.0, 13.2	0.0398*
High Dose	23	2.58	1.74 (3.63)	0.0	0.0, 14.4	-0.85 (3.37)	-0.3	-6.9, 7.2	0.2414

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Age category:>= 65 years (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 26	62	2.49	1.95 (3.36)	0.0	0.0, 15.2	-0.54 (3.50)	-0.1	-6.8, 12.0	0.2274
Low Dose	35	2.68	1.66 (2.43)	0.6	0.0, 10.8	-1.03 (3.05)	-0.6	-6.8, 5.4	0.0545
High Dose	27	2.24	2.33 (4.30)	0.0	0.0, 15.2	0.09 (3.98)	0.0	-6.8, 12.0	0.9123
WEEK 39	53	2.54	1.39 (2.61)	0.0	0.0, 10.8	-1.14 (3.12)	0.0	-7.8, 6.1	0.0102*
Low Dose	33	2.96	1.82 (2.93)	0.0	0.0, 10.8	-1.13 (3.19)	0.0	-7.8, 5.5	0.0496*
High Dose	20	1.84	0.68 (1.83)	0.0	0.0, 6.1	-1.16 (3.08)	-0.1	-7.8, 6.1	0.1089
WEEK 52	39	2.47	1.71 (2.95)	0.0	0.0, 12.0	-0.75 (3.04)	0.0	-7.3, 6.1	0.1312
Low Dose	21	2.51	1.67 (3.11)	0.0	0.0, 12.0	-0.85 (3.33)	-0.4	-6.8, 6.1	0.2577
High Dose	18	2.41	1.77 (2.84)	0.0	0.0, 9.3	-0.64 (2.77)	0.0	-7.3, 2.8	0.3388
Average Daily Normalized 'On' Time With Troublesome Dyskinesia									
BASELINE	119		1.06 (1.90)	0.0	0.0, 10.5				
Low Dose	66		1.47 (2.23)	0.3	0.0, 10.5				
High Dose	53		0.56 (1.23)	0.0	0.0, 5.3				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Age category:>= 65 years (Cont.)									
Average Daily Normalized 'On' Time With Troublesome Dyskinesia (Cont.)									
WEEK 1	113	1.07	1.04 (2.02)	0.0	0.0, 10.5	-0.03 (1.92)	0.0	-6.0, 10.5	0.8544
Low Dose	64	1.51	1.62 (2.46)	0.3	0.0, 10.5	0.11 (2.31)	0.0	-6.0, 10.5	0.7076
High Dose	49	0.50	0.28 (0.72)	0.0	0.0, 3.4	-0.22 (1.22)	0.0	-4.9, 3.4	0.2145
WEEK 6	106	1.02	0.41 (1.24)	0.0	0.0, 5.8	-0.61 (1.77)	0.0	-9.2, 4.1	<=0.001***
Low Dose	59	1.42	0.63 (1.57)	0.0	0.0, 5.8	-0.79 (2.16)	0.0	-9.2, 4.1	0.0069**
High Dose	47	0.52	0.13 (0.51)	0.0	0.0, 2.8	-0.38 (1.08)	0.0	-4.9, 2.1	0.0188*
WEEK 13	58	0.90	0.20 (0.63)	0.0	0.0, 3.5	-0.70 (1.56)	0.0	-7.2, 1.7	0.0012**
Low Dose	35	1.18	0.29 (0.78)	0.0	0.0, 3.5	-0.90 (1.76)	0.0	-7.2, 1.7	0.0048**
High Dose	23	0.46	0.07 (0.24)	0.0	0.0, 0.9	-0.39 (1.17)	0.0	-4.9, 0.9	0.1204
WEEK 26	62	0.80	0.15 (0.57)	0.0	0.0, 3.7	-0.65 (1.60)	0.0	-5.1, 3.7	0.0022**
Low Dose	35	0.90	0.14 (0.63)	0.0	0.0, 3.7	-0.76 (1.63)	0.0	-5.1, 3.7	0.0094**
High Dose	27	0.68	0.17 (0.48)	0.0	0.0, 1.8	-0.51 (1.58)	0.0	-4.9, 1.7	0.1039
WEEK 39	53	0.61	0.20 (0.70)	0.0	0.0, 3.8	-0.40 (1.23)	0.0	-5.1, 2.7	0.0206*
Low Dose	33	0.82	0.24 (0.76)	0.0	0.0, 3.8	-0.58 (1.31)	0.0	-5.1, 0.8	0.0153*
High Dose	20	0.24	0.14 (0.61)	0.0	0.0, 2.7	-0.11 (1.05)	0.0	-3.6, 2.7	0.6557

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Age category:>= 65 years (Cont.)									
Average Daily Normalized 'On' Time With Troublesome Dyskinesia (Cont.)									
WEEK 52	39	0.45	0.55 (1.47)	0.0	0.0, 6.3	0.11 (1.84)	0.0	-3.6, 6.3	0.7200
Low Dose	21	0.62	0.25 (0.75)	0.0	0.0, 3.3	-0.37 (1.26)	0.0	-2.6, 3.3	0.1958
High Dose	18	0.24	0.90 (1.98)	0.0	0.0, 6.3	0.66 (2.26)	0.0	-3.6, 6.3	0.2323
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia									
BASELINE	119		8.91 (2.51)	8.9	0.3, 15.0				
Low Dose	66		8.97 (2.72)	9.0	0.3, 15.0				
High Dose	53		8.83 (2.25)	8.8	2.6, 14.5				
WEEK 1	113	8.90	10.65 (3.69)	10.6	0.0, 16.0	1.74 (4.07)	1.6	-10.4, 11.3	<=0.001***
Low Dose	64	8.87	10.89 (3.67)	10.9	3.0, 16.0	2.02 (3.93)	2.2	-5.9, 11.3	<=0.001***
High Dose	49	8.94	10.33 (3.73)	10.0	0.0, 16.0	1.38 (4.26)	1.4	-10.4, 8.3	0.0277*
WEEK 6	106	8.90	11.59 (3.46)	12.1	0.0, 16.0	2.69 (3.82)	3.0	-9.9, 10.6	<=0.001***
Low Dose	59	8.95	11.96 (3.77)	12.6	0.0, 16.0	3.01 (3.80)	3.1	-9.9, 10.5	<=0.001***
High Dose	47	8.84	11.13 (2.98)	11.5	3.5, 16.0	2.29 (3.86)	2.4	-6.8, 10.6	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Age category:>= 65 years (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia (Cont.)									
WEEK 13	58	9.50	12.65 (3.38)	13.9	2.6, 16.0	3.14 (3.39)	3.8	-4.9, 9.2	<=0.001***
Low Dose	35	9.76	12.63 (3.68)	14.1	2.6, 16.0	2.87 (3.33)	3.8	-4.9, 7.2	<=0.001***
High Dose	23	9.12	12.67 (2.94)	13.1	6.0, 16.0	3.55 (3.51)	3.4	-4.7, 9.2	<=0.001***
WEEK 26	62	8.96	13.15 (3.09)	14.1	1.7, 16.0	4.19 (3.66)	4.3	-5.5, 12.5	<=0.001***
Low Dose	35	9.34	13.51 (3.20)	15.0	1.7, 16.0	4.17 (3.67)	4.3	-4.1, 12.5	<=0.001***
High Dose	27	8.48	12.69 (2.93)	13.8	6.2, 16.0	4.22 (3.71)	4.6	-5.5, 10.6	<=0.001***
WEEK 39	53	9.33	12.69 (3.09)	12.9	2.7, 16.0	3.36 (3.45)	3.2	-9.1, 9.4	<=0.001***
Low Dose	33	9.53	12.70 (3.24)	12.9	2.7, 16.0	3.18 (3.52)	3.1	-9.1, 9.4	<=0.001***
High Dose	20	9.01	12.68 (2.91)	13.0	6.6, 16.0	3.67 (3.40)	3.6	-2.9, 9.1	<=0.001***
WEEK 52	39	9.23	13.11 (2.51)	13.3	7.9, 16.0	3.87 (2.95)	3.5	-2.8, 11.2	<=0.001***
Low Dose	21	9.39	13.39 (2.15)	13.3	9.3, 16.0	4.01 (2.32)	3.5	-1.2, 8.7	<=0.001***
High Dose	18	9.06	12.77 (2.90)	13.1	7.9, 16.0	3.71 (3.61)	3.0	-2.8, 11.2	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Geographic region:NORTH AMERICA									
Average Daily Normalized 'Off' Time									
BASELINE	89		5.54 (2.32)	5.4	0.0, 10.3				
Low Dose	39		4.96 (2.40)	4.9	0.0, 9.9				
High Dose	50		5.99 (2.17)	5.9	0.6, 10.3				
WEEK 1	83	5.50	3.41 (3.08)	2.7	0.0, 11.8	-2.08 (3.32)	-2.2	-8.6, 5.6	<=0.001***
Low Dose	37	5.03	2.79 (3.05)	2.0	0.0, 10.3	-2.24 (3.38)	-2.8	-8.6, 5.6	<=0.001***
High Dose	46	5.87	3.91 (3.03)	3.8	0.0, 11.8	-1.96 (3.30)	-1.8	-8.3, 4.8	<=0.001***
WEEK 6	76	5.49	2.99 (3.29)	1.9	0.0, 14.9	-2.50 (3.57)	-2.9	-9.9, 6.7	<=0.001***
Low Dose	34	4.97	2.40 (3.23)	1.0	0.0, 14.9	-2.57 (3.49)	-2.6	-9.9, 6.3	<=0.001***
High Dose	42	5.92	3.47 (3.30)	2.5	0.0, 10.7	-2.44 (3.68)	-3.1	-8.4, 6.7	<=0.001***
WEEK 13	47	5.16	2.50 (3.15)	1.5	0.0, 10.3	-2.65 (3.43)	-3.2	-9.9, 6.3	<=0.001***
Low Dose	23	4.50	1.45 (2.09)	0.2	0.0, 7.2	-3.05 (2.94)	-3.3	-9.9, 5.0	<=0.001***
High Dose	24	5.79	3.51 (3.68)	2.4	0.0, 10.3	-2.28 (3.87)	-2.1	-9.2, 6.3	0.0084**

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Geographic region:NORTH AMERICA (Cont.)									
Average Daily Normalized 'Off' Time (Cont.)									
WEEK 26	51	5.19	1.83 (2.33)	0.9	0.0, 8.4	-3.37 (2.34)	-2.8	-9.2, 1.5	<=0.001***
Low Dose	25	4.81	1.35 (1.90)	0.3	0.0, 6.1	-3.46 (2.31)	-3.6	-9.2, 0.2	<=0.001***
High Dose	26	5.56	2.28 (2.64)	1.3	0.0, 8.4	-3.28 (2.42)	-2.8	-7.5, 1.5	<=0.001***
WEEK 39	49	5.20	2.19 (2.60)	1.3	0.0, 13.3	-3.01 (3.13)	-3.1	-9.9, 9.6	<=0.001***
Low Dose	26	4.86	2.21 (2.85)	1.4	0.0, 13.3	-2.66 (3.41)	-2.9	-9.9, 9.6	<=0.001***
High Dose	23	5.58	2.18 (2.36)	1.3	0.0, 7.0	-3.40 (2.79)	-3.6	-9.1, 1.9	<=0.001***
WEEK 52	40	5.40	1.83 (2.42)	0.5	0.0, 8.8	-3.57 (2.62)	-3.7	-9.9, 2.8	<=0.001***
Low Dose	19	5.11	1.74 (1.78)	0.9	0.0, 5.9	-3.38 (2.19)	-3.1	-9.9, 0.0	<=0.001***
High Dose	21	5.65	1.91 (2.92)	0.5	0.0, 8.8	-3.74 (3.00)	-4.4	-8.6, 2.8	<=0.001***
Average Daily Normalized 'On' Time Without Dyskinesia									
BASELINE	89		6.91 (3.64)	6.8	0.0, 15.4				
Low Dose	39		6.95 (4.09)	6.8	0.0, 15.4				
High Dose	50		6.87 (3.29)	6.7	0.0, 13.8				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Geographic region:NORTH AMERICA (Cont.)									
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 1	83	6.99	9.25 (4.26)	9.0	0.0, 16.0	2.26 (4.33)	1.7	-8.8, 12.0	<=0.001***
Low Dose	37	6.90	9.06 (4.70)	8.6	0.0, 16.0	2.16 (4.38)	1.7	-8.8, 10.7	0.0049**
High Dose	46	7.07	9.40 (3.91)	9.2	0.5, 16.0	2.33 (4.34)	2.6	-5.1, 12.0	<=0.001***
WEEK 6	76	6.91	10.22 (4.83)	10.4	0.0, 16.0	3.31 (4.87)	3.2	-9.1, 12.0	<=0.001***
Low Dose	34	6.92	9.88 (5.15)	10.0	0.0, 16.0	2.96 (5.17)	2.6	-9.1, 11.7	0.0021**
High Dose	42	6.90	10.50 (4.60)	10.9	0.0, 16.0	3.60 (4.65)	3.4	-6.7, 12.0	<=0.001***
WEEK 13	47	7.21	11.29 (4.62)	12.1	0.0, 16.0	4.07 (4.72)	3.3	-6.3, 15.2	<=0.001***
Low Dose	23	7.77	11.46 (4.79)	13.0	0.0, 16.0	3.70 (4.54)	2.9	-3.9, 15.2	<=0.001***
High Dose	24	6.68	11.12 (4.55)	11.5	0.9, 16.0	4.43 (4.96)	4.9	-6.3, 14.1	<=0.001***
WEEK 26	51	7.28	12.04 (4.04)	13.3	0.0, 16.0	4.76 (4.31)	4.4	-6.6, 14.1	<=0.001***
Low Dose	25	7.85	12.60 (3.68)	13.4	0.5, 16.0	4.75 (4.17)	4.4	-2.4, 11.5	<=0.001***
High Dose	26	6.73	11.50 (4.37)	13.2	0.0, 16.0	4.77 (4.53)	4.6	-6.6, 14.1	<=0.001***
WEEK 39	49	7.49	11.21 (4.58)	12.4	0.0, 16.0	3.72 (4.83)	4.1	-10.6, 13.5	<=0.001***
Low Dose	26	7.61	11.19 (4.71)	12.9	0.6, 16.0	3.58 (5.28)	4.5	-10.6, 11.4	0.0019**
High Dose	23	7.35	11.22 (4.52)	11.8	0.0, 16.0	3.88 (4.37)	3.3	-2.8, 13.5	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Geographic region:NORTH AMERICA (Cont.)									
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 52	40	7.35	10.80 (5.02)	11.6	0.0, 16.0	3.45 (4.83)	3.6	-12.0, 13.8	<=0.001***
Low Dose	19	7.73	11.66 (4.65)	13.0	0.0, 16.0	3.93 (4.05)	4.8	-2.6, 9.9	<=0.001***
High Dose	21	7.01	10.03 (5.32)	10.0	0.0, 16.0	3.01 (5.51)	2.8	-12.0, 13.8	0.0209*
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia									
BASELINE	89		2.82 (2.83)	2.6	0.0, 12.2				
Low Dose	39		3.05 (2.74)	2.9	0.0, 10.3				
High Dose	50		2.64 (2.91)	2.0	0.0, 12.2				
WEEK 1	83	2.84	2.42 (2.99)	1.5	0.0, 13.6	-0.42 (3.43)	0.0	-8.5, 13.6	0.2718
Low Dose	37	3.11	3.02 (3.30)	2.4	0.0, 13.6	-0.09 (3.76)	-0.4	-8.5, 13.6	0.8888
High Dose	46	2.61	1.93 (2.66)	0.3	0.0, 9.7	-0.68 (3.17)	0.0	-8.2, 8.8	0.1506
WEEK 6	76	2.88	2.29 (3.52)	0.6	0.0, 14.6	-0.59 (3.48)	-0.5	-7.8, 9.6	0.1441
Low Dose	34	3.13	2.88 (3.43)	1.4	0.0, 12.2	-0.24 (3.64)	-0.8	-7.6, 9.6	0.7027
High Dose	42	2.68	1.80 (3.56)	0.0	0.0, 14.6	-0.87 (3.37)	-0.1	-7.8, 7.5	0.1005

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Geographic region:NORTH AMERICA (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 13	47	3.01	1.87 (3.81)	0.0	0.0, 15.5	-1.13 (3.90)	-0.6	-12.2, 7.9	0.0520
Low Dose	23	3.00	2.62 (4.37)	0.0	0.0, 15.5	-0.38 (3.97)	-0.6	-8.0, 7.9	0.6477
High Dose	24	3.01	1.16 (3.10)	0.0	0.0, 14.4	-1.85 (3.77)	-0.7	-12.2, 7.2	0.0244*
WEEK 26	51	2.80	1.69 (3.10)	0.0	0.0, 15.2	-1.11 (3.76)	-0.6	-12.2, 12.0	0.0410*
Low Dose	25	2.45	1.35 (1.36)	1.1	0.0, 3.4	-1.10 (2.73)	-0.6	-6.8, 3.1	0.0553
High Dose	26	3.14	2.02 (4.16)	0.0	0.0, 15.2	-1.11 (4.60)	-0.6	-12.2, 12.0	0.2299
WEEK 39	49	2.68	2.18 (3.80)	0.0	0.0, 16.0	-0.49 (4.03)	0.0	-7.8, 15.4	0.3958
Low Dose	26	2.67	2.37 (3.77)	0.6	0.0, 15.4	-0.30 (4.32)	0.0	-7.8, 15.4	0.7267
High Dose	23	2.68	1.97 (3.91)	0.0	0.0, 16.0	-0.71 (3.77)	0.0	-7.8, 6.1	0.3737
WEEK 52	40	2.79	2.89 (4.64)	0.6	0.0, 16.0	0.10 (3.91)	0.0	-7.3, 12.9	0.8777
Low Dose	19	2.59	2.36 (4.41)	0.5	0.0, 16.0	-0.23 (3.34)	-0.4	-6.8, 6.1	0.7683
High Dose	21	2.98	3.37 (4.89)	0.8	0.0, 16.0	0.39 (4.42)	0.0	-7.3, 12.9	0.6909

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Geographic region:NORTH AMERICA (Cont.)									
Average Daily Normalized 'On' Time With Troublesome Dyskinesia									
BASELINE	89		0.74 (1.24)	0.0	0.0, 5.1				
Low Dose	39		1.03 (1.39)	0.3	0.0, 5.1				
High Dose	50		0.51 (1.07)	0.0	0.0, 4.9				
WEEK 1	83	0.67	0.92 (1.73)	0.0	0.0, 7.2	0.24 (1.73)	0.0	-3.7, 7.0	0.2017
Low Dose	37	0.96	1.12 (1.71)	0.0	0.0, 5.4	0.17 (1.61)	0.0	-3.7, 5.2	0.5292
High Dose	46	0.45	0.75 (1.74)	0.0	0.0, 7.2	0.31 (1.84)	0.0	-3.7, 7.0	0.2651
WEEK 6	76	0.72	0.50 (1.55)	0.0	0.0, 9.0	-0.22 (1.68)	0.0	-5.1, 6.9	0.2570
Low Dose	34	0.98	0.84 (2.19)	0.0	0.0, 9.0	-0.15 (2.22)	0.0	-5.1, 6.9	0.7033
High Dose	42	0.50	0.22 (0.59)	0.0	0.0, 2.6	-0.28 (1.09)	0.0	-4.9, 2.1	0.1041
WEEK 13	47	0.62	0.34 (1.07)	0.0	0.0, 5.5	-0.29 (1.04)	0.0	-4.9, 2.6	0.0665
Low Dose	23	0.73	0.46 (1.35)	0.0	0.0, 5.5	-0.27 (0.83)	0.0	-1.7, 1.7	0.1385
High Dose	24	0.52	0.21 (0.72)	0.0	0.0, 3.4	-0.30 (1.23)	0.0	-4.9, 2.6	0.2380

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Geographic region:NORTH AMERICA (Cont.)									
Average Daily Normalized 'On' Time With Troublesome Dyskinesia (Cont.)									
WEEK 26	51	0.73	0.44 (1.80)	0.0	0.0, 12.1	-0.29 (1.76)	0.0	-5.1, 7.2	0.2522
Low Dose	25	0.89	0.70 (2.51)	0.0	0.0, 12.1	-0.19 (2.16)	0.0	-5.1, 7.2	0.6644
High Dose	26	0.57	0.19 (0.58)	0.0	0.0, 2.4	-0.38 (1.30)	0.0	-4.9, 1.6	0.1517
WEEK 39	49	0.63	0.41 (1.30)	0.0	0.0, 8.1	-0.22 (1.60)	0.0	-5.1, 7.3	0.3383
Low Dose	26	0.85	0.22 (0.63)	0.0	0.0, 2.4	-0.63 (1.26)	0.0	-5.1, 0.8	0.0178*
High Dose	23	0.39	0.62 (1.78)	0.0	0.0, 8.1	0.24 (1.84)	0.0	-3.6, 7.3	0.5430
WEEK 52	40	0.46	0.48 (1.41)	0.0	0.0, 6.3	0.02 (1.71)	0.0	-3.6, 6.3	0.9283
Low Dose	19	0.57	0.24 (0.78)	0.0	0.0, 3.3	-0.32 (1.22)	0.0	-2.3, 3.3	0.2625
High Dose	21	0.35	0.69 (1.79)	0.0	0.0, 6.3	0.34 (2.04)	0.0	-3.6, 6.3	0.4532
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia									
BASELINE	89		9.72 (2.47)	9.8	3.7, 16.0				
Low Dose	39		10.01 (3.00)	10.3	3.7, 16.0				
High Dose	50		9.50 (1.97)	9.6	5.7, 14.1				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Geographic region:NORTH AMERICA (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia (Cont.)									
WEEK 1	83	9.83	11.67 (3.27)	11.7	3.0, 16.0	1.84 (3.34)	1.7	-5.6, 8.3	<=0.001***
Low Dose	37	10.01	12.09 (3.25)	12.7	3.0, 16.0	2.07 (3.27)	2.7	-5.6, 7.8	<=0.001***
High Dose	46	9.68	11.33 (3.29)	11.5	4.2, 16.0	1.65 (3.42)	1.4	-4.8, 8.3	0.0021**
WEEK 6	76	9.79	12.51 (3.36)	13.0	1.1, 16.0	2.72 (3.53)	2.9	-6.7, 10.5	<=0.001***
Low Dose	34	10.05	12.76 (3.48)	13.6	1.1, 16.0	2.72 (3.35)	2.7	-3.7, 10.5	<=0.001***
High Dose	42	9.58	12.30 (3.28)	12.7	5.1, 16.0	2.72 (3.70)	3.3	-6.7, 8.4	<=0.001***
WEEK 13	47	10.22	13.16 (3.38)	14.3	5.7, 16.0	2.94 (3.57)	3.3	-6.3, 9.9	<=0.001***
Low Dose	23	10.77	14.08 (2.60)	15.5	8.6, 16.0	3.31 (2.83)	3.8	-3.3, 9.9	<=0.001***
High Dose	24	9.70	12.28 (3.84)	13.5	5.7, 16.0	2.58 (4.19)	2.7	-6.3, 9.2	0.0062**
WEEK 26	51	10.08	13.73 (2.97)	14.9	1.5, 16.0	3.65 (2.92)	3.9	-4.5, 10.5	<=0.001***
Low Dose	25	10.30	13.95 (3.32)	15.7	1.5, 16.0	3.65 (3.25)	3.9	-4.5, 10.5	<=0.001***
High Dose	26	9.87	13.53 (2.64)	14.4	7.6, 16.0	3.66 (2.63)	3.5	-1.0, 7.8	<=0.001***
WEEK 39	49	10.17	13.39 (3.06)	14.3	2.4, 16.0	3.23 (3.47)	3.3	-9.2, 9.9	<=0.001***
Low Dose	26	10.28	13.57 (2.95)	14.3	2.7, 16.0	3.29 (3.45)	3.1	-9.1, 9.9	<=0.001***
High Dose	23	10.03	13.19 (3.24)	14.0	2.4, 16.0	3.16 (3.57)	3.8	-9.2, 9.1	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Geographic region:NORTH AMERICA (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia (Cont.)									
WEEK 52	40	10.15	13.69 (2.55)	14.7	7.2, 16.0	3.54 (2.47)	3.3	-2.8, 9.9	<=0.001***
Low Dose	19	10.32	14.02 (1.88)	13.4	10.1, 16.0	3.70 (2.17)	3.1	0.0, 9.9	<=0.001***
High Dose	21	9.99	13.39 (3.05)	15.2	7.2, 16.0	3.40 (2.76)	3.8	-2.8, 7.5	<=0.001***
Geographic region:EUROPE AND AUSTRALIA									
Average Daily Normalized 'Off' Time									
BASELINE	120		5.97 (2.18)	5.9	0.0, 12.6				
Low Dose	66		5.83 (1.99)	5.8	0.0, 10.2				
High Dose	54		6.15 (2.40)	6.4	0.0, 12.6				
WEEK 1	116	6.01	4.08 (3.63)	2.9	0.0, 16.0	-1.94 (3.92)	-2.3	-10.2, 10.4	<=0.001***
Low Dose	63	5.90	3.73 (3.11)	2.7	0.0, 11.2	-2.16 (3.53)	-2.5	-10.2, 5.9	<=0.001***
High Dose	53	6.16	4.49 (4.15)	3.1	0.0, 16.0	-1.67 (4.35)	-2.1	-8.9, 10.4	0.0074**
WEEK 6	105	6.09	3.41 (2.90)	3.1	0.0, 16.0	-2.67 (3.49)	-3.1	-10.6, 9.9	<=0.001***
Low Dose	58	5.97	3.20 (3.07)	3.1	0.0, 16.0	-2.77 (3.64)	-3.2	-10.2, 9.9	<=0.001***
High Dose	47	6.23	3.68 (2.70)	3.1	0.0, 10.2	-2.55 (3.34)	-2.9	-10.6, 6.8	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Geographic region:EUROPE AND AUSTRALIA (Cont.)									
Average Daily Normalized 'Off' Time (Cont.)									
WEEK 13	58	5.80	3.01 (3.12)	2.0	0.0, 12.6	-2.79 (3.41)	-3.3	-9.3, 7.8	<=0.001***
Low Dose	31	5.95	2.72 (3.07)	1.9	0.0, 12.6	-3.23 (3.46)	-3.5	-9.3, 7.8	<=0.001***
High Dose	27	5.63	3.34 (3.20)	2.0	0.0, 10.7	-2.30 (3.35)	-3.2	-7.5, 5.2	0.0014**
WEEK 26	61	6.35	2.58 (2.65)	1.7	0.0, 9.8	-3.78 (3.34)	-4.5	-10.6, 5.5	<=0.001***
Low Dose	29	6.35	2.00 (2.38)	1.0	0.0, 7.4	-4.35 (2.92)	-4.8	-10.2, 3.3	<=0.001***
High Dose	32	6.36	3.10 (2.81)	2.5	0.0, 9.8	-3.26 (3.65)	-3.5	-10.6, 5.5	<=0.001***
WEEK 39	48	6.25	2.76 (2.72)	2.6	0.0, 11.4	-3.49 (3.18)	-3.1	-9.8, 6.4	<=0.001***
Low Dose	26	6.24	2.37 (2.67)	1.9	0.0, 11.4	-3.87 (3.26)	-3.2	-9.8, 6.4	<=0.001***
High Dose	22	6.26	3.21 (2.78)	3.6	0.0, 7.3	-3.05 (3.09)	-3.0	-9.2, 4.0	<=0.001***
WEEK 52	44	6.12	2.76 (3.15)	1.5	0.0, 11.5	-3.35 (3.45)	-3.4	-11.2, 5.9	<=0.001***
Low Dose	23	6.39	2.73 (3.25)	1.2	0.0, 10.9	-3.66 (3.59)	-4.1	-10.2, 5.9	<=0.001***
High Dose	21	5.83	2.80 (3.11)	1.9	0.0, 11.5	-3.02 (3.34)	-2.8	-11.2, 2.6	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Geographic region:EUROPE AND AUSTRALIA (Cont.)									
Average Daily Normalized 'On' Time Without Dyskinesia									
BASELINE	120		6.41 (3.24)	6.6	0.0, 12.3				
Low Dose	66		6.35 (3.20)	6.7	0.0, 11.9				
High Dose	54		6.47 (3.31)	6.4	0.0, 12.3				
WEEK 1	116	6.33	8.33 (4.69)	8.5	0.0, 16.0	2.00 (3.91)	1.8	-8.2, 10.4	<=0.001***
Low Dose	63	6.17	8.19 (4.49)	8.3	0.0, 16.0	2.02 (3.58)	1.9	-8.2, 10.4	<=0.001***
High Dose	53	6.52	8.51 (4.96)	8.8	0.0, 16.0	1.99 (4.30)	1.8	-8.1, 8.9	0.0015**
WEEK 6	105	6.45	10.06 (4.29)	11.1	0.0, 16.0	3.61 (3.85)	4.0	-8.3, 12.7	<=0.001***
Low Dose	58	6.38	10.10 (4.51)	10.9	0.0, 16.0	3.72 (4.06)	4.1	-8.3, 12.7	<=0.001***
High Dose	47	6.53	10.00 (4.05)	11.1	0.0, 16.0	3.47 (3.61)	3.2	-2.6, 11.2	<=0.001***
WEEK 13	58	6.45	11.22 (3.99)	12.4	2.7, 16.0	4.77 (3.49)	5.2	-3.6, 11.0	<=0.001***
Low Dose	31	6.24	11.60 (4.07)	13.2	3.4, 16.0	5.36 (3.24)	6.0	-1.5, 11.0	<=0.001***
High Dose	27	6.68	10.78 (3.93)	10.6	2.7, 16.0	4.09 (3.71)	3.9	-3.6, 10.4	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Geographic region:EUROPE AND AUSTRALIA (Cont.)									
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 26	61	6.79	11.20 (4.09)	12.0	0.0, 16.0	4.41 (4.41)	5.4	-11.0, 11.0	<=0.001***
Low Dose	29	6.57	12.31 (3.19)	12.8	5.2, 16.0	5.74 (2.57)	5.7	0.4, 11.0	<=0.001***
High Dose	32	6.99	10.20 (4.58)	11.1	0.0, 16.0	3.21 (5.34)	4.6	-11.0, 10.6	0.0019**
WEEK 39	48	6.89	11.31 (3.72)	11.3	4.6, 16.0	4.42 (3.51)	4.4	-2.9, 12.4	<=0.001***
Low Dose	26	6.74	11.83 (3.89)	12.0	4.6, 16.0	5.10 (3.36)	5.1	-2.8, 10.9	<=0.001***
High Dose	22	7.07	10.70 (3.50)	10.7	4.7, 16.0	3.63 (3.60)	2.9	-2.9, 12.4	<=0.001***
WEEK 52	44	6.94	10.84 (4.79)	12.4	0.4, 16.0	3.90 (4.20)	4.3	-6.5, 11.3	<=0.001***
Low Dose	23	6.44	11.27 (4.69)	13.4	1.5, 16.0	4.83 (4.35)	4.8	-6.5, 11.3	<=0.001***
High Dose	21	7.49	10.37 (4.97)	11.9	0.4, 16.0	2.87 (3.88)	2.2	-3.1, 11.2	0.0029**
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia									
BASELINE	120		2.46 (2.28)	2.2	0.0, 10.0				
Low Dose	66		2.28 (1.97)	2.1	0.0, 6.8				
High Dose	54		2.69 (2.61)	2.4	0.0, 10.0				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Geographic region:EUROPE AND AUSTRALIA (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 1	116	2.50	2.48 (3.02)	1.1	0.0, 12.8	-0.02 (2.46)	0.0	-5.3, 8.1	0.9352
Low Dose	63	2.33	2.56 (2.81)	1.8	0.0, 11.6	0.22 (2.59)	0.0	-5.3, 7.1	0.4948
High Dose	53	2.70	2.39 (3.29)	0.8	0.0, 12.8	-0.31 (2.29)	-0.2	-4.5, 8.1	0.3331
WEEK 6	105	2.53	2.04 (3.22)	0.5	0.0, 15.4	-0.49 (2.49)	-0.3	-5.8, 11.6	0.0477*
Low Dose	58	2.35	2.08 (3.18)	0.7	0.0, 15.4	-0.28 (2.64)	-0.0	-5.1, 11.6	0.4304
High Dose	47	2.75	2.00 (3.30)	0.0	0.0, 13.1	-0.75 (2.30)	-0.6	-5.8, 5.7	0.0304*
WEEK 13	58	2.88	1.40 (2.11)	0.3	0.0, 8.2	-1.47 (2.57)	-1.2	-8.6, 4.6	<=0.001***
Low Dose	31	2.77	1.22 (1.93)	0.2	0.0, 8.2	-1.54 (2.16)	-1.8	-5.0, 4.3	<=0.001***
High Dose	27	3.00	1.61 (2.33)	0.6	0.0, 8.0	-1.39 (3.02)	-0.8	-8.6, 4.6	0.0240*
WEEK 26	61	2.10	1.93 (2.80)	0.7	0.0, 11.0	-0.17 (2.87)	0.0	-7.4, 7.2	0.6521
Low Dose	29	2.29	1.64 (2.61)	0.7	0.0, 10.8	-0.64 (2.68)	0.0	-6.5, 5.4	0.2053
High Dose	32	1.93	2.20 (2.98)	0.6	0.0, 11.0	0.27 (3.02)	0.0	-7.4, 7.2	0.6215
WEEK 39	48	2.13	1.63 (2.70)	0.0	0.0, 10.8	-0.50 (2.30)	-0.2	-5.3, 5.5	0.1360
Low Dose	26	2.27	1.47 (2.60)	0.0	0.0, 10.8	-0.80 (2.49)	-0.5	-3.9, 5.5	0.1132
High Dose	22	1.97	1.82 (2.86)	0.0	0.0, 8.5	-0.15 (2.05)	-0.2	-5.3, 4.2	0.7348

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Geographic region:EUROPE AND AUSTRALIA (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 52	44	2.17	1.97 (3.66)	0.0	0.0, 15.6	-0.20 (3.08)	-0.2	-6.5, 9.2	0.6648
Low Dose	23	2.35	1.71 (3.47)	0.0	0.0, 11.8	-0.64 (3.57)	-0.4	-6.5, 9.2	0.3987
High Dose	21	1.97	2.24 (3.93)	0.0	0.0, 15.6	0.28 (2.43)	0.0	-4.9, 6.7	0.6076
Average Daily Normalized 'On' Time With Troublesome Dyskinesia									
BASELINE	120		1.15 (2.00)	0.0	0.0, 10.5				
Low Dose	66		1.54 (2.34)	0.2	0.0, 10.5				
High Dose	54		0.68 (1.36)	0.0	0.0, 5.3				
WEEK 1	116	1.16	1.11 (2.40)	0.0	0.0, 11.7	-0.05 (1.89)	0.0	-5.7, 10.5	0.7777
Low Dose	63	1.60	1.52 (2.81)	0.0	0.0, 11.7	-0.08 (2.16)	0.0	-5.7, 10.5	0.7662
High Dose	53	0.63	0.61 (1.71)	0.0	0.0, 9.8	-0.01 (1.53)	0.0	-4.9, 5.9	0.9541
WEEK 6	105	0.94	0.49 (1.24)	0.0	0.0, 5.8	-0.45 (1.49)	0.0	-9.2, 4.4	0.0026**
Low Dose	58	1.30	0.62 (1.41)	0.0	0.0, 5.8	-0.67 (1.73)	0.0	-9.2, 2.7	0.0043**
High Dose	47	0.49	0.32 (1.00)	0.0	0.0, 4.4	-0.17 (1.08)	0.0	-3.4, 4.4	0.2881

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Geographic region:EUROPE AND AUSTRALIA (Cont.)									
Average Daily Normalized 'On' Time With Troublesome Dyskinesia (Cont.)									
WEEK 13	58	0.88	0.37 (1.24)	0.0	0.0, 8.0	-0.50 (1.43)	0.0	-5.2, 6.0	0.0099**
Low Dose	31	1.05	0.46 (1.50)	0.0	0.0, 8.0	-0.59 (1.80)	0.0	-5.2, 6.0	0.0792
High Dose	27	0.68	0.28 (0.89)	0.0	0.0, 3.7	-0.40 (0.86)	0.0	-3.4, 0.9	0.0217*
WEEK 26	61	0.76	0.29 (1.18)	0.0	0.0, 8.8	-0.47 (1.78)	0.0	-4.9, 8.8	0.0444*
Low Dose	29	0.80	0.05 (0.16)	0.0	0.0, 0.7	-0.74 (1.29)	0.0	-4.7, 0.4	0.0045**
High Dose	32	0.72	0.50 (1.60)	0.0	0.0, 8.8	-0.22 (2.12)	0.0	-4.9, 8.8	0.5603
WEEK 39	48	0.73	0.30 (0.87)	0.0	0.0, 3.8	-0.43 (1.17)	0.0	-5.0, 2.7	0.0150*
Low Dose	26	0.75	0.32 (0.99)	0.0	0.0, 3.8	-0.42 (0.87)	0.0	-3.6, 0.5	0.0202*
High Dose	22	0.71	0.27 (0.73)	0.0	0.0, 2.7	-0.43 (1.48)	0.0	-5.0, 2.7	0.1833
WEEK 52	44	0.77	0.43 (0.91)	0.0	0.0, 3.7	-0.34 (1.41)	0.0	-5.0, 3.7	0.1165
Low Dose	23	0.82	0.29 (0.68)	0.0	0.0, 2.7	-0.53 (1.22)	0.0	-3.0, 1.8	0.0478*
High Dose	21	0.72	0.59 (1.10)	0.0	0.0, 3.7	-0.13 (1.59)	0.0	-5.0, 3.7	0.7160

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Geographic region:EUROPE AND AUSTRALIA (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia									
BASELINE	120		8.87 (2.59)	9.2	0.3, 16.0				
Low Dose	66		8.63 (2.58)	9.0	0.3, 14.2				
High Dose	54		9.17 (2.60)	9.3	2.6, 16.0				
WEEK 1	116	8.83	10.81 (4.00)	11.5	0.0, 16.0	1.99 (4.07)	2.1	-10.4, 11.3	<=0.001***
Low Dose	63	8.50	10.75 (3.91)	11.2	1.6, 16.0	2.24 (3.63)	2.2	-5.9, 11.3	<=0.001***
High Dose	53	9.22	10.90 (4.14)	11.9	0.0, 16.0	1.68 (4.55)	1.8	-10.4, 8.9	0.0097**
WEEK 6	105	8.98	12.10 (3.17)	12.6	0.0, 16.0	3.12 (3.55)	3.7	-9.9, 10.6	<=0.001***
Low Dose	58	8.74	12.18 (3.44)	12.6	0.0, 16.0	3.44 (3.64)	4.0	-9.9, 10.2	<=0.001***
High Dose	47	9.28	12.00 (2.82)	12.3	5.8, 16.0	2.72 (3.44)	3.6	-6.8, 10.6	<=0.001***
WEEK 13	58	9.32	12.62 (3.32)	13.8	3.4, 16.0	3.30 (3.23)	3.7	-5.2, 9.3	<=0.001***
Low Dose	31	9.01	12.82 (3.42)	13.8	3.4, 16.0	3.82 (3.20)	4.4	-4.9, 9.3	<=0.001***
High Dose	27	9.69	12.38 (3.24)	13.9	5.3, 16.0	2.70 (3.22)	3.4	-5.2, 7.5	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Geographic region:EUROPE AND AUSTRALIA (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia (Cont.)									
WEEK 26	61	8.89	13.14 (2.77)	14.3	6.2, 16.0	4.25 (3.68)	4.4	-5.5, 12.5	<=0.001***
Low Dose	29	8.86	13.95 (2.40)	15.0	8.6, 16.0	5.09 (3.39)	4.8	-1.7, 12.5	<=0.001***
High Dose	32	8.92	12.40 (2.91)	13.1	6.2, 16.0	3.48 (3.81)	2.9	-5.5, 10.6	<=0.001***
WEEK 39	48	9.02	12.94 (2.92)	12.9	4.6, 16.0	3.92 (3.35)	3.2	-5.9, 9.8	<=0.001***
Low Dose	26	9.01	13.30 (2.77)	13.0	4.6, 16.0	4.29 (3.50)	3.1	-5.9, 9.8	<=0.001***
High Dose	22	9.03	12.51 (3.11)	12.2	6.6, 16.0	3.48 (3.19)	3.4	-2.9, 9.7	<=0.001***
WEEK 52	44	9.11	12.80 (3.30)	13.9	4.5, 16.0	3.69 (3.57)	3.6	-5.4, 11.2	<=0.001***
Low Dose	23	8.79	12.98 (3.21)	13.9	5.1, 16.0	4.19 (3.65)	4.3	-5.4, 10.2	<=0.001***
High Dose	21	9.46	12.61 (3.46)	13.8	4.5, 16.0	3.15 (3.50)	2.8	-2.3, 11.2	<=0.001***
Geographic region:JAPAN									
Average Daily Normalized 'Off' Time									
BASELINE	27		6.79 (2.05)	6.9	0.0, 10.3				
Low Dose	22		6.50 (2.09)	6.6	0.0, 10.3				
High Dose	5		8.06 (1.42)	8.3	5.7, 9.6				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Geographic region:JAPAN (Cont.)									
Average Daily Normalized 'Off' Time (Cont.)									
WEEK 1	26	6.78	5.25 (3.32)	5.1	0.0, 13.8	-1.53 (3.77)	-1.9	-9.7, 4.7	0.0490*
Low Dose	21	6.47	5.15 (3.26)	4.7	0.0, 13.8	-1.33 (3.66)	-1.9	-9.7, 4.7	0.1122
High Dose	5	8.06	5.67 (3.95)	5.4	0.0, 10.9	-2.39 (4.56)	-3.1	-8.3, 2.8	0.3067
WEEK 6	24	6.72	5.88 (3.71)	4.9	0.0, 13.4	-0.84 (3.94)	-2.5	-7.5, 6.8	0.3088
Low Dose	19	6.37	5.32 (3.62)	4.0	0.0, 13.4	-1.05 (3.86)	-2.4	-7.5, 6.2	0.2497
High Dose	5	8.06	8.04 (3.59)	6.4	4.8, 12.5	-0.02 (4.60)	-2.9	-3.5, 6.8	0.9939
WEEK 13	10	5.81	6.67 (4.86)	7.3	0.0, 13.4	0.86 (5.02)	1.8	-6.6, 8.1	0.6010
Low Dose	10	5.81	6.67 (4.86)	7.3	0.0, 13.4	0.86 (5.02)	1.8	-6.6, 8.1	0.6010
High Dose	0								
WEEK 26	15	6.67	5.79 (4.43)	5.4	0.0, 14.3	-0.89 (4.46)	-0.7	-8.1, 7.1	0.4534
Low Dose	12	6.17	5.92 (4.57)	5.4	0.0, 14.3	-0.26 (4.49)	-0.4	-7.0, 7.1	0.8468
High Dose	3	8.68	5.27 (4.67)	6.9	0.0, 8.9	-3.42 (4.07)	-1.4	-8.1, -0.7	0.2834
WEEK 39	14	6.68	4.36 (3.22)	4.5	0.0, 12.3	-2.32 (3.40)	-1.7	-8.1, 5.1	0.0241*
Low Dose	11	6.13	4.56 (3.30)	4.7	0.0, 12.3	-1.57 (3.14)	-1.3	-7.0, 5.1	0.1294
High Dose	3	8.68	3.61 (3.44)	4.0	0.0, 6.8	-5.07 (3.34)	-5.6	-8.1, -1.5	0.1196

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Geographic region:JAPAN (Cont.)									
Average Daily Normalized 'Off' Time (Cont.)									
WEEK 52	12	6.75	3.83 (3.17)	3.4	0.0, 10.1	-2.92 (3.30)	-3.3	-8.1, 4.1	0.0106*
Low Dose	9	6.11	3.72 (3.24)	3.0	0.0, 10.1	-2.39 (3.33)	-3.1	-7.0, 4.1	0.0634
High Dose	3	8.68	4.17 (3.62)	6.1	0.0, 6.4	-4.51 (3.21)	-3.5	-8.1, -1.9	0.1352
Average Daily Normalized 'On' Time Without Dyskinesia									
BASELINE	27		5.68 (2.73)	5.7	0.0, 10.1				
Low Dose	22		5.30 (2.86)	4.8	0.0, 10.1				
High Dose	5		7.37 (0.91)	7.7	6.4, 8.4				
WEEK 1	26	5.55	6.23 (3.84)	6.8	0.3, 16.0	0.68 (4.00)	0.9	-8.9, 10.2	0.3968
Low Dose	21	5.12	5.49 (3.48)	6.2	0.3, 11.3	0.36 (3.99)	0.8	-8.9, 10.2	0.6805
High Dose	5	7.37	9.36 (4.06)	8.1	5.1, 16.0	1.99 (4.19)	1.3	-2.8, 8.3	0.3494
WEEK 6	24	5.79	8.38 (4.05)	8.4	0.0, 13.8	2.60 (5.07)	3.7	-6.4, 13.8	0.0196*
Low Dose	19	5.37	9.10 (3.56)	8.6	2.6, 13.8	3.73 (4.65)	3.9	-3.5, 13.8	0.0025**
High Dose	5	7.37	5.65 (5.05)	3.5	0.0, 11.2	-1.72 (4.59)	-3.7	-6.4, 3.5	0.4491

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Geographic region:JAPAN (Cont.)									
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 13	10	5.40	5.93 (5.42)	5.2	0.0, 14.7	0.54 (5.57)	0.9	-9.0, 9.6	0.7668
Low Dose	10	5.40	5.93 (5.42)	5.2	0.0, 14.7	0.54 (5.57)	0.9	-9.0, 9.6	0.7668
High Dose	0								
WEEK 26	15	5.94	8.34 (5.26)	8.1	0.0, 16.0	2.40 (5.01)	3.2	-10.1, 9.5	0.0844
Low Dose	12	5.60	7.77 (5.41)	7.8	0.0, 16.0	2.18 (5.33)	3.2	-10.1, 9.5	0.1852
High Dose	3	7.32	10.62 (4.80)	9.1	6.8, 16.0	3.30 (4.19)	1.4	0.4, 8.1	0.3053
WEEK 39	14	5.90	9.83 (4.24)	10.3	0.3, 16.0	3.93 (3.21)	4.0	-1.9, 8.1	<=0.001***
Low Dose	11	5.51	9.36 (4.38)	10.4	0.3, 16.0	3.85 (3.32)	4.9	-1.9, 8.0	0.0032**
High Dose	3	7.32	11.55 (3.86)	9.5	9.2, 16.0	4.23 (3.45)	3.1	1.5, 8.1	0.1679
WEEK 52	12	6.26	10.76 (3.48)	10.9	4.2, 16.0	4.49 (2.45)	3.9	1.7, 8.1	<=0.001***
Low Dose	9	5.91	10.60 (3.48)	11.0	4.2, 16.0	4.69 (2.18)	4.8	1.9, 7.8	<=0.001***
High Dose	3	7.32	11.22 (4.21)	9.6	8.1, 16.0	3.90 (3.64)	1.9	1.7, 8.1	0.2043

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Geographic region:JAPAN (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia									
BASELINE	27		2.74 (2.76)	2.6	0.0, 8.0				
Low Dose	22		3.30 (2.76)	3.1	0.0, 8.0				
High Dose	5		0.26 (0.44)	0.0	0.0, 1.0				
WEEK 1	26	2.84	3.83 (4.01)	2.6	0.0, 14.9	0.99 (3.82)	0.0	-5.4, 13.2	0.2002
Low Dose	21	3.46	4.52 (4.15)	3.4	0.0, 14.9	1.06 (4.24)	0.0	-5.4, 13.2	0.2641
High Dose	5	0.26	0.92 (1.10)	0.6	0.0, 2.6	0.67 (1.16)	0.0	-0.4, 2.3	0.2677
WEEK 6	24	2.64	1.70 (2.87)	0.2	0.0, 9.6	-0.94 (3.53)	0.0	-6.7, 9.6	0.2027
Low Dose	19	3.27	1.54 (2.56)	0.5	0.0, 9.0	-1.73 (2.93)	-1.2	-6.7, 4.4	0.0188*
High Dose	5	0.26	2.31 (4.17)	0.0	0.0, 9.6	2.05 (4.34)	0.0	-1.0, 9.6	0.3496
WEEK 13	10	3.31	3.39 (5.59)	0.7	0.0, 16.0	0.08 (5.72)	-0.5	-6.5, 13.2	0.9655
Low Dose	10	3.31	3.39 (5.59)	0.7	0.0, 16.0	0.08 (5.72)	-0.5	-6.5, 13.2	0.9655
High Dose	0								

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Geographic region:JAPAN (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 26	15	2.91	1.76 (3.26)	0.0	0.0, 12.1	-1.15 (3.11)	0.0	-6.7, 4.6	0.1730
Low Dose	12	3.64	2.17 (3.55)	0.2	0.0, 12.1	-1.47 (3.43)	-2.6	-6.7, 4.6	0.1657
High Dose	3	0.00	0.11 (0.20)	0.0	0.0, 0.3	0.11 (0.20)	0.0	0.0, 0.3	0.4226
WEEK 39	14	2.92	1.72 (3.58)	0.0	0.0, 13.2	-1.20 (3.18)	-0.1	-6.7, 5.2	0.1826
Low Dose	11	3.72	1.96 (3.99)	0.0	0.0, 13.2	-1.75 (3.34)	-1.5	-6.7, 5.2	0.1121
High Dose	3	0.00	0.84 (1.46)	0.0	0.0, 2.5	0.84 (1.46)	0.0	0.0, 2.5	0.4226
WEEK 52	12	2.64	1.41 (2.10)	0.1	0.0, 6.7	-1.23 (2.31)	0.0	-6.7, 1.8	0.0920
Low Dose	9	3.52	1.68 (2.34)	0.3	0.0, 6.7	-1.84 (2.32)	-1.3	-6.7, 0.0	0.0441*
High Dose	3	0.00	0.61 (1.05)	0.0	0.0, 1.8	0.61 (1.05)	0.0	0.0, 1.8	0.4226
Average Daily Normalized 'On' Time With Troublesome Dyskinesia									
BASELINE	27		0.79 (1.74)	0.0	0.0, 7.2				
Low Dose	22		0.90 (1.91)	0.0	0.0, 7.2				
High Dose	5		0.31 (0.43)	0.0	0.0, 0.8				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Geographic region:JAPAN (Cont.)									
Average Daily Normalized 'On' Time With Troublesome Dyskinesia (Cont.)									
WEEK 1	26	0.82	0.69 (1.59)	0.0	0.0, 7.9	-0.13 (2.37)	0.0	-6.0, 7.9	0.7790
Low Dose	21	0.95	0.85 (1.74)	0.0	0.0, 7.9	-0.10 (2.64)	0.0	-6.0, 7.9	0.8639
High Dose	5	0.31	0.05 (0.11)	0.0	0.0, 0.3	-0.26 (0.38)	0.0	-0.8, 0.0	0.1899
WEEK 6	24	0.85	0.04 (0.12)	0.0	0.0, 0.5	-0.82 (1.81)	0.0	-7.2, 0.4	0.0370*
Low Dose	19	0.99	0.04 (0.14)	0.0	0.0, 0.5	-0.95 (2.01)	0.0	-7.2, 0.4	0.0544
High Dose	5	0.31	0.00 (0.00)	0.0	0.0, 0.0	-0.31 (0.43)	0.0	-0.8, 0.0	0.1779
WEEK 13	10	1.48	0.00 (0.00)	0.0	0.0, 0.0	-1.48 (2.59)	0.0	-7.2, 0.0	0.1039
Low Dose	10	1.48	0.00 (0.00)	0.0	0.0, 0.0	-1.48 (2.59)	0.0	-7.2, 0.0	0.1039
High Dose	0								
WEEK 26	15	0.47	0.11 (0.34)	0.0	0.0, 1.3	-0.36 (1.20)	0.0	-3.4, 1.3	0.2645
Low Dose	12	0.59	0.14 (0.37)	0.0	0.0, 1.3	-0.45 (1.33)	0.0	-3.4, 1.3	0.2682
High Dose	3	0.00	0.00 (0.00)	0.0	0.0, 0.0	0.00 (0.00)	0.0	0.0, 0.0	
WEEK 39	14	0.51	0.09 (0.23)	0.0	0.0, 0.7	-0.42 (1.05)	0.0	-3.0, 0.0	0.1610
Low Dose	11	0.64	0.11 (0.26)	0.0	0.0, 0.7	-0.53 (1.17)	0.0	-3.0, 0.0	0.1630
High Dose	3	0.00	0.00 (0.00)	0.0	0.0, 0.0	0.00 (0.00)	0.0	0.0, 0.0	

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Geographic region:JAPAN (Cont.)									
Average Daily Normalized 'On' Time With Troublesome Dyskinesia (Cont.)									
WEEK 52	12	0.34	0.00 (0.00)	0.0	0.0, 0.0	-0.34 (0.97)	0.0	-3.4, 0.0	0.2516
Low Dose	9	0.45	0.00 (0.00)	0.0	0.0, 0.0	-0.45 (1.12)	0.0	-3.4, 0.0	0.2576
High Dose	3	0.00	0.00 (0.00)	0.0	0.0, 0.0	0.00 (0.00)	0.0	0.0, 0.0	
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia									
BASELINE	27		8.42 (1.76)	8.7	4.6, 11.1				
Low Dose	22		8.60 (1.84)	8.9	4.6, 11.1				
High Dose	5		7.63 (1.20)	7.7	6.4, 9.5				
WEEK 1	26	8.40	10.06 (3.19)	9.9	2.2, 16.0	1.66 (3.85)	1.1	-4.0, 9.7	0.0372*
Low Dose	21	8.58	10.00 (3.09)	9.8	2.2, 16.0	1.43 (3.78)	1.0	-4.0, 9.7	0.0996
High Dose	5	7.63	10.28 (3.95)	10.4	5.1, 16.0	2.65 (4.42)	3.7	-2.8, 8.3	0.2511
WEEK 6	24	8.43	10.08 (3.69)	11.1	2.6, 16.0	1.65 (3.82)	3.0	-6.0, 7.5	0.0448*
Low Dose	19	8.64	10.64 (3.60)	11.7	2.6, 16.0	2.00 (3.75)	3.1	-5.7, 7.5	0.0321*
High Dose	5	7.63	7.96 (3.59)	9.6	3.5, 11.2	0.33 (4.19)	2.9	-6.0, 3.5	0.8681

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Geographic region:JAPAN (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia (Cont.)									
WEEK 13	10	8.71	9.33 (4.86)	8.7	2.6, 16.0	0.62 (3.76)	0.1	-5.0, 6.6	0.6148
Low Dose	10	8.71	9.33 (4.86)	8.7	2.6, 16.0	0.62 (3.76)	0.1	-5.0, 6.6	0.6148
High Dose	0								
WEEK 26	15	8.85	10.10 (4.38)	10.5	1.7, 16.0	1.25 (4.00)	0.7	-5.5, 8.1	0.2476
Low Dose	12	9.24	9.94 (4.50)	10.5	1.7, 16.0	0.71 (3.97)	0.5	-5.5, 7.0	0.5513
High Dose	3	7.32	10.73 (4.67)	9.1	7.1, 16.0	3.42 (4.07)	1.4	0.7, 8.1	0.2834
WEEK 39	14	8.82	11.55 (3.17)	11.5	3.7, 16.0	2.73 (2.94)	2.3	-2.1, 8.1	0.0040**
Low Dose	11	9.23	11.32 (3.23)	11.3	3.7, 16.0	2.10 (2.62)	1.9	-2.1, 7.0	0.0244*
High Dose	3	7.32	12.39 (3.44)	12.0	9.2, 16.0	5.07 (3.34)	5.6	1.5, 8.1	0.1196
WEEK 52	12	8.91	12.17 (3.17)	12.6	5.9, 16.0	3.26 (2.79)	3.3	-1.2, 8.1	0.0019**
Low Dose	9	9.43	12.28 (3.24)	13.0	5.9, 16.0	2.85 (2.71)	3.1	-1.2, 7.0	0.0136*
High Dose	3	7.32	11.83 (3.62)	9.9	9.6, 16.0	4.51 (3.21)	3.5	1.9, 8.1	0.1352

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
PD duration (time since diagnosis) category:<10 years									
Average Daily Normalized 'Off' Time									
BASELINE	127		6.04 (2.24)	6.0	0.0, 10.3				
Low Dose	64		6.05 (2.17)	6.0	0.0, 10.3				
High Dose	63		6.04 (2.33)	6.0	0.0, 10.3				
WEEK 1	122	6.02	3.67 (3.21)	2.9	0.0, 14.8	-2.35 (3.42)	-2.1	-9.7, 5.9	<=0.001***
Low Dose	62	6.10	3.78 (3.27)	2.8	0.0, 13.8	-2.32 (3.22)	-2.1	-9.7, 3.9	<=0.001***
High Dose	60	5.94	3.55 (3.18)	2.9	0.0, 14.8	-2.39 (3.64)	-2.2	-8.9, 5.9	<=0.001***
WEEK 6	112	6.05	3.44 (3.00)	3.1	0.0, 12.3	-2.62 (3.39)	-2.9	-9.9, 6.7	<=0.001***
Low Dose	57	5.97	3.29 (2.90)	3.1	0.0, 12.3	-2.68 (3.46)	-2.6	-9.9, 5.7	<=0.001***
High Dose	55	6.14	3.59 (3.11)	3.0	0.0, 10.7	-2.55 (3.34)	-2.9	-8.4, 6.7	<=0.001***
WEEK 13	64	5.63	3.04 (3.44)	1.7	0.0, 12.1	-2.58 (3.48)	-3.2	-9.9, 6.3	<=0.001***
Low Dose	32	5.85	2.42 (3.13)	1.3	0.0, 12.1	-3.42 (3.04)	-3.9	-9.9, 5.0	<=0.001***
High Dose	32	5.40	3.66 (3.66)	2.3	0.0, 10.7	-1.74 (3.74)	-2.1	-9.2, 6.3	0.0130*

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
PD duration (time since diagnosis) category:<10 years (Cont.)									
Average Daily Normalized 'Off' Time (Cont.)									
WEEK 26	69	5.74	2.85 (2.98)	1.7	0.0, 11.2	-2.89 (3.11)	-2.9	-9.2, 5.5	<=0.001***
Low Dose	32	5.77	2.93 (3.23)	1.3	0.0, 11.2	-2.83 (3.36)	-2.9	-9.2, 5.5	<=0.001***
High Dose	37	5.73	2.78 (2.78)	2.0	0.0, 8.4	-2.95 (2.92)	-2.9	-9.2, 4.4	<=0.001***
WEEK 39	59	5.72	2.70 (2.65)	2.0	0.0, 11.4	-3.01 (3.04)	-2.8	-9.9, 6.4	<=0.001***
Low Dose	32	5.84	2.58 (2.70)	1.9	0.0, 11.4	-3.27 (3.26)	-2.9	-9.9, 6.4	<=0.001***
High Dose	27	5.56	2.85 (2.64)	3.1	0.0, 7.2	-2.71 (2.80)	-2.8	-9.2, 4.0	<=0.001***
WEEK 52	58	5.70	2.94 (3.19)	2.3	0.0, 11.5	-2.76 (3.16)	-2.9	-9.9, 5.9	<=0.001***
Low Dose	30	5.95	2.96 (3.18)	2.3	0.0, 10.9	-2.99 (3.53)	-3.3	-9.9, 5.9	<=0.001***
High Dose	28	5.43	2.93 (3.25)	1.6	0.0, 11.5	-2.51 (2.75)	-2.3	-8.6, 2.6	<=0.001***
Average Daily Normalized 'On' Time Without Dyskinesia									
BASELINE	127		6.79 (3.45)	6.9	0.0, 15.4				
Low Dose	64		6.61 (3.83)	7.0	0.0, 15.4				
High Dose	63		6.97 (3.04)	6.9	0.3, 13.8				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
PD duration (time since diagnosis) category:<10 years (Cont.)									
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 1	122	6.73	9.04 (4.69)	9.2	0.0, 16.0	2.30 (4.04)	1.7	-8.9, 12.0	<=0.001***
Low Dose	62	6.45	8.41 (4.96)	8.9	0.0, 16.0	1.96 (3.92)	1.6	-8.9, 10.7	<=0.001***
High Dose	60	7.02	9.69 (4.33)	10.0	0.0, 16.0	2.66 (4.16)	2.6	-5.4, 12.0	<=0.001***
WEEK 6	112	6.96	10.60 (4.19)	11.5	0.0, 16.0	3.64 (4.26)	3.6	-6.7, 13.8	<=0.001***
Low Dose	57	6.92	10.59 (4.36)	11.8	0.0, 16.0	3.67 (4.32)	3.7	-6.1, 13.8	<=0.001***
High Dose	55	6.99	10.61 (4.05)	11.5	0.5, 16.0	3.61 (4.23)	3.5	-6.7, 12.0	<=0.001***
WEEK 13	64	7.16	11.34 (4.50)	12.9	0.0, 16.0	4.18 (4.66)	4.5	-9.0, 15.2	<=0.001***
Low Dose	32	7.36	11.84 (4.80)	13.5	0.0, 16.0	4.48 (4.85)	4.8	-9.0, 15.2	<=0.001***
High Dose	32	6.96	10.84 (4.20)	10.6	2.7, 16.0	3.88 (4.51)	4.0	-6.3, 14.1	<=0.001***
WEEK 26	69	7.44	11.19 (4.31)	12.5	0.0, 16.0	3.75 (4.40)	4.6	-10.1, 14.1	<=0.001***
Low Dose	32	7.76	11.56 (4.52)	13.2	0.0, 16.0	3.80 (4.41)	4.6	-10.1, 11.2	<=0.001***
High Dose	37	7.17	10.87 (4.15)	11.4	0.8, 16.0	3.71 (4.45)	4.6	-6.6, 14.1	<=0.001***
WEEK 39	59	7.41	11.22 (4.15)	11.3	0.0, 16.0	3.81 (3.70)	3.3	-5.0, 12.4	<=0.001***
Low Dose	32	7.49	11.98 (4.05)	12.0	0.3, 16.0	4.49 (3.77)	4.9	-5.0, 11.2	<=0.001***
High Dose	27	7.33	10.33 (4.16)	10.9	0.0, 16.0	3.00 (3.51)	2.7	-2.8, 12.4	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
PD duration (time since diagnosis) category:<10 years (Cont.)									
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 52	58	7.38	10.35 (4.93)	11.3	0.0, 16.0	2.97 (4.12)	3.0	-12.0, 9.9	<=0.001***
Low Dose	30	7.09	11.12 (4.71)	12.5	0.0, 16.0	4.03 (3.78)	4.8	-6.5, 9.9	<=0.001***
High Dose	28	7.69	9.53 (5.11)	9.6	0.0, 16.0	1.84 (4.23)	1.7	-12.0, 8.8	0.0296*
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia									
BASELINE	127		2.35 (2.64)	1.7	0.0, 12.2				
Low Dose	64		2.36 (2.65)	1.7	0.0, 10.3				
High Dose	63		2.35 (2.65)	2.4	0.0, 12.2				
WEEK 1	122	2.43	2.46 (3.22)	1.0	0.0, 14.9	0.03 (2.80)	0.0	-8.5, 13.2	0.8929
Low Dose	62	2.44	2.70 (3.34)	2.1	0.0, 14.9	0.26 (2.80)	0.0	-8.5, 13.2	0.4626
High Dose	60	2.42	2.22 (3.10)	0.6	0.0, 11.9	-0.20 (2.80)	0.0	-8.2, 8.8	0.5775
WEEK 6	112	2.39	1.54 (2.81)	0.0	0.0, 13.9	-0.85 (2.58)	-0.2	-7.6, 8.3	<=0.001***
Low Dose	57	2.41	1.59 (2.72)	0.5	0.0, 10.4	-0.82 (2.77)	0.0	-7.6, 8.3	0.0296*
High Dose	55	2.36	1.49 (2.92)	0.0	0.0, 13.9	-0.87 (2.38)	-0.4	-7.6, 5.7	0.0088**

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
PD duration (time since diagnosis) category:<10 years (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 13	64	2.72	1.41 (2.82)	0.0	0.0, 15.5	-1.31 (3.22)	-0.5	-12.2, 5.2	0.0018**
Low Dose	32	2.48	1.65 (3.48)	0.0	0.0, 15.5	-0.83 (3.11)	0.0	-8.0, 5.2	0.1425
High Dose	32	2.96	1.16 (1.99)	0.0	0.0, 8.0	-1.80 (3.31)	-0.7	-12.2, 4.6	0.0043**
WEEK 26	69	2.28	1.73 (3.07)	0.0	0.0, 15.2	-0.55 (3.36)	0.0	-12.2, 12.0	0.1798
Low Dose	32	2.16	1.29 (2.39)	0.0	0.0, 12.1	-0.87 (2.63)	0.0	-6.8, 4.6	0.0698
High Dose	37	2.38	2.11 (3.55)	0.0	0.0, 15.2	-0.27 (3.91)	0.0	-12.2, 12.0	0.6780
WEEK 39	59	2.36	1.77 (3.37)	0.0	0.0, 16.0	-0.59 (2.82)	0.0	-7.8, 6.1	0.1123
Low Dose	32	2.30	1.27 (2.79)	0.0	0.0, 13.2	-1.02 (2.88)	-0.1	-7.8, 5.2	0.0536
High Dose	27	2.43	2.35 (3.92)	0.0	0.0, 16.0	-0.08 (2.72)	0.0	-6.4, 6.1	0.8744
WEEK 52	58	2.35	2.28 (4.30)	0.0	0.0, 16.0	-0.08 (3.40)	0.0	-6.8, 12.9	0.8653
Low Dose	30	2.43	1.67 (3.73)	0.0	0.0, 16.0	-0.77 (3.28)	0.0	-6.8, 9.2	0.2109
High Dose	28	2.27	2.93 (4.82)	0.3	0.0, 16.0	0.66 (3.44)	0.0	-4.9, 12.9	0.3178

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
PD duration (time since diagnosis) category:<10 years (Cont.)									
Average Daily Normalized 'On' Time With Troublesome Dyskinesia									
BASELINE	127		0.82 (1.65)	0.0	0.0, 9.2				
Low Dose	64		0.98 (1.94)	0.0	0.0, 9.2				
High Dose	63		0.65 (1.28)	0.0	0.0, 5.3				
WEEK 1	122	0.82	0.83 (2.16)	0.0	0.0, 11.7	0.01 (1.78)	0.0	-5.7, 10.5	0.9292
Low Dose	62	1.01	1.11 (2.64)	0.0	0.0, 11.7	0.10 (2.11)	0.0	-5.7, 10.5	0.7154
High Dose	60	0.62	0.55 (1.48)	0.0	0.0, 9.8	-0.07 (1.36)	0.0	-4.9, 4.7	0.6815
WEEK 6	112	0.60	0.42 (1.35)	0.0	0.0, 9.0	-0.18 (1.52)	0.0	-9.2, 6.9	0.2131
Low Dose	57	0.70	0.53 (1.65)	0.0	0.0, 9.0	-0.17 (1.90)	0.0	-9.2, 6.9	0.5010
High Dose	55	0.50	0.31 (0.94)	0.0	0.0, 4.4	-0.19 (1.01)	0.0	-3.4, 4.4	0.1699
WEEK 13	64	0.50	0.21 (0.74)	0.0	0.0, 3.7	-0.29 (0.85)	0.0	-3.4, 2.6	0.0090**
Low Dose	32	0.31	0.08 (0.32)	0.0	0.0, 1.7	-0.23 (0.71)	0.0	-2.7, 1.7	0.0747
High Dose	32	0.68	0.34 (0.99)	0.0	0.0, 3.7	-0.34 (0.98)	0.0	-3.4, 2.6	0.0574

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
PD duration (time since diagnosis) category:<10 years (Cont.)									
Average Daily Normalized 'On' Time With Troublesome Dyskinesia (Cont.)									
WEEK 26	69	0.53	0.23 (0.64)	0.0	0.0, 3.7	-0.31 (1.23)	0.0	-4.9, 3.7	0.0398*
Low Dose	32	0.32	0.22 (0.72)	0.0	0.0, 3.7	-0.10 (1.12)	0.0	-3.4, 3.7	0.6215
High Dose	37	0.72	0.23 (0.57)	0.0	0.0, 2.4	-0.49 (1.30)	0.0	-4.9, 1.7	0.0273*
WEEK 39	59	0.51	0.31 (1.21)	0.0	0.0, 8.1	-0.21 (1.39)	0.0	-5.0, 7.3	0.2619
Low Dose	32	0.37	0.17 (0.65)	0.0	0.0, 3.5	-0.21 (0.61)	0.0	-2.8, 0.8	0.0655
High Dose	27	0.67	0.47 (1.65)	0.0	0.0, 8.1	-0.20 (1.97)	0.0	-5.0, 7.3	0.5944
WEEK 52	58	0.56	0.42 (1.16)	0.0	0.0, 6.3	-0.14 (1.55)	0.0	-5.0, 6.3	0.4965
Low Dose	30	0.52	0.25 (0.80)	0.0	0.0, 3.3	-0.27 (1.23)	0.0	-3.4, 3.3	0.2325
High Dose	28	0.60	0.61 (1.45)	0.0	0.0, 6.3	0.01 (1.84)	0.0	-5.0, 6.3	0.9856
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia									
BASELINE	127		9.14 (2.67)	9.5	0.3, 16.0				
Low Dose	64		8.97 (2.86)	9.2	0.3, 16.0				
High Dose	63		9.31 (2.46)	9.5	2.6, 16.0				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
PD duration (time since diagnosis) category:<10 years (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia (Cont.)									
WEEK 1	122	9.16	11.50 (3.65)	11.6	1.2, 16.0	2.34 (3.53)	2.1	-5.9, 9.7	<=0.001***
Low Dose	62	8.89	11.11 (4.00)	11.1	1.6, 16.0	2.22 (3.24)	1.8	-3.9, 9.7	<=0.001***
High Dose	60	9.44	11.90 (3.23)	12.2	1.2, 16.0	2.46 (3.84)	2.3	-5.9, 8.9	<=0.001***
WEEK 6	112	9.34	12.14 (3.20)	12.7	3.7, 16.0	2.80 (3.44)	3.2	-6.7, 9.9	<=0.001***
Low Dose	57	9.33	12.19 (3.23)	12.7	3.7, 16.0	2.85 (3.41)	3.0	-5.7, 9.9	<=0.001***
High Dose	55	9.36	12.10 (3.19)	12.8	5.1, 16.0	2.74 (3.50)	3.5	-6.7, 8.4	<=0.001***
WEEK 13	64	9.88	12.74 (3.51)	14.2	3.9, 16.0	2.87 (3.50)	3.3	-6.3, 9.9	<=0.001***
Low Dose	32	9.84	13.49 (3.13)	14.6	3.9, 16.0	3.65 (3.06)	3.9	-5.0, 9.9	<=0.001***
High Dose	32	9.92	12.00 (3.76)	13.6	5.3, 16.0	2.08 (3.78)	2.6	-6.3, 9.2	0.0040**
WEEK 26	69	9.72	12.92 (2.97)	14.0	4.8, 16.0	3.20 (3.12)	2.9	-5.5, 10.2	<=0.001***
Low Dose	32	9.92	12.85 (3.26)	14.4	4.8, 16.0	2.93 (3.25)	3.0	-5.5, 9.2	<=0.001***
High Dose	37	9.55	12.99 (2.75)	13.8	7.6, 16.0	3.44 (3.03)	2.9	-4.4, 10.2	<=0.001***
WEEK 39	59	9.77	12.99 (3.00)	13.1	2.4, 16.0	3.22 (3.35)	3.1	-9.2, 9.9	<=0.001***
Low Dose	32	9.78	13.25 (2.73)	13.8	4.6, 16.0	3.47 (3.21)	3.1	-5.9, 9.9	<=0.001***
High Dose	27	9.76	12.68 (3.32)	12.9	2.4, 16.0	2.91 (3.56)	2.8	-9.2, 9.7	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
PD duration (time since diagnosis) category:<10 years (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia (Cont.)									
WEEK 52	58	9.74	12.63 (3.27)	13.2	4.5, 16.0	2.90 (3.00)	2.7	-5.4, 9.9	<=0.001***
Low Dose	30	9.53	12.79 (3.16)	13.4	5.1, 16.0	3.27 (3.25)	3.1	-5.4, 9.9	<=0.001***
High Dose	28	9.96	12.46 (3.44)	12.7	4.5, 16.0	2.50 (2.72)	2.1	-2.3, 8.4	<=0.001***
PD duration (time since diagnosis) category:>=10 years									
Average Daily Normalized 'Off' Time									
BASELINE	109		5.74 (2.24)	5.7	0.0, 12.6				
Low Dose	63		5.30 (2.16)	5.3	0.0, 10.2				
High Dose	46		6.34 (2.23)	6.5	1.5, 12.6				
WEEK 1	103	5.79	4.33 (3.65)	3.7	0.0, 16.0	-1.46 (3.93)	-2.4	-10.2, 10.4	<=0.001***
Low Dose	59	5.35	3.60 (3.14)	2.9	0.0, 11.2	-1.75 (3.77)	-2.5	-10.2, 5.9	<=0.001***
High Dose	44	6.37	5.30 (4.08)	5.5	0.0, 16.0	-1.07 (4.14)	-1.6	-7.5, 10.4	0.0944
WEEK 6	93	5.80	3.68 (3.56)	3.2	0.0, 16.0	-2.12 (3.85)	-2.9	-10.6, 9.9	<=0.001***
Low Dose	54	5.48	3.35 (3.77)	2.9	0.0, 16.0	-2.13 (3.86)	-2.9	-10.2, 9.9	<=0.001***
High Dose	39	6.26	4.14 (3.23)	3.9	0.0, 12.5	-2.11 (3.89)	-2.9	-10.6, 6.8	0.0016**

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
PD duration (time since diagnosis) category:>=10 years (Cont.)									
Average Daily Normalized 'Off' Time (Cont.)									
WEEK 13	51	5.43	3.22 (3.53)	1.9	0.0, 13.4	-2.21 (3.95)	-3.0	-9.3, 8.1	<=0.001***
Low Dose	32	4.97	3.34 (3.88)	1.9	0.0, 13.4	-1.63 (4.30)	-2.6	-9.3, 8.1	0.0407*
High Dose	19	6.21	3.01 (2.96)	2.0	0.0, 9.3	-3.20 (3.13)	-3.3	-8.0, 4.0	<=0.001***
WEEK 26	58	6.14	2.42 (3.09)	1.2	0.0, 14.3	-3.72 (3.36)	-3.8	-10.6, 7.1	<=0.001***
Low Dose	34	5.70	2.03 (3.10)	0.1	0.0, 14.3	-3.68 (3.34)	-3.9	-10.2, 7.1	<=0.001***
High Dose	24	6.76	2.97 (3.05)	1.7	0.0, 9.8	-3.78 (3.46)	-2.8	-10.6, 5.5	<=0.001***
WEEK 39	52	5.98	2.72 (2.98)	2.1	0.0, 13.3	-3.26 (3.34)	-3.4	-9.8, 9.6	<=0.001***
Low Dose	31	5.46	2.80 (3.22)	2.0	0.0, 13.3	-2.66 (3.49)	-2.9	-9.8, 9.6	<=0.001***
High Dose	21	6.76	2.60 (2.66)	2.2	0.0, 7.3	-4.16 (2.97)	-4.4	-8.1, 2.9	<=0.001***
WEEK 52	38	6.20	1.84 (2.32)	0.5	0.0, 8.1	-4.36 (2.73)	-4.3	-11.2, 2.8	<=0.001***
Low Dose	21	5.74	1.93 (2.15)	0.9	0.0, 6.7	-3.81 (2.23)	-4.0	-10.2, 1.2	<=0.001***
High Dose	17	6.76	1.74 (2.58)	0.5	0.0, 8.1	-5.03 (3.17)	-4.9	-11.2, 2.8	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
PD duration (time since diagnosis) category:>=10 years (Cont.)									
Average Daily Normalized 'On' Time Without Dyskinesia									
BASELINE	109		6.19 (3.22)	6.2	0.0, 12.6				
Low Dose	63		6.10 (3.06)	5.9	0.0, 12.6				
High Dose	46		6.32 (3.46)	6.4	0.0, 12.3				
WEEK 1	103	6.19	7.71 (4.22)	7.8	0.0, 16.0	1.52 (4.12)	1.3	-8.8, 10.2	<=0.001***
Low Dose	59	5.96	7.54 (4.03)	7.3	0.0, 16.0	1.58 (3.97)	1.4	-8.8, 10.2	0.0033**
High Dose	44	6.51	7.93 (4.50)	8.0	0.0, 16.0	1.43 (4.37)	1.3	-8.1, 8.0	0.0358*
WEEK 6	93	6.04	9.10 (4.70)	9.8	0.0, 16.0	3.06 (4.54)	3.4	-9.1, 12.7	<=0.001***
Low Dose	54	5.80	9.09 (4.65)	9.8	0.0, 16.0	3.29 (4.71)	4.1	-9.1, 12.7	<=0.001***
High Dose	39	6.38	9.12 (4.84)	9.9	0.0, 16.0	2.74 (4.35)	2.4	-6.4, 11.2	<=0.001***
WEEK 13	51	6.05	10.09 (4.67)	10.4	0.0, 16.0	4.04 (3.97)	4.0	-6.5, 11.0	<=0.001***
Low Dose	32	5.95	9.49 (4.85)	9.6	0.0, 16.0	3.54 (3.94)	3.4	-6.5, 11.0	<=0.001***
High Dose	19	6.23	11.10 (4.30)	11.3	0.9, 16.0	4.87 (3.97)	5.5	-4.7, 10.0	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
PD duration (time since diagnosis) category:>=10 years (Cont.)									
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 26	58	6.23	11.21 (4.40)	12.7	0.0, 16.0	4.98 (4.49)	5.5	-11.0, 12.7	<=0.001***
Low Dose	34	6.05	11.62 (3.95)	12.7	0.5, 16.0	5.57 (3.33)	5.7	-1.6, 11.5	<=0.001***
High Dose	24	6.48	10.63 (5.01)	12.3	0.0, 16.0	4.15 (5.73)	4.9	-11.0, 12.7	0.0017**
WEEK 39	52	6.59	10.91 (4.24)	11.8	0.6, 16.0	4.33 (4.52)	4.6	-10.6, 13.5	<=0.001***
Low Dose	31	6.26	10.27 (4.54)	11.3	0.6, 16.0	4.01 (4.75)	4.8	-10.6, 11.4	<=0.001***
High Dose	21	7.07	11.87 (3.63)	12.6	5.1, 16.0	4.80 (4.24)	4.3	-2.9, 13.5	<=0.001***
WEEK 52	38	6.49	11.51 (4.31)	12.8	1.3, 16.0	5.02 (4.29)	5.1	-2.9, 13.8	<=0.001***
Low Dose	21	6.45	11.54 (4.08)	12.4	1.3, 16.0	5.10 (4.05)	5.1	-2.9, 11.3	<=0.001***
High Dose	17	6.54	11.47 (4.71)	13.8	1.3, 16.0	4.94 (4.70)	5.0	-2.9, 13.8	<=0.001***
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia									
BASELINE	109		2.95 (2.42)	2.7	0.0, 9.3				
Low Dose	63		3.03 (2.07)	2.9	0.0, 7.5				
High Dose	46		2.84 (2.84)	1.9	0.0, 9.3				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
PD duration (time since diagnosis) category:>=10 years (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 1	103	2.94	2.79 (3.09)	1.7	0.0, 13.6	-0.15 (3.31)	0.0	-6.9, 13.6	0.6497
Low Dose	59	3.11	3.40 (3.20)	2.4	0.0, 13.6	0.29 (3.77)	0.0	-6.4, 13.6	0.5614
High Dose	44	2.71	1.98 (2.77)	1.0	0.0, 12.8	-0.73 (2.51)	0.0	-6.9, 5.8	0.0593
WEEK 6	93	3.01	2.75 (3.69)	1.2	0.0, 15.4	-0.26 (3.45)	-0.3	-7.8, 11.6	0.4726
Low Dose	54	3.10	2.90 (3.49)	1.7	0.0, 15.4	-0.19 (3.32)	-0.5	-6.7, 11.6	0.6711
High Dose	39	2.90	2.55 (3.99)	0.6	0.0, 14.6	-0.35 (3.66)	-0.3	-7.8, 9.6	0.5565
WEEK 13	51	3.28	2.22 (3.79)	0.6	0.0, 16.0	-1.06 (3.84)	-1.2	-6.9, 13.2	0.0547
Low Dose	32	3.40	2.48 (3.91)	1.0	0.0, 16.0	-0.92 (4.06)	-1.5	-6.5, 13.2	0.2096
High Dose	19	3.08	1.80 (3.63)	0.0	0.0, 14.4	-1.29 (3.53)	-0.9	-6.9, 7.2	0.1286
WEEK 26	58	2.71	1.92 (2.84)	0.8	0.0, 14.9	-0.79 (3.24)	-0.9	-6.8, 7.8	0.0671
Low Dose	34	3.00	1.95 (2.43)	1.1	0.0, 10.8	-1.06 (3.02)	-1.0	-6.7, 5.4	0.0494*
High Dose	24	2.30	1.88 (3.39)	0.7	0.0, 14.9	-0.42 (3.55)	-0.2	-6.8, 7.8	0.5680
WEEK 39	52	2.60	2.02 (3.29)	0.1	0.0, 15.4	-0.58 (3.72)	-0.1	-7.8, 15.4	0.2659
Low Dose	31	3.10	2.61 (3.76)	0.9	0.0, 15.4	-0.49 (4.03)	-0.7	-6.7, 15.4	0.5028
High Dose	21	1.87	1.16 (2.23)	0.0	0.0, 8.9	-0.71 (3.29)	0.0	-7.8, 5.8	0.3337

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
PD duration (time since diagnosis) category:>=10 years (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 52	38	2.69	2.29 (3.45)	0.6	0.0, 12.0	-0.41 (3.35)	-0.2	-7.3, 7.5	0.4591
Low Dose	21	2.95	2.35 (3.57)	0.7	0.0, 12.0	-0.61 (3.37)	-0.4	-6.7, 6.1	0.4208
High Dose	17	2.37	2.21 (3.39)	0.5	0.0, 10.6	-0.16 (3.40)	0.0	-7.3, 7.5	0.8482
Average Daily Normalized 'On' Time With Troublesome Dyskinesia									
BASELINE	109		1.12 (1.81)	0.0	0.0, 10.5				
Low Dose	63		1.57 (2.08)	0.8	0.0, 10.5				
High Dose	46		0.50 (1.10)	0.0	0.0, 4.9				
WEEK 1	103	1.08	1.17 (1.99)	0.0	0.0, 7.9	0.09 (2.03)	0.0	-6.0, 7.9	0.6507
Low Dose	59	1.58	1.46 (2.00)	0.6	0.0, 7.9	-0.12 (2.08)	0.0	-6.0, 7.9	0.6572
High Dose	44	0.41	0.78 (1.93)	0.0	0.0, 7.3	0.37 (1.96)	0.0	-3.7, 7.0	0.2108
WEEK 6	93	1.14	0.46 (1.25)	0.0	0.0, 5.8	-0.68 (1.66)	0.0	-7.2, 4.1	<=0.001***
Low Dose	54	1.63	0.66 (1.55)	0.0	0.0, 5.8	-0.97 (1.92)	-0.2	-7.2, 4.1	<=0.001***
High Dose	39	0.47	0.19 (0.57)	0.0	0.0, 2.6	-0.28 (1.13)	0.0	-4.9, 2.1	0.1308

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
PD duration (time since diagnosis) category:>=10 years (Cont.)									
Average Daily Normalized 'On' Time With Troublesome Dyskinesia (Cont.)									
WEEK 13	51	1.23	0.47 (1.45)	0.0	0.0, 8.0	-0.77 (1.93)	0.0	-7.2, 6.0	0.0067**
Low Dose	32	1.69	0.69 (1.80)	0.0	0.0, 8.0	-0.99 (2.26)	-0.6	-7.2, 6.0	0.0185*
High Dose	19	0.47	0.09 (0.28)	0.0	0.0, 1.1	-0.38 (1.16)	0.0	-4.9, 0.7	0.1686
WEEK 26	58	0.92	0.45 (1.96)	0.0	0.0, 12.1	-0.47 (2.15)	0.0	-5.1, 8.8	0.1024
Low Dose	34	1.24	0.40 (2.08)	0.0	0.0, 12.1	-0.84 (2.02)	-0.2	-5.1, 7.2	0.0214*
High Dose	24	0.46	0.52 (1.83)	0.0	0.0, 8.8	0.05 (2.26)	0.0	-4.9, 8.8	0.9071
WEEK 39	52	0.83	0.34 (0.81)	0.0	0.0, 3.8	-0.48 (1.32)	0.0	-5.1, 2.7	0.0111*
Low Dose	31	1.18	0.33 (0.85)	0.0	0.0, 3.8	-0.86 (1.35)	-0.1	-5.1, 0.5	0.0013**
High Dose	21	0.30	0.37 (0.78)	0.0	0.0, 2.7	0.07 (1.09)	0.0	-3.6, 2.7	0.7769
WEEK 52	38	0.62	0.36 (1.01)	0.0	0.0, 5.3	-0.26 (1.43)	0.0	-3.6, 5.3	0.2654
Low Dose	21	0.86	0.18 (0.42)	0.0	0.0, 1.5	-0.68 (1.09)	0.0	-2.6, 1.1	0.0099**
High Dose	17	0.33	0.58 (1.43)	0.0	0.0, 5.3	0.25 (1.66)	0.0	-3.6, 5.3	0.5405

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
PD duration (time since diagnosis) category:>=10 years (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia									
BASELINE	109		9.14 (2.31)	9.4	3.4, 14.5				
Low Dose	63		9.13 (2.47)	9.7	3.5, 14.2				
High Dose	46		9.16 (2.09)	9.1	3.4, 14.5				
WEEK 1	103	9.13	10.50 (3.66)	10.6	0.0, 16.0	1.37 (4.00)	1.8	-10.4, 11.3	<=0.001***
Low Dose	59	9.07	10.94 (3.24)	11.5	3.9, 16.0	1.87 (3.84)	2.5	-5.9, 11.3	<=0.001***
High Dose	44	9.22	9.91 (4.13)	9.9	0.0, 16.0	0.69 (4.15)	1.3	-10.4, 7.5	0.2733
WEEK 6	93	9.05	11.86 (3.57)	12.4	0.0, 16.0	2.80 (3.77)	3.3	-9.9, 10.6	<=0.001***
Low Dose	54	8.89	11.99 (3.83)	12.6	0.0, 16.0	3.10 (3.78)	3.6	-9.9, 10.5	<=0.001***
High Dose	39	9.28	11.67 (3.20)	12.0	3.5, 16.0	2.39 (3.77)	2.9	-6.8, 10.6	<=0.001***
WEEK 13	51	9.33	12.31 (3.75)	13.4	2.6, 16.0	2.98 (3.46)	3.3	-4.9, 9.3	<=0.001***
Low Dose	32	9.35	11.97 (4.13)	13.3	2.6, 16.0	2.62 (3.52)	3.0	-4.9, 9.3	<=0.001***
High Dose	19	9.31	12.90 (3.02)	13.5	6.0, 16.0	3.59 (3.37)	3.7	-4.7, 8.2	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
PD duration (time since diagnosis) category:>=10 years (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia (Cont.)									
WEEK 26	58	8.94	13.13 (3.56)	14.4	1.5, 16.0	4.19 (3.92)	4.5	-5.5, 12.5	<=0.001***
Low Dose	34	9.06	13.57 (3.77)	15.6	1.5, 16.0	4.52 (4.05)	4.8	-4.5, 12.5	<=0.001***
High Dose	24	8.78	12.51 (3.20)	13.7	6.2, 16.0	3.73 (3.76)	3.3	-5.5, 10.6	<=0.001***
WEEK 39	52	9.19	12.94 (3.12)	13.6	2.7, 16.0	3.75 (3.37)	3.4	-9.1, 9.8	<=0.001***
Low Dose	31	9.36	12.87 (3.27)	13.5	2.7, 16.0	3.52 (3.63)	3.0	-9.1, 9.8	<=0.001***
High Dose	21	8.94	13.03 (2.96)	13.8	6.6, 16.0	4.09 (3.00)	4.4	-2.9, 8.1	<=0.001***
WEEK 52	38	9.18	13.80 (2.45)	14.7	7.9, 16.0	4.62 (2.81)	4.5	-2.8, 11.2	<=0.001***
Low Dose	21	9.40	13.89 (2.15)	14.0	9.3, 16.0	4.49 (2.49)	3.9	-1.2, 10.2	<=0.001***
High Dose	17	8.91	13.68 (2.83)	15.2	7.9, 16.0	4.78 (3.24)	4.9	-2.8, 11.2	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

表2.7.3.6-12　PD日誌に基づく，標準化した1日あたりの平均「オフ」時間及び「オン」時間の登録時期別の要約（FAS，日本人部分集団）：M15-741試験

[redacted]20[redacted] 10:12 <[redacted]>
ABBV-951
STUDY M15-741 - SECOND INTERIM (CUTOFF [redacted]20[redacted])
R&D/20/1632 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 7

TABLE 14.2__1.7.J

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Enrollment Sample
(FAS - Japan Subjects)

Parameter / Time Point / Sample Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Average Daily Normalized 'Off' Time									
BASELINE	27		6.79 (2.05)	6.9	0.0, 10.3				
Sample 1	18		6.79 (2.31)	7.1	0.0, 9.7				
Sample 2	9		6.79 (1.54)	6.1	5.1, 10.3				
WEEK 1	26	6.78	5.25 (3.32)	5.1	0.0, 13.8	-1.53 (3.77)	-1.9	-9.7, 4.7	0.0490*
Sample 1	18	6.79	5.08 (3.03)	5.1	0.0, 10.9	-1.71 (4.17)	-2.0	-9.7, 4.7	0.1001
Sample 2	8	6.76	5.64 (4.12)	5.6	1.2, 13.8	-1.13 (2.87)	-1.2	-4.7, 3.6	0.3036
WEEK 6	24	6.72	5.88 (3.71)	4.9	0.0, 13.4	-0.84 (3.94)	-2.5	-7.5, 6.8	0.3088
Sample 1	16	6.90	5.84 (3.48)	4.9	2.0, 12.5	-1.06 (4.00)	-2.8	-7.5, 6.8	0.3057
Sample 2	8	6.36	5.97 (4.39)	5.3	0.0, 13.4	-0.39 (4.04)	-0.8	-5.1, 6.2	0.7928
WEEK 13	10	5.81	6.67 (4.86)	7.3	0.0, 13.4	0.86 (5.02)	1.8	-6.6, 8.1	0.6010
Sample 1	6	5.01	4.98 (4.02)	5.0	0.0, 10.4	-0.03 (5.33)	-0.7	-6.6, 8.1	0.9903
Sample 2	4	7.01	9.20 (5.46)	11.1	1.3, 13.4	2.19 (4.92)	3.7	-4.8, 6.1	0.4383
WEEK 26	15	6.67	5.79 (4.43)	5.4	0.0, 14.3	-0.89 (4.46)	-0.7	-8.1, 7.1	0.4534
Sample 1	7	7.03	4.53 (3.67)	5.3	0.0, 8.9	-2.50 (3.78)	-1.4	-8.1, 2.7	0.1313
Sample 2	8	6.36	6.88 (4.97)	7.1	0.0, 14.3	0.52 (4.76)	0.7	-7.0, 7.1	0.7661

Note: Sample 1 contains subjects who were enrolled prior to [redacted]20[redacted].
Sample 2 contains subjects who were enrolled on or after [redacted]20[redacted].
Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.7.J

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Enrollment Sample
(FAS - Japan Subjects)

Parameter / Time Point / Sample Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Average Daily Normalized 'Off' Time (Cont.)									
WEEK 39	14	6.68	4.36 (3.22)	4.5	0.0, 12.3	-2.32 (3.40)	-1.7	-8.1, 5.1	0.0241*
Sample 1	6	7.10	3.96 (2.50)	4.1	0.0, 6.8	-3.14 (3.30)	-2.4	-8.1, 1.1	0.0676
Sample 2	8	6.36	4.66 (3.81)	4.9	0.0, 12.3	-1.70 (3.56)	-1.4	-7.0, 5.1	0.2177
WEEK 52	12	6.75	3.83 (3.17)	3.4	0.0, 10.1	-2.92 (3.30)	-3.3	-8.1, 4.1	0.0106*
Sample 1	5	7.49	4.32 (2.99)	6.1	0.0, 6.7	-3.16 (3.37)	-3.5	-8.1, 1.2	0.1037
Sample 2	7	6.23	3.48 (3.49)	3.0	0.0, 10.1	-2.75 (3.50)	-3.1	-7.0, 4.1	0.0831
Average Daily Normalized 'On' Time Without Dyskinesia									
BASELINE	27		5.68 (2.73)	5.7	0.0, 10.1				
Sample 1	18		5.43 (2.46)	5.7	0.0, 8.7				
Sample 2	9		6.18 (3.30)	5.7	1.1, 10.1				
WEEK 1	26	5.55	6.23 (3.84)	6.8	0.3, 16.0	0.68 (4.00)	0.9	-8.9, 10.2	0.3968
Sample 1	18	5.43	6.19 (4.03)	6.4	0.3, 16.0	0.76 (3.14)	1.1	-6.0, 8.3	0.3180
Sample 2	8	5.83	6.31 (3.63)	7.5	1.0, 11.3	0.48 (5.75)	0.0	-8.9, 10.2	0.8185
WEEK 6	24	5.79	8.38 (4.05)	8.4	0.0, 13.8	2.60 (5.07)	3.7	-6.4, 13.8	0.0196*
Sample 1	16	5.57	7.79 (4.05)	8.0	0.0, 13.8	2.22 (5.21)	3.2	-6.4, 13.8	0.1079
Sample 2	8	6.23	9.57 (4.04)	10.3	2.6, 13.8	3.34 (5.04)	3.9	-3.5, 10.8	0.1030

Note: Sample 1 contains subjects who were enrolled prior to [redacted]20[redacted].
Sample 2 contains subjects who were enrolled on or after [redacted]20[redacted].
Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.7.J

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Enrollment Sample
(FAS - Japan Subjects)

Parameter / Time Point / Sample Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 13	10	5.40	5.93 (5.42)	5.2	0.0, 14.7	0.54 (5.57)	0.9	-9.0, 9.6	0.7668
Sample 1	6	4.04	6.02 (5.31)	5.4	0.0, 14.5	1.97 (5.47)	1.9	-6.5, 9.6	0.4176
Sample 2	4	7.43	5.81 (6.42)	4.3	0.0, 14.7	-1.61 (5.74)	-1.2	-9.0, 4.8	0.6130
WEEK 26	15	5.94	8.34 (5.26)	8.1	0.0, 16.0	2.40 (5.01)	3.2	-10.1, 9.5	0.0844
Sample 1	7	5.61	9.69 (5.22)	9.1	1.2, 16.0	4.08 (4.07)	3.2	-0.9, 9.5	0.0378*
Sample 2	8	6.23	7.16 (5.34)	6.9	0.0, 16.0	0.93 (5.54)	1.9	-10.1, 7.0	0.6492
WEEK 39	14	5.90	9.83 (4.24)	10.3	0.3, 16.0	3.93 (3.21)	4.0	-1.9, 8.1	<=0.001***
Sample 1	6	5.46	9.41 (5.15)	9.6	0.3, 16.0	3.95 (3.88)	4.0	-1.9, 8.1	0.0546
Sample 2	8	6.23	10.14 (3.76)	10.7	3.7, 16.0	3.91 (2.90)	3.9	0.4, 7.8	0.0066**
WEEK 52	12	6.26	10.76 (3.48)	10.9	4.2, 16.0	4.49 (2.45)	3.9	1.7, 8.1	<=0.001***
Sample 1	5	5.57	9.97 (3.54)	9.3	6.9, 16.0	4.40 (2.67)	4.8	1.7, 8.1	0.0212*
Sample 2	7	6.76	11.32 (3.60)	12.0	4.2, 16.0	4.56 (2.49)	3.1	1.9, 7.8	0.0029**
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia									
BASELINE	27		2.74 (2.76)	2.6	0.0, 8.0				
Sample 1	18		2.98 (2.84)	2.7	0.0, 8.0				
Sample 2	9		2.25 (2.70)	0.2	0.0, 5.6				

Note: Sample 1 contains subjects who were enrolled prior to [redacted]20[redacted].
Sample 2 contains subjects who were enrolled on or after [redacted]20[redacted].
Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.7.J

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Enrollment Sample
(FAS - Japan Subjects)

Parameter / Time Point / Sample Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 1	26	2.84	3.83 (4.01)	2.6	0.0, 14.9	0.99 (3.82)	0.0	-5.4, 13.2	0.2002
Sample 1	18	2.98	3.89 (3.87)	2.6	0.0, 14.9	0.90 (3.34)	0.1	-5.4, 8.6	0.2665
Sample 2	8	2.53	3.70 (4.59)	2.2	0.0, 13.2	1.17 (5.00)	0.0	-2.9, 13.2	0.5291
WEEK 6	24	2.64	1.70 (2.87)	0.2	0.0, 9.6	-0.94 (3.53)	0.0	-6.7, 9.6	0.2027
Sample 1	16	2.70	2.32 (3.34)	0.9	0.0, 9.6	-0.38 (3.93)	0.0	-6.7, 9.6	0.7019
Sample 2	8	2.53	0.46 (0.75)	0.2	0.0, 2.2	-2.07 (2.38)	-1.6	-5.1, 0.3	0.0437*
WEEK 13	10	3.31	3.39 (5.59)	0.7	0.0, 16.0	0.08 (5.72)	-0.5	-6.5, 13.2	0.9655
Sample 1	6	4.98	5.00 (6.80)	1.4	0.0, 16.0	0.02 (7.32)	-1.8	-6.5, 13.2	0.9952
Sample 2	4	0.81	0.98 (1.97)	0.0	0.0, 3.9	0.17 (2.94)	0.0	-3.3, 3.9	0.9141
WEEK 26	15	2.91	1.76 (3.26)	0.0	0.0, 12.1	-1.15 (3.11)	0.0	-6.7, 4.6	0.1730
Sample 1	7	3.36	1.77 (4.54)	0.0	0.0, 12.1	-1.59 (3.82)	0.0	-6.7, 4.1	0.3145
Sample 2	8	2.53	1.75 (1.89)	1.6	0.0, 4.8	-0.78 (2.55)	-1.2	-2.9, 4.6	0.4180
WEEK 39	14	2.92	1.72 (3.58)	0.0	0.0, 13.2	-1.20 (3.18)	-0.1	-6.7, 5.2	0.1826
Sample 1	6	3.45	2.63 (5.30)	0.0	0.0, 13.2	-0.82 (4.70)	0.0	-6.7, 5.2	0.6878
Sample 2	8	2.53	1.04 (1.59)	0.0	0.0, 4.1	-1.48 (1.67)	-0.9	-4.0, 0.0	0.0407*

Note: Sample 1 contains subjects who were enrolled prior to [redacted]20[redacted].
Sample 2 contains subjects who were enrolled on or after [redacted]20[redacted].
Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.7.J

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Enrollment Sample
(FAS - Japan Subjects)

Parameter / Time Point / Sample Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 52	12	2.64	1.41 (2.10)	0.1	0.0, 6.7	-1.23 (2.31)	0.0	-6.7, 1.8	0.0920
Sample 1	5	2.95	1.71 (2.91)	0.0	0.0, 6.7	-1.24 (3.27)	0.0	-6.7, 1.8	0.4441
Sample 2	7	2.42	1.20 (1.52)	0.3	0.0, 3.7	-1.23 (1.64)	0.0	-3.8, 0.0	0.0948
Average Daily Normalized 'On' Time With Troublesome Dyskinesia									
BASELINE	27		0.79 (1.74)	0.0	0.0, 7.2				
Sample 1	18		0.80 (1.94)	0.0	0.0, 7.2				
Sample 2	9		0.79 (1.38)	0.0	0.0, 3.4				
WEEK 1	26	0.82	0.69 (1.59)	0.0	0.0, 7.9	-0.13 (2.37)	0.0	-6.0, 7.9	0.7790
Sample 1	18	0.80	0.84 (1.86)	0.0	0.0, 7.9	0.05 (2.69)	0.0	-6.0, 7.9	0.9440
Sample 2	8	0.89	0.36 (0.63)	0.0	0.0, 1.8	-0.53 (1.48)	0.0	-2.7, 1.8	0.3453
WEEK 6	24	0.85	0.04 (0.12)	0.0	0.0, 0.5	-0.82 (1.81)	0.0	-7.2, 0.4	0.0370*
Sample 1	16	0.84	0.05 (0.15)	0.0	0.0, 0.5	-0.78 (2.01)	0.0	-7.2, 0.4	0.1399
Sample 2	8	0.89	0.00 (0.00)	0.0	0.0, 0.0	-0.89 (1.44)	0.0	-3.4, 0.0	0.1260
WEEK 13	10	1.48	0.00 (0.00)	0.0	0.0, 0.0	-1.48 (2.59)	0.0	-7.2, 0.0	0.1039
Sample 1	6	1.97	0.00 (0.00)	0.0	0.0, 0.0	-1.97 (3.16)	0.0	-7.2, 0.0	0.1880
Sample 2	4	0.75	0.00 (0.00)	0.0	0.0, 0.0	-0.75 (1.50)	0.0	-3.0, 0.0	0.3910

Note: Sample 1 contains subjects who were enrolled prior to [redacted]20[redacted].
Sample 2 contains subjects who were enrolled on or after [redacted]20[redacted].
Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.7.J

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Enrollment Sample
(FAS - Japan Subjects)

Parameter / Time Point / Sample Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Average Daily Normalized 'On' Time With Troublesome Dyskinesia (Cont.)									
WEEK 26	15	0.47	0.11 (0.34)	0.0	0.0, 1.3	-0.36 (1.20)	0.0	-3.4, 1.3	0.2645
Sample 1	7	0.00	0.00 (0.00)	0.0	0.0, 0.0	0.00 (0.00)	0.0	0.0, 0.0	
Sample 2	8	0.89	0.21 (0.45)	0.0	0.0, 1.3	-0.67 (1.62)	0.0	-3.4, 1.3	0.2780
WEEK 39	14	0.51	0.09 (0.23)	0.0	0.0, 0.7	-0.42 (1.05)	0.0	-3.0, 0.0	0.1610
Sample 1	6	0.00	0.00 (0.00)	0.0	0.0, 0.0	0.00 (0.00)	0.0	0.0, 0.0	
Sample 2	8	0.89	0.16 (0.29)	0.0	0.0, 0.7	-0.73 (1.33)	0.0	-3.0, 0.0	0.1663
WEEK 52	12	0.34	0.00 (0.00)	0.0	0.0, 0.0	-0.34 (0.97)	0.0	-3.4, 0.0	0.2516
Sample 1	5	0.00	0.00 (0.00)	0.0	0.0, 0.0	0.00 (0.00)	0.0	0.0, 0.0	
Sample 2	7	0.58	0.00 (0.00)	0.0	0.0, 0.0	-0.58 (1.25)	0.0	-3.4, 0.0	0.2647
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia									
BASELINE	27		8.42 (1.76)	8.7	4.6, 11.1				
Sample 1	18		8.42 (1.75)	8.5	4.6, 11.1				
Sample 2	9		8.42 (1.90)	9.0	5.7, 10.3				
WEEK 1	26	8.40	10.06 (3.19)	9.9	2.2, 16.0	1.66 (3.85)	1.1	-4.0, 9.7	0.0372*
Sample 1	18	8.42	10.08 (2.89)	10.2	5.1, 16.0	1.66 (4.07)	1.1	-4.0, 9.7	0.1009
Sample 2	8	8.35	10.01 (3.99)	9.4	2.2, 14.2	1.66 (3.57)	2.0	-3.6, 7.3	0.2306

Note: Sample 1 contains subjects who were enrolled prior to [redacted]20[redacted].
Sample 2 contains subjects who were enrolled on or after [redacted]20[redacted].
Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.7.J

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Enrollment Sample
(FAS - Japan Subjects)

Parameter Time Point Sample Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia (Cont.)									
WEEK 6	24	8.43	10.08 (3.69)	11.1	2.6, 16.0	1.65 (3.82)	3.0	-6.0, 7.5	0.0448*
Sample 1	16	8.27	10.11 (3.44)	11.1	3.5, 13.8	1.84 (3.86)	3.0	-6.0, 7.5	0.0757
Sample 2	8	8.75	10.03 (4.39)	10.7	2.6, 16.0	1.28 (3.96)	1.6	-3.3, 5.8	0.3922
WEEK 13	10	8.71	9.33 (4.86)	8.7	2.6, 16.0	0.62 (3.76)	0.1	-5.0, 6.6	0.6148
Sample 1	6	9.03	11.02 (4.02)	11.0	5.6, 16.0	1.99 (2.94)	1.8	-1.1, 6.6	0.1572
Sample 2	4	8.24	6.80 (5.46)	4.9	2.6, 14.7	-1.44 (4.30)	-2.8	-5.0, 4.8	0.5510
WEEK 26	15	8.85	10.10 (4.38)	10.5	1.7, 16.0	1.25 (4.00)	0.7	-5.5, 8.1	0.2476
Sample 1	7	8.97	11.47 (3.67)	10.7	7.1, 16.0	2.50 (3.78)	1.4	-2.7, 8.1	0.1313
Sample 2	8	8.75	8.91 (4.82)	8.8	1.7, 16.0	0.15 (4.11)	0.5	-5.5, 7.0	0.9191
WEEK 39	14	8.82	11.55 (3.17)	11.5	3.7, 16.0	2.73 (2.94)	2.3	-2.1, 8.1	0.0040**
Sample 1	6	8.90	12.04 (2.50)	11.9	9.2, 16.0	3.14 (3.30)	2.4	-1.1, 8.1	0.0676
Sample 2	8	8.75	11.18 (3.72)	11.1	3.7, 16.0	2.43 (2.82)	2.3	-2.1, 7.0	0.0451*
WEEK 52	12	8.91	12.17 (3.17)	12.6	5.9, 16.0	3.26 (2.79)	3.3	-1.2, 8.1	0.0019**
Sample 1	5	8.51	11.68 (2.99)	9.9	9.3, 16.0	3.16 (3.37)	3.5	-1.2, 8.1	0.1037
Sample 2	7	9.18	12.52 (3.49)	13.0	5.9, 16.0	3.33 (2.59)	3.1	-0.8, 7.0	0.0143*

Note: Sample 1 contains subjects who were enrolled prior to [redacted]20[redacted].
Sample 2 contains subjects who were enrolled on or after [redacted]20[redacted].
Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

表2.7.3.6-13　PD日誌に基づく，標準化した1日あたりの平均「オフ」時間及び「オン」時間の要約（FAS，部分集団別）：M15-737試験

TABLE 14.2__1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Gender:Female									
Average Daily Normalized 'Off' Time									
BASELINE	24		2.09 (2.55)	1.0	0.0, 8.8				
Low Dose	15		2.29 (2.49)	1.2	0.0, 6.7				
High Dose	9		1.76 (2.78)	0.8	0.0, 8.8				
WEEK 12	20	2.35	2.27 (1.89)	2.3	0.0, 5.9	-0.08 (2.36)	0.0	-6.4, 4.2	0.8803
Low Dose	14	2.26	2.04 (1.86)	2.3	0.0, 5.9	-0.22 (1.67)	0.0	-4.2, 2.8	0.6332
High Dose	6	2.55	2.79 (2.01)	2.2	0.3, 5.7	0.24 (3.70)	0.9	-6.4, 4.2	0.8797
WEEK 24	21	1.89	3.80 (4.80)	1.7	0.0, 16.0	1.91 (3.53)	0.1	-2.3, 13.3	0.0223*
Low Dose	12	1.99	3.74 (5.34)	0.7	0.0, 16.0	1.74 (4.35)	0.0	-2.3, 13.3	0.1925
High Dose	9	1.76	3.88 (4.30)	2.7	0.0, 13.4	2.12 (2.24)	2.2	0.0, 6.2	0.0217*
WEEK 36	13	2.16	1.63 (2.01)	1.2	0.0, 6.5	-0.53 (2.01)	0.0	-5.5, 1.4	0.3625
Low Dose	8	1.87	1.33 (2.22)	0.4	0.0, 6.5	-0.54 (2.11)	0.0	-5.5, 1.4	0.4932
High Dose	5	2.62	2.11 (1.76)	2.0	0.0, 4.9	-0.51 (2.10)	0.0	-3.9, 1.2	0.6134

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Gender:Female (Cont.)									
Average Daily Normalized 'Off' Time (Cont.)									
WEEK 48	9	1.73	2.43 (4.57)	0.7	0.0, 14.3	0.70 (2.05)	0.0	-1.2, 5.5	0.3377
Low Dose	5	0.83	0.67 (1.15)	0.0	0.0, 2.7	-0.16 (0.62)	0.0	-1.2, 0.5	0.6037
High Dose	4	2.86	4.62 (6.52)	2.0	0.3, 14.3	1.76 (2.83)	1.2	-0.8, 5.5	0.3007
WEEK 60	2	0.25	0.71 (1.00)	0.7	0.0, 1.4	0.46 (0.64)	0.5	0.0, 0.9	0.5000
Low Dose	1	0.00	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	1	0.50	1.41 (N/A)	1.4	1.4, 1.4	0.91 (N/A)	0.9	0.9, 0.9	
WEEK 72	1	0.00	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
Low Dose	1	0.00	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	0								
Average Daily Normalized 'On' Time Without Dyskinesia									
BASELINE	24		11.23 (5.19)	13.3	0.0, 16.0				
Low Dose	15		11.32 (5.30)	13.3	1.3, 16.0				
High Dose	9		11.07 (5.32)	13.3	0.0, 16.0				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Gender:Female (Cont.)									
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 12	20	11.38	12.25 (3.78)	13.4	4.2, 16.0	0.86 (4.08)	0.0	-6.6, 14.2	0.3554
Low Dose	14	12.04	12.64 (3.75)	13.7	4.5, 16.0	0.61 (4.57)	0.0	-6.6, 14.2	0.6281
High Dose	6	9.85	11.32 (4.04)	11.9	4.2, 15.8	1.46 (2.86)	0.9	-2.0, 5.4	0.2653
WEEK 24	21	11.39	11.70 (5.17)	14.3	0.0, 16.0	0.31 (5.31)	0.0	-13.3, 14.2	0.7935
Low Dose	12	11.63	12.20 (5.36)	15.3	0.0, 16.0	0.57 (6.08)	0.0	-13.3, 14.2	0.7524
High Dose	9	11.07	11.03 (5.14)	13.3	2.6, 16.0	-0.04 (4.40)	0.0	-4.5, 10.6	0.9789
WEEK 36	13	11.00	14.00 (2.72)	14.8	8.0, 16.0	3.00 (5.29)	0.7	-1.4, 14.2	0.0631
Low Dose	8	12.14	14.49 (2.58)	15.6	8.4, 16.0	2.35 (5.22)	0.0	-1.4, 14.2	0.2432
High Dose	5	9.17	13.22 (3.04)	14.0	8.0, 16.0	4.05 (5.83)	1.0	0.0, 14.0	0.1957
WEEK 48	9	12.33	13.37 (4.65)	15.3	1.4, 16.0	1.04 (5.19)	0.0	-5.6, 13.7	0.5646
Low Dose	5	12.28	15.18 (1.09)	15.3	13.3, 16.0	2.91 (6.09)	0.0	-0.5, 13.7	0.3464
High Dose	4	12.40	11.11 (6.62)	13.6	1.4, 15.7	-1.29 (3.04)	-0.4	-5.6, 1.3	0.4577
WEEK 60	2	12.25	14.35 (2.33)	14.4	12.7, 16.0	2.10 (2.97)	2.1	0.0, 4.2	0.5000
Low Dose	1	16.00	16.00 (N/A)	16.0	16.0, 16.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	1	8.50	12.71 (N/A)	12.7	12.7, 12.7	4.21 (N/A)	4.2	4.2, 4.2	

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Gender:Female (Cont.)									
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 72	1	16.00	16.00 (N/A)	16.0	16.0, 16.0	0.00 (N/A)	0.0	0.0, 0.0	
Low Dose	1	16.00	16.00 (N/A)	16.0	16.0, 16.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	0								
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia									
BASELINE	24		2.24 (4.13)	0.1	0.0, 12.9				
Low Dose	15		2.10 (4.15)	0.0	0.0, 12.0				
High Dose	9		2.48 (4.33)	0.6	0.0, 12.9				
WEEK 12	20	2.05	1.45 (2.76)	0.0	0.0, 8.7	-0.60 (3.61)	0.0	-11.6, 7.4	0.4680
Low Dose	14	1.39	1.26 (2.90)	0.0	0.0, 8.7	-0.12 (3.91)	0.0	-11.6, 7.4	0.9075
High Dose	6	3.59	1.89 (2.58)	0.6	0.0, 6.1	-1.70 (2.78)	-1.1	-6.9, 1.0	0.1934
WEEK 24	21	2.29	0.15 (0.42)	0.0	0.0, 1.8	-2.14 (4.30)	0.0	-12.9, 0.1	0.0337*
Low Dose	12	2.15	0.04 (0.10)	0.0	0.0, 0.3	-2.11 (4.53)	0.0	-12.0, 0.0	0.1354
High Dose	9	2.48	0.29 (0.63)	0.0	0.0, 1.8	-2.19 (4.25)	-0.2	-12.9, 0.1	0.1613

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Gender:Female (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 36	13	2.64	0.33 (0.86)	0.0	0.0, 3.1	-2.31 (4.80)	0.0	-12.9, 2.9	0.1091
Low Dose	8	1.66	0.12 (0.25)	0.0	0.0, 0.7	-1.54 (4.05)	0.0	-11.6, 0.0	0.3187
High Dose	5	4.20	0.67 (1.37)	0.0	0.0, 3.1	-3.53 (6.12)	-2.0	-12.9, 2.9	0.2661
WEEK 48	9	1.64	0.20 (0.32)	0.0	0.0, 0.8	-1.44 (3.65)	0.0	-11.1, 0.1	0.2706
Low Dose	5	2.36	0.15 (0.33)	0.0	0.0, 0.7	-2.22 (4.96)	0.0	-11.1, 0.0	0.3739
High Dose	4	0.74	0.27 (0.36)	0.2	0.0, 0.8	-0.47 (0.73)	-0.3	-1.5, 0.1	0.2890
WEEK 60	2	0.38	0.94 (1.33)	0.9	0.0, 1.9	0.57 (0.80)	0.6	0.0, 1.1	0.5000
Low Dose	1	0.00	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	1	0.75	1.88 (N/A)	1.9	1.9, 1.9	1.13 (N/A)	1.1	1.1, 1.1	
WEEK 72	1	0.00	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
Low Dose	1	0.00	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	0								

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Gender:Female (Cont.)									
Average Daily Normalized 'On' Time With Troublesome Dyskinesia									
BASELINE	24		0.44 (1.38)	0.0	0.0, 6.3				
Low Dose	15		0.29 (0.76)	0.0	0.0, 2.7				
High Dose	9		0.69 (2.08)	0.0	0.0, 6.3				
WEEK 12	20	0.22	0.03 (0.15)	0.0	0.0, 0.7	-0.19 (0.69)	0.0	-2.7, 0.7	0.2449
Low Dose	14	0.31	0.05 (0.18)	0.0	0.0, 0.7	-0.26 (0.82)	0.0	-2.7, 0.7	0.2493
High Dose	6	0.00	0.00 (0.00)	0.0	0.0, 0.0	0.00 (0.00)	0.0	0.0, 0.0	
WEEK 24	21	0.42	0.35 (1.56)	0.0	0.0, 7.2	-0.07 (0.63)	0.0	-2.7, 0.9	0.6100
Low Dose	12	0.22	0.02 (0.07)	0.0	0.0, 0.3	-0.20 (0.78)	0.0	-2.7, 0.3	0.3901
High Dose	9	0.69	0.80 (2.39)	0.0	0.0, 7.2	0.10 (0.31)	0.0	0.0, 0.9	0.3466
WEEK 36	13	0.21	0.04 (0.13)	0.0	0.0, 0.5	-0.17 (0.76)	0.0	-2.7, 0.5	0.4362
Low Dose	8	0.33	0.06 (0.16)	0.0	0.0, 0.5	-0.28 (0.98)	0.0	-2.7, 0.5	0.4511
High Dose	5	0.00	0.00 (0.00)	0.0	0.0, 0.0	0.00 (0.00)	0.0	0.0, 0.0	

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Gender:Female (Cont.)									
Average Daily Normalized 'On' Time With Troublesome Dyskinesia (Cont.)									
WEEK 48	9	0.30	0.00 (0.00)	0.0	0.0, 0.0	-0.30 (0.89)	0.0	-2.7, 0.0	0.3466
Low Dose	5	0.53	0.00 (0.00)	0.0	0.0, 0.0	-0.53 (1.19)	0.0	-2.7, 0.0	0.3739
High Dose	4	0.00	0.00 (0.00)	0.0	0.0, 0.0	0.00 (0.00)	0.0	0.0, 0.0	
WEEK 60	2	3.13	0.00 (0.00)	0.0	0.0, 0.0	-3.13 (4.42)	-3.1	-6.3, 0.0	0.5000
Low Dose	1	0.00	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	1	6.25	0.00 (N/A)	0.0	0.0, 0.0	-6.25 (N/A)	-6.3	-6.3, -6.3	
WEEK 72	1	0.00	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
Low Dose	1	0.00	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	0								
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia									
BASELINE	24		13.47 (2.75)	14.8	7.2, 16.0				
Low Dose	15		13.42 (2.58)	13.3	8.7, 16.0				
High Dose	9		13.55 (3.18)	14.9	7.2, 16.0				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Gender:Female (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia (Cont.)									
WEEK 12	20	13.43	13.70 (1.85)	13.7	10.1, 16.0	0.27 (2.54)	-0.0	-4.2, 6.4	0.6457
Low Dose	14	13.43	13.91 (1.81)	13.7	10.1, 16.0	0.48 (2.00)	0.0	-2.8, 4.4	0.3842
High Dose	6	13.45	13.21 (2.01)	13.8	10.3, 15.8	-0.24 (3.70)	-0.9	-4.2, 6.4	0.8797
WEEK 24	21	13.68	11.85 (5.05)	14.3	0.0, 16.0	-1.83 (3.69)	-0.1	-13.3, 2.7	0.0337*
Low Dose	12	13.78	12.24 (5.37)	15.3	0.0, 16.0	-1.54 (4.54)	0.0	-13.3, 2.7	0.2646
High Dose	9	13.55	11.32 (4.86)	13.3	2.6, 16.0	-2.23 (2.31)	-2.2	-6.2, 0.0	0.0202*
WEEK 36	13	13.63	14.33 (2.11)	14.8	9.1, 16.0	0.70 (2.12)	0.0	-1.4, 5.5	0.2572
Low Dose	8	13.80	14.61 (2.37)	15.6	9.1, 16.0	0.81 (2.26)	0.0	-1.4, 5.5	0.3430
High Dose	5	13.38	13.89 (1.76)	14.0	11.1, 16.0	0.51 (2.10)	0.0	-1.2, 3.9	0.6134
WEEK 48	9	13.97	13.57 (4.57)	15.3	1.7, 16.0	-0.40 (2.34)	0.0	-5.5, 2.7	0.6207
Low Dose	5	14.64	15.33 (1.15)	16.0	13.3, 16.0	0.69 (1.26)	0.0	-0.5, 2.7	0.2898
High Dose	4	13.14	11.38 (6.52)	14.0	1.7, 15.7	-1.76 (2.83)	-1.2	-5.5, 0.8	0.3007
WEEK 60	2	12.63	15.29 (1.00)	15.3	14.6, 16.0	2.67 (3.77)	2.7	0.0, 5.3	0.5000
Low Dose	1	16.00	16.00 (N/A)	16.0	16.0, 16.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	1	9.25	14.59 (N/A)	14.6	14.6, 14.6	5.34 (N/A)	5.3	5.3, 5.3	

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Gender:Female (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia (Cont.)									
WEEK 72	1	16.00	16.00 (N/A)	16.0	16.0, 16.0	0.00 (N/A)	0.0	0.0, 0.0	
Low Dose	1	16.00	16.00 (N/A)	16.0	16.0, 16.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	0								
Gender:Male									
Average Daily Normalized 'Off' Time									
BASELINE	49		2.54 (2.75)	1.4	0.0, 10.1				
Low Dose	15		3.74 (2.72)	3.0	0.0, 10.1				
High Dose	34		2.01 (2.64)	0.5	0.0, 8.1				
WEEK 12	34	2.81	2.88 (2.81)	2.3	0.0, 7.6	0.07 (2.09)	0.0	-4.3, 6.8	0.8498
Low Dose	11	3.89	3.07 (2.69)	2.7	0.0, 7.3	-0.83 (1.97)	0.0	-4.1, 1.8	0.1942
High Dose	23	2.29	2.79 (2.92)	2.0	0.0, 7.6	0.50 (2.05)	0.0	-4.3, 6.8	0.2578
WEEK 24	41	2.24	2.53 (3.05)	1.9	0.0, 10.9	0.29 (2.15)	0.0	-5.7, 5.2	0.3953
Low Dose	13	3.14	2.62 (2.99)	1.9	0.0, 10.8	-0.51 (2.38)	-0.5	-5.7, 4.3	0.4528
High Dose	28	1.83	2.49 (3.12)	1.6	0.0, 10.9	0.66 (1.97)	0.0	-3.3, 5.2	0.0873

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Gender:Male (Cont.)									
Average Daily Normalized 'Off' Time (Cont.)									
WEEK 36	21	2.77	3.24 (2.92)	3.4	0.0, 12.1	0.47 (2.02)	0.3	-3.5, 5.6	0.2963
Low Dose	9	3.88	4.75 (3.28)	3.7	1.9, 12.1	0.87 (1.94)	0.4	-1.0, 5.6	0.2138
High Dose	12	1.94	2.11 (2.12)	1.3	0.0, 6.1	0.17 (2.10)	0.0	-3.5, 3.9	0.7840
WEEK 48	16	1.84	2.94 (3.07)	2.0	0.0, 8.6	1.10 (2.46)	0.2	-3.0, 6.1	0.0944
Low Dose	5	2.00	1.64 (1.76)	1.7	0.0, 4.2	-0.36 (1.70)	-0.0	-3.0, 1.6	0.6622
High Dose	11	1.77	3.53 (3.42)	4.0	0.0, 8.6	1.76 (2.53)	0.4	-1.0, 6.1	0.0436*
WEEK 60	2	0.27	2.42 (0.00)	2.4	2.4, 2.4	2.16 (0.38)	2.2	1.9, 2.4	0.0783
Low Dose	1	0.53	2.42 (N/A)	2.4	2.4, 2.4	1.89 (N/A)	1.9	1.9, 1.9	
High Dose	1	0.00	2.42 (N/A)	2.4	2.4, 2.4	2.42 (N/A)	2.4	2.4, 2.4	
WEEK 72	1	0.00	5.45 (N/A)	5.5	5.5, 5.5	5.45 (N/A)	5.5	5.5, 5.5	
Low Dose	0								
High Dose	1	0.00	5.45 (N/A)	5.5	5.5, 5.5	5.45 (N/A)	5.5	5.5, 5.5	

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Gender:Male (Cont.)									
Average Daily Normalized 'On' Time Without Dyskinesia									
BASELINE	49		9.87 (4.88)	10.7	0.0, 16.0				
Low Dose	15		10.79 (2.94)	11.5	4.2, 14.6				
High Dose	34		9.46 (5.51)	9.8	0.0, 16.0				
WEEK 12	34	9.70	10.39 (4.99)	10.5	0.0, 16.0	0.69 (3.20)	0.4	-9.6, 9.0	0.2172
Low Dose	11	10.38	11.30 (4.49)	12.2	1.0, 16.0	0.93 (3.13)	0.6	-5.9, 6.1	0.3500
High Dose	23	9.37	9.95 (5.25)	10.1	0.0, 16.0	0.58 (3.30)	0.0	-9.6, 9.0	0.4095
WEEK 24	41	10.55	10.78 (4.38)	10.6	0.0, 16.0	0.23 (4.01)	0.0	-9.2, 13.7	0.7169
Low Dose	13	11.30	11.01 (4.60)	10.7	1.0, 16.0	-0.29 (3.73)	-0.1	-5.9, 7.4	0.7835
High Dose	28	10.21	10.68 (4.35)	10.4	0.0, 16.0	0.47 (4.18)	0.0	-9.2, 13.7	0.5569
WEEK 36	21	10.81	8.95 (4.76)	9.9	0.0, 15.8	-1.86 (3.20)	-0.6	-11.2, 2.4	0.0148*
Low Dose	9	10.76	8.94 (4.51)	10.9	1.3, 14.0	-1.82 (2.52)	-0.8	-5.9, 1.0	0.0616
High Dose	12	10.85	8.96 (5.14)	9.6	0.0, 15.8	-1.89 (3.75)	-0.4	-11.2, 2.4	0.1078

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Gender:Male (Cont.)									
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 48	16	10.35	10.29 (4.34)	10.2	1.8, 16.0	-0.06 (4.01)	0.0	-5.1, 7.9	0.9532
Low Dose	5	10.68	10.42 (5.96)	10.2	1.8, 16.0	-0.26 (5.27)	-3.2	-5.1, 7.4	0.9167
High Dose	11	10.20	10.24 (3.76)	10.2	4.9, 16.0	0.03 (3.61)	0.1	-5.1, 7.9	0.9771
WEEK 60	2	4.32	9.94 (5.14)	9.9	6.3, 13.6	5.62 (0.97)	5.6	4.9, 6.3	0.0775
Low Dose	1	8.65	13.58 (N/A)	13.6	13.6, 13.6	4.93 (N/A)	4.9	4.9, 4.9	
High Dose	1	0.00	6.30 (N/A)	6.3	6.3, 6.3	6.30 (N/A)	6.3	6.3, 6.3	
WEEK 72	1	11.29	1.43 (N/A)	1.4	1.4, 1.4	-9.87 (N/A)	-9.9	-9.9, -9.9	
Low Dose	0								
High Dose	1	11.29	1.43 (N/A)	1.4	1.4, 1.4	-9.87 (N/A)	-9.9	-9.9, -9.9	
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia									
BASELINE	49		3.16 (4.82)	0.7	0.0, 16.0				
Low Dose	15		1.23 (1.91)	0.3	0.0, 6.7				
High Dose	34		4.01 (5.46)	0.8	0.0, 16.0				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Gender:Male (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 12	34	2.94	2.13 (4.32)	0.0	0.0, 16.0	-0.81 (4.18)	0.0	-15.8, 6.7	0.2695
Low Dose	11	1.40	1.63 (3.72)	0.0	0.0, 12.4	0.23 (2.21)	0.0	-3.5, 5.7	0.7382
High Dose	23	3.67	2.37 (4.64)	0.0	0.0, 16.0	-1.30 (4.82)	0.0	-15.8, 6.7	0.2091
WEEK 24	41	2.71	2.37 (3.66)	0.0	0.0, 16.0	-0.34 (3.84)	0.0	-16.0, 6.1	0.5746
Low Dose	13	1.29	2.24 (3.46)	1.5	0.0, 12.4	0.95 (2.25)	0.1	-3.5, 5.7	0.1544
High Dose	28	3.37	2.43 (3.81)	0.0	0.0, 16.0	-0.94 (4.29)	0.0	-16.0, 6.1	0.2580
WEEK 36	21	2.04	3.50 (5.01)	0.5	0.0, 16.0	1.46 (2.86)	0.0	-1.0, 11.2	0.0299*
Low Dose	9	1.32	2.17 (3.56)	0.5	0.0, 11.1	0.85 (1.53)	0.2	-0.6, 4.4	0.1354
High Dose	12	2.57	4.49 (5.82)	2.4	0.0, 16.0	1.92 (3.56)	0.0	-1.0, 11.2	0.0884
WEEK 48	16	3.31	2.53 (3.43)	0.9	0.0, 11.9	-0.78 (4.73)	0.0	-12.8, 5.2	0.5174
Low Dose	5	2.66	3.75 (5.18)	0.9	0.0, 11.9	1.09 (3.25)	0.9	-3.5, 5.2	0.4949
High Dose	11	3.61	1.97 (2.43)	1.0	0.0, 6.4	-1.64 (5.18)	0.0	-12.8, 4.9	0.3195
WEEK 60	2	9.75	2.91 (4.11)	2.9	0.0, 5.8	-6.84 (4.72)	-6.8	-10.2, -3.5	0.2890
Low Dose	1	3.50	0.00 (N/A)	0.0	0.0, 0.0	-3.50 (N/A)	-3.5	-3.5, -3.5	
High Dose	1	16.00	5.82 (N/A)	5.8	5.8, 5.8	-10.18 (N/A)	-10.2	-10.2, -10.2	

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Gender:Male (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 72	1	4.71	4.16 (N/A)	4.2	4.2, 4.2	-0.55 (N/A)	-0.5	-0.5, -0.5	
Low Dose	0								
High Dose	1	4.71	4.16 (N/A)	4.2	4.2, 4.2	-0.55 (N/A)	-0.5	-0.5, -0.5	
Average Daily Normalized 'On' Time With Troublesome Dyskinesia									
BASELINE	49		0.43 (1.08)	0.0	0.0, 5.3				
Low Dose	15		0.24 (0.85)	0.0	0.0, 3.3				
High Dose	34		0.51 (1.17)	0.0	0.0, 5.3				
WEEK 12	34	0.56	0.60 (2.08)	0.0	0.0, 11.0	0.05 (2.38)	0.0	-5.3, 11.0	0.9112
Low Dose	11	0.33	0.00 (0.00)	0.0	0.0, 0.0	-0.33 (0.99)	0.0	-3.3, 0.0	0.3006
High Dose	23	0.67	0.89 (2.49)	0.0	0.0, 11.0	0.22 (2.82)	0.0	-5.3, 11.0	0.7062
WEEK 24	41	0.50	0.32 (0.88)	0.0	0.0, 4.3	-0.18 (1.40)	0.0	-5.3, 4.3	0.4205
Low Dose	13	0.28	0.13 (0.32)	0.0	0.0, 0.9	-0.15 (1.01)	0.0	-3.3, 0.9	0.6135
High Dose	28	0.60	0.41 (1.04)	0.0	0.0, 4.3	-0.19 (1.57)	0.0	-5.3, 4.3	0.5193

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Gender:Male (Cont.)									
Average Daily Normalized 'On' Time With Troublesome Dyskinesia (Cont.)									
WEEK 36	21	0.38	0.31 (0.75)	0.0	0.0, 2.8	-0.07 (1.30)	0.0	-5.3, 1.8	0.8106
Low Dose	9	0.03	0.13 (0.40)	0.0	0.0, 1.2	0.10 (0.43)	0.0	-0.3, 1.2	0.4897
High Dose	12	0.63	0.44 (0.93)	0.0	0.0, 2.8	-0.20 (1.70)	0.0	-5.3, 1.8	0.6951
WEEK 48	16	0.49	0.24 (0.42)	0.0	0.0, 1.6	-0.26 (1.06)	0.0	-3.3, 0.7	0.3504
Low Dose	5	0.66	0.19 (0.31)	0.0	0.0, 0.7	-0.47 (1.62)	0.0	-3.3, 0.7	0.5513
High Dose	11	0.42	0.26 (0.48)	0.0	0.0, 1.6	-0.16 (0.78)	0.0	-2.5, 0.4	0.5162
WEEK 60	2	1.66	0.73 (1.03)	0.7	0.0, 1.5	-0.93 (3.37)	-0.9	-3.3, 1.5	0.7633
Low Dose	1	3.31	0.00 (N/A)	0.0	0.0, 0.0	-3.31 (N/A)	-3.3	-3.3, -3.3	
High Dose	1	0.00	1.45 (N/A)	1.5	1.5, 1.5	1.45 (N/A)	1.5	1.5, 1.5	
WEEK 72	1	0.00	4.96 (N/A)	5.0	5.0, 5.0	4.96 (N/A)	5.0	5.0, 5.0	
Low Dose	0								
High Dose	1	0.00	4.96 (N/A)	5.0	5.0, 5.0	4.96 (N/A)	5.0	5.0, 5.0	

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Gender:Male (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia									
BASELINE	49		13.03 (2.82)	13.6	5.9, 16.0				
Low Dose	15		12.02 (2.55)	12.4	5.9, 16.0				
High Dose	34		13.48 (2.85)	14.9	7.9, 16.0				
WEEK 12	34	12.63	12.52 (3.22)	12.9	5.0, 16.0	-0.11 (3.07)	0.0	-11.0, 5.3	0.8295
Low Dose	11	11.78	12.93 (2.69)	13.3	8.8, 16.0	1.16 (1.93)	0.5	-1.5, 4.1	0.0751
High Dose	23	13.04	12.32 (3.49)	12.2	5.0, 16.0	-0.72 (3.36)	0.0	-11.0, 5.3	0.3139
WEEK 24	41	13.26	13.15 (3.08)	13.7	5.1, 16.0	-0.11 (2.38)	0.0	-5.2, 5.7	0.7682
Low Dose	13	12.59	13.25 (3.08)	14.1	5.2, 16.0	0.66 (2.67)	0.9	-4.3, 5.7	0.3925
High Dose	28	13.57	13.11 (3.13)	13.7	5.1, 16.0	-0.47 (2.20)	-0.1	-5.2, 3.3	0.2707
WEEK 36	21	12.85	12.45 (2.82)	12.4	3.9, 16.0	-0.40 (2.27)	-0.2	-5.6, 4.3	0.4265
Low Dose	9	12.09	11.11 (3.25)	11.5	3.9, 14.1	-0.98 (2.01)	-0.4	-5.6, 1.0	0.1835
High Dose	12	13.42	13.45 (2.06)	13.4	9.9, 16.0	0.03 (2.45)	0.0	-3.9, 4.3	0.9697

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Gender:Male (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia (Cont.)									
WEEK 48	16	13.67	12.82 (3.08)	13.9	7.3, 16.0	-0.84 (2.62)	-0.3	-6.1, 3.8	0.2169
Low Dose	5	13.34	14.16 (2.03)	14.1	11.1, 16.0	0.83 (2.56)	0.0	-2.3, 3.8	0.5101
High Dose	11	13.81	12.21 (3.36)	12.0	7.3, 16.0	-1.60 (2.38)	-0.4	-6.1, 1.0	0.0491*
WEEK 60	2	14.08	12.85 (1.03)	12.8	12.1, 13.6	-1.23 (3.75)	-1.2	-3.9, 1.4	0.7239
Low Dose	1	12.15	13.58 (N/A)	13.6	13.6, 13.6	1.42 (N/A)	1.4	1.4, 1.4	
High Dose	1	16.00	12.12 (N/A)	12.1	12.1, 12.1	-3.88 (N/A)	-3.9	-3.9, -3.9	
WEEK 72	1	16.00	5.59 (N/A)	5.6	5.6, 5.6	-10.41 (N/A)	-10.4	-10.4, -10.4	
Low Dose	0								
High Dose	1	16.00	5.59 (N/A)	5.6	5.6, 5.6	-10.41 (N/A)	-10.4	-10.4, -10.4	
Race:WHITE									
Average Daily Normalized 'Off' Time									
BASELINE	64		1.98 (2.41)	0.9	0.0, 8.8				
Low Dose	25		2.41 (2.23)	2.3	0.0, 6.9				
High Dose	39		1.71 (2.51)	0.5	0.0, 8.8				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:WHITE (Cont.)									
Average Daily Normalized 'Off' Time (Cont.)									
WEEK 12	45	2.10	2.29 (2.44)	1.7	0.0, 7.5	0.18 (2.13)	0.0	-6.4, 6.8	0.5669
Low Dose	20	2.21	2.08 (2.18)	1.9	0.0, 7.3	-0.13 (1.55)	0.0	-4.1, 2.8	0.7206
High Dose	25	2.02	2.45 (2.66)	1.7	0.0, 7.5	0.43 (2.51)	0.0	-6.4, 6.8	0.3987
WEEK 24	56	1.87	2.67 (3.67)	1.2	0.0, 16.0	0.80 (2.81)	0.0	-5.7, 13.3	0.0377*
Low Dose	23	2.42	2.94 (4.24)	1.2	0.0, 16.0	0.52 (3.72)	0.0	-5.7, 13.3	0.5076
High Dose	33	1.49	2.48 (3.28)	1.1	0.0, 13.4	0.99 (1.98)	0.0	-3.1, 6.2	0.0072**
WEEK 36	28	2.13	2.48 (2.86)	1.9	0.0, 12.1	0.35 (1.58)	0.1	-3.9, 5.6	0.2477
Low Dose	15	2.72	3.24 (3.44)	2.3	0.0, 12.1	0.52 (1.56)	0.3	-1.0, 5.6	0.2145
High Dose	13	1.44	1.60 (1.76)	1.0	0.0, 4.9	0.16 (1.65)	0.0	-3.9, 3.6	0.7368
WEEK 48	21	1.44	2.40 (3.76)	0.7	0.0, 14.3	0.96 (2.36)	0.0	-3.0, 6.1	0.0766
Low Dose	9	1.31	1.03 (1.52)	0.0	0.0, 4.2	-0.28 (1.28)	0.0	-3.0, 1.6	0.5297
High Dose	12	1.53	3.42 (4.61)	1.0	0.0, 14.3	1.89 (2.59)	0.3	-0.8, 6.1	0.0281*
WEEK 60	4	0.26	1.57 (1.15)	1.9	0.0, 2.4	1.31 (1.07)	1.4	0.0, 2.4	0.0928
Low Dose	2	0.27	1.21 (1.71)	1.2	0.0, 2.4	0.95 (1.34)	0.9	0.0, 1.9	0.5000
High Dose	2	0.25	1.92 (0.72)	1.9	1.4, 2.4	1.67 (1.07)	1.7	0.9, 2.4	0.2710

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:WHITE (Cont.)									
Average Daily Normalized 'Off' Time (Cont.)									
WEEK 72	2	0.00	2.73 (3.85)	2.7	0.0, 5.5	2.73 (3.85)	2.7	0.0, 5.5	0.5000
Low Dose	1	0.00	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	1	0.00	5.45 (N/A)	5.5	5.5, 5.5	5.45 (N/A)	5.5	5.5, 5.5	
Average Daily Normalized 'On' Time Without Dyskinesia									
BASELINE	64		10.62 (5.07)	11.7	0.0, 16.0				
Low Dose	25		11.85 (4.02)	13.0	1.3, 16.0				
High Dose	39		9.84 (5.55)	11.2	0.0, 16.0				
WEEK 12	45	10.76	11.61 (4.53)	12.5	0.0, 16.0	0.85 (3.62)	0.0	-9.6, 14.2	0.1236
Low Dose	20	12.36	13.16 (3.12)	14.1	4.5, 16.0	0.80 (4.00)	0.0	-6.6, 14.2	0.3839
High Dose	25	9.48	10.37 (5.13)	10.7	0.0, 16.0	0.89 (3.37)	0.4	-9.6, 9.0	0.2004
WEEK 24	56	11.04	11.54 (4.48)	13.4	0.0, 16.0	0.51 (4.53)	0.0	-13.3, 14.2	0.4047
Low Dose	23	11.75	12.23 (4.47)	14.5	0.0, 16.0	0.48 (4.93)	0.0	-13.3, 14.2	0.6468
High Dose	33	10.54	11.07 (4.49)	11.8	0.0, 16.0	0.53 (4.30)	0.0	-9.2, 13.7	0.4851

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:WHITE (Cont.)									
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 36	28	11.29	11.33 (4.73)	12.6	0.0, 16.0	0.04 (4.90)	-0.1	-11.2, 14.2	0.9667
Low Dose	15	11.85	12.02 (3.97)	13.3	3.4, 16.0	0.17 (4.25)	-0.3	-5.9, 14.2	0.8819
High Dose	13	10.65	10.54 (5.54)	11.9	0.0, 16.0	-0.11 (5.73)	0.0	-11.2, 14.0	0.9471
WEEK 48	21	11.24	12.17 (4.26)	14.0	1.4, 16.0	0.93 (4.45)	0.0	-5.6, 13.7	0.3475
Low Dose	9	11.99	14.02 (2.94)	15.3	8.1, 16.0	2.04 (5.46)	0.0	-3.4, 13.7	0.2957
High Dose	12	10.68	10.79 (4.67)	11.3	1.4, 16.0	0.11 (3.54)	0.0	-5.6, 7.9	0.9189
WEEK 60	4	8.29	12.15 (4.14)	13.1	6.3, 16.0	3.86 (2.72)	4.6	0.0, 6.3	0.0655
Low Dose	2	12.32	14.79 (1.71)	14.8	13.6, 16.0	2.46 (3.48)	2.5	0.0, 4.9	0.5000
High Dose	2	4.25	9.50 (4.53)	9.5	6.3, 12.7	5.25 (1.48)	5.3	4.2, 6.3	0.1254
WEEK 72	2	13.65	8.71 (10.30)	8.7	1.4, 16.0	-4.93 (6.98)	-4.9	-9.9, 0.0	0.5000
Low Dose	1	16.00	16.00 (N/A)	16.0	16.0, 16.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	1	11.29	1.43 (N/A)	1.4	1.4, 1.4	-9.87 (N/A)	-9.9	-9.9, -9.9	

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:WHITE (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia									
BASELINE	64		2.96 (4.82)	0.5	0.0, 16.0				
Low Dose	25		1.49 (3.28)	0.0	0.0, 12.0				
High Dose	39		3.91 (5.42)	0.8	0.0, 16.0				
WEEK 12	45	2.70	1.74 (3.71)	0.0	0.0, 16.0	-0.97 (4.16)	0.0	-15.8, 7.4	0.1257
Low Dose	20	1.10	0.72 (2.01)	0.0	0.0, 8.7	-0.38 (3.27)	0.0	-11.6, 7.4	0.6102
High Dose	25	3.98	2.54 (4.52)	0.2	0.0, 16.0	-1.44 (4.76)	0.0	-15.8, 6.7	0.1444
WEEK 24	56	2.61	1.46 (2.95)	0.0	0.0, 16.0	-1.15 (4.15)	0.0	-16.0, 6.1	0.0432*
Low Dose	23	1.56	0.75 (1.37)	0.0	0.0, 4.6	-0.81 (3.71)	0.0	-12.0, 3.3	0.3054
High Dose	33	3.34	1.96 (3.61)	0.0	0.0, 16.0	-1.38 (4.47)	0.0	-16.0, 6.1	0.0854
WEEK 36	28	2.28	2.04 (4.23)	0.1	0.0, 16.0	-0.24 (4.42)	0.0	-12.9, 11.2	0.7744
Low Dose	15	1.23	0.63 (1.05)	0.0	0.0, 3.0	-0.60 (3.10)	0.0	-11.6, 1.8	0.4634
High Dose	13	3.50	3.67 (5.80)	0.2	0.0, 16.0	0.18 (5.69)	0.0	-12.9, 11.2	0.9131

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:WHITE (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 48	21	2.82	1.25 (2.11)	0.2	0.0, 6.4	-1.57 (4.40)	0.0	-12.8, 4.9	0.1169
Low Dose	9	2.04	0.84 (1.95)	0.0	0.0, 6.0	-1.20 (4.05)	0.0	-11.1, 2.9	0.4008
High Dose	12	3.41	1.55 (2.26)	0.5	0.0, 6.4	-1.85 (4.80)	-0.3	-12.8, 4.9	0.2079
WEEK 60	4	5.06	1.93 (2.74)	0.9	0.0, 5.8	-3.14 (5.09)	-1.8	-10.2, 1.1	0.3056
Low Dose	2	1.75	0.00 (0.00)	0.0	0.0, 0.0	-1.75 (2.48)	-1.8	-3.5, 0.0	0.5000
High Dose	2	8.38	3.85 (2.78)	3.9	1.9, 5.8	-4.52 (8.00)	-4.5	-10.2, 1.1	0.5705
WEEK 72	2	2.35	2.08 (2.94)	2.1	0.0, 4.2	-0.27 (0.39)	-0.3	-0.5, 0.0	0.5000
Low Dose	1	0.00	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	1	4.71	4.16 (N/A)	4.2	4.2, 4.2	-0.55 (N/A)	-0.5	-0.5, -0.5	
Average Daily Normalized 'On' Time With Troublesome Dyskinesia									
BASELINE	64		0.43 (1.22)	0.0	0.0, 6.3				
Low Dose	25		0.26 (0.83)	0.0	0.0, 3.3				
High Dose	39		0.55 (1.42)	0.0	0.0, 6.3				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:WHITE (Cont.)									
Average Daily Normalized 'On' Time With Troublesome Dyskinesia (Cont.)									
WEEK 12	45	0.43	0.37 (1.71)	0.0	0.0, 11.0	-0.06 (2.07)	0.0	-5.3, 11.0	0.8387
Low Dose	20	0.33	0.03 (0.15)	0.0	0.0, 0.7	-0.29 (0.95)	0.0	-3.3, 0.7	0.1825
High Dose	25	0.52	0.64 (2.28)	0.0	0.0, 11.0	0.12 (2.67)	0.0	-5.3, 11.0	0.8239
WEEK 24	56	0.48	0.32 (1.17)	0.0	0.0, 7.2	-0.16 (1.25)	0.0	-5.3, 4.3	0.3453
Low Dose	23	0.27	0.09 (0.25)	0.0	0.0, 0.9	-0.19 (0.93)	0.0	-3.3, 0.9	0.3432
High Dose	33	0.63	0.49 (1.49)	0.0	0.0, 7.2	-0.14 (1.45)	0.0	-5.3, 4.3	0.5834
WEEK 36	28	0.30	0.15 (0.42)	0.0	0.0, 1.8	-0.15 (1.22)	0.0	-5.3, 1.8	0.5196
Low Dose	15	0.20	0.11 (0.33)	0.0	0.0, 1.2	-0.09 (0.79)	0.0	-2.7, 1.2	0.6817
High Dose	13	0.41	0.18 (0.51)	0.0	0.0, 1.8	-0.23 (1.62)	0.0	-5.3, 1.8	0.6240
WEEK 48	21	0.50	0.18 (0.38)	0.0	0.0, 1.6	-0.32 (1.07)	0.0	-3.3, 0.7	0.1831
Low Dose	9	0.66	0.11 (0.24)	0.0	0.0, 0.7	-0.56 (1.41)	0.0	-3.3, 0.7	0.2693
High Dose	12	0.38	0.24 (0.46)	0.0	0.0, 1.6	-0.14 (0.74)	0.0	-2.5, 0.4	0.5139
WEEK 60	4	2.39	0.36 (0.73)	0.0	0.0, 1.5	-2.03 (3.45)	-1.7	-6.3, 1.5	0.3247
Low Dose	2	1.66	0.00 (0.00)	0.0	0.0, 0.0	-1.66 (2.34)	-1.7	-3.3, 0.0	0.5000
High Dose	2	3.13	0.73 (1.03)	0.7	0.0, 1.5	-2.40 (5.45)	-2.4	-6.3, 1.5	0.6456

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:WHITE (Cont.)									
Average Daily Normalized 'On' Time With Troublesome Dyskinesia (Cont.)									
WEEK 72	2	0.00	2.48 (3.51)	2.5	0.0, 5.0	2.48 (3.51)	2.5	0.0, 5.0	0.5000
Low Dose	1	0.00	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	1	0.00	4.96 (N/A)	5.0	5.0, 5.0	4.96 (N/A)	5.0	5.0, 5.0	
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia									
BASELINE	64		13.58 (2.52)	14.4	7.2, 16.0				
Low Dose	25		13.33 (2.15)	13.3	9.1, 16.0				
High Dose	39		13.75 (2.75)	15.2	7.2, 16.0				
WEEK 12	45	13.46	13.34 (2.70)	13.9	5.0, 16.0	-0.12 (2.90)	0.0	-11.0, 6.4	0.7818
Low Dose	20	13.46	13.88 (2.15)	14.1	8.8, 16.0	0.42 (1.72)	0.0	-2.8, 4.1	0.2892
High Dose	25	13.46	12.91 (3.04)	13.9	5.0, 16.0	-0.55 (3.55)	0.0	-11.0, 6.4	0.4450
WEEK 24	56	13.64	13.00 (3.79)	14.2	0.0, 16.0	-0.64 (3.03)	0.0	-13.3, 5.7	0.1193
Low Dose	23	13.31	12.98 (4.29)	14.8	0.0, 16.0	-0.34 (3.93)	0.0	-13.3, 5.7	0.6860
High Dose	33	13.88	13.02 (3.47)	13.8	2.6, 16.0	-0.85 (2.24)	-0.2	-6.2, 3.3	0.0362*

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:WHITE (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia (Cont.)									
WEEK 36	28	13.58	13.38 (2.87)	14.1	3.9, 16.0	-0.20 (1.95)	0.0	-5.6, 4.3	0.5861
Low Dose	15	13.08	12.65 (3.50)	13.8	3.9, 16.0	-0.44 (1.83)	0.0	-5.6, 2.7	0.3709
High Dose	13	14.15	14.22 (1.67)	14.3	11.1, 16.0	0.07 (2.11)	0.0	-3.6, 4.3	0.9092
WEEK 48	21	14.06	13.42 (3.79)	15.1	1.7, 16.0	-0.64 (2.58)	-0.2	-6.1, 3.8	0.2694
Low Dose	9	14.03	14.86 (1.73)	16.0	11.1, 16.0	0.84 (2.00)	0.0	-2.3, 3.8	0.2452
High Dose	12	14.09	12.34 (4.58)	14.5	1.7, 16.0	-1.75 (2.46)	-0.3	-6.1, 0.8	0.0319*
WEEK 60	4	13.35	14.07 (1.64)	14.1	12.1, 16.0	0.72 (3.81)	0.7	-3.9, 5.3	0.7302
Low Dose	2	14.08	14.79 (1.71)	14.8	13.6, 16.0	0.71 (1.01)	0.7	0.0, 1.4	0.5000
High Dose	2	12.63	13.35 (1.74)	13.4	12.1, 14.6	0.73 (6.52)	0.7	-3.9, 5.3	0.9000
WEEK 72	2	16.00	10.79 (7.36)	10.8	5.6, 16.0	-5.21 (7.36)	-5.2	-10.4, 0.0	0.5000
Low Dose	1	16.00	16.00 (N/A)	16.0	16.0, 16.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	1	16.00	5.59 (N/A)	5.6	5.6, 5.6	-10.41 (N/A)	-10.4	-10.4, -10.4	

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:ASIAN									
Average Daily Normalized 'Off' Time									
BASELINE	9		5.33 (2.83)	5.8	0.0, 10.1				
Low Dose	5		6.05 (2.79)	5.8	2.4, 10.1				
High Dose	4		4.41 (2.99)	5.6	0.0, 6.4				
WEEK 12	9	5.33	4.49 (2.10)	4.3	2.1, 7.6	-0.84 (2.30)	0.2	-4.2, 2.1	0.3054
Low Dose	5	6.05	4.13 (2.09)	2.9	2.5, 6.9	-1.93 (2.16)	-3.0	-4.2, 0.6	0.1162
High Dose	4	4.41	4.94 (2.34)	5.0	2.1, 7.6	0.52 (1.84)	1.1	-2.1, 2.1	0.6096
WEEK 24	6	4.46	5.64 (3.60)	4.5	2.5, 10.9	1.18 (2.66)	1.5	-3.3, 4.5	0.3253
Low Dose	2	4.55	5.66 (4.41)	5.7	2.5, 8.8	1.11 (1.32)	1.1	0.2, 2.0	0.4455
High Dose	4	4.41	5.64 (3.89)	4.5	2.6, 10.9	1.22 (3.35)	1.8	-3.3, 4.5	0.5178
WEEK 36	6	4.46	3.32 (1.77)	3.5	1.2, 6.1	-1.14 (3.44)	-1.5	-5.5, 3.9	0.4526
Low Dose	2	4.55	2.41 (1.71)	2.4	1.2, 3.6	-2.15 (4.80)	-2.1	-5.5, 1.2	0.6410
High Dose	4	4.41	3.77 (1.85)	3.7	1.6, 6.1	-0.64 (3.32)	-1.5	-3.5, 3.9	0.7249

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:ASIAN (Cont.)									
Average Daily Normalized 'Off' Time (Cont.)									
WEEK 48	4	3.72	4.64 (1.95)	4.7	2.3, 6.9	0.92 (2.18)	0.4	-1.0, 4.0	0.4612
Low Dose	1	2.37	2.32 (N/A)	2.3	2.3, 2.3	-0.04 (N/A)	-0.0	-0.0, -0.0	
High Dose	3	4.17	5.41 (1.45)	5.3	4.0, 6.9	1.24 (2.56)	0.8	-1.0, 4.0	0.4888
Average Daily Normalized 'On' Time Without Dyskinesia									
BASELINE	9		8.12 (3.88)	8.1	4.0, 16.0				
Low Dose	5		7.09 (2.92)	6.9	4.2, 10.7				
High Dose	4		9.42 (4.99)	8.8	4.0, 16.0				
WEEK 12	9	8.12	8.42 (4.42)	8.4	1.0, 13.9	0.29 (3.09)	0.3	-5.9, 4.2	0.7819
Low Dose	5	7.09	7.64 (4.70)	7.8	1.0, 13.5	0.55 (4.08)	1.4	-5.9, 4.2	0.7791
High Dose	4	9.42	9.39 (4.51)	10.1	3.6, 13.9	-0.02 (1.73)	-0.1	-2.1, 2.1	0.9824
WEEK 24	6	8.97	6.87 (4.27)	6.1	1.0, 13.4	-2.10 (2.95)	-2.3	-5.9, 1.6	0.1411
Low Dose	2	8.09	4.12 (4.39)	4.1	1.0, 7.2	-3.97 (2.73)	-4.0	-5.9, -2.0	0.2883
High Dose	4	9.42	8.25 (4.04)	7.3	5.0, 13.4	-1.17 (2.91)	-0.8	-4.5, 1.6	0.4816

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:ASIAN (Cont.)									
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 36	6	8.97	8.78 (4.70)	9.0	1.3, 14.8	-0.20 (4.07)	0.2	-5.6, 5.5	0.9110
Low Dose	2	8.09	8.05 (9.55)	8.0	1.3, 14.8	-0.04 (7.89)	-0.0	-5.6, 5.5	0.9950
High Dose	4	9.42	9.14 (2.43)	9.0	6.4, 12.1	-0.27 (2.62)	0.2	-3.9, 2.4	0.8494
WEEK 48	4	10.14	7.34 (4.81)	7.8	1.8, 12.0	-2.80 (2.69)	-3.6	-5.1, 1.0	0.1286
Low Dose	1	6.92	1.81 (N/A)	1.8	1.8, 1.8	-5.11 (N/A)	-5.1	-5.1, -5.1	
High Dose	3	11.22	9.19 (3.77)	10.7	4.9, 12.0	-2.03 (2.70)	-3.1	-4.0, 1.0	0.3225
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia									
BASELINE	9		2.13 (2.51)	1.7	0.0, 6.7				
Low Dose	5		2.56 (2.93)	1.7	0.0, 6.7				
High Dose	4		1.60 (2.16)	0.9	0.0, 4.6				
WEEK 12	9	2.13	2.60 (4.41)	0.0	0.0, 12.4	0.46 (2.48)	0.0	-2.3, 5.7	0.5894
Low Dose	5	2.56	4.23 (5.52)	1.3	0.0, 12.4	1.67 (2.66)	0.0	-0.4, 5.7	0.2333
High Dose	4	1.60	0.56 (1.11)	0.0	0.0, 2.2	-1.04 (1.22)	-0.9	-2.3, 0.0	0.1867

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:ASIAN (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 24	6	2.19	3.08 (4.83)	1.2	0.0, 12.4	0.89 (2.67)	0.0	-2.1, 5.7	0.4487
Low Dose	2	3.36	6.22 (8.80)	6.2	0.0, 12.4	2.86 (4.05)	2.9	0.0, 5.7	0.5000
High Dose	4	1.60	1.51 (1.80)	1.2	0.0, 3.6	-0.09 (1.59)	0.0	-2.1, 1.8	0.9172
WEEK 36	6	2.19	3.43 (4.42)	2.2	0.0, 11.1	1.25 (1.82)	0.3	0.0, 4.4	0.1551
Low Dose	2	3.36	5.55 (7.85)	5.5	0.0, 11.1	2.19 (3.10)	2.2	0.0, 4.4	0.5000
High Dose	4	1.60	2.37 (2.76)	2.2	0.0, 5.1	0.77 (1.20)	0.3	0.0, 2.5	0.2893
WEEK 48	4	2.14	4.02 (5.60)	2.1	0.0, 11.9	1.88 (2.45)	1.2	0.0, 5.2	0.2223
Low Dose	1	6.72	11.87 (N/A)	11.9	11.9, 11.9	5.15 (N/A)	5.2	5.2, 5.2	
High Dose	3	0.61	1.40 (2.42)	0.0	0.0, 4.2	0.79 (1.37)	0.0	0.0, 2.4	0.4226
Average Daily Normalized 'On' Time With Troublesome Dyskinesia									
BASELINE	9		0.42 (0.85)	0.0	0.0, 2.3				
Low Dose	5		0.29 (0.65)	0.0	0.0, 1.5				
High Dose	4		0.57 (1.14)	0.0	0.0, 2.3				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:ASIAN (Cont.)									
Average Daily Normalized 'On' Time With Troublesome Dyskinesia (Cont.)									
WEEK 12	9	0.42	0.49 (1.48)	0.0	0.0, 4.4	0.08 (0.92)	0.0	-1.5, 2.2	0.8043
Low Dose	5	0.29	0.00 (0.00)	0.0	0.0, 0.0	-0.29 (0.65)	0.0	-1.5, 0.0	0.3739
High Dose	4	0.57	1.11 (2.22)	0.0	0.0, 4.4	0.54 (1.08)	0.0	0.0, 2.2	0.3910
WEEK 24	6	0.38	0.40 (0.99)	0.0	0.0, 2.4	0.02 (0.05)	0.0	0.0, 0.1	0.3632
Low Dose	2	0.00	0.00 (0.00)	0.0	0.0, 0.0	0.00 (0.00)	0.0	0.0, 0.0	
High Dose	4	0.57	0.60 (1.21)	0.0	0.0, 2.4	0.03 (0.07)	0.0	0.0, 0.1	0.3910
WEEK 36	6	0.38	0.47 (1.16)	0.0	0.0, 2.8	0.09 (0.23)	0.0	0.0, 0.6	0.3632
Low Dose	2	0.00	0.00 (0.00)	0.0	0.0, 0.0	0.00 (0.00)	0.0	0.0, 0.0	
High Dose	4	0.57	0.71 (1.42)	0.0	0.0, 2.8	0.14 (0.28)	0.0	0.0, 0.6	0.3910
WEEK 48	4	0.00	0.00 (0.00)	0.0	0.0, 0.0	0.00 (0.00)	0.0	0.0, 0.0	
Low Dose	1	0.00	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	3	0.00	0.00 (0.00)	0.0	0.0, 0.0	0.00 (0.00)	0.0	0.0, 0.0	

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Race:ASIAN (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia									
BASELINE	9		10.26 (2.96)	9.6	5.9, 16.0				
Low Dose	5		9.65 (2.83)	9.3	5.9, 13.6				
High Dose	4		11.01 (3.37)	9.7	8.6, 16.0				
WEEK 12	9	10.26	11.02 (2.84)	11.7	5.8, 13.9	0.76 (2.77)	-0.2	-2.8, 4.4	0.4347
Low Dose	5	9.65	11.87 (2.09)	13.1	9.1, 13.5	2.22 (2.41)	3.2	-0.6, 4.4	0.1090
High Dose	4	11.01	9.95 (3.59)	10.1	5.8, 13.9	-1.06 (2.17)	-1.8	-2.8, 2.1	0.4000
WEEK 24	6	11.16	9.95 (3.80)	10.3	5.1, 13.5	-1.21 (2.66)	-1.6	-4.5, 3.3	0.3171
Low Dose	2	11.45	10.34 (4.41)	10.3	7.2, 13.5	-1.11 (1.32)	-1.1	-2.0, -0.2	0.4455
High Dose	4	11.01	9.76 (4.18)	10.3	5.1, 13.4	-1.26 (3.35)	-1.9	-4.5, 3.3	0.5073
WEEK 36	6	11.16	12.21 (1.60)	12.2	9.9, 14.8	1.05 (3.37)	1.5	-3.9, 5.5	0.4798
Low Dose	2	11.45	13.59 (1.71)	13.6	12.4, 14.8	2.15 (4.80)	2.1	-1.2, 5.5	0.6410
High Dose	4	11.01	11.52 (1.18)	11.8	9.9, 12.6	0.50 (3.17)	1.5	-3.9, 2.9	0.7722

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:ASIAN (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia (Cont.)									
WEEK 48	4	12.28	11.36 (1.95)	11.3	9.1, 13.7	-0.92 (2.18)	-0.4	-4.0, 1.0	0.4612
Low Dose	1	13.63	13.68 (N/A)	13.7	13.7, 13.7	0.04 (N/A)	0.0	0.0, 0.0	
High Dose	3	11.83	10.59 (1.45)	10.7	9.1, 12.0	-1.24 (2.56)	-0.8	-4.0, 1.0	0.4888
Age category:< 65 years									
Average Daily Normalized 'Off' Time									
BASELINE	41		2.46 (2.73)	1.3	0.0, 10.1				
Low Dose	18		2.92 (2.92)	2.0	0.0, 10.1				
High Dose	23		2.10 (2.59)	0.5	0.0, 8.8				
WEEK 12	29	2.73	2.95 (2.68)	2.5	0.0, 7.6	0.22 (2.43)	0.0	-6.4, 6.8	0.6347
Low Dose	14	2.80	2.55 (2.17)	2.6	0.0, 6.9	-0.26 (1.92)	0.0	-4.1, 2.8	0.6249
High Dose	15	2.67	3.33 (3.12)	2.3	0.0, 7.6	0.66 (2.83)	0.0	-6.4, 6.8	0.3809
WEEK 24	34	2.27	2.43 (3.02)	1.6	0.0, 13.4	0.16 (2.12)	0.0	-5.7, 5.2	0.6706
Low Dose	14	2.16	1.68 (1.79)	1.2	0.0, 5.9	-0.48 (1.79)	0.0	-5.7, 2.3	0.3346
High Dose	20	2.35	2.95 (3.59)	2.3	0.0, 13.4	0.60 (2.26)	0.0	-3.3, 5.2	0.2497

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Age category:< 65 years (Cont.)									
Average Daily Normalized 'Off' Time (Cont.)									
WEEK 36	21	2.41	2.20 (2.08)	2.0	0.0, 7.7	-0.21 (1.67)	0.0	-3.9, 3.6	0.5661
Low Dose	12	2.22	2.43 (2.28)	2.1	0.0, 7.7	0.22 (0.81)	0.1	-1.0, 1.4	0.3722
High Dose	9	2.68	1.89 (1.86)	1.6	0.0, 4.9	-0.79 (2.32)	0.0	-3.9, 3.6	0.3389
WEEK 48	17	1.81	3.11 (4.14)	0.9	0.0, 14.3	1.31 (2.34)	0.3	-1.2, 6.1	0.0349*
Low Dose	7	1.12	1.27 (1.58)	0.7	0.0, 4.2	0.15 (0.82)	0.0	-1.2, 1.6	0.6444
High Dose	10	2.29	4.40 (4.94)	2.7	0.0, 14.3	2.11 (2.74)	0.6	-0.8, 6.1	0.0372*
WEEK 60	2	0.00	1.21 (1.71)	1.2	0.0, 2.4	1.21 (1.71)	1.2	0.0, 2.4	0.5000
Low Dose	1	0.00	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	1	0.00	2.42 (N/A)	2.4	2.4, 2.4	2.42 (N/A)	2.4	2.4, 2.4	
WEEK 72	1	0.00	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
Low Dose	1	0.00	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	0								

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Age category:< 65 years (Cont.)									
Average Daily Normalized 'On' Time Without Dyskinesia									
BASELINE	41		9.61 (5.40)	10.7	0.0, 16.0				
Low Dose	18		11.09 (4.46)	11.9	1.5, 16.0				
High Dose	23		8.46 (5.87)	8.1	0.0, 16.0				
WEEK 12	29	9.35	10.79 (4.62)	11.4	0.0, 16.0	1.44 (3.75)	0.4	-5.9, 14.2	0.0477*
Low Dose	14	10.85	11.56 (4.32)	12.7	1.0, 15.8	0.71 (4.51)	-0.2	-5.9, 14.2	0.5677
High Dose	15	7.96	10.08 (4.93)	9.0	0.0, 16.0	2.13 (2.86)	0.5	-0.4, 9.0	0.0121*
WEEK 24	34	10.47	11.46 (4.24)	11.9	1.0, 16.0	1.00 (4.59)	0.0	-6.3, 14.2	0.2147
Low Dose	14	11.82	12.10 (4.38)	14.0	1.0, 16.0	0.28 (4.75)	-0.1	-5.9, 14.2	0.8271
High Dose	20	9.52	11.02 (4.20)	11.2	2.6, 16.0	1.50 (4.53)	0.7	-6.3, 13.7	0.1564
WEEK 36	21	10.82	11.65 (4.29)	13.3	1.3, 16.0	0.83 (4.76)	0.0	-5.6, 14.2	0.4337
Low Dose	12	11.58	11.86 (4.59)	13.5	1.3, 16.0	0.28 (4.76)	-0.2	-5.6, 14.2	0.8443
High Dose	9	9.81	11.38 (4.10)	11.9	6.4, 16.0	1.57 (4.93)	0.2	-3.6, 14.0	0.3686

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Age category:< 65 years (Cont.)									
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 48	17	10.39	10.56 (5.23)	10.2	1.4, 16.0	0.17 (4.90)	0.0	-5.6, 13.7	0.8884
Low Dose	7	11.41	11.81 (5.41)	15.3	1.8, 16.0	0.40 (6.29)	-0.5	-5.1, 13.7	0.8729
High Dose	10	9.68	9.69 (5.20)	8.6	1.4, 16.0	0.01 (4.02)	0.3	-5.6, 7.9	0.9940
WEEK 60	2	8.00	11.15 (6.86)	11.2	6.3, 16.0	3.15 (4.46)	3.2	0.0, 6.3	0.5000
Low Dose	1	16.00	16.00 (N/A)	16.0	16.0, 16.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	1	0.00	6.30 (N/A)	6.3	6.3, 6.3	6.30 (N/A)	6.3	6.3, 6.3	
WEEK 72	1	16.00	16.00 (N/A)	16.0	16.0, 16.0	0.00 (N/A)	0.0	0.0, 0.0	
Low Dose	1	16.00	16.00 (N/A)	16.0	16.0, 16.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	0								
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia									
BASELINE	41		3.55 (5.04)	0.8	0.0, 16.0				
Low Dose	18		1.75 (3.12)	0.3	0.0, 11.8				
High Dose	23		4.95 (5.82)	1.8	0.0, 16.0				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Age category:< 65 years (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 12	29	3.44	2.01 (3.89)	0.2	0.0, 16.0	-1.43 (4.29)	0.0	-15.8, 5.7	0.0828
Low Dose	14	2.03	1.85 (3.67)	0.2	0.0, 12.4	-0.18 (3.72)	0.0	-11.6, 5.7	0.8581
High Dose	15	4.76	2.16 (4.21)	0.2	0.0, 16.0	-2.60 (4.58)	-0.6	-15.8, 1.0	0.0449*
WEEK 24	34	2.86	1.85 (3.00)	0.0	0.0, 12.4	-1.01 (4.92)	0.0	-16.0, 6.1	0.2404
Low Dose	14	1.81	2.10 (3.36)	0.9	0.0, 12.4	0.29 (3.85)	0.1	-11.6, 5.7	0.7858
High Dose	20	3.59	1.67 (2.79)	0.0	0.0, 10.2	-1.92 (5.46)	-0.1	-16.0, 6.1	0.1334
WEEK 36	21	2.51	1.92 (3.05)	0.2	0.0, 11.1	-0.59 (4.09)	0.0	-12.9, 4.4	0.5168
Low Dose	12	1.96	1.61 (3.20)	0.1	0.0, 11.1	-0.35 (3.78)	0.0	-11.6, 4.4	0.7544
High Dose	9	3.26	2.35 (2.97)	0.5	0.0, 8.1	-0.91 (4.70)	0.0	-12.9, 2.9	0.5775
WEEK 48	17	3.37	2.12 (3.29)	0.7	0.0, 11.9	-1.26 (5.18)	0.0	-12.8, 5.2	0.3326
Low Dose	7	3.08	2.78 (4.54)	0.7	0.0, 11.9	-0.30 (5.13)	0.0	-11.1, 5.2	0.8804
High Dose	10	3.58	1.65 (2.22)	0.7	0.0, 6.4	-1.92 (5.38)	-0.3	-12.8, 4.9	0.2882
WEEK 60	2	8.00	2.91 (4.11)	2.9	0.0, 5.8	-5.09 (7.20)	-5.1	-10.2, 0.0	0.5000
Low Dose	1	0.00	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	1	16.00	5.82 (N/A)	5.8	5.8, 5.8	-10.18 (N/A)	-10.2	-10.2, -10.2	

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Age category:< 65 years (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 72	1	0.00	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
Low Dose	1	0.00	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	0								
Average Daily Normalized 'On' Time With Troublesome Dyskinesia									
BASELINE	41		0.38 (0.85)	0.0	0.0, 3.0				
Low Dose	18		0.24 (0.70)	0.0	0.0, 2.7				
High Dose	23		0.49 (0.95)	0.0	0.0, 3.0				
WEEK 12	29	0.47	0.25 (0.90)	0.0	0.0, 4.4	-0.22 (0.93)	0.0	-3.0, 2.2	0.2067
Low Dose	14	0.31	0.05 (0.18)	0.0	0.0, 0.7	-0.27 (0.82)	0.0	-2.7, 0.7	0.2450
High Dose	15	0.61	0.43 (1.23)	0.0	0.0, 4.4	-0.18 (1.05)	0.0	-3.0, 2.2	0.5119
WEEK 24	34	0.40	0.26 (0.66)	0.0	0.0, 2.4	-0.14 (0.91)	0.0	-3.0, 1.9	0.3677
Low Dose	14	0.21	0.12 (0.31)	0.0	0.0, 0.9	-0.09 (0.81)	0.0	-2.7, 0.9	0.6890
High Dose	20	0.54	0.36 (0.81)	0.0	0.0, 2.4	-0.18 (1.00)	0.0	-3.0, 1.9	0.4269

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Age category:< 65 years (Cont.)									
Average Daily Normalized 'On' Time With Troublesome Dyskinesia (Cont.)									
WEEK 36	21	0.25	0.22 (0.67)	0.0	0.0, 2.8	-0.03 (0.68)	0.0	-2.7, 1.2	0.8529
Low Dose	12	0.25	0.10 (0.35)	0.0	0.0, 1.2	-0.15 (0.87)	0.0	-2.7, 1.2	0.5772
High Dose	9	0.25	0.38 (0.94)	0.0	0.0, 2.8	0.13 (0.25)	0.0	0.0, 0.6	0.1692
WEEK 48	17	0.43	0.21 (0.42)	0.0	0.0, 1.6	-0.22 (0.90)	0.0	-2.7, 0.7	0.3319
Low Dose	7	0.38	0.14 (0.27)	0.0	0.0, 0.7	-0.24 (1.10)	0.0	-2.7, 0.7	0.5804
High Dose	10	0.46	0.25 (0.50)	0.0	0.0, 1.6	-0.20 (0.80)	0.0	-2.5, 0.4	0.4448
WEEK 60	2	0.00	0.73 (1.03)	0.7	0.0, 1.5	0.73 (1.03)	0.7	0.0, 1.5	0.5000
Low Dose	1	0.00	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	1	0.00	1.45 (N/A)	1.5	1.5, 1.5	1.45 (N/A)	1.5	1.5, 1.5	
WEEK 72	1	0.00	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
Low Dose	1	0.00	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	0								

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Age category:< 65 years (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia									
BASELINE	41		13.16 (2.88)	13.9	5.9, 16.0				
Low Dose	18		12.84 (2.92)	13.5	5.9, 16.0				
High Dose	23		13.41 (2.88)	14.2	7.2, 16.0				
WEEK 12	29	12.80	12.80 (2.89)	13.5	5.8, 16.0	0.01 (2.55)	0.0	-6.8, 6.4	0.9899
Low Dose	14	12.88	13.40 (2.11)	13.4	9.1, 16.0	0.52 (2.19)	-0.1	-2.8, 4.4	0.3870
High Dose	15	12.72	12.24 (3.44)	13.7	5.8, 16.0	-0.48 (2.82)	0.0	-6.8, 6.4	0.5230
WEEK 24	34	13.33	13.31 (3.09)	13.9	2.6, 16.0	-0.01 (2.21)	0.0	-5.2, 5.7	0.9724
Low Dose	14	13.63	14.20 (1.99)	14.8	9.3, 16.0	0.57 (2.02)	0.0	-3.1, 5.7	0.3111
High Dose	20	13.11	12.69 (3.59)	13.7	2.6, 16.0	-0.42 (2.29)	-0.1	-5.2, 3.3	0.4218
WEEK 36	21	13.34	13.58 (2.17)	14.0	8.3, 16.0	0.24 (1.78)	0.0	-3.6, 3.9	0.5435
Low Dose	12	13.54	13.47 (2.36)	13.9	8.3, 16.0	-0.07 (1.31)	0.0	-2.3, 2.7	0.8494
High Dose	9	13.07	13.73 (2.00)	14.0	11.1, 16.0	0.66 (2.29)	0.0	-3.6, 3.9	0.4126

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Age category:< 65 years (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia (Cont.)									
WEEK 48	17	13.76	12.68 (4.16)	14.2	1.7, 16.0	-1.09 (2.41)	-0.4	-6.1, 2.7	0.0814
Low Dose	7	14.50	14.59 (1.82)	15.3	11.1, 16.0	0.09 (1.54)	0.0	-2.3, 2.7	0.8791
High Dose	10	13.25	11.34 (4.87)	12.7	1.7, 16.0	-1.91 (2.62)	-0.6	-6.1, 0.8	0.0468*
WEEK 60	2	16.00	14.06 (2.74)	14.1	12.1, 16.0	-1.94 (2.74)	-1.9	-3.9, 0.0	0.5000
Low Dose	1	16.00	16.00 (N/A)	16.0	16.0, 16.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	1	16.00	12.12 (N/A)	12.1	12.1, 12.1	-3.88 (N/A)	-3.9	-3.9, -3.9	
WEEK 72	1	16.00	16.00 (N/A)	16.0	16.0, 16.0	0.00 (N/A)	0.0	0.0, 0.0	
Low Dose	1	16.00	16.00 (N/A)	16.0	16.0, 16.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	0								
Age category:>= 65 years									
Average Daily Normalized 'Off' Time									
BASELINE	32		2.31 (2.65)	1.0	0.0, 8.1				
Low Dose	12		3.16 (2.35)	2.9	0.0, 6.7				
High Dose	20		1.80 (2.75)	0.4	0.0, 8.1				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Age category:>= 65 years (Cont.)									
Average Daily Normalized 'Off' Time (Cont.)									
WEEK 12	25	2.53	2.31 (2.29)	2.1	0.0, 7.3	-0.22 (1.85)	0.0	-4.3, 4.2	0.5520
Low Dose	11	3.20	2.42 (2.51)	2.5	0.0, 7.3	-0.78 (1.66)	0.0	-4.2, 0.8	0.1521
High Dose	14	2.00	2.22 (2.20)	1.9	0.0, 6.1	0.21 (1.93)	0.0	-4.3, 4.2	0.6859
WEEK 24	28	1.94	3.61 (4.45)	2.0	0.0, 16.0	1.66 (3.26)	0.3	-3.0, 13.3	0.0118*
Low Dose	11	3.14	5.04 (5.64)	2.4	0.0, 16.0	1.90 (4.80)	0.0	-3.0, 13.3	0.2178
High Dose	17	1.17	2.68 (3.34)	1.7	0.0, 10.9	1.51 (1.85)	0.9	-0.2, 6.2	0.0040**
WEEK 36	13	2.74	3.31 (3.47)	2.0	0.0, 12.1	0.58 (2.54)	0.3	-5.5, 5.6	0.4292
Low Dose	5	4.66	4.85 (4.80)	4.5	0.0, 12.1	0.19 (3.95)	0.3	-5.5, 5.6	0.9209
High Dose	8	1.54	2.36 (2.18)	1.8	0.0, 6.1	0.82 (1.41)	0.5	-0.3, 3.9	0.1430
WEEK 48	8	1.78	1.99 (2.03)	1.9	0.0, 5.3	0.21 (2.13)	-0.0	-3.0, 4.0	0.7890
Low Dose	3	2.09	0.89 (1.53)	0.0	0.0, 2.7	-1.21 (1.61)	-0.5	-3.0, -0.0	0.3251
High Dose	5	1.60	2.66 (2.14)	2.8	0.0, 5.3	1.06 (2.06)	0.0	-1.0, 4.0	0.3145
WEEK 60	2	0.52	1.92 (0.72)	1.9	1.4, 2.4	1.40 (0.69)	1.4	0.9, 1.9	0.2140
Low Dose	1	0.53	2.42 (N/A)	2.4	2.4, 2.4	1.89 (N/A)	1.9	1.9, 1.9	
High Dose	1	0.50	1.41 (N/A)	1.4	1.4, 1.4	0.91 (N/A)	0.9	0.9, 0.9	

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Age category:>= 65 years (Cont.)									
Average Daily Normalized 'Off' Time (Cont.)									
WEEK 72	1	0.00	5.45 (N/A)	5.5	5.5, 5.5	5.45 (N/A)	5.5	5.5, 5.5	
Low Dose	0								
High Dose	1	0.00	5.45 (N/A)	5.5	5.5, 5.5	5.45 (N/A)	5.5	5.5, 5.5	
Average Daily Normalized 'On' Time Without Dyskinesia									
BASELINE	32		11.22 (4.32)	11.5	0.0, 16.0				
Low Dose	12		11.01 (4.02)	11.5	1.3, 16.0				
High Dose	20		11.35 (4.58)	11.5	0.0, 16.0				
WEEK 12	25	11.44	11.40 (4.71)	12.3	0.0, 16.0	-0.04 (3.11)	0.0	-9.6, 6.1	0.9479
Low Dose	11	11.88	12.68 (3.81)	13.5	4.5, 16.0	0.80 (3.27)	0.3	-6.6, 6.1	0.4358
High Dose	14	11.10	10.39 (5.23)	11.0	0.0, 16.0	-0.70 (2.93)	-0.3	-9.6, 2.8	0.3865
WEEK 24	28	11.28	10.64 (5.12)	11.6	0.0, 16.0	-0.64 (4.17)	0.0	-13.3, 7.4	0.4207
Low Dose	11	11.00	10.91 (5.66)	13.6	0.0, 16.0	-0.08 (5.32)	1.0	-13.3, 7.4	0.9592
High Dose	17	11.47	10.46 (4.91)	9.7	0.0, 16.0	-1.01 (3.36)	-0.6	-9.2, 6.5	0.2341

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Age category:>= 65 years (Cont.)									
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 36	13	10.99	9.64 (5.38)	11.5	0.0, 16.0	-1.35 (4.47)	-0.3	-11.2, 5.5	0.2991
Low Dose	5	11.00	10.82 (5.12)	11.5	3.4, 16.0	-0.18 (4.04)	-0.3	-5.9, 5.5	0.9242
High Dose	8	10.98	8.90 (5.75)	10.9	0.0, 14.1	-2.07 (4.84)	-0.5	-11.2, 4.5	0.2647
WEEK 48	8	12.50	13.19 (2.27)	12.9	10.2, 16.0	0.69 (3.35)	0.0	-4.0, 7.4	0.5788
Low Dose	3	11.64	15.11 (1.53)	16.0	13.3, 16.0	3.48 (3.68)	3.0	0.0, 7.4	0.2430
High Dose	5	13.01	12.03 (1.83)	12.0	10.2, 14.9	-0.98 (1.89)	-0.9	-4.0, 1.0	0.3081
WEEK 60	2	8.57	13.14 (0.62)	13.1	12.7, 13.6	4.57 (0.51)	4.6	4.2, 4.9	0.0502
Low Dose	1	8.65	13.58 (N/A)	13.6	13.6, 13.6	4.93 (N/A)	4.9	4.9, 4.9	
High Dose	1	8.50	12.71 (N/A)	12.7	12.7, 12.7	4.21 (N/A)	4.2	4.2, 4.2	
WEEK 72	1	11.29	1.43 (N/A)	1.4	1.4, 1.4	-9.87 (N/A)	-9.9	-9.9, -9.9	
Low Dose	0								
High Dose	1	11.29	1.43 (N/A)	1.4	1.4, 1.4	-9.87 (N/A)	-9.9	-9.9, -9.9	

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Age category:>= 65 years (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia									
BASELINE	32		1.98 (3.86)	0.0	0.0, 16.0				
Low Dose	12		1.54 (3.46)	0.0	0.0, 12.0				
High Dose	20		2.24 (4.15)	0.0	0.0, 16.0				
WEEK 12	25	1.64	1.73 (3.77)	0.0	0.0, 16.0	0.09 (3.40)	0.0	-11.0, 7.4	0.8946
Low Dose	11	0.59	0.89 (2.60)	0.0	0.0, 8.7	0.30 (2.57)	0.0	-3.5, 7.4	0.7046
High Dose	14	2.46	2.39 (4.46)	0.0	0.0, 16.0	-0.08 (4.02)	0.0	-11.0, 6.7	0.9453
WEEK 24	28	2.21	1.34 (3.38)	0.0	0.0, 16.0	-0.88 (2.75)	0.0	-12.0, 5.1	0.1034
Low Dose	11	1.56	0.02 (0.07)	0.0	0.0, 0.2	-1.54 (3.63)	0.0	-12.0, 0.0	0.1890
High Dose	17	2.63	2.19 (4.16)	0.0	0.0, 16.0	-0.45 (2.02)	0.0	-3.9, 5.1	0.3744
WEEK 36	13	1.87	2.87 (5.76)	0.0	0.0, 16.0	1.01 (4.07)	0.0	-5.7, 11.2	0.3906
Low Dose	5	0.34	0.24 (0.34)	0.0	0.0, 0.7	-0.10 (0.39)	0.0	-0.8, 0.3	0.6153
High Dose	8	2.82	4.51 (6.98)	0.1	0.0, 16.0	1.69 (5.19)	0.0	-5.7, 11.2	0.3866

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Age category:>= 65 years (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 48	8	1.30	0.78 (1.93)	0.0	0.0, 5.5	-0.52 (1.36)	0.0	-3.5, 0.8	0.3131
Low Dose	3	1.17	0.00 (0.00)	0.0	0.0, 0.0	-1.17 (2.02)	0.0	-3.5, 0.0	0.4226
High Dose	5	1.39	1.25 (2.40)	0.0	0.0, 5.5	-0.13 (0.82)	0.0	-1.5, 0.8	0.7345
WEEK 60	2	2.13	0.94 (1.33)	0.9	0.0, 1.9	-1.19 (3.28)	-1.2	-3.5, 1.1	0.6989
Low Dose	1	3.50	0.00 (N/A)	0.0	0.0, 0.0	-3.50 (N/A)	-3.5	-3.5, -3.5	
High Dose	1	0.75	1.88 (N/A)	1.9	1.9, 1.9	1.13 (N/A)	1.1	1.1, 1.1	
WEEK 72	1	4.71	4.16 (N/A)	4.2	4.2, 4.2	-0.55 (N/A)	-0.5	-0.5, -0.5	
Low Dose	0								
High Dose	1	4.71	4.16 (N/A)	4.2	4.2, 4.2	-0.55 (N/A)	-0.5	-0.5, -0.5	
Average Daily Normalized 'On' Time With Troublesome Dyskinesia									
BASELINE	32		0.50 (1.52)	0.0	0.0, 6.3				
Low Dose	12		0.30 (0.95)	0.0	0.0, 3.3				
High Dose	20		0.62 (1.78)	0.0	0.0, 6.3				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Age category:>= 65 years (Cont.)									
Average Daily Normalized 'On' Time With Troublesome Dyskinesia (Cont.)									
WEEK 12	25	0.39	0.56 (2.26)	0.0	0.0, 11.0	0.17 (2.66)	0.0	-5.3, 11.0	0.7479
Low Dose	11	0.32	0.00 (0.00)	0.0	0.0, 0.0	-0.32 (0.99)	0.0	-3.3, 0.0	0.3053
High Dose	14	0.44	1.00 (2.99)	0.0	0.0, 11.0	0.56 (3.46)	0.0	-5.3, 11.0	0.5521
WEEK 24	28	0.56	0.42 (1.55)	0.0	0.0, 7.2	-0.14 (1.48)	0.0	-5.3, 4.3	0.6194
Low Dose	11	0.30	0.02 (0.08)	0.0	0.0, 0.3	-0.28 (1.01)	0.0	-3.3, 0.3	0.3817
High Dose	17	0.73	0.68 (1.97)	0.0	0.0, 7.2	-0.05 (1.74)	0.0	-5.3, 4.3	0.9052
WEEK 36	13	0.41	0.17 (0.51)	0.0	0.0, 1.8	-0.24 (1.61)	0.0	-5.3, 1.8	0.6071
Low Dose	5	0.00	0.09 (0.20)	0.0	0.0, 0.5	0.09 (0.20)	0.0	0.0, 0.5	0.3739
High Dose	8	0.67	0.23 (0.64)	0.0	0.0, 1.8	-0.44 (2.08)	0.0	-5.3, 1.8	0.5669
WEEK 48	8	0.41	0.04 (0.10)	0.0	0.0, 0.3	-0.38 (1.19)	0.0	-3.3, 0.3	0.4002
Low Dose	3	1.10	0.00 (0.00)	0.0	0.0, 0.0	-1.10 (1.91)	0.0	-3.3, 0.0	0.4226
High Dose	5	0.00	0.06 (0.13)	0.0	0.0, 0.3	0.06 (0.13)	0.0	0.0, 0.3	0.3739
WEEK 60	2	4.78	0.00 (0.00)	0.0	0.0, 0.0	-4.78 (2.08)	-4.8	-6.3, -3.3	0.1896
Low Dose	1	3.31	0.00 (N/A)	0.0	0.0, 0.0	-3.31 (N/A)	-3.3	-3.3, -3.3	
High Dose	1	6.25	0.00 (N/A)	0.0	0.0, 0.0	-6.25 (N/A)	-6.3	-6.3, -6.3	

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Age category:>= 65 years (Cont.)									
Average Daily Normalized 'On' Time With Troublesome Dyskinesia (Cont.)									
WEEK 72	1	0.00	4.96 (N/A)	5.0	5.0, 5.0	4.96 (N/A)	5.0	5.0, 5.0	
Low Dose	0								
High Dose	1	0.00	4.96 (N/A)	5.0	5.0, 5.0	4.96 (N/A)	5.0	5.0, 5.0	
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia									
BASELINE	32		13.20 (2.71)	13.5	7.9, 16.0				
Low Dose	12		12.55 (2.20)	12.7	9.3, 16.0				
High Dose	20		13.59 (2.96)	15.2	7.9, 16.0				
WEEK 12	25	13.08	13.13 (2.82)	13.5	5.0, 16.0	0.05 (3.26)	0.0	-11.0, 5.3	0.9396
Low Dose	11	12.47	13.58 (2.51)	13.5	8.8, 16.0	1.10 (1.66)	0.5	-0.8, 4.2	0.0529
High Dose	14	13.56	12.78 (3.09)	13.1	5.0, 16.0	-0.78 (3.97)	-0.3	-11.0, 5.3	0.4775
WEEK 24	28	13.50	11.98 (4.60)	13.6	0.0, 16.0	-1.52 (3.58)	-0.3	-13.3, 3.8	0.0326*
Low Dose	11	12.56	10.94 (5.66)	13.6	0.0, 16.0	-1.63 (5.10)	0.0	-13.3, 3.8	0.3149
High Dose	17	14.10	12.65 (3.80)	13.7	5.1, 16.0	-1.45 (2.30)	-0.9	-6.2, 3.0	0.0193*

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Age category:>= 65 years (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia (Cont.)									
WEEK 36	13	12.85	12.51 (3.40)	14.0	3.9, 16.0	-0.34 (2.90)	-0.3	-5.6, 5.5	0.6797
Low Dose	5	11.34	11.06 (4.84)	11.5	3.9, 16.0	-0.28 (3.96)	-0.3	-5.6, 5.5	0.8830
High Dose	8	13.80	13.42 (1.98)	14.1	9.9, 16.0	-0.38 (2.33)	-0.6	-3.9, 4.3	0.6592
WEEK 48	8	13.80	13.97 (2.00)	14.1	10.7, 16.0	0.17 (2.58)	0.0	-4.0, 3.8	0.8592
Low Dose	3	12.80	15.11 (1.53)	16.0	13.3, 16.0	2.31 (2.01)	3.0	0.0, 3.8	0.1847
High Dose	5	14.40	13.28 (2.05)	13.2	10.7, 15.7	-1.12 (2.03)	-0.3	-4.0, 1.0	0.2848
WEEK 60	2	10.70	14.08 (0.72)	14.1	13.6, 14.6	3.38 (2.77)	3.4	1.4, 5.3	0.3341
Low Dose	1	12.15	13.58 (N/A)	13.6	13.6, 13.6	1.42 (N/A)	1.4	1.4, 1.4	
High Dose	1	9.25	14.59 (N/A)	14.6	14.6, 14.6	5.34 (N/A)	5.3	5.3, 5.3	
WEEK 72	1	16.00	5.59 (N/A)	5.6	5.6, 5.6	-10.41 (N/A)	-10.4	-10.4, -10.4	
Low Dose	0								
High Dose	1	16.00	5.59 (N/A)	5.6	5.6, 5.6	-10.41 (N/A)	-10.4	-10.4, -10.4	

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Geographic region:NORTH AMERICA									
Average Daily Normalized 'Off' Time									
BASELINE	32		1.71 (2.30)	0.5	0.0, 8.1				
Low Dose	10		2.35 (1.91)	2.6	0.0, 5.9				
High Dose	22		1.41 (2.44)	0.1	0.0, 8.1				
WEEK 12	22	1.86	2.32 (2.32)	2.1	0.0, 6.8	0.46 (2.28)	0.0	-4.3, 6.8	0.3596
Low Dose	8	2.27	2.35 (1.93)	2.5	0.0, 5.9	0.07 (1.67)	-0.0	-3.0, 2.8	0.9044
High Dose	14	1.63	2.30 (2.59)	1.6	0.0, 6.8	0.67 (2.60)	0.0	-4.3, 6.8	0.3501
WEEK 24	27	1.30	2.16 (2.86)	0.9	0.0, 10.3	0.86 (2.18)	0.0	-3.0, 7.6	0.0506
Low Dose	9	2.23	2.51 (3.50)	1.1	0.0, 10.3	0.28 (2.95)	-0.0	-3.0, 7.6	0.7844
High Dose	18	0.84	1.99 (2.57)	0.4	0.0, 7.4	1.15 (1.70)	0.3	-0.5, 6.2	0.0107*
WEEK 36	14	1.32	1.72 (1.98)	1.4	0.0, 6.5	0.40 (0.69)	0.3	-1.1, 1.4	0.0496*
Low Dose	6	2.30	2.85 (2.52)	3.0	0.0, 6.5	0.55 (0.57)	0.4	-0.0, 1.4	0.0639
High Dose	8	0.57	0.86 (0.92)	0.6	0.0, 2.0	0.29 (0.79)	0.1	-1.1, 1.2	0.3349

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Geographic region:NORTH AMERICA (Cont.)									
Average Daily Normalized 'Off' Time (Cont.)									
WEEK 48	9	0.83	1.46 (1.87)	0.7	0.0, 4.5	0.63 (2.07)	0.4	-3.0, 4.5	0.3904
Low Dose	5	1.29	0.98 (1.82)	0.0	0.0, 4.2	-0.31 (1.72)	0.0	-3.0, 1.6	0.7077
High Dose	4	0.25	2.05 (2.00)	1.9	0.0, 4.5	1.80 (2.06)	1.4	0.0, 4.5	0.1794
WEEK 60	4	0.26	1.57 (1.15)	1.9	0.0, 2.4	1.31 (1.07)	1.4	0.0, 2.4	0.0928
Low Dose	2	0.27	1.21 (1.71)	1.2	0.0, 2.4	0.95 (1.34)	0.9	0.0, 1.9	0.5000
High Dose	2	0.25	1.92 (0.72)	1.9	1.4, 2.4	1.67 (1.07)	1.7	0.9, 2.4	0.2710
WEEK 72	2	0.00	2.73 (3.85)	2.7	0.0, 5.5	2.73 (3.85)	2.7	0.0, 5.5	0.5000
Low Dose	1	0.00	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	1	0.00	5.45 (N/A)	5.5	5.5, 5.5	5.45 (N/A)	5.5	5.5, 5.5	
Average Daily Normalized 'On' Time Without Dyskinesia									
BASELINE	32		10.40 (5.28)	11.2	0.0, 16.0				
Low Dose	10		11.47 (4.43)	12.4	1.3, 16.0				
High Dose	22		9.91 (5.66)	10.6	0.0, 16.0				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Geographic region:NORTH AMERICA (Cont.)									
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 12	22	10.31	10.53 (4.97)	11.0	0.0, 16.0	0.22 (3.82)	0.2	-9.6, 9.0	0.7939
Low Dose	8	12.50	12.43 (3.90)	13.5	4.5, 16.0	-0.08 (3.76)	0.2	-6.6, 6.1	0.9565
High Dose	14	9.06	9.44 (5.31)	10.0	0.0, 16.0	0.38 (3.98)	0.2	-9.6, 9.0	0.7255
WEEK 24	27	11.14	12.31 (3.82)	13.6	4.4, 16.0	1.17 (4.48)	0.0	-9.2, 13.7	0.1869
Low Dose	9	11.52	13.14 (3.71)	14.9	5.5, 16.0	1.62 (2.92)	1.1	-2.6, 7.4	0.1343
High Dose	18	10.95	11.89 (3.92)	12.6	4.4, 16.0	0.94 (5.15)	0.0	-9.2, 13.7	0.4487
WEEK 36	14	11.66	11.39 (5.41)	13.9	0.0, 16.0	-0.28 (5.45)	-0.3	-11.2, 14.0	0.8530
Low Dose	6	13.46	12.72 (2.99)	12.6	8.4, 16.0	-0.74 (1.01)	-0.3	-2.5, 0.0	0.1319
High Dose	8	10.32	10.40 (6.73)	14.0	0.0, 16.0	0.07 (7.36)	-0.1	-11.2, 14.0	0.9784
WEEK 48	9	11.78	13.23 (3.13)	15.1	7.9, 16.0	1.46 (3.86)	0.0	-3.2, 7.9	0.2896
Low Dose	5	13.35	14.70 (2.54)	16.0	10.2, 16.0	1.35 (4.02)	0.0	-3.2, 7.4	0.4941
High Dose	4	9.81	11.40 (3.08)	11.3	7.9, 15.1	1.59 (4.25)	-0.2	-1.1, 7.9	0.5085
WEEK 60	4	8.29	12.15 (4.14)	13.1	6.3, 16.0	3.86 (2.72)	4.6	0.0, 6.3	0.0655
Low Dose	2	12.32	14.79 (1.71)	14.8	13.6, 16.0	2.46 (3.48)	2.5	0.0, 4.9	0.5000
High Dose	2	4.25	9.50 (4.53)	9.5	6.3, 12.7	5.25 (1.48)	5.3	4.2, 6.3	0.1254

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Geographic region:NORTH AMERICA (Cont.)									
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 72	2	13.65	8.71 (10.30)	8.7	1.4, 16.0	-4.93 (6.98)	-4.9	-9.9, 0.0	0.5000
Low Dose	1	16.00	16.00 (N/A)	16.0	16.0, 16.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	1	11.29	1.43 (N/A)	1.4	1.4, 1.4	-9.87 (N/A)	-9.9	-9.9, -9.9	
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia									
BASELINE	32		3.33 (5.03)	0.6	0.0, 16.0				
Low Dose	10		1.82 (3.75)	0.0	0.0, 12.0				
High Dose	22		4.01 (5.45)	0.8	0.0, 16.0				
WEEK 12	22	3.31	2.93 (4.93)	0.1	0.0, 16.0	-0.38 (4.62)	0.0	-15.8, 7.4	0.7050
Low Dose	8	0.78	1.23 (3.04)	0.0	0.0, 8.7	0.45 (3.06)	0.0	-3.5, 7.4	0.6916
High Dose	14	4.75	3.90 (5.61)	1.1	0.0, 16.0	-0.85 (5.36)	0.0	-15.8, 6.7	0.5636
WEEK 24	27	2.91	1.04 (1.96)	0.0	0.0, 5.8	-1.87 (4.64)	0.0	-16.0, 5.1	0.0462*
Low Dose	9	1.88	0.22 (0.57)	0.0	0.0, 1.7	-1.67 (4.12)	0.0	-12.0, 1.7	0.2599
High Dose	18	3.42	1.45 (2.28)	0.0	0.0, 5.8	-1.97 (4.99)	0.0	-16.0, 5.1	0.1121

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Geographic region:NORTH AMERICA (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 36	14	2.64	2.65 (5.59)	0.0	0.0, 16.0	0.01 (5.41)	0.0	-12.9, 11.2	0.9961
Low Dose	6	0.24	0.15 (0.28)	0.0	0.0, 0.7	-0.09 (0.34)	0.0	-0.8, 0.2	0.5663
High Dose	8	4.44	4.51 (6.98)	0.1	0.0, 16.0	0.08 (7.36)	0.0	-12.9, 11.2	0.9771
WEEK 48	9	3.03	1.15 (1.94)	0.0	0.0, 5.5	-1.88 (4.31)	0.0	-12.8, 0.9	0.2274
Low Dose	5	0.70	0.18 (0.40)	0.0	0.0, 0.9	-0.52 (1.71)	0.0	-3.5, 0.9	0.5316
High Dose	4	5.94	2.37 (2.50)	2.0	0.0, 5.5	-3.57 (6.22)	-1.1	-12.8, 0.8	0.3344
WEEK 60	4	5.06	1.93 (2.74)	0.9	0.0, 5.8	-3.14 (5.09)	-1.8	-10.2, 1.1	0.3056
Low Dose	2	1.75	0.00 (0.00)	0.0	0.0, 0.0	-1.75 (2.48)	-1.8	-3.5, 0.0	0.5000
High Dose	2	8.38	3.85 (2.78)	3.9	1.9, 5.8	-4.52 (8.00)	-4.5	-10.2, 1.1	0.5705
WEEK 72	2	2.35	2.08 (2.94)	2.1	0.0, 4.2	-0.27 (0.39)	-0.3	-0.5, 0.0	0.5000
Low Dose	1	0.00	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	1	4.71	4.16 (N/A)	4.2	4.2, 4.2	-0.55 (N/A)	-0.5	-0.5, -0.5	

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Geographic region:NORTH AMERICA (Cont.)									
Average Daily Normalized 'On' Time With Troublesome Dyskinesia									
BASELINE	32		0.57 (1.56)	0.0	0.0, 6.3				
Low Dose	10		0.36 (1.04)	0.0	0.0, 3.3				
High Dose	22		0.66 (1.75)	0.0	0.0, 6.3				
WEEK 12	22	0.52	0.23 (0.75)	0.0	0.0, 3.0	-0.29 (1.49)	0.0	-5.3, 3.0	0.3665
Low Dose	8	0.45	0.00 (0.00)	0.0	0.0, 0.0	-0.45 (1.16)	0.0	-3.3, 0.0	0.3143
High Dose	14	0.56	0.36 (0.93)	0.0	0.0, 3.0	-0.21 (1.69)	0.0	-5.3, 3.0	0.6542
WEEK 24	27	0.65	0.49 (1.58)	0.0	0.0, 7.2	-0.16 (1.56)	0.0	-5.3, 4.3	0.6024
Low Dose	9	0.37	0.13 (0.31)	0.0	0.0, 0.9	-0.24 (1.19)	0.0	-3.3, 0.9	0.5690
High Dose	18	0.79	0.67 (1.92)	0.0	0.0, 7.2	-0.12 (1.75)	0.0	-5.3, 4.3	0.7751
WEEK 36	14	0.38	0.25 (0.56)	0.0	0.0, 1.8	-0.13 (1.60)	0.0	-5.3, 1.8	0.7608
Low Dose	6	0.00	0.28 (0.49)	0.0	0.0, 1.2	0.28 (0.49)	0.0	0.0, 1.2	0.2252
High Dose	8	0.67	0.23 (0.64)	0.0	0.0, 1.8	-0.44 (2.08)	0.0	-5.3, 1.8	0.5669

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Geographic region:NORTH AMERICA (Cont.)									
Average Daily Normalized 'On' Time With Troublesome Dyskinesia (Cont.)									
WEEK 48	9	0.37	0.16 (0.26)	0.0	0.0, 0.7	-0.21 (1.19)	0.0	-3.3, 0.7	0.6145
Low Dose	5	0.66	0.14 (0.32)	0.0	0.0, 0.7	-0.52 (1.59)	0.0	-3.3, 0.7	0.5073
High Dose	4	0.00	0.18 (0.21)	0.1	0.0, 0.4	0.18 (0.21)	0.1	0.0, 0.4	0.1912
WEEK 60	4	2.39	0.36 (0.73)	0.0	0.0, 1.5	-2.03 (3.45)	-1.7	-6.3, 1.5	0.3247
Low Dose	2	1.66	0.00 (0.00)	0.0	0.0, 0.0	-1.66 (2.34)	-1.7	-3.3, 0.0	0.5000
High Dose	2	3.13	0.73 (1.03)	0.7	0.0, 1.5	-2.40 (5.45)	-2.4	-6.3, 1.5	0.6456
WEEK 72	2	0.00	2.48 (3.51)	2.5	0.0, 5.0	2.48 (3.51)	2.5	0.0, 5.0	0.5000
Low Dose	1	0.00	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	1	0.00	4.96 (N/A)	5.0	5.0, 5.0	4.96 (N/A)	5.0	5.0, 5.0	
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia									
BASELINE	32		13.73 (2.47)	14.7	7.9, 16.0				
Low Dose	10		13.30 (1.86)	13.1	10.1, 16.0				
High Dose	22		13.92 (2.72)	15.5	7.9, 16.0				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Geographic region:NORTH AMERICA (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia (Cont.)									
WEEK 12	22	13.62	13.46 (2.27)	13.9	9.2, 16.0	-0.16 (2.78)	0.0	-6.8, 5.3	0.7869
Low Dose	8	13.28	13.65 (1.93)	13.5	10.1, 16.0	0.37 (1.90)	0.3	-2.8, 3.0	0.5967
High Dose	14	13.81	13.34 (2.51)	13.9	9.2, 16.0	-0.47 (3.21)	0.0	-6.8, 5.3	0.5947
WEEK 24	27	14.05	13.35 (3.29)	14.9	5.2, 16.0	-0.70 (2.64)	0.0	-7.8, 3.8	0.1789
Low Dose	9	13.40	13.36 (3.59)	14.9	5.5, 16.0	-0.04 (3.34)	0.0	-7.8, 3.8	0.9712
High Dose	18	14.37	13.34 (3.24)	14.4	5.2, 16.0	-1.03 (2.24)	-0.3	-6.2, 3.0	0.0678
WEEK 36	14	14.30	14.04 (2.11)	14.3	9.1, 16.0	-0.27 (1.57)	-0.3	-2.3, 4.3	0.5345
Low Dose	6	13.70	12.87 (2.77)	12.6	9.1, 16.0	-0.83 (0.91)	-0.7	-2.3, 0.0	0.0758
High Dose	8	14.76	14.91 (0.90)	14.6	14.0, 16.0	0.15 (1.88)	-0.1	-1.6, 4.3	0.8278
WEEK 48	9	14.80	14.38 (2.06)	15.3	11.1, 16.0	-0.42 (2.69)	-0.4	-4.9, 3.8	0.6518
Low Dose	5	14.05	14.88 (2.14)	16.0	11.1, 16.0	0.83 (2.56)	0.0	-2.3, 3.8	0.5094
High Dose	4	15.75	13.77 (2.08)	14.1	11.1, 15.7	-1.98 (2.17)	-1.4	-4.9, -0.3	0.1653
WEEK 60	4	13.35	14.07 (1.64)	14.1	12.1, 16.0	0.72 (3.81)	0.7	-3.9, 5.3	0.7302
Low Dose	2	14.08	14.79 (1.71)	14.8	13.6, 16.0	0.71 (1.01)	0.7	0.0, 1.4	0.5000
High Dose	2	12.63	13.35 (1.74)	13.4	12.1, 14.6	0.73 (6.52)	0.7	-3.9, 5.3	0.9000

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Geographic region:NORTH AMERICA (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia (Cont.)									
WEEK 72	2	16.00	10.79 (7.36)	10.8	5.6, 16.0	-5.21 (7.36)	-5.2	-10.4, 0.0	0.5000
Low Dose	1	16.00	16.00 (N/A)	16.0	16.0, 16.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	1	16.00	5.59 (N/A)	5.6	5.6, 5.6	-10.41 (N/A)	-10.4	-10.4, -10.4	
Geographic region:EUROPE AND AUSTRALIA									
Average Daily Normalized 'Off' Time									
BASELINE	34		2.45 (2.56)	1.4	0.0, 8.8				
Low Dose	16		2.66 (2.54)	2.0	0.0, 6.9				
High Dose	18		2.26 (2.63)	1.1	0.0, 8.8				
WEEK 12	25	2.59	2.42 (2.58)	1.7	0.0, 7.5	-0.16 (2.00)	0.0	-6.4, 2.9	0.6862
Low Dose	13	2.45	1.98 (2.30)	1.5	0.0, 7.3	-0.47 (1.65)	0.0	-4.1, 1.8	0.3263
High Dose	12	2.73	2.90 (2.88)	2.0	0.0, 7.5	0.16 (2.36)	0.3	-6.4, 2.9	0.8138
WEEK 24	30	2.49	3.25 (4.26)	1.5	0.0, 16.0	0.75 (3.27)	0.0	-5.7, 13.3	0.2177
Low Dose	14	2.54	3.22 (4.77)	1.2	0.0, 16.0	0.68 (4.25)	0.0	-5.7, 13.3	0.5593
High Dose	16	2.45	3.27 (3.92)	2.0	0.0, 13.4	0.82 (2.24)	0.0	-3.1, 5.2	0.1666

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Geographic region:EUROPE AND AUSTRALIA (Cont.)									
Average Daily Normalized 'Off' Time (Cont.)									
WEEK 36	15	3.08	3.14 (3.34)	2.0	0.0, 12.1	0.05 (2.31)	0.0	-3.9, 5.6	0.9317
Low Dose	9	3.00	3.50 (4.07)	2.0	0.0, 12.1	0.51 (2.01)	0.0	-1.0, 5.6	0.4715
High Dose	6	3.22	2.59 (2.05)	2.9	0.0, 4.9	-0.63 (2.75)	-0.1	-3.9, 3.6	0.5990
WEEK 48	12	1.89	3.10 (4.68)	0.7	0.0, 14.3	1.21 (2.61)	0.0	-1.2, 6.1	0.1366
Low Dose	4	1.33	1.09 (1.32)	0.8	0.0, 2.7	-0.24 (0.65)	-0.0	-1.2, 0.3	0.5086
High Dose	8	2.17	4.11 (5.49)	0.7	0.0, 14.3	1.94 (2.96)	0.1	-0.8, 6.1	0.1060
Average Daily Normalized 'On' Time Without Dyskinesia									
BASELINE	34		10.45 (5.03)	12.0	0.0, 16.0				
Low Dose	16		11.61 (4.20)	12.8	1.5, 16.0				
High Dose	18		9.42 (5.59)	9.9	0.0, 16.0				
WEEK 12	25	10.63	12.00 (4.36)	12.7	0.0, 16.0	1.37 (3.27)	0.0	-1.3, 14.2	0.0467*
Low Dose	13	11.66	13.03 (3.29)	14.5	5.7, 16.0	1.38 (4.03)	0.0	-1.3, 14.2	0.2413
High Dose	12	9.51	10.88 (5.20)	11.6	0.0, 16.0	1.36 (2.37)	0.2	-0.9, 6.2	0.0716

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Geographic region:EUROPE AND AUSTRALIA (Cont.)									
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 24	30	10.71	10.64 (5.00)	11.1	0.0, 16.0	-0.07 (4.48)	0.0	-13.3, 14.2	0.9305
Low Dose	14	11.90	11.64 (4.93)	14.0	0.0, 16.0	-0.26 (5.86)	0.0	-13.3, 14.2	0.8707
High Dose	16	9.66	9.76 (5.05)	9.9	0.0, 16.0	0.09 (3.01)	0.0	-6.3, 5.5	0.9040
WEEK 36	15	10.46	10.95 (4.19)	11.9	3.4, 16.0	0.49 (4.33)	0.2	-5.9, 14.2	0.6687
Low Dose	9	10.79	11.56 (4.63)	13.3	3.4, 16.0	0.77 (5.48)	0.0	-5.9, 14.2	0.6843
High Dose	6	9.98	10.04 (3.64)	9.9	6.4, 15.5	0.07 (2.04)	0.6	-3.6, 2.4	0.9390
WEEK 48	12	10.84	11.38 (4.93)	13.7	1.4, 16.0	0.54 (4.97)	0.1	-5.6, 13.7	0.7140
Low Dose	4	10.28	13.18 (3.57)	14.3	8.1, 16.0	2.89 (7.50)	0.6	-3.4, 13.7	0.4965
High Dose	8	11.12	10.48 (5.47)	11.7	1.4, 16.0	-0.64 (3.16)	0.0	-5.6, 3.6	0.5870
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia									
BASELINE	34		2.71 (4.54)	0.5	0.0, 16.0				
Low Dose	16		1.45 (3.04)	0.1	0.0, 11.8				
High Dose	18		3.82 (5.39)	0.7	0.0, 16.0				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Geographic region:EUROPE AND AUSTRALIA (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 12	25	2.31	0.93 (1.82)	0.0	0.0, 7.4	-1.38 (3.64)	0.0	-11.6, 3.1	0.0704
Low Dose	13	1.55	0.93 (2.14)	0.0	0.0, 7.4	-0.62 (3.45)	0.0	-11.6, 3.1	0.5281
High Dose	12	3.14	0.94 (1.51)	0.0	0.0, 5.0	-2.20 (3.81)	-0.6	-11.0, 1.0	0.0709
WEEK 24	30	2.40	1.87 (3.57)	0.0	0.0, 16.0	-0.53 (3.53)	0.0	-11.6, 6.1	0.4181
Low Dose	14	1.35	1.08 (1.63)	0.0	0.0, 4.6	-0.26 (3.48)	0.0	-11.6, 3.3	0.7800
High Dose	16	3.32	2.56 (4.60)	0.0	0.0, 16.0	-0.76 (3.68)	-0.1	-10.7, 6.1	0.4207
WEEK 36	15	2.10	1.68 (2.39)	0.5	0.0, 8.1	-0.42 (3.24)	0.0	-11.6, 2.9	0.6224
Low Dose	9	1.89	0.94 (1.27)	0.3	0.0, 3.0	-0.95 (4.05)	0.0	-11.6, 1.8	0.5024
High Dose	6	2.43	2.80 (3.30)	1.8	0.0, 8.1	0.37 (1.35)	0.0	-1.0, 2.9	0.5307
WEEK 48	12	2.67	1.32 (2.32)	0.3	0.0, 6.4	-1.34 (4.64)	0.0	-11.1, 4.9	0.3372
Low Dose	4	3.72	1.67 (2.88)	0.4	0.0, 6.0	-2.04 (6.18)	0.0	-11.1, 2.9	0.5557
High Dose	8	2.14	1.14 (2.18)	0.3	0.0, 6.4	-1.00 (4.13)	0.0	-9.7, 4.9	0.5175

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Geographic region:EUROPE AND AUSTRALIA (Cont.)									
Average Daily Normalized 'On' Time With Troublesome Dyskinesia									
BASELINE	34		0.39 (0.84)	0.0	0.0, 3.0				
Low Dose	16		0.28 (0.73)	0.0	0.0, 2.7				
High Dose	18		0.50 (0.93)	0.0	0.0, 3.0				
WEEK 12	25	0.47	0.65 (2.34)	0.0	0.0, 11.0	0.17 (2.47)	0.0	-3.0, 11.0	0.7307
Low Dose	13	0.34	0.05 (0.19)	0.0	0.0, 0.7	-0.29 (0.85)	0.0	-2.7, 0.7	0.2461
High Dose	12	0.62	1.29 (3.32)	0.0	0.0, 11.0	0.67 (3.47)	0.0	-3.0, 11.0	0.5171
WEEK 24	30	0.40	0.25 (0.68)	0.0	0.0, 2.4	-0.15 (0.89)	0.0	-3.0, 1.9	0.3625
Low Dose	14	0.21	0.06 (0.21)	0.0	0.0, 0.8	-0.16 (0.76)	0.0	-2.7, 0.8	0.4557
High Dose	16	0.56	0.42 (0.90)	0.0	0.0, 2.4	-0.15 (1.02)	0.0	-3.0, 1.9	0.5748
WEEK 36	15	0.35	0.23 (0.74)	0.0	0.0, 2.8	-0.12 (0.74)	0.0	-2.7, 0.6	0.5396
Low Dose	9	0.33	0.00 (0.00)	0.0	0.0, 0.0	-0.33 (0.88)	0.0	-2.7, 0.0	0.2969
High Dose	6	0.38	0.57 (1.14)	0.0	0.0, 2.8	0.19 (0.30)	0.0	0.0, 0.6	0.1749

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Geographic region:EUROPE AND AUSTRALIA (Cont.)									
Average Daily Normalized 'On' Time With Troublesome Dyskinesia (Cont.)									
WEEK 48	12	0.60	0.20 (0.46)	0.0	0.0, 1.6	-0.41 (1.01)	0.0	-2.7, 0.2	0.1912
Low Dose	4	0.67	0.06 (0.12)	0.0	0.0, 0.2	-0.61 (1.38)	0.0	-2.7, 0.2	0.4440
High Dose	8	0.57	0.27 (0.56)	0.0	0.0, 1.6	-0.31 (0.87)	0.0	-2.5, 0.0	0.3521
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia									
BASELINE	34		13.16 (2.77)	14.0	7.2, 16.0				
Low Dose	16		13.07 (2.57)	13.5	8.7, 16.0				
High Dose	18		13.24 (3.00)	14.7	7.2, 16.0				
WEEK 12	25	12.94	12.93 (3.32)	13.7	5.0, 16.0	-0.01 (3.12)	0.0	-11.0, 6.4	0.9892
Low Dose	13	13.21	13.97 (2.26)	14.5	8.8, 16.0	0.75 (1.94)	0.0	-1.5, 4.4	0.1865
High Dose	12	12.65	11.81 (3.98)	12.2	5.0, 16.0	-0.84 (3.96)	-0.2	-11.0, 6.4	0.4800
WEEK 24	30	13.11	12.51 (4.28)	14.1	0.0, 16.0	-0.60 (3.34)	0.0	-13.3, 5.7	0.3311
Low Dose	14	13.25	12.73 (4.80)	14.8	0.0, 16.0	-0.52 (4.38)	0.0	-13.3, 5.7	0.6610
High Dose	16	12.98	12.32 (3.91)	13.7	2.6, 16.0	-0.67 (2.22)	-0.4	-5.2, 3.3	0.2457

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Geographic region:EUROPE AND AUSTRALIA (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia (Cont.)									
WEEK 36	15	12.57	12.64 (3.30)	13.3	3.9, 16.0	0.07 (2.37)	0.0	-5.6, 3.9	0.9134
Low Dose	9	12.68	12.50 (4.07)	14.0	3.9, 16.0	-0.18 (2.28)	0.0	-5.6, 2.7	0.8196
High Dose	6	12.40	12.84 (2.00)	11.9	11.1, 16.0	0.44 (2.69)	0.1	-3.6, 3.9	0.7063
WEEK 48	12	13.50	12.70 (4.66)	14.5	1.7, 16.0	-0.81 (2.61)	-0.0	-6.1, 2.7	0.3076
Low Dose	4	14.00	14.85 (1.36)	15.0	13.3, 16.0	0.85 (1.40)	0.6	-0.5, 2.7	0.3131
High Dose	8	13.26	11.62 (5.42)	14.5	1.7, 16.0	-1.63 (2.74)	-0.1	-6.1, 0.8	0.1354
Geographic region:JAPAN									
Average Daily Normalized 'Off' Time									
BASELINE	7		5.28 (3.26)	6.1	0.0, 10.1				
Low Dose	4		6.11 (3.22)	6.0	2.4, 10.1				
High Dose	3		4.17 (3.62)	6.1	0.0, 6.4				
WEEK 12	7	5.28	4.54 (2.27)	4.3	2.1, 7.6	-0.74 (2.43)	0.2	-4.2, 2.1	0.4483
Low Dose	4	6.11	4.44 (2.27)	4.2	2.5, 6.9	-1.67 (2.40)	-1.5	-4.2, 0.6	0.2582
High Dose	3	4.17	4.66 (2.78)	4.3	2.1, 7.6	0.49 (2.26)	1.5	-2.1, 2.1	0.7445

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Geographic region:JAPAN (Cont.)									
Average Daily Normalized 'Off' Time (Cont.)									
WEEK 24	5	4.32	5.54 (4.01)	2.8	2.5, 10.9	1.21 (2.97)	2.0	-3.3, 4.5	0.4127
Low Dose	2	4.55	5.66 (4.41)	5.7	2.5, 8.8	1.11 (1.32)	1.1	0.2, 2.0	0.4455
High Dose	3	4.17	5.46 (4.74)	2.8	2.6, 10.9	1.29 (4.10)	2.6	-3.3, 4.5	0.6410
WEEK 36	5	4.32	3.65 (1.75)	3.6	1.2, 6.1	-0.67 (3.62)	-0.3	-5.5, 3.9	0.6997
Low Dose	2	4.55	2.41 (1.71)	2.4	1.2, 3.6	-2.15 (4.80)	-2.1	-5.5, 1.2	0.6410
High Dose	3	4.17	4.48 (1.45)	3.9	3.4, 6.1	0.31 (3.34)	-0.3	-2.7, 3.9	0.8866
WEEK 48	4	3.72	4.64 (1.95)	4.7	2.3, 6.9	0.92 (2.18)	0.4	-1.0, 4.0	0.4612
Low Dose	1	2.37	2.32 (N/A)	2.3	2.3, 2.3	-0.04 (N/A)	-0.0	-0.0, -0.0	
High Dose	3	4.17	5.41 (1.45)	5.3	4.0, 6.9	1.24 (2.56)	0.8	-1.0, 4.0	0.4888
Average Daily Normalized 'On' Time Without Dyskinesia									
BASELINE	7		9.25 (3.66)	9.3	4.2, 16.0				
Low Dose	4		7.77 (2.87)	8.1	4.2, 10.7				
High Dose	3		11.22 (4.21)	9.6	8.1, 16.0				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Geographic region:JAPAN (Cont.)									
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 12	7	9.25	9.50 (4.42)	10.2	1.0, 13.9	0.25 (3.52)	0.3	-5.9, 4.2	0.8578
Low Dose	4	7.77	8.12 (5.28)	9.0	1.0, 13.5	0.35 (4.68)	1.5	-5.9, 4.2	0.8918
High Dose	3	11.22	11.34 (2.78)	11.7	8.4, 13.9	0.12 (2.10)	0.3	-2.1, 2.1	0.9298
WEEK 24	5	9.97	7.26 (4.65)	7.2	1.0, 13.4	-2.71 (2.84)	-2.6	-5.9, 1.6	0.0994
Low Dose	2	8.09	4.12 (4.39)	4.1	1.0, 7.2	-3.97 (2.73)	-4.0	-5.9, -2.0	0.2883
High Dose	3	11.22	9.35 (4.16)	9.6	5.1, 13.4	-1.87 (3.12)	-2.6	-4.5, 1.6	0.4076
WEEK 36	5	9.97	9.26 (5.09)	9.9	1.3, 14.8	-0.71 (4.33)	0.2	-5.6, 5.5	0.7320
Low Dose	2	8.09	8.05 (9.55)	8.0	1.3, 14.8	-0.04 (7.89)	-0.0	-5.6, 5.5	0.9950
High Dose	3	11.22	10.06 (1.95)	9.9	8.2, 12.1	-1.16 (2.37)	0.2	-3.9, 0.3	0.4870
WEEK 48	4	10.14	7.34 (4.81)	7.8	1.8, 12.0	-2.80 (2.69)	-3.6	-5.1, 1.0	0.1286
Low Dose	1	6.92	1.81 (N/A)	1.8	1.8, 1.8	-5.11 (N/A)	-5.1	-5.1, -5.1	
High Dose	3	11.22	9.19 (3.77)	10.7	4.9, 12.0	-2.03 (2.70)	-3.1	-4.0, 1.0	0.3225

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Geographic region:JAPAN (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia									
BASELINE	7		1.47 (2.46)	0.0	0.0, 6.7				
Low Dose	4		2.11 (3.18)	0.9	0.0, 6.7				
High Dose	3		0.61 (1.05)	0.0	0.0, 1.8				
WEEK 12	7	1.47	1.96 (4.65)	0.0	0.0, 12.4	0.50 (2.40)	0.0	-1.8, 5.7	0.6046
Low Dose	4	2.11	3.44 (6.04)	0.6	0.0, 12.4	1.32 (2.94)	0.0	-0.4, 5.7	0.4347
High Dose	3	0.61	0.00 (0.00)	0.0	0.0, 0.0	-0.61 (1.05)	0.0	-1.8, 0.0	0.4226
WEEK 24	5	1.71	3.21 (5.39)	0.0	0.0, 12.4	1.50 (2.48)	0.0	0.0, 5.7	0.2490
Low Dose	2	3.36	6.22 (8.80)	6.2	0.0, 12.4	2.86 (4.05)	2.9	0.0, 5.7	0.5000
High Dose	3	0.61	1.19 (2.07)	0.0	0.0, 3.6	0.59 (1.02)	0.0	0.0, 1.8	0.4226
WEEK 36	5	1.71	3.09 (4.86)	0.0	0.0, 11.1	1.38 (2.00)	0.0	0.0, 4.4	0.1974
Low Dose	2	3.36	5.55 (7.85)	5.5	0.0, 11.1	2.19 (3.10)	2.2	0.0, 4.4	0.5000
High Dose	3	0.61	1.45 (2.52)	0.0	0.0, 4.4	0.85 (1.46)	0.0	0.0, 2.5	0.4226

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Geographic region:JAPAN (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 48	4	2.14	4.02 (5.60)	2.1	0.0, 11.9	1.88 (2.45)	1.2	0.0, 5.2	0.2223
Low Dose	1	6.72	11.87 (N/A)	11.9	11.9, 11.9	5.15 (N/A)	5.2	5.2, 5.2	
High Dose	3	0.61	1.40 (2.42)	0.0	0.0, 4.2	0.79 (1.37)	0.0	0.0, 2.4	0.4226
Average Daily Normalized 'On' Time With Troublesome Dyskinesia									
BASELINE	7		0.00 (0.00)	0.0	0.0, 0.0				
Low Dose	4		0.00 (0.00)	0.0	0.0, 0.0				
High Dose	3		0.00 (0.00)	0.0	0.0, 0.0				
WEEK 12	7	0.00	0.00 (0.00)	0.0	0.0, 0.0	0.00 (0.00)	0.0	0.0, 0.0	
Low Dose	4	0.00	0.00 (0.00)	0.0	0.0, 0.0	0.00 (0.00)	0.0	0.0, 0.0	
High Dose	3	0.00	0.00 (0.00)	0.0	0.0, 0.0	0.00 (0.00)	0.0	0.0, 0.0	
WEEK 24	5	0.00	0.00 (0.00)	0.0	0.0, 0.0	0.00 (0.00)	0.0	0.0, 0.0	
Low Dose	2	0.00	0.00 (0.00)	0.0	0.0, 0.0	0.00 (0.00)	0.0	0.0, 0.0	
High Dose	3	0.00	0.00 (0.00)	0.0	0.0, 0.0	0.00 (0.00)	0.0	0.0, 0.0	

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Geographic region:JAPAN (Cont.)									
Average Daily Normalized 'On' Time With Troublesome Dyskinesia (Cont.)									
WEEK 36	5	0.00	0.00 (0.00)	0.0	0.0, 0.0	0.00 (0.00)	0.0	0.0, 0.0	
Low Dose	2	0.00	0.00 (0.00)	0.0	0.0, 0.0	0.00 (0.00)	0.0	0.0, 0.0	
High Dose	3	0.00	0.00 (0.00)	0.0	0.0, 0.0	0.00 (0.00)	0.0	0.0, 0.0	
WEEK 48	4	0.00	0.00 (0.00)	0.0	0.0, 0.0	0.00 (0.00)	0.0	0.0, 0.0	
Low Dose	1	0.00	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	3	0.00	0.00 (0.00)	0.0	0.0, 0.0	0.00 (0.00)	0.0	0.0, 0.0	
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia									
BASELINE	7		10.72 (3.26)	9.9	5.9, 16.0				
Low Dose	4		9.89 (3.22)	10.0	5.9, 13.6				
High Dose	3		11.83 (3.62)	9.9	9.6, 16.0				
WEEK 12	7	10.72	11.46 (2.27)	11.7	8.4, 13.9	0.74 (2.43)	-0.2	-2.1, 4.2	0.4483
Low Dose	4	9.89	11.56 (2.27)	11.8	9.1, 13.5	1.67 (2.40)	1.5	-0.6, 4.2	0.2582
High Dose	3	11.83	11.34 (2.78)	11.7	8.4, 13.9	-0.49 (2.26)	-1.5	-2.1, 2.1	0.7445

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Geographic region:JAPAN (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia (Cont.)									
WEEK 24	5	11.68	10.46 (4.01)	13.2	5.1, 13.5	-1.21 (2.97)	-2.0	-4.5, 3.3	0.4127
Low Dose	2	11.45	10.34 (4.41)	10.3	7.2, 13.5	-1.11 (1.32)	-1.1	-2.0, -0.2	0.4455
High Dose	3	11.83	10.54 (4.74)	13.2	5.1, 13.4	-1.29 (4.10)	-2.6	-4.5, 3.3	0.6410
WEEK 36	5	11.68	12.35 (1.75)	12.4	9.9, 14.8	0.67 (3.62)	0.3	-3.9, 5.5	0.6997
Low Dose	2	11.45	13.59 (1.71)	13.6	12.4, 14.8	2.15 (4.80)	2.1	-1.2, 5.5	0.6410
High Dose	3	11.83	11.52 (1.45)	12.1	9.9, 12.6	-0.31 (3.34)	0.3	-3.9, 2.7	0.8866
WEEK 48	4	12.28	11.36 (1.95)	11.3	9.1, 13.7	-0.92 (2.18)	-0.4	-4.0, 1.0	0.4612
Low Dose	1	13.63	13.68 (N/A)	13.7	13.7, 13.7	0.04 (N/A)	0.0	0.0, 0.0	
High Dose	3	11.83	10.59 (1.45)	10.7	9.1, 12.0	-1.24 (2.56)	-0.8	-4.0, 1.0	0.4888
PD duration (time since diagnosis) category:<10 years									
Average Daily Normalized 'Off' Time									
BASELINE	42		2.63 (2.83)	1.3	0.0, 10.1				
Low Dose	18		3.19 (2.89)	2.5	0.0, 10.1				
High Dose	24		2.22 (2.78)	0.7	0.0, 8.8				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
PD duration (time since diagnosis) category:<10 years (Cont.)									
Average Daily Normalized 'Off' Time (Cont.)									
WEEK 12	33	2.86	2.61 (2.55)	2.1	0.0, 7.5	-0.26 (2.27)	0.0	-6.4, 6.8	0.5197
Low Dose	15	3.18	2.41 (2.34)	2.5	0.0, 6.9	-0.77 (1.89)	0.0	-4.1, 2.8	0.1373
High Dose	18	2.59	2.76 (2.77)	2.1	0.0, 7.5	0.17 (2.51)	0.0	-6.4, 6.8	0.7768
WEEK 24	35	2.33	2.60 (3.26)	1.7	0.0, 13.4	0.27 (2.21)	0.0	-5.7, 6.2	0.4776
Low Dose	14	2.50	1.61 (1.85)	1.2	0.0, 6.0	-0.90 (1.67)	-0.0	-5.7, 0.5	0.0663
High Dose	21	2.22	3.27 (3.84)	2.3	0.0, 13.4	1.04 (2.21)	0.0	-3.1, 6.2	0.0430*
WEEK 36	21	2.83	2.62 (2.45)	2.0	0.0, 7.7	-0.21 (1.31)	0.0	-3.9, 1.2	0.4654
Low Dose	12	2.53	2.77 (2.73)	2.7	0.0, 7.7	0.24 (0.66)	0.1	-0.9, 1.2	0.2410
High Dose	9	3.23	2.41 (2.16)	2.0	0.0, 6.1	-0.81 (1.73)	-0.2	-3.9, 1.2	0.1979
WEEK 48	16	1.80	2.16 (3.70)	0.5	0.0, 14.3	0.36 (2.06)	0.0	-3.0, 5.5	0.4913
Low Dose	9	1.27	0.99 (1.48)	0.0	0.0, 4.2	-0.28 (1.28)	0.0	-3.0, 1.6	0.5285
High Dose	7	2.48	3.67 (5.15)	1.1	0.0, 14.3	1.19 (2.65)	0.0	-1.0, 5.5	0.2792
WEEK 60	4	0.26	1.57 (1.15)	1.9	0.0, 2.4	1.31 (1.07)	1.4	0.0, 2.4	0.0928
Low Dose	2	0.27	1.21 (1.71)	1.2	0.0, 2.4	0.95 (1.34)	0.9	0.0, 1.9	0.5000
High Dose	2	0.25	1.92 (0.72)	1.9	1.4, 2.4	1.67 (1.07)	1.7	0.9, 2.4	0.2710

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
PD duration (time since diagnosis) category:<10 years (Cont.)									
Average Daily Normalized 'Off' Time (Cont.)									
WEEK 72	1	0.00	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
Low Dose	1	0.00	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	0								
Average Daily Normalized 'On' Time Without Dyskinesia									
BASELINE	42		9.89 (5.07)	10.0	0.0, 16.0				
Low Dose	18		10.51 (4.33)	11.1	1.5, 16.0				
High Dose	24		9.42 (5.60)	9.6	0.0, 16.0				
WEEK 12	33	9.96	11.38 (4.56)	12.3	0.0, 16.0	1.42 (3.49)	0.4	-5.9, 14.2	0.0259*
Low Dose	15	10.26	11.87 (4.52)	13.3	1.0, 16.0	1.61 (4.46)	0.5	-5.9, 14.2	0.1841
High Dose	18	9.71	10.97 (4.69)	11.2	0.0, 16.0	1.26 (2.55)	0.4	-0.9, 9.0	0.0507
WEEK 24	35	10.61	11.55 (4.51)	12.1	1.0, 16.0	0.94 (4.49)	0.0	-5.9, 14.2	0.2253
Low Dose	14	11.08	12.50 (4.30)	14.2	1.0, 16.0	1.42 (4.75)	0.5	-5.9, 14.2	0.2846
High Dose	21	10.30	10.92 (4.64)	11.8	2.6, 16.0	0.62 (4.40)	0.0	-4.5, 13.7	0.5270

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
PD duration (time since diagnosis) category:<10 years (Cont.)									
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 36	21	10.19	11.39 (4.25)	11.5	1.3, 16.0	1.19 (4.70)	0.0	-5.6, 14.2	0.2580
Low Dose	12	11.21	11.43 (4.75)	11.3	1.3, 16.0	0.21 (4.74)	-0.3	-5.6, 14.2	0.8789
High Dose	9	8.83	11.34 (3.74)	11.9	6.4, 15.8	2.50 (4.58)	1.0	-0.6, 14.0	0.1400
WEEK 48	16	11.12	11.91 (5.06)	15.1	1.4, 16.0	0.79 (5.26)	0.0	-5.6, 13.7	0.5558
Low Dose	9	11.28	12.74 (5.04)	15.3	1.8, 16.0	1.46 (5.94)	0.0	-5.1, 13.7	0.4810
High Dose	7	10.92	10.85 (5.27)	10.7	1.4, 16.0	-0.07 (4.54)	0.0	-5.6, 7.9	0.9683
WEEK 60	4	8.29	12.15 (4.14)	13.1	6.3, 16.0	3.86 (2.72)	4.6	0.0, 6.3	0.0655
Low Dose	2	12.32	14.79 (1.71)	14.8	13.6, 16.0	2.46 (3.48)	2.5	0.0, 4.9	0.5000
High Dose	2	4.25	9.50 (4.53)	9.5	6.3, 12.7	5.25 (1.48)	5.3	4.2, 6.3	0.1254
WEEK 72	1	16.00	16.00 (N/A)	16.0	16.0, 16.0	0.00 (N/A)	0.0	0.0, 0.0	
Low Dose	1	16.00	16.00 (N/A)	16.0	16.0, 16.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	0								

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
PD duration (time since diagnosis) category:<10 years (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia									
BASELINE	42		3.00 (4.81)	0.4	0.0, 16.0				
Low Dose	18		1.89 (3.14)	0.0	0.0, 11.8				
High Dose	24		3.84 (5.67)	0.6	0.0, 16.0				
WEEK 12	33	2.77	1.82 (3.73)	0.0	0.0, 16.0	-0.95 (3.83)	0.0	-15.8, 5.7	0.1650
Low Dose	15	2.06	1.72 (3.58)	0.0	0.0, 12.4	-0.34 (3.69)	0.0	-11.6, 5.7	0.7232
High Dose	18	3.36	1.91 (3.95)	0.0	0.0, 16.0	-1.45 (3.98)	0.0	-15.8, 1.0	0.1403
WEEK 24	35	2.53	1.48 (2.88)	0.0	0.0, 12.4	-1.05 (4.36)	0.0	-16.0, 5.7	0.1633
Low Dose	14	1.99	1.83 (3.44)	0.1	0.0, 12.4	-0.16 (3.92)	0.0	-11.6, 5.7	0.8805
High Dose	21	2.89	1.25 (2.50)	0.0	0.0, 10.2	-1.64 (4.63)	0.0	-16.0, 4.5	0.1193
WEEK 36	21	2.74	1.75 (3.01)	0.2	0.0, 11.1	-0.99 (4.17)	0.0	-12.9, 4.4	0.2901
Low Dose	12	2.03	1.66 (3.18)	0.3	0.0, 11.1	-0.37 (3.78)	0.0	-11.6, 4.4	0.7439
High Dose	9	3.68	1.86 (2.96)	0.0	0.0, 8.1	-1.82 (4.74)	0.0	-12.9, 2.9	0.2825

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
PD duration (time since diagnosis) category:<10 years (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 48	16	2.71	1.84 (3.42)	0.0	0.0, 11.9	-0.87 (4.81)	0.0	-12.8, 5.2	0.4810
Low Dose	9	2.79	2.16 (4.12)	0.0	0.0, 11.9	-0.63 (4.57)	0.0	-11.1, 5.2	0.6920
High Dose	7	2.60	1.42 (2.50)	0.0	0.0, 6.4	-1.18 (5.46)	0.0	-12.8, 4.9	0.5875
WEEK 60	4	5.06	1.93 (2.74)	0.9	0.0, 5.8	-3.14 (5.09)	-1.8	-10.2, 1.1	0.3056
Low Dose	2	1.75	0.00 (0.00)	0.0	0.0, 0.0	-1.75 (2.48)	-1.8	-3.5, 0.0	0.5000
High Dose	2	8.38	3.85 (2.78)	3.9	1.9, 5.8	-4.52 (8.00)	-4.5	-10.2, 1.1	0.5705
WEEK 72	1	0.00	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
Low Dose	1	0.00	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	0								
Average Daily Normalized 'On' Time With Troublesome Dyskinesia									
BASELINE	42		0.47 (1.24)	0.0	0.0, 6.3				
Low Dose	18		0.41 (1.00)	0.0	0.0, 3.3				
High Dose	24		0.52 (1.42)	0.0	0.0, 6.3				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
PD duration (time since diagnosis) category:<10 years (Cont.)									
Average Daily Normalized 'On' Time With Troublesome Dyskinesia (Cont.)									
WEEK 12	33	0.41	0.20 (0.84)	0.0	0.0, 4.4	-0.22 (0.89)	0.0	-3.3, 2.2	0.1725
Low Dose	15	0.50	0.00 (0.00)	0.0	0.0, 0.0	-0.50 (1.09)	0.0	-3.3, 0.0	0.0990
High Dose	18	0.34	0.36 (1.13)	0.0	0.0, 4.4	0.02 (0.63)	0.0	-1.3, 2.2	0.9127
WEEK 24	35	0.53	0.37 (1.30)	0.0	0.0, 7.2	-0.16 (0.92)	0.0	-3.3, 1.9	0.3238
Low Dose	14	0.43	0.07 (0.25)	0.0	0.0, 0.9	-0.36 (1.15)	0.0	-3.3, 0.9	0.2615
High Dose	21	0.59	0.57 (1.65)	0.0	0.0, 7.2	-0.02 (0.73)	0.0	-2.1, 1.9	0.9048
WEEK 36	21	0.24	0.24 (0.67)	0.0	0.0, 2.8	0.01 (0.69)	0.0	-2.7, 1.2	0.9611
Low Dose	12	0.22	0.14 (0.36)	0.0	0.0, 1.2	-0.08 (0.89)	0.0	-2.7, 1.2	0.7523
High Dose	9	0.25	0.38 (0.94)	0.0	0.0, 2.8	0.13 (0.25)	0.0	0.0, 0.6	0.1692
WEEK 48	16	0.37	0.09 (0.21)	0.0	0.0, 0.7	-0.29 (1.08)	0.0	-3.3, 0.7	0.3048
Low Dose	9	0.66	0.11 (0.24)	0.0	0.0, 0.7	-0.56 (1.41)	0.0	-3.3, 0.7	0.2693
High Dose	7	0.00	0.06 (0.16)	0.0	0.0, 0.4	0.06 (0.16)	0.0	0.0, 0.4	0.3559
WEEK 60	4	2.39	0.36 (0.73)	0.0	0.0, 1.5	-2.03 (3.45)	-1.7	-6.3, 1.5	0.3247
Low Dose	2	1.66	0.00 (0.00)	0.0	0.0, 0.0	-1.66 (2.34)	-1.7	-3.3, 0.0	0.5000
High Dose	2	3.13	0.73 (1.03)	0.7	0.0, 1.5	-2.40 (5.45)	-2.4	-6.3, 1.5	0.6456

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
PD duration (time since diagnosis) category:<10 years (Cont.)									
Average Daily Normalized 'On' Time With Troublesome Dyskinesia (Cont.)									
WEEK 72	1	0.00	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
Low Dose	1	0.00	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	0								
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia									
BASELINE	42		12.89 (2.94)	13.4	5.9, 16.0				
Low Dose	18		12.40 (2.78)	13.1	5.9, 16.0				
High Dose	24		13.27 (3.05)	14.9	7.2, 16.0				
WEEK 12	33	12.73	13.20 (2.78)	13.9	5.8, 16.0	0.47 (2.43)	0.0	-6.8, 6.4	0.2713
Low Dose	15	12.32	13.59 (2.34)	13.5	9.1, 16.0	1.27 (2.06)	0.5	-2.8, 4.4	0.0318*
High Dose	18	13.06	12.88 (3.14)	13.9	5.8, 16.0	-0.19 (2.57)	0.0	-6.8, 6.4	0.7612
WEEK 24	35	13.14	13.03 (3.59)	14.1	2.6, 16.0	-0.11 (2.49)	0.0	-6.2, 5.7	0.7907
Low Dose	14	13.07	14.33 (1.90)	14.8	10.0, 16.0	1.26 (1.92)	0.5	-0.9, 5.7	0.0294*
High Dose	21	13.19	12.16 (4.19)	13.7	2.6, 16.0	-1.02 (2.44)	-0.6	-6.2, 3.3	0.0683

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
PD duration (time since diagnosis) category:<10 years (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia (Cont.)									
WEEK 36	21	12.93	13.14 (2.52)	14.0	8.3, 16.0	0.21 (1.47)	0.0	-2.3, 3.9	0.5298
Low Dose	12	13.24	13.09 (2.84)	13.3	8.3, 16.0	-0.15 (1.25)	-0.1	-2.3, 2.7	0.6798
High Dose	9	12.52	13.20 (2.18)	14.0	9.9, 16.0	0.68 (1.69)	0.2	-1.2, 3.9	0.2594
WEEK 48	16	13.83	13.75 (3.74)	15.5	1.7, 16.0	-0.08 (2.51)	0.0	-5.5, 3.8	0.9044
Low Dose	9	14.06	14.90 (1.69)	16.0	11.1, 16.0	0.84 (2.00)	0.0	-2.3, 3.8	0.2447
High Dose	7	13.52	12.27 (5.17)	14.9	1.7, 16.0	-1.25 (2.74)	-0.0	-5.5, 1.0	0.2724
WEEK 60	4	13.35	14.07 (1.64)	14.1	12.1, 16.0	0.72 (3.81)	0.7	-3.9, 5.3	0.7302
Low Dose	2	14.08	14.79 (1.71)	14.8	13.6, 16.0	0.71 (1.01)	0.7	0.0, 1.4	0.5000
High Dose	2	12.63	13.35 (1.74)	13.4	12.1, 14.6	0.73 (6.52)	0.7	-3.9, 5.3	0.9000
WEEK 72	1	16.00	16.00 (N/A)	16.0	16.0, 16.0	0.00 (N/A)	0.0	0.0, 0.0	
Low Dose	1	16.00	16.00 (N/A)	16.0	16.0, 16.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	0								

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
PD duration (time since diagnosis) category:>=10 years									
Average Daily Normalized 'Off' Time									
BASELINE	31		2.07 (2.46)	0.9	0.0, 8.1				
Low Dose	12		2.75 (2.38)	2.7	0.0, 6.7				
High Dose	19		1.64 (2.48)	0.5	0.0, 8.1				
WEEK 12	21	2.29	2.73 (2.50)	2.5	0.0, 7.6	0.44 (1.99)	0.0	-4.3, 4.2	0.3254
Low Dose	10	2.67	2.61 (2.29)	2.6	0.0, 7.3	-0.06 (1.64)	0.0	-4.2, 1.8	0.9104
High Dose	11	1.94	2.83 (2.79)	2.1	0.0, 7.6	0.89 (2.25)	0.8	-4.3, 4.2	0.2176
WEEK 24	27	1.85	3.42 (4.31)	2.3	0.0, 16.0	1.57 (3.27)	0.2	-3.3, 13.3	0.0191*
Low Dose	11	2.69	5.13 (5.55)	2.5	0.0, 16.0	2.43 (4.50)	0.2	-2.3, 13.3	0.1032
High Dose	16	1.27	2.25 (2.83)	1.6	0.0, 7.7	0.98 (2.03)	0.4	-3.3, 5.2	0.0720
WEEK 36	13	2.06	2.64 (3.17)	2.0	0.0, 12.1	0.58 (2.86)	0.3	-5.5, 5.6	0.4811
Low Dose	5	3.90	4.04 (4.54)	2.3	1.2, 12.1	0.15 (4.02)	0.3	-5.5, 5.6	0.9393
High Dose	8	0.92	1.77 (1.80)	1.4	0.0, 4.1	0.85 (2.14)	0.5	-2.7, 3.9	0.3002

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
PD duration (time since diagnosis) category:>=10 years (Cont.)									
Average Daily Normalized 'Off' Time (Cont.)									
WEEK 48	9	1.80	3.81 (3.35)	2.8	0.0, 8.6	2.01 (2.40)	0.8	-0.3, 6.1	0.0368*
Low Dose	1	2.69	2.66 (N/A)	2.7	2.7, 2.7	-0.04 (N/A)	-0.0	-0.0, -0.0	
High Dose	8	1.69	3.95 (3.55)	3.4	0.0, 8.6	2.26 (2.44)	1.6	-0.3, 6.1	0.0342*
WEEK 72	1	0.00	5.45 (N/A)	5.5	5.5, 5.5	5.45 (N/A)	5.5	5.5, 5.5	
Low Dose	0								
High Dose	1	0.00	5.45 (N/A)	5.5	5.5, 5.5	5.45 (N/A)	5.5	5.5, 5.5	
Average Daily Normalized 'On' Time Without Dyskinesia									
BASELINE	31		10.89 (4.90)	12.4	0.0, 16.0				
Low Dose	12		11.87 (4.09)	12.8	1.3, 16.0				
High Dose	19		10.28 (5.36)	11.3	0.0, 16.0				
WEEK 12	21	10.89	10.60 (4.81)	11.4	0.0, 16.0	-0.29 (3.36)	0.0	-9.6, 6.2	0.6946
Low Dose	10	12.88	12.33 (3.46)	13.1	4.5, 16.0	-0.55 (2.66)	-0.6	-6.6, 4.2	0.5306
High Dose	11	9.09	9.03 (5.45)	8.9	0.0, 16.0	-0.06 (4.02)	0.0	-9.6, 6.2	0.9616

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
PD duration (time since diagnosis) category:>=10 years (Cont.)									
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 24	27	11.13	10.50 (4.82)	9.7	0.0, 16.0	-0.63 (4.31)	0.0	-13.3, 6.5	0.4542
Low Dose	11	11.94	10.42 (5.59)	13.5	0.0, 16.0	-1.53 (4.80)	-0.1	-13.3, 4.2	0.3164
High Dose	16	10.57	10.56 (4.41)	9.7	0.0, 16.0	-0.01 (3.97)	0.0	-9.2, 6.5	0.9900
WEEK 36	13	12.00	10.06 (5.57)	12.1	0.0, 16.0	-1.94 (4.19)	-1.3	-11.2, 5.5	0.1213
Low Dose	5	11.88	11.85 (4.77)	13.8	3.4, 14.8	-0.03 (4.13)	0.6	-5.9, 5.5	0.9874
High Dose	8	12.07	8.95 (6.04)	10.6	0.0, 16.0	-3.13 (4.01)	-2.5	-11.2, 0.8	0.0631
WEEK 48	9	10.97	10.49 (3.80)	12.0	4.9, 15.1	-0.48 (2.22)	0.0	-4.0, 3.6	0.5368
Low Dose	1	13.31	13.34 (N/A)	13.3	13.3, 13.3	0.04 (N/A)	0.0	0.0, 0.0	
High Dose	8	10.68	10.14 (3.89)	11.1	4.9, 15.1	-0.54 (2.36)	-0.4	-4.0, 3.6	0.5377
WEEK 72	1	11.29	1.43 (N/A)	1.4	1.4, 1.4	-9.87 (N/A)	-9.9	-9.9, -9.9	
Low Dose	0								
High Dose	1	11.29	1.43 (N/A)	1.4	1.4, 1.4	-9.87 (N/A)	-9.9	-9.9, -9.9	

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
PD duration (time since diagnosis) category:>=10 years (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia									
BASELINE	31		2.66 (4.36)	0.5	0.0, 16.0				
Low Dose	12		1.33 (3.40)	0.1	0.0, 12.0				
High Dose	19		3.50 (4.77)	0.8	0.0, 16.0				
WEEK 12	21	2.36	1.97 (4.00)	0.0	0.0, 16.0	-0.38 (4.19)	0.0	-11.0, 7.4	0.6790
Low Dose	10	0.40	0.99 (2.71)	0.0	0.0, 8.7	0.59 (2.40)	0.0	-0.6, 7.4	0.4541
High Dose	11	4.14	2.87 (4.86)	1.0	0.0, 16.0	-1.27 (5.30)	-0.8	-11.0, 6.7	0.4437
WEEK 24	27	2.62	1.80 (3.54)	0.0	0.0, 16.0	-0.82 (3.71)	0.0	-12.0, 6.1	0.2611
Low Dose	11	1.34	0.36 (0.84)	0.0	0.0, 2.5	-0.97 (3.75)	0.0	-12.0, 2.5	0.4091
High Dose	16	3.49	2.78 (4.32)	0.1	0.0, 16.0	-0.71 (3.79)	0.0	-10.7, 6.1	0.4641
WEEK 36	13	1.50	3.15 (5.73)	0.0	0.0, 16.0	1.65 (3.55)	0.0	-2.0, 11.2	0.1190
Low Dose	5	0.16	0.11 (0.24)	0.0	0.0, 0.5	-0.06 (0.31)	0.0	-0.6, 0.3	0.7011
High Dose	8	2.34	5.06 (6.74)	2.3	0.0, 16.0	2.72 (4.26)	1.3	-2.0, 11.2	0.1137

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
PD duration (time since diagnosis) category:>=10 years (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 48	9	2.72	1.43 (2.02)	0.8	0.0, 5.5	-1.29 (3.48)	0.0	-9.7, 2.4	0.2987
Low Dose	1	0.00	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	8	3.06	1.61 (2.08)	0.9	0.0, 5.5	-1.45 (3.69)	-0.4	-9.7, 2.4	0.3023
WEEK 72	1	4.71	4.16 (N/A)	4.2	4.2, 4.2	-0.55 (N/A)	-0.5	-0.5, -0.5	
Low Dose	0								
High Dose	1	4.71	4.16 (N/A)	4.2	4.2, 4.2	-0.55 (N/A)	-0.5	-0.5, -0.5	
Average Daily Normalized 'On' Time With Troublesome Dyskinesia									
BASELINE	31		0.38 (1.10)	0.0	0.0, 5.3				
Low Dose	12		0.04 (0.10)	0.0	0.0, 0.3				
High Dose	19		0.59 (1.38)	0.0	0.0, 5.3				
WEEK 12	21	0.46	0.70 (2.46)	0.0	0.0, 11.0	0.24 (2.90)	0.0	-5.3, 11.0	0.7111
Low Dose	10	0.05	0.07 (0.21)	0.0	0.0, 0.7	0.01 (0.26)	0.0	-0.3, 0.7	0.8739
High Dose	11	0.83	1.27 (3.36)	0.0	0.0, 11.0	0.44 (4.08)	0.0	-5.3, 11.0	0.7271

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
PD duration (time since diagnosis) category:>=10 years (Cont.)									
Average Daily Normalized 'On' Time With Troublesome Dyskinesia (Cont.)									
WEEK 24	27	0.41	0.28 (0.93)	0.0	0.0, 4.3	-0.12 (1.49)	0.0	-5.3, 4.3	0.6694
Low Dose	11	0.03	0.09 (0.24)	0.0	0.0, 0.8	0.07 (0.26)	0.0	-0.3, 0.8	0.4177
High Dose	16	0.67	0.41 (1.19)	0.0	0.0, 4.3	-0.26 (1.94)	0.0	-5.3, 4.3	0.6063
WEEK 36	13	0.43	0.14 (0.50)	0.0	0.0, 1.8	-0.29 (1.60)	0.0	-5.3, 1.8	0.5208
Low Dose	5	0.06	0.00 (0.00)	0.0	0.0, 0.0	-0.06 (0.13)	0.0	-0.3, 0.0	0.3739
High Dose	8	0.67	0.23 (0.64)	0.0	0.0, 1.8	-0.44 (2.08)	0.0	-5.3, 1.8	0.5669
WEEK 48	9	0.51	0.27 (0.52)	0.0	0.0, 1.6	-0.24 (0.84)	0.0	-2.5, 0.3	0.4162
Low Dose	1	0.00	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	8	0.57	0.30 (0.55)	0.0	0.0, 1.6	-0.27 (0.89)	0.0	-2.5, 0.3	0.4205
WEEK 72	1	0.00	4.96 (N/A)	5.0	5.0, 5.0	4.96 (N/A)	5.0	5.0, 5.0	
Low Dose	0								
High Dose	1	0.00	4.96 (N/A)	5.0	5.0, 5.0	4.96 (N/A)	5.0	5.0, 5.0	

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
PD duration (time since diagnosis) category:>=10 years (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia									
BASELINE	31		13.55 (2.56)	14.2	7.9, 16.0				
Low Dose	12		13.20 (2.38)	13.3	9.3, 16.0				
High Dose	19		13.78 (2.70)	15.2	7.9, 16.0				
WEEK 12	21	13.25	12.57 (2.94)	12.7	5.0, 16.0	-0.68 (3.39)	-0.6	-11.0, 5.3	0.3718
Low Dose	10	13.27	13.32 (2.22)	13.4	8.8, 16.0	0.05 (1.63)	-0.3	-1.5, 4.2	0.9298
High Dose	11	13.23	11.89 (3.43)	11.9	5.0, 16.0	-1.33 (4.43)	-1.5	-11.0, 5.3	0.3415
WEEK 24	27	13.74	12.30 (4.24)	13.7	0.0, 16.0	-1.45 (3.41)	-0.2	-13.3, 3.3	0.0364*
Low Dose	11	13.28	10.78 (5.59)	13.5	0.0, 16.0	-2.50 (4.56)	-0.2	-13.3, 2.3	0.0986
High Dose	16	14.06	13.34 (2.73)	13.7	8.3, 16.0	-0.73 (2.23)	-0.5	-5.2, 3.3	0.2134
WEEK 36	13	13.50	13.22 (3.09)	14.0	3.9, 16.0	-0.28 (3.18)	0.0	-5.6, 5.5	0.7529
Low Dose	5	12.05	11.96 (4.54)	13.8	3.9, 14.8	-0.09 (4.02)	0.0	-5.6, 5.5	0.9631
High Dose	8	14.41	14.01 (1.65)	14.3	11.9, 16.0	-0.41 (2.84)	-0.6	-3.9, 4.3	0.6975

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.3

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
PD duration (time since diagnosis) category:>=10 years (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia (Cont.)									
WEEK 48	9	13.69	11.92 (3.23)	13.2	7.3, 15.7	-1.77 (2.15)	-0.8	-6.1, 0.3	0.0390*
Low Dose	1	13.31	13.34 (N/A)	13.3	13.3, 13.3	0.04 (N/A)	0.0	0.0, 0.0	
High Dose	8	13.73	11.74 (3.41)	12.6	7.3, 15.7	-1.99 (2.18)	-1.6	-6.1, 0.3	0.0364*
WEEK 72	1	16.00	5.59 (N/A)	5.6	5.6, 5.6	-10.41 (N/A)	-10.4	-10.4, -10.4	
Low Dose	0								
High Dose	1	16.00	5.59 (N/A)	5.6	5.6, 5.6	-10.41 (N/A)	-10.4	-10.4, -10.4	

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

表2.7.3.6-14　MDS-UPDRSスコア（FAS，日本人部分集団）：M15-741試験

[redacted]20[redacted] 10:12 <[redacted]>
ABBV-951
STUDY M15-741 - SECOND INTERIM (CUTOFF [redacted]20[redacted])
R&D/20/1632 - CLINICAL/STATISTICAL

TABLE 14.2__2.1.J

Change from Baseline to Each Planned Visit in Parkinson's Disease Symptoms as Assessed
by The Movement Disorder Society-Unified Parkinson's Disease Rating Scale Score by Part and Total
(FAS - Japan Subjects)

Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
MDS-UPDRS Total Score of Parts I-III									
BASELINE	27		41.0 (17.88)	37.0	13, 83				
Low dose	22		37.9 (16.32)	37.0	13, 68				
High dose	5		54.6 (19.92)	47.0	35, 83				
DAY 2	26	41.0	37.5 (21.58)	30.5	6, 91	-3.5 (11.09)	-3.5	-37, 24	0.1163
Low dose	21	37.8	32.1 (16.25)	28.0	6, 63	-5.6 (10.19)	-5.0	-37, 13	0.0200*
High dose	5	54.6	59.8 (28.58)	51.0	30, 91	5.2 (11.48)	4.0	-5, 24	0.3683
WEEK 1	25	42.2	47.0 (24.91)	42.0	18, 114	4.8 (20.22)	-2.0	-18, 68	0.2474
Low dose	20	39.1	42.1 (21.08)	40.0	18, 109	3.0 (17.47)	-1.0	-17, 68	0.4457
High dose	5	54.6	66.4 (31.98)	65.0	31, 114	11.8 (30.43)	-2.0	-18, 47	0.4349
WEEK 2	24	43.4	50.0 (26.57)	43.5	19, 114	6.6 (21.88)	-1.5	-25, 60	0.1532
Low dose	19	40.4	47.2 (24.72)	40.0	19, 101	6.8 (19.79)	-1.0	-19, 60	0.1538
High dose	5	54.6	60.6 (33.67)	58.0	30, 114	6.0 (31.47)	-11.0	-25, 47	0.6925
WEEK 3	21	41.3	50.2 (28.13)	44.0	14, 135	8.9 (24.14)	5.0	-28, 94	0.1065
Low dose	18	38.7	50.7 (30.40)	44.5	14, 135	12.0 (24.17)	9.0	-18, 94	0.0504
High dose	3	57.0	47.3 (6.66)	44.0	43, 55	-9.7 (16.07)	-3.0	-28, 2	0.4069
WEEK 4	20	41.5	50.6 (25.42)	46.5	16, 106	9.1 (20.05)	5.5	-27, 56	0.0571
Low dose	17	38.8	52.1 (26.98)	50.0	16, 106	13.3 (18.30)	12.0	-14, 56	0.0084**
High dose	3	57.0	42.0 (13.53)	41.0	29, 56	-15.0 (10.82)	-12.0	-27, -6	0.1383

&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 2.1.J

Change from Baseline to Each Planned Visit in Parkinson's Disease Symptoms as Assessed
by The Movement Disorder Society-Unified Parkinson's Disease Rating Scale Score by Part and Total
(FAS - Japan Subjects)

Parameter Time Point Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
MDS-UPDRS Total Score of Parts I-III									
WEEK 6	18	40.1	48.2 (27.44)	43.0	12, 113	8.1 (25.37)	2.5	-45, 72	0.1929
Low dose	15	36.7	50.7 (29.50)	47.0	12, 113	13.9 (22.37)	11.0	-15, 72	0.0302*
High dose	3	57.0	36.0 (6.24)	38.0	29, 41	-21.0 (21.00)	-12.0	-45, -6	0.2254
WEEK 13	17	41.2	51.9 (24.01)	56.0	13, 96	10.6 (23.19)	17.0	-32, 66	0.0766
Low dose	14	37.9	53.8 (25.22)	59.0	13, 96	15.9 (20.59)	18.0	-19, 66	0.0126*
High dose	3	57.0	43.0 (18.36)	51.0	22, 56	-14.0 (20.95)	-19.0	-32, 9	0.3667
WEEK 26	15	42.6	46.8 (22.02)	42.0	14, 84	4.2 (17.96)	-1.0	-28, 39	0.3803
Low dose	12	39.0	48.5 (23.68)	43.5	14, 84	9.5 (15.39)	9.5	-10, 39	0.0558
High dose	3	57.0	40.0 (15.00)	40.0	25, 55	-17.0 (10.54)	-16.0	-28, -7	0.1077
WEEK 39	12	39.3	42.7 (23.13)	41.5	17, 95	3.3 (21.23)	-1.0	-20, 54	0.5974
Low dose	9	33.4	41.7 (24.43)	40.0	17, 95	8.2 (21.86)	-1.0	-14, 54	0.2919
High dose	3	57.0	45.7 (23.18)	49.0	21, 67	-11.3 (11.72)	-16.0	-20, 2	0.2359
WEEK 52	11	39.9	43.5 (19.24)	47.0	15, 71	3.5 (17.51)	-2.0	-26, 30	0.5170
Low dose	8	33.5	43.4 (17.44)	47.0	17, 66	9.9 (15.11)	8.5	-6, 30	0.1071
High dose	3	57.0	43.7 (28.02)	45.0	15, 71	-13.3 (12.06)	-12.0	-26, -2	0.1955

&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 2.1.J

Change from Baseline to Each Planned Visit in Parkinson's Disease Symptoms as Assessed
by The Movement Disorder Society-Unified Parkinson's Disease Rating Scale Score by Part and Total
(FAS - Japan Subjects)

Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
MDS-UPDRS Part I Score									
BASELINE	27		7.9 (4.53)	7.0	2, 19				
Low dose	22		7.3 (4.62)	6.0	2, 19				
High dose	5		10.4 (3.36)	9.0	7, 14				
DAY 2	26	8.0	7.0 (3.89)	6.5	0, 14	-1.0 (2.16)	-1.0	-7, 2	0.0217*
Low dose	21	7.4	6.5 (4.09)	6.0	0, 14	-1.0 (2.18)	-1.0	-7, 2	0.0589
High dose	5	10.4	9.0 (2.12)	9.0	7, 12	-1.4 (2.30)	-1.0	-5, 1	0.2455
WEEK 1	25	8.2	8.4 (5.70)	7.0	1, 22	0.1 (3.76)	-1.0	-4, 11	0.8744
Low dose	20	7.7	7.6 (5.51)	7.0	1, 22	-0.2 (3.23)	-0.5	-4, 9	0.8378
High dose	5	10.4	11.6 (5.86)	10.0	6, 20	1.2 (5.76)	-1.0	-4, 11	0.6657
WEEK 2	24	7.9	7.5 (4.32)	7.0	1, 19	-0.4 (2.99)	0.0	-7, 4	0.5018
Low dose	19	7.2	7.2 (4.67)	6.0	1, 19	0.0 (2.54)	0.0	-4, 4	>0.999
High dose	5	10.4	8.4 (2.79)	7.0	6, 13	-2.0 (4.30)	-2.0	-7, 4	0.3572
WEEK 3	21	7.3	9.0 (6.16)	7.0	1, 23	1.7 (3.62)	2.0	-4, 8	0.0479*
Low dose	18	6.9	8.8 (6.53)	6.5	1, 23	1.9 (3.80)	2.0	-4, 8	0.0442*
High dose	3	9.7	9.7 (4.04)	9.0	6, 14	0.0 (2.00)	0.0	-2, 2	>0.999
WEEK 4	20	7.5	8.9 (6.93)	7.0	1, 29	1.4 (5.03)	0.0	-8, 17	0.2447
Low dose	17	7.1	9.4 (7.43)	8.0	1, 29	2.2 (4.76)	1.0	-3, 17	0.0709
High dose	3	9.7	6.0 (0.00)	6.0	6, 6	-3.7 (3.79)	-2.0	-8, -1	0.2354

&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 2.1.J

Change from Baseline to Each Planned Visit in Parkinson's Disease Symptoms as Assessed
by The Movement Disorder Society-Unified Parkinson's Disease Rating Scale Score by Part and Total
(FAS - Japan Subjects)

Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
MDS-UPDRS Part I Score									
WEEK 6	18	7.7	9.0 (6.68)	7.5	1, 25	1.3 (5.28)	0.0	-8, 10	0.3188
Low dose	15	7.3	9.9 (6.92)	9.0	1, 25	2.5 (4.58)	1.0	-4, 10	0.0503
High dose	3	9.7	4.7 (3.21)	6.0	1, 7	-5.0 (4.36)	-7.0	-8, 0	0.1853
WEEK 13	17	7.9	9.2 (5.95)	7.0	0, 20	1.2 (5.43)	1.0	-10, 14	0.3619
Low dose	14	7.6	10.0 (6.21)	8.0	0, 20	2.4 (4.78)	2.0	-7, 14	0.0799
High dose	3	9.7	5.3 (2.31)	4.0	4, 8	-4.3 (5.51)	-4.0	-10, 1	0.3061
WEEK 26	15	8.3	7.9 (5.33)	8.0	1, 23	-0.4 (3.25)	0.0	-6, 4	0.6406
Low dose	12	7.9	8.3 (5.58)	8.5	1, 23	0.4 (3.00)	1.0	-6, 4	0.6397
High dose	3	9.7	6.0 (4.58)	5.0	2, 11	-3.7 (2.08)	-3.0	-6, -2	0.0927
WEEK 39	12	7.1	6.0 (3.77)	6.5	0, 12	-1.1 (3.58)	-1.0	-6, 4	0.3169
Low dose	9	6.2	5.7 (4.33)	5.0	0, 12	-0.6 (3.75)	1.0	-6, 4	0.6681
High dose	3	9.7	7.0 (1.00)	7.0	6, 8	-2.7 (3.06)	-2.0	-6, 0	0.2697
WEEK 52	11	7.5	7.5 (3.17)	6.0	3, 14	0.1 (4.74)	1.0	-11, 7	0.9506
Low dose	8	6.6	8.3 (3.24)	8.0	5, 14	1.6 (3.42)	1.0	-4, 7	0.2209
High dose	3	9.7	5.7 (2.52)	6.0	3, 8	-4.0 (6.08)	-1.0	-11, 0	0.3727

&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 2.1.J

Change from Baseline to Each Planned Visit in Parkinson's Disease Symptoms as Assessed
by The Movement Disorder Society-Unified Parkinson's Disease Rating Scale Score by Part and Total
(FAS - Japan Subjects)

Parameter Time Point Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
MDS-UPDRS Part II Score									
BASELINE	27		14.4 (7.84)	13.0	1, 33				
Low dose	22		12.9 (7.38)	11.5	1, 27				
High dose	5		21.0 (6.82)	18.0	17, 33				
DAY 2	26	14.7	11.9 (7.77)	11.5	0, 33	-2.8 (3.82)	-1.5	-15, 3	0.0011**
Low dose	21	13.1	9.8 (6.28)	10.0	0, 21	-3.4 (3.90)	-2.0	-15, 3	<=0.001***
High dose	5	21.0	20.8 (7.56)	17.0	14, 33	-0.2 (2.17)	0.0	-3, 3	0.8466
WEEK 1	25	14.6	11.5 (6.75)	10.0	3, 29	-3.1 (5.80)	-3.0	-17, 9	0.0129*
Low dose	20	13.1	10.1 (5.88)	8.5	3, 26	-3.0 (5.03)	-2.5	-17, 4	0.0152*
High dose	5	21.0	17.4 (7.40)	18.0	10, 29	-3.6 (9.04)	-6.0	-15, 9	0.4237
WEEK 2	24	15.7	12.7 (7.62)	11.0	3, 37	-3.0 (7.48)	-3.0	-18, 17	0.0615
Low dose	19	14.3	10.9 (5.60)	9.0	3, 21	-3.3 (5.80)	-3.0	-18, 8	0.0227*
High dose	5	21.0	19.2 (11.19)	17.0	9, 37	-1.8 (12.95)	-6.0	-16, 17	0.7715
WEEK 3	21	15.4	13.0 (7.97)	11.0	3, 37	-2.5 (6.19)	-2.0	-17, 12	0.0819
Low dose	18	14.2	12.8 (8.58)	11.0	3, 37	-1.4 (5.51)	-1.5	-10, 12	0.2817
High dose	3	22.7	14.0 (2.65)	15.0	11, 16	-8.7 (7.64)	-7.0	-17, -2	0.1883
WEEK 4	20	15.6	14.2 (7.42)	14.0	3, 27	-1.4 (5.90)	-1.5	-17, 8	0.3017
Low dose	17	14.4	14.4 (7.99)	14.0	3, 27	0.1 (4.55)	-1.0	-9, 8	0.9581
High dose	3	22.7	13.0 (3.00)	13.0	10, 16	-9.7 (6.66)	-8.0	-17, -4	0.1284

&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 2.1.J

Change from Baseline to Each Planned Visit in Parkinson's Disease Symptoms as Assessed
by The Movement Disorder Society-Unified Parkinson's Disease Rating Scale Score by Part and Total
(FAS - Japan Subjects)

Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
MDS-UPDRS Part II Score									
WEEK 6	18	14.8	13.1 (8.29)	11.0	3, 32	-1.7 (6.62)	-0.5	-21, 6	0.2853
Low dose	15	13.3	13.4 (9.09)	10.0	3, 32	0.1 (4.45)	1.0	-9, 6	0.9093
High dose	3	22.7	11.7 (1.53)	12.0	10, 13	-11.0 (8.89)	-8.0	-21, -4	0.1653
WEEK 13	17	15.2	14.1 (7.72)	14.0	1, 29	-1.1 (8.81)	-1.0	-21, 15	0.6081
Low dose	14	13.6	14.4 (8.38)	15.0	1, 29	0.8 (7.59)	0.5	-10, 15	0.7047
High dose	3	22.7	12.7 (4.04)	12.0	9, 17	-10.0 (10.15)	-8.0	-21, -1	0.2300
WEEK 26	15	16.2	12.9 (8.29)	14.0	0, 30	-3.3 (7.38)	-2.0	-18, 13	0.1023
Low dose	12	14.6	13.5 (8.91)	15.5	0, 30	-1.1 (5.93)	-1.0	-8, 13	0.5398
High dose	3	22.7	10.3 (5.69)	12.0	4, 15	-12.3 (6.03)	-13.0	-18, -6	0.0712
WEEK 39	12	15.0	11.5 (8.90)	10.0	1, 28	-3.5 (7.01)	-3.5	-15, 10	0.1118
Low dose	9	12.4	11.8 (9.60)	9.0	1, 28	-0.7 (4.97)	-1.0	-7, 10	0.6982
High dose	3	22.7	10.7 (8.08)	12.0	2, 18	-12.0 (5.20)	-15.0	-15, -6	0.0572
WEEK 52	11	15.6	12.3 (6.33)	10.0	5, 22	-3.4 (7.09)	-3.0	-17, 8	0.1466
Low dose	8	13.0	13.0 (6.89)	10.5	5, 22	0.0 (4.41)	-1.0	-5, 8	>0.999
High dose	3	22.7	10.3 (5.13)	9.0	6, 16	-12.3 (4.16)	-11.0	-17, -9	0.0359*

&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 2.1.J

Change from Baseline to Each Planned Visit in Parkinson's Disease Symptoms as Assessed
by The Movement Disorder Society-Unified Parkinson's Disease Rating Scale Score by Part and Total
(FAS - Japan Subjects)

Parameter Time Point Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
MDS-UPDRS Part III Score									
BASELINE	27		18.7 (10.66)	18.0	2, 42				
Low dose	22		17.7 (9.78)	17.0	2, 36				
High dose	5		23.2 (14.38)	22.0	9, 42				
DAY 2	26	18.3	18.6 (14.95)	14.0	2, 59	0.3 (8.79)	-0.5	-19, 26	0.8772
Low dose	21	17.2	15.9 (11.30)	14.0	2, 44	-1.3 (7.55)	-1.0	-19, 14	0.4444
High dose	5	23.2	30.0 (23.60)	27.0	6, 59	6.8 (11.50)	5.0	-3, 26	0.2566
WEEK 1	25	19.3	27.1 (18.35)	27.0	0, 76	7.8 (16.56)	1.0	-8, 67	0.0268*
Low dose	20	18.3	24.5 (17.07)	23.0	0, 76	6.2 (16.28)	0.5	-8, 67	0.1041
High dose	5	23.2	37.4 (21.66)	39.0	11, 70	14.2 (17.96)	5.0	-2, 37	0.1519
WEEK 2	24	19.8	29.9 (19.79)	23.5	5, 77	10.1 (17.20)	4.5	-7, 68	0.0087**
Low dose	19	18.9	29.1 (19.78)	23.0	5, 77	10.1 (17.42)	5.0	-5, 68	0.0206*
High dose	5	23.2	33.0 (21.80)	32.0	12, 68	9.8 (18.34)	2.0	-7, 35	0.2977
WEEK 3	21	18.6	28.3 (18.14)	24.0	6, 84	9.7 (17.24)	4.0	-9, 75	0.0178*
Low dose	18	17.6	29.1 (19.29)	24.5	6, 84	11.5 (17.89)	7.0	-4, 75	0.0143*
High dose	3	24.7	23.7 (9.50)	24.0	14, 33	-1.0 (7.00)	2.0	-9, 4	0.8277
WEEK 4	20	18.4	27.5 (15.42)	26.0	6, 62	9.1 (14.33)	3.0	-8, 53	0.0102*
Low dose	17	17.3	28.3 (16.10)	27.0	6, 62	11.1 (14.63)	13.0	-3, 53	0.0067**
High dose	3	24.7	23.0 (12.12)	25.0	10, 34	-1.7 (5.69)	0.0	-8, 3	0.6621

&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 2.1.J

Change from Baseline to Each Planned Visit in Parkinson's Disease Symptoms as Assessed
by The Movement Disorder Society-Unified Parkinson's Disease Rating Scale Score by Part and Total
(FAS - Japan Subjects)

Parameter Time Point Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
MDS-UPDRS Part III Score									
WEEK 6	18	17.6	26.1 (16.34)	24.0	5, 69	8.6 (16.93)	3.0	-17, 60	0.0466*
Low dose	15	16.1	27.4 (17.42)	24.0	5, 69	11.3 (16.88)	10.0	-7, 60	0.0215*
High dose	3	24.7	19.7 (8.39)	24.0	10, 25	-5.0 (10.44)	0.0	-17, 2	0.4941
WEEK 13	17	18.1	28.6 (15.08)	29.0	1, 57	10.5 (12.99)	9.0	-9, 37	0.0042**
Low dose	14	16.6	29.3 (15.69)	27.9	1, 57	12.7 (12.99)	14.0	-9, 37	0.0029**
High dose	3	24.7	25.0 (14.00)	31.0	9, 35	0.3 (8.08)	-1.0	-7, 9	0.9496
WEEK 26	15	18.1	26.1 (15.72)	28.0	4, 51	7.9 (13.75)	1.0	-6, 39	0.0423*
Low dose	12	16.5	26.7 (16.64)	28.0	4, 51	10.2 (14.57)	6.0	-6, 39	0.0341*
High dose	3	24.7	23.7 (14.01)	23.0	10, 38	-1.0 (2.65)	0.0	-4, 1	0.5799
WEEK 39	12	17.3	25.2 (17.46)	24.5	4, 56	7.9 (15.40)	2.0	-7, 47	0.1026
Low dose	9	14.8	24.2 (18.72)	24.0	4, 56	9.4 (17.65)	2.0	-7, 47	0.1471
High dose	3	24.7	28.0 (16.09)	30.0	11, 43	3.3 (4.04)	1.0	1, 8	0.2893
WEEK 52	11	16.8	23.6 (17.17)	30.0	1, 51	6.8 (11.56)	5.0	-9, 23	0.0789
Low dose	8	13.9	22.1 (17.03)	23.5	1, 51	8.3 (13.08)	6.5	-9, 23	0.1176
High dose	3	24.7	27.7 (20.60)	30.0	6, 47	3.0 (6.24)	5.0	-4, 8	0.4929

&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 2.1.J

Change from Baseline to Each Planned Visit in Parkinson's Disease Symptoms as Assessed
by The Movement Disorder Society-Unified Parkinson's Disease Rating Scale Score by Part and Total
(FAS - Japan Subjects)

Parameter Time Point Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
MDS-UPDRS Part IV Score									
BASELINE	27		8.7 (2.84)	9.0	0, 14				
Low dose	22		8.6 (3.02)	8.5	0, 14				
High dose	5		9.0 (2.12)	9.0	7, 12				
DAY 2	26	8.8	6.5 (3.78)	6.0	0, 14	-2.3 (3.76)	-1.0	-12, 6	0.0044**
Low dose	21	8.7	6.5 (3.97)	6.0	0, 14	-2.2 (3.95)	-1.0	-12, 6	0.0172*
High dose	5	9.0	6.4 (3.21)	8.0	1, 9	-2.6 (3.21)	-1.0	-6, 1	0.1443
WEEK 1	25	8.7	7.9 (3.40)	8.0	1, 15	-0.8 (3.76)	-1.0	-8, 9	0.2985
Low dose	20	8.6	8.0 (2.96)	8.0	2, 15	-0.7 (3.65)	-1.0	-6, 9	0.4351
High dose	5	9.0	7.6 (5.22)	6.0	1, 15	-1.4 (4.62)	-1.0	-8, 5	0.5348
WEEK 2	24	8.7	7.4 (2.95)	7.5	2, 12	-1.3 (2.87)	-1.5	-7, 5	0.0375*
Low dose	19	8.6	7.7 (2.67)	8.0	3, 12	-0.9 (2.66)	-1.0	-7, 5	0.1374
High dose	5	9.0	6.4 (4.04)	7.0	2, 12	-2.6 (3.58)	-4.0	-7, 2	0.1795
WEEK 3	21	8.0	8.3 (2.87)	8.0	3, 15	0.2 (3.36)	0.0	-5, 8	0.7488
Low dose	18	8.1	8.5 (3.00)	8.5	3, 15	0.4 (3.52)	0.0	-5, 8	0.6449
High dose	3	7.7	7.0 (1.73)	6.0	6, 9	-0.7 (2.52)	-1.0	-3, 2	0.6914
WEEK 4	20	8.0	6.8 (2.78)	7.0	2, 12	-1.2 (2.76)	-1.0	-5, 5	0.0672
Low dose	17	8.1	7.2 (2.66)	8.0	2, 12	-0.8 (2.65)	-1.0	-5, 5	0.2186
High dose	3	7.7	4.3 (2.52)	4.0	2, 7	-3.3 (2.89)	-5.0	-5, 0	0.1835

&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 2.1.J

Change from Baseline to Each Planned Visit in Parkinson's Disease Symptoms as Assessed
by The Movement Disorder Society-Unified Parkinson's Disease Rating Scale Score by Part and Total
(FAS - Japan Subjects)

Parameter Time Point Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
MDS-UPDRS Part IV Score									
WEEK 6	18	7.8	6.4 (2.73)	6.0	2, 12	-1.4 (3.20)	-1.5	-8, 5	0.0727
Low dose	15	7.9	6.5 (2.88)	6.0	2, 12	-1.3 (3.33)	-1.0	-8, 5	0.1434
High dose	3	7.7	5.7 (2.08)	5.0	4, 8	-2.0 (3.00)	-2.0	-5, 1	0.3675
WEEK 13	17	7.5	6.1 (2.82)	6.0	2, 11	-1.4 (3.97)	-2.0	-6, 10	0.1619
Low dose	14	7.4	6.4 (3.00)	6.5	2, 11	-1.1 (4.25)	-2.0	-6, 10	0.3629
High dose	3	7.7	4.7 (1.15)	4.0	4, 6	-3.0 (2.00)	-3.0	-5, -1	0.1217
WEEK 26	15	7.6	5.8 (3.03)	5.0	2, 12	-1.8 (3.59)	-1.0	-10, 5	0.0725
Low dose	12	7.6	6.1 (3.23)	6.0	2, 12	-1.5 (3.83)	-1.0	-10, 5	0.2016
High dose	3	7.7	4.7 (2.08)	4.0	3, 7	-3.0 (2.65)	-4.0	-5, 0	0.1885
WEEK 39	12	7.3	5.7 (2.90)	5.5	0, 9	-1.7 (3.23)	-2.0	-6, 5	0.1013
Low dose	9	7.2	5.9 (2.85)	6.0	0, 9	-1.3 (3.12)	-2.0	-6, 5	0.2361
High dose	3	7.7	5.0 (3.61)	4.0	2, 9	-2.7 (4.04)	-5.0	-5, 2	0.3715
WEEK 52	11	7.4	5.9 (2.59)	6.0	2, 10	-1.5 (3.93)	-3.0	-5, 6	0.2481
Low dose	8	7.3	6.4 (2.45)	6.5	3, 10	-0.9 (4.16)	-1.5	-5, 6	0.5702
High dose	3	7.7	4.7 (3.06)	4.0	2, 8	-3.0 (3.46)	-5.0	-5, 1	0.2724

&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

表2.7.3.6-15　MDS-UPDRSスコア（FAS，日本人部分集団）：M15-737試験

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ABBV-951
STUDY M15-737 - SECOND INTERIM (CUTOFF [redacted]20[redacted])
R&D/20/1639 - CLINICAL/STATISTICAL

TABLE 14.2__2.1.J

Change from Baseline to Each Planned Visit in Parkinson's Disease Symptoms as Assessed
by The Movement Disorder Society-Unified Parkinson's Disease Rating Scale Score by Part and Total
(FAS - Japan Subjects)

Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
MDS-UPDRS Part I Score									
BASELINE	7		7.4 (3.64)	6.0	3, 14				
Low dose	4		8.8 (4.11)	8.0	5, 14				
High dose	3		5.7 (2.52)	6.0	3, 8				
WEEK 24	5	7.4	10.0 (6.40)	7.0	5, 21	2.6 (2.51)	2.0	1, 7	0.0815
Low dose	2	10.0	14.0 (9.90)	14.0	7, 21	4.0 (4.24)	4.0	1, 7	0.4097
High dose	3	5.7	7.3 (2.52)	7.0	5, 10	1.7 (0.58)	2.0	1, 2	0.0377*
WEEK 48	4	5.8	7.3 (2.75)	7.5	4, 10	1.5 (1.29)	1.5	0, 3	0.1027
Low dose	1	6.0	6.0 (N/A)	6.0	6, 6	0.0 (N/A)	0.0	0, 0	
High dose	3	5.7	7.7 (3.21)	9.0	4, 10	2.0 (1.00)	2.0	1, 3	0.0742
MDS-UPDRS Part II Score									
BASELINE	7		12.4 (7.14)	9.0	5, 22				
Low dose	4		14.0 (8.76)	14.5	5, 22				
High dose	3		10.3 (5.13)	9.0	6, 16				
WEEK 24	5	11.6	15.4 (10.36)	11.0	5, 32	3.8 (4.27)	2.0	-1, 10	0.1172
Low dose	2	13.5	21.5 (14.85)	21.5	11, 32	8.0 (2.83)	8.0	6, 10	0.1560
High dose	3	10.3	11.3 (6.51)	11.0	5, 18	1.0 (1.73)	2.0	-1, 2	0.4226
WEEK 48	4	9.0	11.5 (6.14)	11.5	4, 19	2.5 (3.70)	2.5	-2, 7	0.2691
Low dose	1	5.0	12.0 (N/A)	12.0	12, 12	7.0 (N/A)	7.0	7, 7	
High dose	3	10.3	11.3 (7.51)	11.0	4, 19	1.0 (2.65)	2.0	-2, 3	0.5799

&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 2.1.J

Change from Baseline to Each Planned Visit in Parkinson's Disease Symptoms as Assessed
by The Movement Disorder Society-Unified Parkinson's Disease Rating Scale Score by Part and Total
(FAS - Japan Subjects)

Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
MDS-UPDRS Part III Score									
BASELINE	7		22.0 (17.56)	30.0	1, 47				
Low dose	4		17.8 (16.66)	18.0	1, 34				
High dose	3		27.7 (20.60)	30.0	6, 47				
WEEK 24	5	23.8	28.0 (20.74)	30.0	6, 52	4.2 (10.11)	0.0	-3, 22	0.4055
Low dose	2	18.0	30.0 (31.11)	30.0	8, 52	12.0 (14.14)	12.0	2, 22	0.4423
High dose	3	27.7	26.7 (19.22)	30.0	6, 44	-1.0 (1.73)	0.0	-3, 0	0.4226
WEEK 48	4	22.3	22.3 (18.71)	19.5	5, 45	0.0 (2.16)	-0.5	-2, 3	>0.999
Low dose	1	6.0	9.0 (N/A)	9.0	9, 9	3.0 (N/A)	3.0	3, 3	
High dose	3	27.7	26.7 (20.21)	30.0	5, 45	-1.0 (1.00)	-1.0	-2, 0	0.2254
MDS-UPDRS Part IV Score									
BASELINE	7		5.9 (2.19)	6.0	2, 8				
Low dose	4		6.8 (0.96)	6.5	6, 8				
High dose	3		4.7 (3.06)	4.0	2, 8				
WEEK 24	5	5.6	5.6 (2.61)	6.0	2, 8	0.0 (0.00)	0.0	0, 0	
Low dose	2	7.0	7.0 (1.41)	7.0	6, 8	0.0 (0.00)	0.0	0, 0	
High dose	3	4.7	4.7 (3.06)	4.0	2, 8	0.0 (0.00)	0.0	0, 0	
WEEK 48	4	5.5	6.0 (2.94)	6.0	3, 9	0.5 (0.58)	0.5	0, 1	0.1817
Low dose	1	8.0	8.0 (N/A)	8.0	8, 8	0.0 (N/A)	0.0	0, 0	
High dose	3	4.7	5.3 (3.21)	4.0	3, 9	0.7 (0.58)	1.0	0, 1	0.1835

&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 2.1.J

Change from Baseline to Each Planned Visit in Parkinson's Disease Symptoms as Assessed
by The Movement Disorder Society-Unified Parkinson's Disease Rating Scale Score by Part and Total
(FAS - Japan Subjects)

Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
MDS-UPDRS Total Score of Parts I-III									
BASELINE	7		41.9 (22.00)	45.0	15, 71				
Low dose	4		40.5 (20.95)	39.5	17, 66				
High dose	3		43.7 (28.02)	45.0	15, 71				
WEEK 24	5	42.8	53.4 (36.01)	48.0	16, 105	10.6 (16.21)	3.0	1, 39	0.2175
Low dose	2	41.5	65.5 (55.86)	65.5	26, 105	24.0 (21.21)	24.0	9, 39	0.3556
High dose	3	43.7	45.3 (28.10)	48.0	16, 72	1.7 (1.15)	1.0	1, 3	0.1296
WEEK 48	4	37.0	41.0 (26.77)	38.5	13, 74	4.0 (4.97)	4.0	-2, 10	0.2056
Low dose	1	17.0	27.0 (N/A)	27.0	27, 27	10.0 (N/A)	10.0	10, 10	
High dose	3	43.7	45.7 (30.73)	50.0	13, 74	2.0 (3.61)	3.0	-2, 5	0.4380

&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

表2.7.3.6-16　PDSS-2スコア（FAS，日本人部分集団）：M15-741試験

[redacted]20[redacted] 10:12 <[redacted]>
ABBV-951
STUDY M15-741 - SECOND INTERIM (CUTOFF [redacted]20[redacted])
R&D/20/1632 - CLINICAL/STATISTICAL

TABLE 14.2__3.J

Change from Baseline to Each Planned Visit in Sleep Symptoms as Assessed
by The Parkinson's Disease Sleep Scale - 2
(FAS - Japan Subjects)

Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
PDSS-2 Total Score									
BASELINE	27		16.1 (6.58)	14.0	5.0, 29.0				
Low dose	22		15.4 (6.45)	13.5	5.0, 26.0				
High dose	5		19.2 (6.94)	21.0	12.0, 29.0				
WEEK 6	19	16.3	17.9 (10.61)	15.0	4.0, 45.0	1.6 (10.82)	-1.0	-15.0, 27.0	0.5327
Low dose	16	15.4	18.2 (11.33)	15.5	4.0, 45.0	2.8 (10.94)	0.0	-11.0, 27.0	0.3306
High dose	3	21.0	16.3 (6.81)	14.0	11.0, 24.0	-4.7 (9.29)	-2.0	-15.0, 3.0	0.4761
WEEK 13	17	16.4	18.0 (8.66)	17.0	0.0, 36.0	1.6 (11.02)	1.0	-18.0, 17.0	0.5608
Low dose	14	15.4	18.7 (9.41)	19.5	0.0, 36.0	3.3 (11.08)	3.5	-18.0, 17.0	0.2871
High dose	3	21.0	14.7 (2.08)	14.0	13.0, 17.0	-6.3 (7.77)	-4.0	-15.0, 0.0	0.2934
WEEK 26	15	17.1	21.0 (8.68)	19.0	8.0, 42.0	3.9 (9.32)	3.0	-12.0, 19.0	0.1304
Low dose	12	16.2	22.1 (8.59)	19.5	8.0, 42.0	5.9 (8.90)	6.5	-8.0, 19.0	0.0418*
High dose	3	21.0	16.7 (9.29)	14.0	9.0, 27.0	-4.3 (6.81)	-2.0	-12.0, 1.0	0.3851
WEEK 39	12	17.3	15.6 (4.70)	16.5	7.0, 22.0	-1.8 (8.85)	-2.5	-16.0, 12.0	0.5077
Low dose	9	16.1	16.0 (4.85)	18.0	7.0, 22.0	-0.1 (9.57)	4.0	-16.0, 12.0	0.9731
High dose	3	21.0	14.3 (4.93)	12.0	11.0, 20.0	-6.7 (4.04)	-9.0	-9.0, -2.0	0.1038
WEEK 52	11	17.7	18.5 (4.13)	17.0	12.0, 25.0	0.7 (9.05)	3.0	-14.0, 14.0	0.7951
Low dose	8	16.5	18.4 (4.50)	18.5	12.0, 25.0	1.9 (10.13)	3.5	-14.0, 14.0	0.6169
High dose	3	21.0	18.7 (3.79)	17.0	16.0, 23.0	-2.3 (5.51)	-5.0	-6.0, 4.0	0.5394

&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 3.J

Change from Baseline to Each Planned Visit in Sleep Symptoms as Assessed
by The Parkinson's Disease Sleep Scale - 2
(FAS - Japan Subjects)

Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
PDSS-2 Motor Symptoms at Night Score									
BASELINE	27		3.1 (3.07)	2.0	0.0, 9.0				
Low dose	22		2.7 (2.77)	2.0	0.0, 9.0				
High dose	5		5.0 (3.94)	4.0	0.0, 9.0				
WEEK 6	19	3.1	4.7 (4.08)	5.0	0.0, 13.0	1.6 (4.21)	0.0	-6.0, 10.0	0.1081
Low dose	16	2.7	4.8 (4.31)	5.0	0.0, 13.0	2.1 (4.03)	0.5	-3.0, 10.0	0.0522
High dose	3	5.3	4.3 (3.21)	3.0	2.0, 8.0	-1.0 (5.00)	-1.0	-6.0, 4.0	0.7621
WEEK 13	17	3.2	4.2 (3.85)	4.0	0.0, 13.0	1.1 (4.67)	1.0	-9.0, 9.0	0.3638
Low dose	14	2.7	4.6 (4.07)	4.5	0.0, 13.0	1.9 (4.28)	1.5	-6.0, 9.0	0.1281
High dose	3	5.3	2.7 (2.52)	3.0	0.0, 5.0	-2.7 (5.51)	0.0	-9.0, 1.0	0.4899
WEEK 26	15	3.6	5.7 (4.15)	5.0	0.0, 16.0	2.1 (4.53)	2.0	-4.0, 11.0	0.0988
Low dose	12	3.2	6.4 (4.21)	7.0	0.0, 16.0	3.3 (4.18)	3.5	-3.0, 11.0	0.0209*
High dose	3	5.3	2.7 (2.52)	3.0	0.0, 5.0	-2.7 (2.31)	-4.0	-4.0, 0.0	0.1835
WEEK 39	12	3.8	3.3 (2.22)	3.5	0.0, 7.0	-0.5 (3.12)	-1.0	-5.0, 4.0	0.5898
Low dose	9	3.2	3.6 (2.30)	4.0	0.0, 7.0	0.3 (3.04)	0.0	-4.0, 4.0	0.7508
High dose	3	5.3	2.3 (2.08)	3.0	0.0, 4.0	-3.0 (2.00)	-3.0	-5.0, -1.0	0.1217
WEEK 52	11	3.9	4.5 (2.46)	4.0	1.0, 10.0	0.5 (4.37)	0.0	-6.0, 10.0	0.6874
Low dose	8	3.4	4.9 (2.59)	4.5	2.0, 10.0	1.5 (4.72)	2.0	-6.0, 10.0	0.3987
High dose	3	5.3	3.3 (2.08)	4.0	1.0, 5.0	-2.0 (2.00)	-2.0	-4.0, 0.0	0.2254

&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 3.J

Change from Baseline to Each Planned Visit in Sleep Symptoms as Assessed
by The Parkinson's Disease Sleep Scale - 2
(FAS - Japan Subjects)

Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
PDSS-2 PD Symptoms at Night Score									
BASELINE	27		4.0 (2.90)	3.0	0.0, 10.0				
Low dose	22		3.9 (2.96)	3.0	0.0, 10.0				
High dose	5		4.8 (2.77)	6.0	1.0, 8.0				
WEEK 6	19	4.4	4.0 (4.77)	2.0	0.0, 18.0	-0.4 (4.02)	-1.0	-6.0, 12.0	0.6533
Low dose	16	4.3	4.1 (5.09)	2.0	0.0, 18.0	-0.3 (4.34)	-1.0	-6.0, 12.0	0.8210
High dose	3	5.0	3.7 (3.21)	5.0	0.0, 6.0	-1.3 (1.53)	-1.0	-3.0, 0.0	0.2697
WEEK 13	17	4.3	4.0 (3.26)	4.0	0.0, 10.0	-0.3 (4.25)	0.0	-7.0, 7.0	0.7792
Low dose	14	4.1	4.3 (3.36)	4.0	0.0, 10.0	0.1 (4.31)	1.0	-7.0, 7.0	0.9032
High dose	3	5.0	2.7 (2.89)	1.0	1.0, 6.0	-2.3 (4.04)	0.0	-7.0, 0.0	0.4226
WEEK 26	15	4.7	5.7 (3.43)	5.0	1.0, 12.0	1.0 (3.21)	1.0	-3.0, 6.0	0.2472
Low dose	12	4.7	6.0 (3.25)	5.5	1.0, 12.0	1.3 (3.37)	1.5	-3.0, 6.0	0.1974
High dose	3	5.0	4.7 (4.73)	3.0	1.0, 10.0	-0.3 (2.52)	0.0	-3.0, 2.0	0.8399
WEEK 39	12	4.3	3.7 (2.46)	4.0	0.0, 8.0	-0.7 (3.37)	-1.5	-6.0, 6.0	0.5069
Low dose	9	4.1	3.8 (2.44)	4.0	0.0, 8.0	-0.3 (3.87)	0.0	-6.0, 6.0	0.8028
High dose	3	5.0	3.3 (3.06)	4.0	0.0, 6.0	-1.7 (0.58)	-2.0	-2.0, -1.0	0.0377*
WEEK 52	11	4.5	4.1 (1.45)	4.0	2.0, 7.0	-0.4 (2.98)	-2.0	-3.0, 5.0	0.6938
Low dose	8	4.3	3.9 (1.55)	4.0	2.0, 7.0	-0.4 (3.20)	-1.5	-3.0, 5.0	0.7503
High dose	3	5.0	4.7 (1.15)	4.0	4.0, 6.0	-0.3 (2.89)	-2.0	-2.0, 3.0	0.8600

&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 3.J

Change from Baseline to Each Planned Visit in Sleep Symptoms as Assessed
by The Parkinson's Disease Sleep Scale - 2
(FAS - Japan Subjects)

Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
PDSS-2 Disturbed Sleep Score									
BASELINE	27		9.0 (3.11)	9.0	2.0, 14.0				
Low dose	22		8.9 (3.30)	9.0	2.0, 14.0				
High dose	5		9.4 (2.30)	9.0	6.0, 12.0				
WEEK 6	19	8.8	9.2 (3.64)	9.0	3.0, 19.0	0.4 (5.00)	0.0	-6.0, 17.0	0.7519
Low dose	16	8.4	9.3 (3.89)	9.0	3.0, 19.0	0.9 (5.19)	0.0	-4.0, 17.0	0.5102
High dose	3	10.7	8.3 (2.08)	9.0	6.0, 10.0	-2.3 (3.21)	-1.0	-6.0, 0.0	0.3356
WEEK 13	17	8.9	9.8 (4.32)	10.0	0.0, 15.0	0.8 (4.84)	1.0	-7.0, 11.0	0.4928
Low dose	14	8.6	9.9 (4.59)	11.0	0.0, 15.0	1.3 (5.09)	1.0	-7.0, 11.0	0.3619
High dose	3	10.7	9.3 (3.51)	9.0	6.0, 13.0	-1.3 (3.21)	0.0	-5.0, 1.0	0.5471
WEEK 26	15	8.8	9.6 (2.47)	10.0	5.0, 14.0	0.8 (3.05)	1.0	-5.0, 8.0	0.3272
Low dose	12	8.3	9.7 (2.46)	10.0	5.0, 14.0	1.3 (2.90)	1.0	-2.0, 8.0	0.1398
High dose	3	10.7	9.3 (3.06)	10.0	6.0, 12.0	-1.3 (3.21)	0.0	-5.0, 1.0	0.5471
WEEK 39	12	9.3	8.7 (2.71)	9.0	4.0, 13.0	-0.6 (4.25)	-1.0	-7.0, 7.0	0.6439
Low dose	9	8.8	8.7 (2.74)	9.0	4.0, 13.0	-0.1 (4.46)	-1.0	-7.0, 7.0	0.9422
High dose	3	10.7	8.7 (3.21)	10.0	5.0, 11.0	-2.0 (4.00)	-2.0	-6.0, 2.0	0.4778
WEEK 52	11	9.4	9.9 (2.47)	11.0	6.0, 13.0	0.5 (3.56)	0.0	-5.0, 6.0	0.6223
Low dose	8	8.9	9.6 (2.62)	10.5	6.0, 13.0	0.8 (3.92)	0.5	-5.0, 6.0	0.6051
High dose	3	10.7	10.7 (2.31)	12.0	8.0, 12.0	0.0 (3.00)	0.0	-3.0, 3.0	>0.999

&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

表2.7.3.6-17　MMSEスコア（FAS，日本人部分集団）：M15-737試験

[redacted]20[redacted] 04:20 <[redacted]>
ABBV-951
STUDY M15-737 - SECOND INTERIM (CUTOFF [redacted]20[redacted])
R&D/20/1639 - CLINICAL/STATISTICAL

TABLE 14.2__5.J

Change from Baseline to Each Planned Visit
in Mini-Mental State Examination (MMSE) Total Score
(FAS - Japan Subjects)

Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
MMSE - Attention/Calculation									
BASELINE	7		4.6 (0.79)	5.0	3.0, 5.0				
Low dose	4		4.3 (0.96)	4.5	3.0, 5.0				
High dose	3		5.0 (0.00)	5.0	5.0, 5.0				
WEEK 24	5	4.6	4.2 (1.79)	5.0	1.0, 5.0	-0.4 (0.89)	0.0	-2.0, 0.0	0.3739
Low dose	2	4.0	3.0 (2.83)	3.0	1.0, 5.0	-1.0 (1.41)	-1.0	-2.0, 0.0	0.5000
High dose	3	5.0	5.0 (0.00)	5.0	5.0, 5.0	0.0 (0.00)	0.0	0.0, 0.0	
WEEK 48	4	5.0	5.0 (0.00)	5.0	5.0, 5.0	0.0 (0.00)	0.0	0.0, 0.0	
Low dose	1	5.0	5.0 (N/A)	5.0	5.0, 5.0	0.0 (N/A)	0.0	0.0, 0.0	
High dose	3	5.0	5.0 (0.00)	5.0	5.0, 5.0	0.0 (0.00)	0.0	0.0, 0.0	
POST-BASELINE MINIMUM	5	4.6	4.2 (1.79)	5.0	1.0, 5.0	-0.4 (0.89)	0.0	-2.0, 0.0	0.3739
Low dose	2	4.0	3.0 (2.83)	3.0	1.0, 5.0	-1.0 (1.41)	-1.0	-2.0, 0.0	0.5000
High dose	3	5.0	5.0 (0.00)	5.0	5.0, 5.0	0.0 (0.00)	0.0	0.0, 0.0	
POST-BASELINE MAXIMUM	5	4.6	4.2 (1.79)	5.0	1.0, 5.0	-0.4 (0.89)	0.0	-2.0, 0.0	0.3739
Low dose	2	4.0	3.0 (2.83)	3.0	1.0, 5.0	-1.0 (1.41)	-1.0	-2.0, 0.0	0.5000
High dose	3	5.0	5.0 (0.00)	5.0	5.0, 5.0	0.0 (0.00)	0.0	0.0, 0.0	
MMSE - Comprehension									
BASELINE	7		3.0 (0.00)	3.0	3.0, 3.0				
Low dose	4		3.0 (0.00)	3.0	3.0, 3.0				
High dose	3		3.0 (0.00)	3.0	3.0, 3.0				

&: P-value is obtained from two-sided paired-sample t-test.

Program Source Code: [redacted]

TABLE 14.2 5.J

Change from Baseline to Each Planned Visit
in Mini-Mental State Examination (MMSE) Total Score
(FAS - Japan Subjects)

Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
MMSE - Comprehension									
WEEK 24	5	3.0	3.0 (0.00)	3.0	3.0, 3.0	0.0 (0.00)	0.0	0.0, 0.0	
Low dose	2	3.0	3.0 (0.00)	3.0	3.0, 3.0	0.0 (0.00)	0.0	0.0, 0.0	
High dose	3	3.0	3.0 (0.00)	3.0	3.0, 3.0	0.0 (0.00)	0.0	0.0, 0.0	
WEEK 48	4	3.0	3.0 (0.00)	3.0	3.0, 3.0	0.0 (0.00)	0.0	0.0, 0.0	
Low dose	1	3.0	3.0 (N/A)	3.0	3.0, 3.0	0.0 (N/A)	0.0	0.0, 0.0	
High dose	3	3.0	3.0 (0.00)	3.0	3.0, 3.0	0.0 (0.00)	0.0	0.0, 0.0	
POST-BASELINE MINIMUM	5	3.0	3.0 (0.00)	3.0	3.0, 3.0	0.0 (0.00)	0.0	0.0, 0.0	
Low dose	2	3.0	3.0 (0.00)	3.0	3.0, 3.0	0.0 (0.00)	0.0	0.0, 0.0	
High dose	3	3.0	3.0 (0.00)	3.0	3.0, 3.0	0.0 (0.00)	0.0	0.0, 0.0	
POST-BASELINE MAXIMUM	5	3.0	3.0 (0.00)	3.0	3.0, 3.0	0.0 (0.00)	0.0	0.0, 0.0	
Low dose	2	3.0	3.0 (0.00)	3.0	3.0, 3.0	0.0 (0.00)	0.0	0.0, 0.0	
High dose	3	3.0	3.0 (0.00)	3.0	3.0, 3.0	0.0 (0.00)	0.0	0.0, 0.0	
MMSE - Drawing									
BASELINE	7		1.0 (0.00)	1.0	1.0, 1.0				
Low dose	4		1.0 (0.00)	1.0	1.0, 1.0				
High dose	3		1.0 (0.00)	1.0	1.0, 1.0				
WEEK 24	5	1.0	0.8 (0.45)	1.0	0.0, 1.0	-0.2 (0.45)	0.0	-1.0, 0.0	0.3739
Low dose	2	1.0	0.5 (0.71)	0.5	0.0, 1.0	-0.5 (0.71)	-0.5	-1.0, 0.0	0.5000
High dose	3	1.0	1.0 (0.00)	1.0	1.0, 1.0	0.0 (0.00)	0.0	0.0, 0.0	

&: P-value is obtained from two-sided paired-sample t-test.

Program Source Code: [redacted]

TABLE 14.2 5.J

Change from Baseline to Each Planned Visit
in Mini-Mental State Examination (MMSE) Total Score
(FAS - Japan Subjects)

Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
MMSE - Drawing									
WEEK 48	4	1.0	1.0 (0.00)	1.0	1.0, 1.0	0.0 (0.00)	0.0	0.0, 0.0	
Low dose	1	1.0	1.0 (N/A)	1.0	1.0, 1.0	0.0 (N/A)	0.0	0.0, 0.0	
High dose	3	1.0	1.0 (0.00)	1.0	1.0, 1.0	0.0 (0.00)	0.0	0.0, 0.0	
POST-BASELINE MINIMUM	5	1.0	0.8 (0.45)	1.0	0.0, 1.0	-0.2 (0.45)	0.0	-1.0, 0.0	0.3739
Low dose	2	1.0	0.5 (0.71)	0.5	0.0, 1.0	-0.5 (0.71)	-0.5	-1.0, 0.0	0.5000
High dose	3	1.0	1.0 (0.00)	1.0	1.0, 1.0	0.0 (0.00)	0.0	0.0, 0.0	
POST-BASELINE MAXIMUM	5	1.0	0.8 (0.45)	1.0	0.0, 1.0	-0.2 (0.45)	0.0	-1.0, 0.0	0.3739
Low dose	2	1.0	0.5 (0.71)	0.5	0.0, 1.0	-0.5 (0.71)	-0.5	-1.0, 0.0	0.5000
High dose	3	1.0	1.0 (0.00)	1.0	1.0, 1.0	0.0 (0.00)	0.0	0.0, 0.0	
MMSE - Naming									
BASELINE	7		2.0 (0.00)	2.0	2.0, 2.0				
Low dose	4		2.0 (0.00)	2.0	2.0, 2.0				
High dose	3		2.0 (0.00)	2.0	2.0, 2.0				
WEEK 24	5	2.0	2.0 (0.00)	2.0	2.0, 2.0	0.0 (0.00)	0.0	0.0, 0.0	
Low dose	2	2.0	2.0 (0.00)	2.0	2.0, 2.0	0.0 (0.00)	0.0	0.0, 0.0	
High dose	3	2.0	2.0 (0.00)	2.0	2.0, 2.0	0.0 (0.00)	0.0	0.0, 0.0	
WEEK 48	4	2.0	2.0 (0.00)	2.0	2.0, 2.0	0.0 (0.00)	0.0	0.0, 0.0	
Low dose	1	2.0	2.0 (N/A)	2.0	2.0, 2.0	0.0 (N/A)	0.0	0.0, 0.0	
High dose	3	2.0	2.0 (0.00)	2.0	2.0, 2.0	0.0 (0.00)	0.0	0.0, 0.0	

&: P-value is obtained from two-sided paired-sample t-test.

Program Source Code: [redacted]

TABLE 14.2 5.J

Change from Baseline to Each Planned Visit
in Mini-Mental State Examination (MMSE) Total Score
(FAS - Japan Subjects)

Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
MMSE - Naming									
POST-BASELINE MINIMUM	5	2.0	2.0 (0.00)	2.0	2.0, 2.0	0.0 (0.00)	0.0	0.0, 0.0	
Low dose	2	2.0	2.0 (0.00)	2.0	2.0, 2.0	0.0 (0.00)	0.0	0.0, 0.0	
High dose	3	2.0	2.0 (0.00)	2.0	2.0, 2.0	0.0 (0.00)	0.0	0.0, 0.0	
POST-BASELINE MAXIMUM	5	2.0	2.0 (0.00)	2.0	2.0, 2.0	0.0 (0.00)	0.0	0.0, 0.0	
Low dose	2	2.0	2.0 (0.00)	2.0	2.0, 2.0	0.0 (0.00)	0.0	0.0, 0.0	
High dose	3	2.0	2.0 (0.00)	2.0	2.0, 2.0	0.0 (0.00)	0.0	0.0, 0.0	
MMSE - Orientation to Place									
BASELINE	7		4.6 (1.13)	5.0	2.0, 5.0				
Low dose	4		4.3 (1.50)	5.0	2.0, 5.0				
High dose	3		5.0 (0.00)	5.0	5.0, 5.0				
WEEK 24	5	4.4	4.2 (1.79)	5.0	1.0, 5.0	-0.2 (0.45)	0.0	-1.0, 0.0	0.3739
Low dose	2	3.5	3.0 (2.83)	3.0	1.0, 5.0	-0.5 (0.71)	-0.5	-1.0, 0.0	0.5000
High dose	3	5.0	5.0 (0.00)	5.0	5.0, 5.0	0.0 (0.00)	0.0	0.0, 0.0	
WEEK 48	4	5.0	5.0 (0.00)	5.0	5.0, 5.0	0.0 (0.00)	0.0	0.0, 0.0	
Low dose	1	5.0	5.0 (N/A)	5.0	5.0, 5.0	0.0 (N/A)	0.0	0.0, 0.0	
High dose	3	5.0	5.0 (0.00)	5.0	5.0, 5.0	0.0 (0.00)	0.0	0.0, 0.0	
POST-BASELINE MINIMUM	5	4.4	4.2 (1.79)	5.0	1.0, 5.0	-0.2 (0.45)	0.0	-1.0, 0.0	0.3739
Low dose	2	3.5	3.0 (2.83)	3.0	1.0, 5.0	-0.5 (0.71)	-0.5	-1.0, 0.0	0.5000
High dose	3	5.0	5.0 (0.00)	5.0	5.0, 5.0	0.0 (0.00)	0.0	0.0, 0.0	

&: P-value is obtained from two-sided paired-sample t-test.

Program Source Code: [redacted]

TABLE 14.2 5.J

Change from Baseline to Each Planned Visit
in Mini-Mental State Examination (MMSE) Total Score
(FAS - Japan Subjects)

Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
MMSE - Orientation to Place									
POST-BASELINE MAXIMUM	5	4.4	4.2 (1.79)	5.0	1.0, 5.0	-0.2 (0.45)	0.0	-1.0, 0.0	0.3739
Low dose	2	3.5	3.0 (2.83)	3.0	1.0, 5.0	-0.5 (0.71)	-0.5	-1.0, 0.0	0.5000
High dose	3	5.0	5.0 (0.00)	5.0	5.0, 5.0	0.0 (0.00)	0.0	0.0, 0.0	
MMSE - Orientation to Time									
BASELINE	7		4.6 (1.13)	5.0	2.0, 5.0				
Low dose	4		4.3 (1.50)	5.0	2.0, 5.0				
High dose	3		5.0 (0.00)	5.0	5.0, 5.0				
WEEK 24	5	4.4	4.2 (1.79)	5.0	1.0, 5.0	-0.2 (0.45)	0.0	-1.0, 0.0	0.3739
Low dose	2	3.5	3.0 (2.83)	3.0	1.0, 5.0	-0.5 (0.71)	-0.5	-1.0, 0.0	0.5000
High dose	3	5.0	5.0 (0.00)	5.0	5.0, 5.0	0.0 (0.00)	0.0	0.0, 0.0	
WEEK 48	4	5.0	5.0 (0.00)	5.0	5.0, 5.0	0.0 (0.00)	0.0	0.0, 0.0	
Low dose	1	5.0	5.0 (N/A)	5.0	5.0, 5.0	0.0 (N/A)	0.0	0.0, 0.0	
High dose	3	5.0	5.0 (0.00)	5.0	5.0, 5.0	0.0 (0.00)	0.0	0.0, 0.0	
POST-BASELINE MINIMUM	5	4.4	4.2 (1.79)	5.0	1.0, 5.0	-0.2 (0.45)	0.0	-1.0, 0.0	0.3739
Low dose	2	3.5	3.0 (2.83)	3.0	1.0, 5.0	-0.5 (0.71)	-0.5	-1.0, 0.0	0.5000
High dose	3	5.0	5.0 (0.00)	5.0	5.0, 5.0	0.0 (0.00)	0.0	0.0, 0.0	
POST-BASELINE MAXIMUM	5	4.4	4.2 (1.79)	5.0	1.0, 5.0	-0.2 (0.45)	0.0	-1.0, 0.0	0.3739
Low dose	2	3.5	3.0 (2.83)	3.0	1.0, 5.0	-0.5 (0.71)	-0.5	-1.0, 0.0	0.5000
High dose	3	5.0	5.0 (0.00)	5.0	5.0, 5.0	0.0 (0.00)	0.0	0.0, 0.0	

&: P-value is obtained from two-sided paired-sample t-test.

Program Source Code: [redacted]

TABLE 14.2 5.J

Change from Baseline to Each Planned Visit
in Mini-Mental State Examination (MMSE) Total Score
(FAS - Japan Subjects)

Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
MMSE - Reading									
BASELINE	7		1.0 (0.00)	1.0	1.0, 1.0				
Low dose	4		1.0 (0.00)	1.0	1.0, 1.0				
High dose	3		1.0 (0.00)	1.0	1.0, 1.0				
WEEK 24	5	1.0	1.0 (0.00)	1.0	1.0, 1.0	0.0 (0.00)	0.0	0.0, 0.0	
Low dose	2	1.0	1.0 (0.00)	1.0	1.0, 1.0	0.0 (0.00)	0.0	0.0, 0.0	
High dose	3	1.0	1.0 (0.00)	1.0	1.0, 1.0	0.0 (0.00)	0.0	0.0, 0.0	
WEEK 48	4	1.0	1.0 (0.00)	1.0	1.0, 1.0	0.0 (0.00)	0.0	0.0, 0.0	
Low dose	1	1.0	1.0 (N/A)	1.0	1.0, 1.0	0.0 (N/A)	0.0	0.0, 0.0	
High dose	3	1.0	1.0 (0.00)	1.0	1.0, 1.0	0.0 (0.00)	0.0	0.0, 0.0	
POST-BASELINE MINIMUM	5	1.0	1.0 (0.00)	1.0	1.0, 1.0	0.0 (0.00)	0.0	0.0, 0.0	
Low dose	2	1.0	1.0 (0.00)	1.0	1.0, 1.0	0.0 (0.00)	0.0	0.0, 0.0	
High dose	3	1.0	1.0 (0.00)	1.0	1.0, 1.0	0.0 (0.00)	0.0	0.0, 0.0	
POST-BASELINE MAXIMUM	5	1.0	1.0 (0.00)	1.0	1.0, 1.0	0.0 (0.00)	0.0	0.0, 0.0	
Low dose	2	1.0	1.0 (0.00)	1.0	1.0, 1.0	0.0 (0.00)	0.0	0.0, 0.0	
High dose	3	1.0	1.0 (0.00)	1.0	1.0, 1.0	0.0 (0.00)	0.0	0.0, 0.0	
MMSE - Recall									
BASELINE	7		2.4 (0.79)	3.0	1.0, 3.0				
Low dose	4		2.5 (0.58)	2.5	2.0, 3.0				
High dose	3		2.3 (1.15)	3.0	1.0, 3.0				

&: P-value is obtained from two-sided paired-sample t-test.

Program Source Code: [redacted]

TABLE 14.2 5.J

Change from Baseline to Each Planned Visit
in Mini-Mental State Examination (MMSE) Total Score
(FAS - Japan Subjects)

Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
MMSE - Recall									
WEEK 24	5	2.4	2.6 (0.89)	3.0	1.0, 3.0	0.2 (1.10)	0.0	-1.0, 2.0	0.7040
Low dose	2	2.5	2.0 (1.41)	2.0	1.0, 3.0	-0.5 (0.71)	-0.5	-1.0, 0.0	0.5000
High dose	3	2.3	3.0 (0.00)	3.0	3.0, 3.0	0.7 (1.15)	0.0	0.0, 2.0	0.4226
WEEK 48	4	2.5	2.8 (0.50)	3.0	2.0, 3.0	0.3 (0.50)	0.0	0.0, 1.0	0.3910
Low dose	1	3.0	3.0 (N/A)	3.0	3.0, 3.0	0.0 (N/A)	0.0	0.0, 0.0	
High dose	3	2.3	2.7 (0.58)	3.0	2.0, 3.0	0.3 (0.58)	0.0	0.0, 1.0	0.4226
POST-BASELINE MINIMUM	5	2.4	2.4 (0.89)	3.0	1.0, 3.0	0.0 (0.71)	0.0	-1.0, 1.0	>0.999
Low dose	2	2.5	2.0 (1.41)	2.0	1.0, 3.0	-0.5 (0.71)	-0.5	-1.0, 0.0	0.5000
High dose	3	2.3	2.7 (0.58)	3.0	2.0, 3.0	0.3 (0.58)	0.0	0.0, 1.0	0.4226
POST-BASELINE MAXIMUM	5	2.4	2.6 (0.89)	3.0	1.0, 3.0	0.2 (1.10)	0.0	-1.0, 2.0	0.7040
Low dose	2	2.5	2.0 (1.41)	2.0	1.0, 3.0	-0.5 (0.71)	-0.5	-1.0, 0.0	0.5000
High dose	3	2.3	3.0 (0.00)	3.0	3.0, 3.0	0.7 (1.15)	0.0	0.0, 2.0	0.4226
MMSE - Registration									
BASELINE	7		3.0 (0.00)	3.0	3.0, 3.0				
Low dose	4		3.0 (0.00)	3.0	3.0, 3.0				
High dose	3		3.0 (0.00)	3.0	3.0, 3.0				
WEEK 24	5	3.0	3.0 (0.00)	3.0	3.0, 3.0	0.0 (0.00)	0.0	0.0, 0.0	
Low dose	2	3.0	3.0 (0.00)	3.0	3.0, 3.0	0.0 (0.00)	0.0	0.0, 0.0	
High dose	3	3.0	3.0 (0.00)	3.0	3.0, 3.0	0.0 (0.00)	0.0	0.0, 0.0	

&: P-value is obtained from two-sided paired-sample t-test.

Program Source Code: [redacted]

TABLE 14.2 5.J

Change from Baseline to Each Planned Visit
in Mini-Mental State Examination (MMSE) Total Score
(FAS - Japan Subjects)

Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
MMSE - Registration									
WEEK 48	4	3.0	3.0 (0.00)	3.0	3.0, 3.0	0.0 (0.00)	0.0	0.0, 0.0	
Low dose	1	3.0	3.0 (N/A)	3.0	3.0, 3.0	0.0 (N/A)	0.0	0.0, 0.0	
High dose	3	3.0	3.0 (0.00)	3.0	3.0, 3.0	0.0 (0.00)	0.0	0.0, 0.0	
POST-BASELINE MINIMUM	5	3.0	3.0 (0.00)	3.0	3.0, 3.0	0.0 (0.00)	0.0	0.0, 0.0	
Low dose	2	3.0	3.0 (0.00)	3.0	3.0, 3.0	0.0 (0.00)	0.0	0.0, 0.0	
High dose	3	3.0	3.0 (0.00)	3.0	3.0, 3.0	0.0 (0.00)	0.0	0.0, 0.0	
POST-BASELINE MAXIMUM	5	3.0	3.0 (0.00)	3.0	3.0, 3.0	0.0 (0.00)	0.0	0.0, 0.0	
Low dose	2	3.0	3.0 (0.00)	3.0	3.0, 3.0	0.0 (0.00)	0.0	0.0, 0.0	
High dose	3	3.0	3.0 (0.00)	3.0	3.0, 3.0	0.0 (0.00)	0.0	0.0, 0.0	
MMSE - Repetition									
BASELINE	7		1.0 (0.00)	1.0	1.0, 1.0				
Low dose	4		1.0 (0.00)	1.0	1.0, 1.0				
High dose	3		1.0 (0.00)	1.0	1.0, 1.0				
WEEK 24	5	1.0	1.0 (0.00)	1.0	1.0, 1.0	0.0 (0.00)	0.0	0.0, 0.0	
Low dose	2	1.0	1.0 (0.00)	1.0	1.0, 1.0	0.0 (0.00)	0.0	0.0, 0.0	
High dose	3	1.0	1.0 (0.00)	1.0	1.0, 1.0	0.0 (0.00)	0.0	0.0, 0.0	
WEEK 48	4	1.0	1.0 (0.00)	1.0	1.0, 1.0	0.0 (0.00)	0.0	0.0, 0.0	
Low dose	1	1.0	1.0 (N/A)	1.0	1.0, 1.0	0.0 (N/A)	0.0	0.0, 0.0	
High dose	3	1.0	1.0 (0.00)	1.0	1.0, 1.0	0.0 (0.00)	0.0	0.0, 0.0	

&: P-value is obtained from two-sided paired-sample t-test.

Program Source Code: [redacted]

TABLE 14.2 5.J

Change from Baseline to Each Planned Visit
in Mini-Mental State Examination (MMSE) Total Score
(FAS - Japan Subjects)

Parameter / Time Point / Dose Category	N	Baseline Mean	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
MMSE - Repetition									
POST-BASELINE MINIMUM	5	1.0	1.0 (0.00)	1.0	1.0, 1.0	0.0 (0.00)	0.0	0.0, 0.0	
Low dose	2	1.0	1.0 (0.00)	1.0	1.0, 1.0	0.0 (0.00)	0.0	0.0, 0.0	
High dose	3	1.0	1.0 (0.00)	1.0	1.0, 1.0	0.0 (0.00)	0.0	0.0, 0.0	
POST-BASELINE MAXIMUM	5	1.0	1.0 (0.00)	1.0	1.0, 1.0	0.0 (0.00)	0.0	0.0, 0.0	
Low dose	2	1.0	1.0 (0.00)	1.0	1.0, 1.0	0.0 (0.00)	0.0	0.0, 0.0	
High dose	3	1.0	1.0 (0.00)	1.0	1.0, 1.0	0.0 (0.00)	0.0	0.0, 0.0	
MMSE - Total									
BASELINE	7		28.1 (3.29)	30.0	21.0, 30.0				
Low dose	4		27.3 (4.27)	29.0	21.0, 30.0				
High dose	3		29.3 (1.15)	30.0	28.0, 30.0				
WEEK 24	5	27.8	27.0 (6.71)	30.0	15.0, 30.0	-0.8 (3.03)	0.0	-6.0, 2.0	0.5870
Low dose	2	25.5	22.5 (10.61)	22.5	15.0, 30.0	-3.0 (4.24)	-3.0	-6.0, 0.0	0.5000
High dose	3	29.3	30.0 (0.00)	30.0	30.0, 30.0	0.7 (1.15)	0.0	0.0, 2.0	0.4226
WEEK 48	4	29.5	29.8 (0.50)	30.0	29.0, 30.0	0.3 (0.50)	0.0	0.0, 1.0	0.3910
Low dose	1	30.0	30.0 (N/A)	30.0	30.0, 30.0	0.0 (N/A)	0.0	0.0, 0.0	
High dose	3	29.3	29.7 (0.58)	30.0	29.0, 30.0	0.3 (0.58)	0.0	0.0, 1.0	0.4226
POST-BASELINE MINIMUM	5	27.8	26.8 (6.61)	30.0	15.0, 30.0	-1.0 (2.83)	0.0	-6.0, 1.0	0.4734
Low dose	2	25.5	22.5 (10.61)	22.5	15.0, 30.0	-3.0 (4.24)	-3.0	-6.0, 0.0	0.5000
High dose	3	29.3	29.7 (0.58)	30.0	29.0, 30.0	0.3 (0.58)	0.0	0.0, 1.0	0.4226

&: P-value is obtained from two-sided paired-sample t-test.

Program Source Code: [redacted]

TABLE 14.2 5.J

Change from Baseline to Each Planned Visit
in Mini-Mental State Examination (MMSE) Total Score
(FAS - Japan Subjects)

Parameter Time Point Dose Category	N	Baseline Mean	Visit Mean (SD)	Visit Median	Visit Min, Max	Change from Baseline Mean (SD)	Change from Baseline Median	Change from Baseline Min, Max	P-Value &
MMSE - Total									
POST-BASELINE MAXIMUM	5	27.8	27.0 (6.71)	30.0	15.0, 30.0	-0.8 (3.03)	0.0	-6.0, 2.0	0.5870
Low dose	2	25.5	22.5 (10.61)	22.5	15.0, 30.0	-3.0 (4.24)	-3.0	-6.0, 0.0	0.5000
High dose	3	29.3	30.0 (0.00)	30.0	30.0, 30.0	0.7 (1.15)	0.0	0.0, 2.0	0.4226
MMSE - Writing									
BASELINE	7		1.0 (0.00)	1.0	1.0, 1.0				
Low dose	4		1.0 (0.00)	1.0	1.0, 1.0				
High dose	3		1.0 (0.00)	1.0	1.0, 1.0				
WEEK 24	5	1.0	1.0 (0.00)	1.0	1.0, 1.0	0.0 (0.00)	0.0	0.0, 0.0	
Low dose	2	1.0	1.0 (0.00)	1.0	1.0, 1.0	0.0 (0.00)	0.0	0.0, 0.0	
High dose	3	1.0	1.0 (0.00)	1.0	1.0, 1.0	0.0 (0.00)	0.0	0.0, 0.0	
WEEK 48	4	1.0	1.0 (0.00)	1.0	1.0, 1.0	0.0 (0.00)	0.0	0.0, 0.0	
Low dose	1	1.0	1.0 (N/A)	1.0	1.0, 1.0	0.0 (N/A)	0.0	0.0, 0.0	
High dose	3	1.0	1.0 (0.00)	1.0	1.0, 1.0	0.0 (0.00)	0.0	0.0, 0.0	
POST-BASELINE MINIMUM	5	1.0	1.0 (0.00)	1.0	1.0, 1.0	0.0 (0.00)	0.0	0.0, 0.0	
Low dose	2	1.0	1.0 (0.00)	1.0	1.0, 1.0	0.0 (0.00)	0.0	0.0, 0.0	
High dose	3	1.0	1.0 (0.00)	1.0	1.0, 1.0	0.0 (0.00)	0.0	0.0, 0.0	
POST-BASELINE MAXIMUM	5	1.0	1.0 (0.00)	1.0	1.0, 1.0	0.0 (0.00)	0.0	0.0, 0.0	
Low dose	2	1.0	1.0 (0.00)	1.0	1.0, 1.0	0.0 (0.00)	0.0	0.0, 0.0	
High dose	3	1.0	1.0 (0.00)	1.0	1.0, 1.0	0.0 (0.00)	0.0	0.0, 0.0	

&: P-value is obtained from two-sided paired-sample t-test.

Program Source Code: [redacted]

表2.7.3.6-18　PD日誌に基づく，標準化した1日あたりの平均「オフ」時間及び「オン」時間の要約（FAS）：M15-741試験（更新時）

[redacted]20[redacted] 10:49 <[redacted]>
ABBV-951
STUDY M15-741 - THIRD INTERIM (CUTOFF [redacted]20[redacted])
R&D/22/0153 - CLINICAL/STATISTICAL

TABLE 14.2__1.1

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary
(FAS)

Parameter Time Point Dose Category	N	Baseline Mean (SD)	Visit Mean (SD)	Visit Median	Visit Min, Max	Change from Baseline Mean (SD)	Change from Baseline Median	Change from Baseline Min, Max	Change from Baseline P-Value &
Average Daily Normalized 'Off' Time									
BASELINE	236		5.90 (2.24)	5.9	0.0, 12.6				
Low Dose	127		5.68 (2.19)	5.8	0.0, 10.3				
High Dose	109		6.16 (2.28)	6.4	0.0, 12.6				
WEEK 1	225	5.91 (2.25)	3.97 (3.43)	3.1	0.0, 16.0	-1.94 (3.68)	-2.2	-10.2, 10.4	<=0.001***
Low Dose	121	5.73 (2.21)	3.69 (3.19)	2.9	0.0, 13.8	-2.04 (3.49)	-2.2	-10.2, 5.9	<=0.001***
High Dose	104	6.12 (2.29)	4.29 (3.67)	3.6	0.0, 16.0	-1.83 (3.89)	-2.1	-8.9, 10.4	<=0.001***
WEEK 6	205	5.94 (2.24)	3.55 (3.26)	3.1	0.0, 16.0	-2.39 (3.60)	-2.9	-10.6, 9.9	<=0.001***
Low Dose	111	5.73 (2.12)	3.32 (3.33)	3.1	0.0, 16.0	-2.41 (3.65)	-2.9	-10.2, 9.9	<=0.001***
High Dose	94	6.19 (2.35)	3.82 (3.16)	3.1	0.0, 12.5	-2.37 (3.57)	-2.9	-10.6, 6.8	<=0.001***
WEEK 13	114	5.52 (2.28)	3.09 (3.46)	1.8	0.0, 13.4	-2.43 (3.70)	-3.2	-9.9, 8.1	<=0.001***
Low Dose	64	5.41 (2.22)	2.88 (3.53)	1.6	0.0, 13.4	-2.52 (3.80)	-3.3	-9.9, 8.1	<=0.001***
High Dose	50	5.66 (2.36)	3.35 (3.40)	2.1	0.0, 10.7	-2.31 (3.60)	-2.8	-9.2, 6.3	<=0.001***
WEEK 26	131	5.95 (2.23)	2.61 (3.02)	1.4	0.0, 14.3	-3.34 (3.25)	-3.4	-10.6, 7.1	<=0.001***
Low Dose	69	5.77 (1.96)	2.45 (3.17)	0.9	0.0, 14.3	-3.31 (3.36)	-3.8	-10.2, 7.1	<=0.001***
High Dose	62	6.15 (2.50)	2.79 (2.86)	1.8	0.0, 9.8	-3.36 (3.15)	-2.9	-10.6, 5.5	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours
(i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.1

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary
(FAS)

Parameter Time Point Dose Category	N	Baseline Mean (SD)	Visit Mean (SD)	Visit Median	Visit Min, Max	Change from Baseline Mean (SD)	Change from Baseline Median	Change from Baseline Min, Max	Change from Baseline P-Value &
Average Daily Normalized 'Off' Time (Cont.)									
WEEK 39	119	5.89 (2.22)	2.65 (2.78)	2.0	0.0, 13.3	-3.24 (3.14)	-3.2	-9.9, 9.6	<=0.001***
Low Dose	67	5.63 (1.95)	2.54 (2.91)	1.7	0.0, 13.3	-3.08 (3.29)	-3.1	-9.9, 9.6	<=0.001***
High Dose	52	6.23 (2.49)	2.79 (2.63)	2.4	0.0, 7.7	-3.44 (2.94)	-3.4	-9.2, 4.0	<=0.001***
WEEK 52	104	5.88 (2.27)	2.52 (2.88)	1.3	0.0, 11.5	-3.36 (3.12)	-3.5	-11.2, 5.9	<=0.001***
Low Dose	56	5.80 (2.02)	2.63 (2.81)	2.2	0.0, 10.9	-3.18 (3.12)	-3.4	-10.2, 5.9	<=0.001***
High Dose	48	5.96 (2.55)	2.39 (2.98)	0.7	0.0, 11.5	-3.57 (3.15)	-3.6	-11.2, 2.8	<=0.001***
Average Daily Normalized 'On' Time Without Dyskinesia									
BASELINE	236		6.51 (3.35)	6.6	0.0, 15.4				
Low Dose	127		6.35 (3.47)	6.4	0.0, 15.4				
High Dose	109		6.70 (3.22)	6.7	0.0, 13.8				
WEEK 1	225	6.48 (3.31)	8.43 (4.52)	8.3	0.0, 16.0	1.94 (4.09)	1.6	-8.9, 12.0	<=0.001***
Low Dose	121	6.21 (3.38)	7.99 (4.53)	8.3	0.0, 16.0	1.78 (3.93)	1.6	-8.9, 10.7	<=0.001***
High Dose	104	6.80 (3.21)	8.94 (4.47)	9.0	0.0, 16.0	2.14 (4.27)	1.9	-8.1, 12.0	<=0.001***
WEEK 6	205	6.54 (3.36)	9.92 (4.48)	10.6	0.0, 16.0	3.38 (4.39)	3.5	-9.1, 13.8	<=0.001***
Low Dose	111	6.37 (3.45)	9.86 (4.55)	10.5	0.0, 16.0	3.49 (4.50)	3.9	-9.1, 13.8	<=0.001***
High Dose	94	6.74 (3.26)	9.99 (4.43)	10.7	0.0, 16.0	3.25 (4.28)	3.2	-6.7, 12.0	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.1

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary
(FAS)

Parameter Time Point Dose Category	N	Baseline Mean (SD)	Visit Mean (SD)	Visit Median	Visit Min, Max	Change from Baseline Mean (SD)	Change from Baseline Median	Change from Baseline Min, Max	Change from Baseline P-Value &
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 13	114	6.67 (3.42)	10.80 (4.61)	11.5	0.0, 16.0	4.12 (4.36)	4.3	-9.0, 15.2	<=0.001***
Low Dose	64	6.66 (3.46)	10.66 (4.92)	12.4	0.0, 16.0	4.00 (4.41)	4.0	-9.0, 15.2	<=0.001***
High Dose	50	6.70 (3.41)	10.98 (4.23)	11.1	0.9, 16.0	4.28 (4.34)	4.5	-6.3, 14.1	<=0.001***
WEEK 26	131	6.85 (3.37)	11.29 (4.33)	12.6	0.0, 16.0	4.44 (4.47)	4.9	-11.0, 14.1	<=0.001***
Low Dose	69	6.78 (3.46)	11.69 (4.18)	12.8	0.0, 16.0	4.91 (3.99)	5.4	-10.1, 11.5	<=0.001***
High Dose	62	6.93 (3.28)	10.84 (4.48)	11.6	0.0, 16.0	3.92 (4.93)	4.6	-11.0, 14.1	<=0.001***
WEEK 39	119	6.96 (3.28)	10.97 (4.37)	11.3	0.0, 16.0	4.00 (4.10)	4.2	-10.6, 13.5	<=0.001***
Low Dose	67	6.90 (3.28)	11.24 (4.45)	11.8	0.3, 16.0	4.35 (4.23)	4.9	-10.6, 11.4	<=0.001***
High Dose	52	7.05 (3.32)	10.61 (4.29)	11.3	0.0, 16.0	3.56 (3.92)	3.1	-3.8, 13.5	<=0.001***
WEEK 52	104	7.03 (3.30)	10.83 (4.67)	11.8	0.0, 16.0	3.79 (4.21)	4.1	-12.0, 13.8	<=0.001***
Low Dose	56	6.77 (3.29)	11.32 (4.33)	12.7	0.0, 16.0	4.55 (3.85)	4.8	-6.5, 11.3	<=0.001***
High Dose	48	7.34 (3.32)	10.25 (5.02)	11.2	0.0, 16.0	2.91 (4.48)	2.4	-12.0, 13.8	<=0.001***
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia									
BASELINE	236		2.63 (2.55)	2.4	0.0, 12.2				
Low Dose	127		2.69 (2.39)	2.6	0.0, 10.3				
High Dose	109		2.55 (2.73)	1.9	0.0, 12.2				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.1

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary
(FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 1	225	2.66 (2.56)	2.61 (3.16)	1.5	0.0, 14.9	-0.05 (3.04)	0.0	-8.5, 13.6	0.8070
Low Dose	121	2.77 (2.40)	3.04 (3.28)	2.2	0.0, 14.9	0.27 (3.29)	0.0	-8.5, 13.6	0.3612
High Dose	104	2.54 (2.74)	2.12 (2.95)	0.7	0.0, 12.8	-0.43 (2.68)	0.0	-8.2, 8.8	0.1075
WEEK 6	205	2.67 (2.62)	2.09 (3.29)	0.5	0.0, 15.4	-0.58 (3.01)	-0.3	-7.8, 11.6	0.0064**
Low Dose	111	2.75 (2.42)	2.23 (3.17)	0.8	0.0, 15.4	-0.51 (3.05)	-0.2	-7.6, 11.6	0.0785
High Dose	94	2.58 (2.85)	1.93 (3.43)	0.0	0.0, 14.6	-0.66 (2.97)	-0.3	-7.8, 9.6	0.0352*
WEEK 13	114	2.98 (2.75)	1.78 (3.31)	0.0	0.0, 16.0	-1.19 (3.51)	-0.9	-12.2, 13.2	<=0.001***
Low Dose	64	2.94 (2.58)	2.07 (3.69)	0.2	0.0, 16.0	-0.87 (3.58)	-1.1	-8.0, 13.2	0.0571
High Dose	50	3.03 (2.98)	1.42 (2.72)	0.0	0.0, 14.4	-1.61 (3.40)	-0.7	-12.2, 7.2	0.0016**
WEEK 26	131	2.43 (2.47)	1.78 (2.93)	0.3	0.0, 15.2	-0.65 (3.24)	-0.1	-12.2, 12.0	0.0227*
Low Dose	69	2.54 (2.27)	1.56 (2.39)	0.6	0.0, 12.1	-0.99 (2.76)	-0.6	-6.8, 5.4	0.0042**
High Dose	62	2.31 (2.69)	2.03 (3.43)	0.0	0.0, 15.2	-0.28 (3.69)	0.0	-12.2, 12.0	0.5507
WEEK 39	119	2.43 (2.54)	2.03 (3.53)	0.0	0.0, 16.0	-0.40 (3.48)	0.0	-7.8, 15.4	0.2135
Low Dose	67	2.68 (2.38)	1.94 (3.47)	0.0	0.0, 15.4	-0.74 (3.56)	-0.2	-7.8, 15.4	0.0954
High Dose	52	2.11 (2.72)	2.15 (3.63)	0.0	0.0, 16.0	0.04 (3.35)	0.0	-7.8, 9.9	0.9391

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.1

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary
(FAS)

Parameter Time Point Dose Category	N	Baseline Mean (SD)	Visit Mean (SD)	Visit Median	Visit Min, Max	Change from Baseline Mean (SD)	Change from Baseline Median	Change from Baseline Min, Max	Change from Baseline P-Value &
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 52	104	2.49 (2.71)	2.16 (3.85)	0.2	0.0, 16.0	-0.33 (3.38)	0.0	-7.3, 12.9	0.3224
Low Dose	56	2.72 (2.52)	1.85 (3.52)	0.1	0.0, 16.0	-0.86 (3.38)	-0.5	-6.8, 9.2	0.0609
High Dose	48	2.22 (2.91)	2.52 (4.21)	0.4	0.0, 16.0	0.29 (3.30)	0.0	-7.3, 12.9	0.5392
Average Daily Normalized 'On' Time With Troublesome Dyskinesia									
BASELINE	236		0.96 (1.73)	0.0	0.0, 10.5				
Low Dose	127		1.27 (2.02)	0.0	0.0, 10.5				
High Dose	109		0.59 (1.20)	0.0	0.0, 5.3				
WEEK 1	225	0.94 (1.71)	0.99 (2.09)	0.0	0.0, 11.7	0.05 (1.89)	0.0	-6.0, 10.5	0.6962
Low Dose	121	1.29 (2.03)	1.28 (2.35)	0.0	0.0, 11.7	-0.01 (2.09)	0.0	-6.0, 10.5	0.9647
High Dose	104	0.53 (1.11)	0.65 (1.68)	0.0	0.0, 9.8	0.12 (1.65)	0.0	-4.9, 7.0	0.4714
WEEK 6	205	0.85 (1.61)	0.44 (1.30)	0.0	0.0, 9.0	-0.41 (1.60)	0.0	-9.2, 6.9	<=0.001***
Low Dose	111	1.15 (1.92)	0.59 (1.59)	0.0	0.0, 9.0	-0.56 (1.94)	0.0	-9.2, 6.9	0.0030**
High Dose	94	0.49 (1.05)	0.26 (0.81)	0.0	0.0, 4.4	-0.23 (1.06)	0.0	-4.9, 4.4	0.0402*
WEEK 13	114	0.83 (1.43)	0.33 (1.12)	0.0	0.0, 8.0	-0.50 (1.45)	0.0	-7.2, 6.0	<=0.001***
Low Dose	64	1.00 (1.57)	0.39 (1.32)	0.0	0.0, 8.0	-0.61 (1.70)	0.0	-7.2, 6.0	0.0059**
High Dose	50	0.62 (1.22)	0.25 (0.81)	0.0	0.0, 3.7	-0.36 (1.05)	0.0	-4.9, 2.6	0.0178*

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.1

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary
(FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Average Daily Normalized 'On' Time With Troublesome Dyskinesia (Cont.)									
WEEK 26	131	0.77 (1.51)	0.32 (1.38)	0.0	0.0, 12.1	-0.45 (1.85)	0.0	-9.2, 8.8	0.0063**
Low Dose	69	0.91 (1.65)	0.30 (1.53)	0.0	0.0, 12.1	-0.61 (1.95)	0.0	-9.2, 7.2	0.0119*
High Dose	62	0.61 (1.32)	0.34 (1.21)	0.0	0.0, 8.8	-0.27 (1.73)	0.0	-4.9, 8.8	0.2200
WEEK 39	119	0.72 (1.30)	0.35 (1.06)	0.0	0.0, 8.1	-0.37 (1.34)	0.0	-5.1, 7.3	0.0033**
Low Dose	67	0.80 (1.31)	0.27 (0.78)	0.0	0.0, 3.8	-0.53 (1.06)	0.0	-5.1, 0.8	<=0.001***
High Dose	52	0.61 (1.29)	0.46 (1.34)	0.0	0.0, 8.1	-0.16 (1.61)	0.0	-5.0, 7.3	0.4835
WEEK 52	104	0.60 (1.17)	0.50 (1.67)	0.0	0.0, 13.5	-0.10 (1.99)	0.0	-5.1, 13.0	0.5986
Low Dose	56	0.70 (1.21)	0.20 (0.63)	0.0	0.0, 3.3	-0.50 (1.29)	0.0	-5.1, 3.3	0.0050**
High Dose	48	0.48 (1.12)	0.84 (2.33)	0.0	0.0, 13.5	0.36 (2.52)	0.0	-5.0, 13.0	0.3230
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia									
BASELINE	236		9.14 (2.50)	9.4	0.3, 16.0				
Low Dose	127		9.05 (2.67)	9.7	0.3, 16.0				
High Dose	109		9.25 (2.30)	9.4	2.6, 16.0				
WEEK 1	225	9.15 (2.50)	11.04 (3.68)	11.2	0.0, 16.0	1.89 (3.77)	1.8	-10.4, 11.3	<=0.001***
Low Dose	121	8.98 (2.66)	11.03 (3.64)	11.2	1.6, 16.0	2.05 (3.53)	2.2	-5.9, 11.3	<=0.001***
High Dose	104	9.35 (2.31)	11.06 (3.75)	11.5	0.0, 16.0	1.71 (4.05)	1.6	-10.4, 8.9	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.1

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary
(FAS)

Parameter Time Point Dose Category	N	Baseline Mean (SD)	Visit Mean (SD)	Visit Median	Visit Min, Max	Change from Baseline Mean (SD)	Change from Baseline Median	Change from Baseline Min, Max	Change from Baseline P-Value &
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia (Cont.)									
WEEK 6	205	9.21 (2.44)	12.01 (3.36)	12.4	0.0, 16.0	2.80 (3.59)	3.2	-9.9, 10.6	<=0.001***
Low Dose	111	9.12 (2.54)	12.09 (3.52)	12.6	0.0, 16.0	2.97 (3.58)	3.3	-9.9, 10.5	<=0.001***
High Dose	94	9.32 (2.32)	11.92 (3.18)	12.3	3.5, 16.0	2.60 (3.60)	3.2	-6.8, 10.6	<=0.001***
WEEK 13	114	9.65 (2.35)	12.58 (3.61)	13.9	2.6, 16.0	2.93 (3.48)	3.3	-6.3, 9.9	<=0.001***
Low Dose	64	9.59 (2.37)	12.72 (3.71)	14.2	2.6, 16.0	3.13 (3.31)	3.7	-5.0, 9.9	<=0.001***
High Dose	50	9.73 (2.33)	12.40 (3.50)	13.6	5.3, 16.0	2.67 (3.70)	3.1	-6.3, 9.2	<=0.001***
WEEK 26	131	9.28 (2.60)	13.07 (3.24)	14.3	1.5, 16.0	3.79 (3.54)	3.9	-5.5, 12.5	<=0.001***
Low Dose	69	9.33 (2.66)	13.25 (3.51)	14.9	1.5, 16.0	3.92 (3.76)	4.1	-5.5, 12.5	<=0.001***
High Dose	62	9.24 (2.55)	12.87 (2.93)	14.0	6.2, 16.0	3.64 (3.30)	3.0	-5.5, 10.6	<=0.001***
WEEK 39	119	9.39 (2.47)	13.00 (3.01)	13.5	2.4, 16.0	3.60 (3.32)	3.4	-9.2, 9.9	<=0.001***
Low Dose	67	9.57 (2.42)	13.19 (2.95)	13.7	2.7, 16.0	3.61 (3.32)	3.1	-9.1, 9.9	<=0.001***
High Dose	52	9.16 (2.55)	12.75 (3.09)	13.1	2.4, 16.0	3.60 (3.35)	3.4	-9.2, 9.7	<=0.001***
WEEK 52	104	9.52 (2.43)	12.99 (3.14)	13.7	2.5, 16.0	3.46 (3.11)	3.5	-5.4, 11.2	<=0.001***
Low Dose	56	9.49 (2.44)	13.17 (2.81)	13.7	5.1, 16.0	3.68 (3.07)	3.5	-5.4, 10.2	<=0.001***
High Dose	48	9.56 (2.46)	12.77 (3.51)	14.0	2.5, 16.0	3.21 (3.17)	3.2	-3.8, 11.2	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

表2.7.3.6-19　PD日誌に基づく，標準化した1日あたりの平均「オフ」時間及び「オン」時間の登録時期別の要約（FAS）：M15-741試験（更新時）

[redacted]20[redacted] 10:49 <[redacted]>
ABBV-951
STUDY M15-741 - THIRD INTERIM (CUTOFF [redacted]20[redacted])
R&D/22/0153 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 7

TABLE 14.2__1.7

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Enrollment Sample
(FAS)

Parameter / Time Point / Sample Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Average Daily Normalized 'Off' Time									
BASELINE	236		5.90 (2.24)	5.9	0.0, 12.6				
Sample 1	150		5.82 (2.36)	5.9	0.0, 12.6				
Sample 2	86		6.04 (2.03)	5.9	0.6, 10.3				
WEEK 1	225	5.91 (2.25)	3.97 (3.43)	3.1	0.0, 16.0	-1.94 (3.68)	-2.2	-10.2, 10.4	<=0.001***
Sample 1	143	5.81 (2.35)	4.33 (3.34)	3.9	0.0, 16.0	-1.48 (3.57)	-1.5	-9.7, 8.0	<=0.001***
Sample 2	82	6.09 (2.06)	3.34 (3.50)	2.2	0.0, 14.8	-2.75 (3.75)	-3.4	-10.2, 10.4	<=0.001***
WEEK 6	205	5.94 (2.24)	3.55 (3.26)	3.1	0.0, 16.0	-2.39 (3.60)	-2.9	-10.6, 9.9	<=0.001***
Sample 1	129	5.89 (2.38)	3.70 (3.23)	3.2	0.0, 14.9	-2.19 (3.51)	-2.6	-10.6, 8.1	<=0.001***
Sample 2	76	6.02 (1.99)	3.29 (3.31)	3.0	0.0, 16.0	-2.73 (3.76)	-3.6	-10.2, 9.9	<=0.001***
WEEK 13	114	5.52 (2.28)	3.09 (3.46)	1.8	0.0, 13.4	-2.43 (3.70)	-3.2	-9.9, 8.1	<=0.001***
Sample 1	74	5.29 (2.33)	2.77 (3.12)	1.6	0.0, 10.7	-2.52 (3.46)	-3.0	-9.9, 8.1	<=0.001***
Sample 2	40	5.93 (2.14)	3.68 (4.00)	1.9	0.0, 13.4	-2.26 (4.15)	-3.3	-9.3, 7.8	0.0014**
WEEK 26	131	5.95 (2.23)	2.61 (3.02)	1.4	0.0, 14.3	-3.34 (3.25)	-3.4	-10.6, 7.1	<=0.001***
Sample 1	77	5.79 (2.39)	2.53 (2.60)	1.6	0.0, 8.9	-3.26 (2.77)	-2.9	-10.6, 4.4	<=0.001***
Sample 2	54	6.18 (1.98)	2.72 (3.56)	1.1	0.0, 14.3	-3.45 (3.86)	-4.3	-10.2, 7.1	<=0.001***

Note: Sample 1 contains subjects who were enrolled prior to [redacted]20[redacted].
Sample 2 contains subjects who were enrolled on or after [redacted]20[redacted].
Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.7

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Enrollment Sample
(FAS)

Parameter Time Point Sample Category	N	Baseline Mean (SD)	Visit Mean (SD)	Visit Median	Visit Min, Max	Change from Baseline Mean (SD)	Change from Baseline Median	Change from Baseline Min, Max	Change from Baseline P-Value &
Average Daily Normalized 'Off' Time (Cont.)									
WEEK 39	119	5.89 (2.22)	2.65 (2.78)	2.0	0.0, 13.3	-3.24 (3.14)	-3.2	-9.9, 9.6	<=0.001***
Sample 1	70	5.69 (2.38)	2.51 (2.69)	1.9	0.0, 13.3	-3.18 (3.13)	-3.1	-9.9, 9.6	<=0.001***
Sample 2	49	6.17 (1.94)	2.85 (2.92)	2.0	0.0, 12.3	-3.32 (3.17)	-3.4	-9.8, 6.4	<=0.001***
WEEK 52	104	5.88 (2.27)	2.52 (2.88)	1.3	0.0, 11.5	-3.36 (3.12)	-3.5	-11.2, 5.9	<=0.001***
Sample 1	66	5.68 (2.37)	2.13 (2.45)	1.0	0.0, 8.8	-3.55 (2.82)	-3.5	-11.2, 3.1	<=0.001***
Sample 2	38	6.21 (2.07)	3.19 (3.43)	2.4	0.0, 11.5	-3.02 (3.61)	-3.4	-10.2, 5.9	<=0.001***
Average Daily Normalized 'On' Time Without Dyskinesia									
BASELINE	236		6.51 (3.35)	6.6	0.0, 15.4				
Sample 1	150		6.66 (3.29)	6.6	0.0, 15.4				
Sample 2	86		6.26 (3.47)	6.5	0.0, 12.6				
WEEK 1	225	6.48 (3.31)	8.43 (4.52)	8.3	0.0, 16.0	1.94 (4.09)	1.6	-8.9, 12.0	<=0.001***
Sample 1	143	6.60 (3.27)	8.18 (4.27)	8.1	0.0, 16.0	1.58 (3.52)	1.3	-8.2, 8.7	<=0.001***
Sample 2	82	6.29 (3.39)	8.87 (4.92)	8.9	0.0, 16.0	2.58 (4.88)	2.3	-8.9, 12.0	<=0.001***
WEEK 6	205	6.54 (3.36)	9.92 (4.48)	10.6	0.0, 16.0	3.38 (4.39)	3.5	-9.1, 13.8	<=0.001***
Sample 1	129	6.71 (3.33)	9.86 (4.54)	10.6	0.0, 16.0	3.14 (4.37)	3.3	-9.1, 13.8	<=0.001***
Sample 2	76	6.25 (3.42)	10.03 (4.42)	10.5	0.0, 16.0	3.78 (4.42)	4.0	-7.5, 12.0	<=0.001***

Note: Sample 1 contains subjects who were enrolled prior to [redacted]20[redacted].
Sample 2 contains subjects who were enrolled on or after [redacted]20[redacted].
Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.7

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Enrollment Sample
(FAS)

Parameter Time Point Sample Category	N	Baseline Mean (SD)	Visit Mean (SD)	Visit Median	Visit Min, Max	Change from Baseline Mean (SD)	Change from Baseline Median	Change from Baseline Min, Max	Change from Baseline P-Value &
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 13	114	6.67 (3.42)	10.80 (4.61)	11.5	0.0, 16.0	4.12 (4.36)	4.3	-9.0, 15.2	<=0.001***
Sample 1	74	6.68 (3.48)	10.79 (4.57)	11.1	0.0, 16.0	4.11 (4.14)	4.4	-6.5, 11.2	<=0.001***
Sample 2	40	6.66 (3.34)	10.82 (4.75)	12.8	0.0, 16.0	4.16 (4.80)	4.0	-9.0, 15.2	<=0.001***
WEEK 26	131	6.85 (3.37)	11.29 (4.33)	12.6	0.0, 16.0	4.44 (4.47)	4.9	-11.0, 14.1	<=0.001***
Sample 1	77	7.12 (3.30)	11.45 (3.96)	12.8	0.0, 16.0	4.33 (4.24)	4.6	-9.6, 12.7	<=0.001***
Sample 2	54	6.47 (3.45)	11.06 (4.84)	11.9	0.0, 16.0	4.60 (4.82)	5.2	-11.0, 14.1	<=0.001***
WEEK 39	119	6.96 (3.28)	10.97 (4.37)	11.3	0.0, 16.0	4.00 (4.10)	4.2	-10.6, 13.5	<=0.001***
Sample 1	70	7.21 (3.20)	11.38 (4.14)	11.8	0.3, 16.0	4.17 (3.98)	4.2	-6.4, 13.5	<=0.001***
Sample 2	49	6.61 (3.39)	10.37 (4.66)	11.0	0.0, 16.0	3.76 (4.29)	4.2	-10.6, 12.4	<=0.001***
WEEK 52	104	7.03 (3.30)	10.83 (4.67)	11.8	0.0, 16.0	3.79 (4.21)	4.1	-12.0, 13.8	<=0.001***
Sample 1	66	6.90 (3.41)	10.64 (4.83)	11.5	0.0, 16.0	3.74 (4.55)	4.3	-12.0, 13.8	<=0.001***
Sample 2	38	7.26 (3.13)	11.14 (4.42)	12.2	0.0, 16.0	3.88 (3.61)	3.5	-2.8, 10.1	<=0.001***
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia									
BASELINE	236		2.63 (2.55)	2.4	0.0, 12.2				
Sample 1	150		2.71 (2.55)	2.6	0.0, 10.3				
Sample 2	86		2.49 (2.56)	1.9	0.0, 12.2				

Note: Sample 1 contains subjects who were enrolled prior to [redacted]20[redacted].
Sample 2 contains subjects who were enrolled on or after [redacted]20[redacted].
Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.7

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Enrollment Sample
(FAS)

Parameter / Time Point / Sample Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 1	225	2.66 (2.56)	2.61 (3.16)	1.5	0.0, 14.9	-0.05 (3.04)	0.0	-8.5, 13.6	0.8070
Sample 1	143	2.77 (2.58)	2.57 (2.98)	1.5	0.0, 14.9	-0.20 (2.64)	0.0	-6.9, 8.8	0.3663
Sample 2	82	2.47 (2.53)	2.68 (3.46)	1.1	0.0, 13.6	0.21 (3.64)	0.0	-8.5, 13.6	0.5974
WEEK 6	205	2.67 (2.62)	2.09 (3.29)	0.5	0.0, 15.4	-0.58 (3.01)	-0.3	-7.8, 11.6	0.0064**
Sample 1	129	2.71 (2.62)	2.11 (3.34)	0.5	0.0, 15.4	-0.61 (3.10)	-0.3	-7.8, 11.6	0.0276*
Sample 2	76	2.60 (2.63)	2.07 (3.21)	0.5	0.0, 14.6	-0.53 (2.87)	-0.4	-7.6, 7.5	0.1119
WEEK 13	114	2.98 (2.75)	1.78 (3.31)	0.0	0.0, 16.0	-1.19 (3.51)	-0.9	-12.2, 13.2	<=0.001***
Sample 1	74	3.19 (2.57)	2.08 (3.53)	0.2	0.0, 16.0	-1.11 (3.51)	-1.2	-7.1, 13.2	0.0081**
Sample 2	40	2.59 (3.05)	1.24 (2.81)	0.0	0.0, 14.4	-1.35 (3.55)	-0.3	-12.2, 7.2	0.0213*
WEEK 26	131	2.43 (2.47)	1.78 (2.93)	0.3	0.0, 15.2	-0.65 (3.24)	-0.1	-12.2, 12.0	0.0227*
Sample 1	77	2.57 (2.45)	1.69 (2.92)	0.0	0.0, 15.2	-0.88 (3.29)	-0.1	-7.4, 12.0	0.0211*
Sample 2	54	2.23 (2.51)	1.91 (2.95)	0.6	0.0, 14.9	-0.32 (3.16)	-0.1	-12.2, 7.8	0.4563
WEEK 39	119	2.43 (2.54)	2.03 (3.53)	0.0	0.0, 16.0	-0.40 (3.48)	0.0	-7.8, 15.4	0.2135
Sample 1	70	2.53 (2.51)	1.70 (2.89)	0.0	0.0, 13.2	-0.83 (3.02)	-0.2	-7.8, 6.1	0.0248*
Sample 2	49	2.28 (2.60)	2.50 (4.27)	0.0	0.0, 16.0	0.22 (3.99)	0.0	-7.8, 15.4	0.7071

Note: Sample 1 contains subjects who were enrolled prior to [redacted]20[redacted].
Sample 2 contains subjects who were enrolled on or after [redacted]20[redacted].
Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.7

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Enrollment Sample
(FAS)

Parameter Time Point Sample Category	N	Baseline Mean (SD)	Visit Mean (SD)	Visit Median	Visit Min, Max	Change from Baseline Mean (SD)	Change from Baseline Median	Change from Baseline Min, Max	Change from Baseline P-Value &
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 52	104	2.49 (2.71)	2.16 (3.85)	0.2	0.0, 16.0	-0.33 (3.38)	0.0	-7.3, 12.9	0.3224
Sample 1	66	2.78 (2.73)	2.71 (4.24)	0.5	0.0, 16.0	-0.07 (3.79)	0.0	-7.3, 12.9	0.8829
Sample 2	38	1.99 (2.63)	1.21 (2.85)	0.0	0.0, 16.0	-0.78 (2.48)	-0.1	-5.2, 4.6	0.0594
Average Daily Normalized 'On' Time With Troublesome Dyskinesia									
BASELINE	236		0.96 (1.73)	0.0	0.0, 10.5				
Sample 1	150		0.81 (1.57)	0.0	0.0, 10.5				
Sample 2	86		1.21 (1.95)	0.0	0.0, 9.2				
WEEK 1	225	0.94 (1.71)	0.99 (2.09)	0.0	0.0, 11.7	0.05 (1.89)	0.0	-6.0, 10.5	0.6962
Sample 1	143	0.82 (1.59)	0.92 (1.97)	0.0	0.0, 10.5	0.10 (1.96)	0.0	-6.0, 10.5	0.5414
Sample 2	82	1.15 (1.90)	1.11 (2.28)	0.0	0.0, 11.7	-0.04 (1.79)	0.0	-4.9, 6.1	0.8432
WEEK 6	205	0.85 (1.61)	0.44 (1.30)	0.0	0.0, 9.0	-0.41 (1.60)	0.0	-9.2, 6.9	<=0.001***
Sample 1	129	0.68 (1.48)	0.34 (1.23)	0.0	0.0, 9.0	-0.34 (1.36)	0.0	-7.2, 5.3	0.0051**
Sample 2	76	1.13 (1.79)	0.61 (1.41)	0.0	0.0, 6.9	-0.52 (1.95)	0.0	-9.2, 6.9	0.0233*
WEEK 13	114	0.83 (1.43)	0.33 (1.12)	0.0	0.0, 8.0	-0.50 (1.45)	0.0	-7.2, 6.0	<=0.001***
Sample 1	74	0.84 (1.49)	0.37 (1.20)	0.0	0.0, 8.0	-0.47 (1.61)	0.0	-7.2, 6.0	0.0139*
Sample 2	40	0.81 (1.34)	0.26 (0.96)	0.0	0.0, 5.5	-0.56 (1.13)	0.0	-4.9, 1.3	0.0036**

Note: Sample 1 contains subjects who were enrolled prior to [redacted]20[redacted].
Sample 2 contains subjects who were enrolled on or after [redacted]20[redacted].
Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.7

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Enrollment Sample
(FAS)

Parameter Time Point Sample Category	N	Baseline Mean (SD)	Visit Mean (SD)	Visit Median	Visit Min, Max	Change from Baseline Mean (SD)	Change from Baseline Median	Change from Baseline Min, Max	Change from Baseline P-Value &
Average Daily Normalized 'On' Time With Troublesome Dyskinesia (Cont.)									
WEEK 26	131	0.77 (1.51)	0.32 (1.38)	0.0	0.0, 12.1	-0.45 (1.85)	0.0	-9.2, 8.8	0.0063**
Sample 1	77	0.52 (1.03)	0.33 (1.17)	0.0	0.0, 8.8	-0.19 (1.52)	0.0	-4.0, 8.8	0.2824
Sample 2	54	1.13 (1.96)	0.30 (1.65)	0.0	0.0, 12.1	-0.82 (2.20)	0.0	-9.2, 7.2	0.0083**
WEEK 39	119	0.72 (1.30)	0.35 (1.06)	0.0	0.0, 8.1	-0.37 (1.34)	0.0	-5.1, 7.3	0.0033**
Sample 1	70	0.57 (1.08)	0.41 (1.21)	0.0	0.0, 8.1	-0.16 (1.43)	0.0	-5.0, 7.3	0.3453
Sample 2	49	0.93 (1.55)	0.27 (0.82)	0.0	0.0, 3.5	-0.66 (1.14)	0.0	-5.1, 0.2	<=0.001***
WEEK 52	104	0.60 (1.17)	0.50 (1.67)	0.0	0.0, 13.5	-0.10 (1.99)	0.0	-5.1, 13.0	0.5986
Sample 1	66	0.63 (1.14)	0.52 (1.29)	0.0	0.0, 6.3	-0.12 (1.69)	0.0	-5.0, 6.3	0.5789
Sample 2	38	0.54 (1.23)	0.46 (2.20)	0.0	0.0, 13.5	-0.08 (2.46)	0.0	-5.1, 13.0	0.8397
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia									
BASELINE	236		9.14 (2.50)	9.4	0.3, 16.0				
Sample 1	150		9.37 (2.29)	9.5	3.4, 16.0				
Sample 2	86		8.75 (2.81)	9.1	0.3, 14.5				
WEEK 1	225	9.15 (2.50)	11.04 (3.68)	11.2	0.0, 16.0	1.89 (3.77)	1.8	-10.4, 11.3	<=0.001***
Sample 1	143	9.37 (2.27)	10.75 (3.43)	10.6	0.0, 16.0	1.38 (3.51)	1.3	-8.0, 9.7	<=0.001***
Sample 2	82	8.76 (2.84)	11.55 (4.05)	12.6	1.2, 16.0	2.79 (4.07)	3.2	-10.4, 11.3	<=0.001***

Note: Sample 1 contains subjects who were enrolled prior to [redacted]20[redacted].
Sample 2 contains subjects who were enrolled on or after [redacted]20[redacted].
Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.7

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary by Enrollment Sample
(FAS)

Parameter Time Point Sample Category	N	Baseline Mean (SD)	Visit Mean (SD)	Visit Median	Visit Min, Max	Change from Baseline Mean (SD)	Change from Baseline Median	Change from Baseline Min, Max	Change from Baseline P-Value &
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia (Cont.)									
WEEK 6	205	9.21 (2.44)	12.01 (3.36)	12.4	0.0, 16.0	2.80 (3.59)	3.2	-9.9, 10.6	<=0.001***
Sample 1	129	9.43 (2.28)	11.96 (3.28)	12.3	1.1, 16.0	2.54 (3.27)	2.9	-6.7, 10.6	<=0.001***
Sample 2	76	8.85 (2.65)	12.10 (3.53)	12.6	0.0, 16.0	3.25 (4.05)	4.0	-9.9, 10.5	<=0.001***
WEEK 13	114	9.65 (2.35)	12.58 (3.61)	13.9	2.6, 16.0	2.93 (3.48)	3.3	-6.3, 9.9	<=0.001***
Sample 1	74	9.86 (2.38)	12.86 (3.37)	14.1	5.3, 16.0	3.00 (3.14)	3.3	-6.3, 9.9	<=0.001***
Sample 2	40	9.26 (2.26)	12.07 (4.01)	13.6	2.6, 16.0	2.81 (4.07)	3.8	-5.0, 9.3	<=0.001***
WEEK 26	131	9.28 (2.60)	13.07 (3.24)	14.3	1.5, 16.0	3.79 (3.54)	3.9	-5.5, 12.5	<=0.001***
Sample 1	77	9.69 (2.43)	13.14 (2.71)	14.0	7.1, 16.0	3.45 (2.81)	3.0	-2.7, 10.6	<=0.001***
Sample 2	54	8.70 (2.74)	12.97 (3.90)	14.9	1.5, 16.0	4.27 (4.36)	4.8	-5.5, 12.5	<=0.001***
WEEK 39	119	9.39 (2.47)	13.00 (3.01)	13.5	2.4, 16.0	3.60 (3.32)	3.4	-9.2, 9.9	<=0.001***
Sample 1	70	9.74 (2.35)	13.08 (3.08)	13.5	2.4, 16.0	3.34 (3.37)	3.2	-9.2, 9.9	<=0.001***
Sample 2	49	8.90 (2.59)	12.87 (2.92)	12.9	3.7, 16.0	3.98 (3.24)	4.2	-5.9, 9.8	<=0.001***
WEEK 52	104	9.52 (2.43)	12.99 (3.14)	13.7	2.5, 16.0	3.46 (3.11)	3.5	-5.4, 11.2	<=0.001***
Sample 1	66	9.68 (2.44)	13.35 (2.61)	14.0	7.2, 16.0	3.67 (2.81)	3.5	-3.1, 11.2	<=0.001***
Sample 2	38	9.25 (2.43)	12.35 (3.86)	13.4	2.5, 16.0	3.10 (3.58)	3.5	-5.4, 10.2	<=0.001***

Note: Sample 1 contains subjects who were enrolled prior to [redacted]20[redacted].
Sample 2 contains subjects who were enrolled on or after [redacted]20[redacted].
Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

表2.7.3.6-20　PD日誌に基づく，標準化した1日あたりの平均「オフ」時間及び「オン」時間の要約（FAS）：M15-737試験（更新時）

[redacted]20[redacted] 10:46 <[redacted]>
ABBV-951
STUDY M15-737 - THIRD INTERIM (CUTOFF [redacted]20[redacted])
R&D/22/0154 - CLINICAL/STATISTICAL

TABLE 14.2__1.1

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary
(FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Average Daily Normalized 'Off' Time									
BASELINE	97		2.55 (2.96)	1.2	0.0, 11.5				
Low Dose	45		2.94 (2.91)	2.6	0.0, 10.9				
High Dose	52		2.21 (2.98)	0.5	0.0, 11.5				
WEEK 12	75	2.84 (3.14)	2.98 (2.83)	2.3	0.0, 10.9	0.14 (2.59)	0.0	-8.2, 10.9	0.6297
Low Dose	38	3.00 (3.09)	2.64 (2.35)	2.5	0.0, 8.0	-0.36 (2.26)	0.0	-8.2, 3.8	0.3332
High Dose	37	2.67 (3.22)	3.33 (3.25)	2.3	0.0, 10.9	0.66 (2.83)	0.0	-6.4, 10.9	0.1630
WEEK 24	75	2.35 (2.64)	3.12 (3.58)	2.3	0.0, 16.0	0.76 (2.99)	0.0	-6.1, 13.3	0.0301*
Low Dose	36	3.03 (2.70)	3.23 (3.75)	2.5	0.0, 16.0	0.20 (3.48)	0.0	-6.1, 13.3	0.7311
High Dose	39	1.73 (2.45)	3.01 (3.47)	2.3	0.0, 13.4	1.28 (2.38)	0.6	-3.3, 7.7	0.0018**
WEEK 36	39	2.27 (2.65)	2.34 (2.66)	1.7	0.0, 12.1	0.07 (1.91)	0.0	-5.5, 5.6	0.8096
Low Dose	21	2.48 (2.52)	2.65 (3.15)	1.9	0.0, 12.1	0.16 (1.87)	0.0	-5.5, 5.6	0.6950
High Dose	18	2.02 (2.85)	1.99 (1.97)	1.7	0.0, 6.1	-0.03 (2.00)	0.0	-3.9, 3.9	0.9516

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours
(i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.1

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary
(FAS)

Parameter Time Point Dose Category	N	Baseline Mean (SD)	Visit Mean (SD)	Visit Median	Visit Min, Max	Change from Baseline Mean (SD)	Change from Baseline Median	Change from Baseline Min, Max	Change from Baseline P-Value &
Average Daily Normalized 'Off' Time (Cont.)									
WEEK 48	52	2.01 (2.42)	2.81 (3.58)	1.2	0.0, 14.3	0.79 (2.27)	0.0	-3.0, 7.4	0.0149*
Low Dose	21	2.11 (2.30)	2.32 (3.11)	0.7	0.0, 10.1	0.21 (2.12)	0.0	-3.0, 7.4	0.6586
High Dose	31	1.95 (2.53)	3.14 (3.88)	1.2	0.0, 14.3	1.19 (2.32)	0.2	-2.0, 6.6	0.0077**
WEEK 60	29	2.54 (2.68)	3.04 (2.84)	2.4	0.0, 10.4	0.50 (1.62)	0.0	-3.0, 3.9	0.1088
Low Dose	16	2.70 (2.44)	2.86 (3.13)	2.2	0.0, 10.4	0.16 (1.59)	-0.0	-3.0, 3.9	0.6897
High Dose	13	2.34 (3.05)	3.26 (2.53)	3.0	0.0, 7.1	0.91 (1.63)	0.9	-2.0, 3.9	0.0660
WEEK 72	12	2.46 (2.66)	3.36 (3.37)	2.8	0.0, 10.4	0.90 (2.48)	-0.0	-2.2, 5.5	0.2342
Low Dose	6	2.16 (2.50)	1.69 (1.66)	1.3	0.0, 3.7	-0.47 (1.03)	-0.2	-2.2, 0.8	0.3183
High Dose	6	2.76 (3.02)	5.03 (3.94)	4.7	0.0, 10.4	2.27 (2.83)	3.0	-1.7, 5.5	0.1064
WEEK 84	2	3.06 (4.33)	5.71 (8.08)	5.7	0.0, 11.4	2.65 (3.75)	2.7	0.0, 5.3	0.5000
Low Dose	1	0.00 (N/A)	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	1	6.13 (N/A)	11.43 (N/A)	11.4	11.4, 11.4	5.30 (N/A)	5.3	5.3, 5.3	

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.1

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary
(FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Average Daily Normalized 'Off' Time (Cont.)									
WEEK 96	1	0.00 (N/A)	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
Low Dose	1	0.00 (N/A)	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	0								
Average Daily Normalized 'On' Time Without Dyskinesia									
BASELINE	97		10.66 (4.84)	11.6	0.0, 16.0				
Low Dose	45		10.82 (4.46)	11.7	0.0, 16.0				
High Dose	52		10.52 (5.19)	11.5	0.0, 16.0				
WEEK 12	75	10.66 (4.91)	10.83 (4.63)	11.7	0.0, 16.0	0.17 (3.71)	0.0	-10.9, 14.2	0.6998
Low Dose	38	10.94 (4.51)	11.18 (4.68)	12.8	0.0, 16.0	0.24 (3.79)	0.0	-6.7, 14.2	0.6931
High Dose	37	10.38 (5.33)	10.47 (4.62)	10.8	0.0, 16.0	0.09 (3.69)	0.0	-10.9, 9.0	0.8886
WEEK 24	75	10.66 (4.81)	10.58 (4.76)	10.7	0.0, 16.0	-0.09 (4.47)	0.0	-13.3, 14.2	0.8695
Low Dose	36	10.64 (4.39)	10.50 (5.14)	10.7	0.0, 16.0	-0.14 (4.57)	0.0	-13.3, 14.2	0.8590
High Dose	39	10.69 (5.22)	10.65 (4.44)	10.6	0.0, 16.0	-0.04 (4.43)	0.0	-9.6, 13.7	0.9578

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.1

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary
(FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 36	39	11.45 (4.51)	11.47 (4.73)	12.1	0.0, 16.0	0.02 (4.39)	0.0	-11.2, 14.2	0.9723
Low Dose	21	12.11 (3.82)	12.28 (4.45)	14.0	1.3, 16.0	0.16 (3.99)	0.0	-5.9, 14.2	0.8524
High Dose	18	10.67 (5.21)	10.53 (4.99)	11.9	0.0, 16.0	-0.14 (4.94)	0.1	-11.2, 14.0	0.9070
WEEK 48	52	10.49 (5.06)	10.98 (4.69)	11.4	0.0, 16.0	0.49 (4.82)	0.0	-9.4, 14.9	0.4648
Low Dose	21	10.83 (5.04)	11.33 (4.75)	12.4	1.1, 16.0	0.50 (5.34)	0.0	-8.0, 13.7	0.6710
High Dose	31	10.26 (5.15)	10.74 (4.71)	10.7	0.0, 16.0	0.49 (4.53)	0.0	-9.4, 14.9	0.5549
WEEK 60	29	10.16 (4.90)	10.85 (4.09)	10.3	0.8, 16.0	0.69 (4.13)	0.0	-6.1, 13.9	0.3752
Low Dose	16	10.42 (4.59)	10.73 (4.54)	10.2	0.8, 16.0	0.31 (4.96)	-0.7	-6.1, 13.9	0.8086
High Dose	13	9.83 (5.43)	10.99 (3.63)	12.1	4.3, 16.0	1.16 (2.92)	0.3	-3.9, 6.3	0.1757
WEEK 72	12	10.96 (4.52)	11.11 (4.62)	12.2	1.4, 16.0	0.15 (4.68)	0.0	-9.9, 9.8	0.9155
Low Dose	6	13.60 (2.96)	14.03 (1.84)	14.1	11.9, 16.0	0.42 (1.43)	0.0	-0.8, 3.2	0.5010
High Dose	6	8.32 (4.40)	8.19 (4.81)	8.6	1.4, 14.1	-0.13 (6.78)	-0.2	-9.9, 9.8	0.9641

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.1

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary
(FAS)

Parameter Time Point Dose Category	N	Baseline Mean (SD)	Visit Mean (SD)	Visit Median	Visit Min, Max	Change from Baseline Mean (SD)	Change from Baseline Median	Change from Baseline Min, Max	Change from Baseline P-Value &
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 84	2	12.03 (5.62)	10.29 (8.08)	10.3	4.6, 16.0	-1.74 (2.46)	-1.7	-3.5, 0.0	0.5000
Low Dose	1	16.00 (N/A)	16.00 (N/A)	16.0	16.0, 16.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	1	8.05 (N/A)	4.57 (N/A)	4.6	4.6, 4.6	-3.48 (N/A)	-3.5	-3.5, -3.5	
WEEK 96	1	16.00 (N/A)	16.00 (N/A)	16.0	16.0, 16.0	0.00 (N/A)	0.0	0.0, 0.0	
Low Dose	1	16.00 (N/A)	16.00 (N/A)	16.0	16.0, 16.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	0								
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia									
BASELINE	97		2.31 (4.14)	0.3	0.0, 16.0				
Low Dose	45		1.75 (3.51)	0.0	0.0, 16.0				
High Dose	52		2.78 (4.60)	0.4	0.0, 16.0				
WEEK 12	75	1.98 (3.99)	1.83 (3.55)	0.0	0.0, 16.0	-0.15 (3.77)	0.0	-15.8, 11.6	0.7321
Low Dose	38	1.49 (3.32)	1.75 (3.28)	0.0	0.0, 12.4	0.26 (3.82)	0.0	-11.6, 11.6	0.6791
High Dose	37	2.49 (4.56)	1.92 (3.85)	0.0	0.0, 16.0	-0.57 (3.72)	0.0	-15.8, 6.7	0.3589

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.1

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary
(FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	Change from Baseline: P-Value &
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 24	75	2.57 (4.21)	1.90 (3.44)	0.0	0.0, 16.0	-0.67 (3.87)	0.0	-16.0, 6.2	0.1385
Low Dose	36	2.11 (3.84)	1.94 (3.56)	0.0	0.0, 16.0	-0.17 (3.49)	0.0	-12.0, 6.2	0.7708
High Dose	39	2.99 (4.52)	1.86 (3.37)	0.0	0.0, 16.0	-1.13 (4.18)	0.0	-16.0, 6.1	0.0997
WEEK 36	39	2.01 (3.45)	2.01 (4.01)	0.0	0.0, 16.0	-0.00 (3.83)	0.0	-12.9, 11.2	0.9937
Low Dose	21	1.26 (2.89)	1.00 (2.49)	0.0	0.0, 11.1	-0.27 (2.83)	0.0	-11.6, 4.4	0.6718
High Dose	18	2.88 (3.92)	3.18 (5.10)	0.1	0.0, 16.0	0.30 (4.81)	0.0	-12.9, 11.2	0.7954
WEEK 48	52	3.16 (4.69)	1.90 (3.31)	0.1	0.0, 14.9	-1.25 (4.17)	0.0	-12.9, 8.0	0.0351*
Low Dose	21	2.76 (4.75)	2.30 (4.26)	0.0	0.0, 14.9	-0.47 (4.14)	0.0	-11.1, 8.0	0.6105
High Dose	31	3.42 (4.70)	1.64 (2.53)	0.2	0.0, 9.8	-1.78 (4.17)	0.0	-12.9, 4.9	0.0238*
WEEK 60	29	2.71 (4.41)	1.98 (2.73)	0.9	0.0, 11.6	-0.73 (3.81)	0.0	-11.3, 5.7	0.3101
Low Dose	16	2.51 (4.11)	2.36 (3.21)	1.0	0.0, 11.6	-0.15 (4.24)	0.0	-11.3, 5.7	0.8919
High Dose	13	2.95 (4.91)	1.50 (2.01)	0.0	0.0, 5.8	-1.45 (3.21)	-0.2	-10.2, 1.1	0.1298

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.1

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary
(FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 72	12	2.06 (4.60)	0.94 (1.30)	0.2	0.0, 4.2	-1.12 (4.18)	0.0	-14.2, 1.4	0.3725
Low Dose	6	0.24 (0.59)	0.28 (0.50)	0.0	0.0, 1.2	0.04 (0.71)	0.0	-1.0, 1.2	0.8905
High Dose	6	3.88 (6.19)	1.59 (1.55)	1.6	0.0, 4.2	-2.29 (5.90)	-0.2	-14.2, 1.4	0.3855
WEEK 84	2	0.91 (1.29)	0.00 (0.00)	0.0	0.0, 0.0	-0.91 (1.29)	-0.9	-1.8, 0.0	0.5000
Low Dose	1	0.00 (N/A)	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	1	1.82 (N/A)	0.00 (N/A)	0.0	0.0, 0.0	-1.82 (N/A)	-1.8	-1.8, -1.8	
WEEK 96	1	0.00 (N/A)	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
Low Dose	1	0.00 (N/A)	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	0								
Average Daily Normalized 'On' Time With Troublesome Dyskinesia									
BASELINE	97		0.48 (1.69)	0.0	0.0, 13.5				
Low Dose	45		0.48 (2.09)	0.0	0.0, 13.5				
High Dose	52		0.49 (1.27)	0.0	0.0, 6.3				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.1

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary
(FAS)

Parameter Time Point Dose Category	N	Baseline Mean (SD)	Visit Mean (SD)	Visit Median	Visit Min, Max	Change from Baseline Mean (SD)	Change from Baseline Median	Change from Baseline Min, Max	Change from Baseline P-Value &
Average Daily Normalized 'On' Time With Troublesome Dyskinesia (Cont.)									
WEEK 12	75	0.52 (1.79)	0.36 (1.49)	0.0	0.0, 11.0	-0.16 (2.31)	0.0	-13.5, 11.0	0.5486
Low Dose	38	0.57 (2.27)	0.43 (1.90)	0.0	0.0, 11.0	-0.14 (3.04)	0.0	-13.5, 11.0	0.7716
High Dose	37	0.46 (1.12)	0.28 (0.92)	0.0	0.0, 4.4	-0.18 (1.24)	0.0	-5.3, 3.0	0.3861
WEEK 24	75	0.41 (1.17)	0.41 (1.36)	0.0	0.0, 7.8	-0.01 (1.32)	0.0	-5.3, 6.4	0.9538
Low Dose	36	0.22 (0.73)	0.33 (1.31)	0.0	0.0, 7.8	0.11 (1.32)	0.0	-3.3, 6.4	0.6330
High Dose	39	0.59 (1.45)	0.48 (1.42)	0.0	0.0, 7.2	-0.12 (1.33)	0.0	-5.3, 4.3	0.5931
WEEK 36	39	0.27 (1.00)	0.18 (0.57)	0.0	0.0, 2.8	-0.09 (1.04)	0.0	-5.3, 1.8	0.5758
Low Dose	21	0.14 (0.58)	0.08 (0.28)	0.0	0.0, 1.2	-0.06 (0.66)	0.0	-2.7, 1.2	0.6773
High Dose	18	0.42 (1.34)	0.29 (0.77)	0.0	0.0, 2.8	-0.13 (1.37)	0.0	-5.3, 1.8	0.6888
WEEK 48	52	0.34 (0.86)	0.31 (1.00)	0.0	0.0, 6.2	-0.03 (1.26)	0.0	-3.3, 6.2	0.8428
Low Dose	21	0.30 (0.90)	0.06 (0.17)	0.0	0.0, 0.7	-0.24 (0.94)	0.0	-3.3, 0.7	0.2516
High Dose	31	0.37 (0.85)	0.48 (1.27)	0.0	0.0, 6.2	0.11 (1.44)	0.0	-3.0, 6.2	0.6876

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.1

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary
(FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Average Daily Normalized 'On' Time With Troublesome Dyskinesia (Cont.)									
WEEK 60	29	0.60 (1.42)	0.14 (0.36)	0.0	0.0, 1.5	-0.46 (1.46)	0.0	-6.3, 1.5	0.1021
Low Dose	16	0.37 (1.03)	0.05 (0.16)	0.0	0.0, 0.6	-0.32 (1.06)	0.0	-3.3, 0.6	0.2452
High Dose	13	0.88 (1.79)	0.25 (0.50)	0.0	0.0, 1.5	-0.63 (1.88)	0.0	-6.3, 1.5	0.2504
WEEK 72	12	0.52 (1.80)	0.60 (1.46)	0.0	0.0, 5.0	0.08 (2.04)	0.0	-4.6, 5.0	0.9006
Low Dose	6	0.00 (0.00)	0.00 (0.00)	0.0	0.0, 0.0	0.00 (0.00)	0.0	0.0, 0.0	
High Dose	6	1.04 (2.55)	1.19 (1.96)	0.3	0.0, 5.0	0.15 (3.02)	0.0	-4.6, 5.0	0.9077
WEEK 84	2	0.00 (0.00)	0.00 (0.00)	0.0	0.0, 0.0	0.00 (0.00)	0.0	0.0, 0.0	
Low Dose	1	0.00 (N/A)	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	1	0.00 (N/A)	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
WEEK 96	1	0.00 (N/A)	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
Low Dose	1	0.00 (N/A)	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	0								

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.1

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary
(FAS)

Parameter Time Point Dose Category	N	Baseline Mean (SD)	Visit Mean (SD)	Visit Median	Visit Min, Max	Change from Baseline Mean (SD)	Change from Baseline Median	Change from Baseline Min, Max	Change from Baseline P-Value &
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia									
BASELINE	97		12.96 (3.22)	13.7	2.5, 16.0				
Low Dose	45		12.57 (3.24)	13.3	2.5, 16.0				
High Dose	52		13.30 (3.19)	15.1	4.5, 16.0				
WEEK 12	75	12.65 (3.40)	12.66 (3.09)	13.5	5.0, 16.0	0.02 (3.35)	0.0	-11.0, 11.6	0.9662
Low Dose	38	12.43 (3.44)	12.93 (2.86)	13.4	5.0, 16.0	0.50 (3.57)	0.0	-11.0, 11.6	0.3906
High Dose	37	12.87 (3.39)	12.38 (3.33)	13.7	5.1, 16.0	-0.48 (3.07)	0.0	-10.9, 6.4	0.3455
WEEK 24	75	13.23 (2.75)	12.48 (3.78)	13.6	0.0, 16.0	-0.75 (3.10)	-0.1	-13.3, 6.1	0.0386*
Low Dose	36	12.75 (2.66)	12.45 (3.98)	13.5	0.0, 16.0	-0.31 (3.57)	0.0	-13.3, 6.1	0.6089
High Dose	39	13.67 (2.79)	12.51 (3.64)	13.7	2.6, 16.0	-1.17 (2.57)	-0.7	-7.7, 3.3	0.0074**
WEEK 36	39	13.46 (2.72)	13.48 (2.68)	14.1	3.9, 16.0	0.02 (2.10)	0.0	-5.6, 5.5	0.9535
Low Dose	21	13.38 (2.45)	13.28 (3.21)	14.1	3.9, 16.0	-0.10 (2.03)	0.0	-5.6, 5.5	0.8212
High Dose	18	13.55 (3.08)	13.72 (1.96)	14.1	9.9, 16.0	0.16 (2.23)	0.0	-3.9, 4.3	0.7629

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.1

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary
(FAS)

Parameter Time Point Dose Category	N	Baseline Mean (SD)	Visit Mean (SD)	Visit Median	Visit Min, Max	Change from Baseline Mean (SD)	Change from Baseline Median	Change from Baseline Min, Max	Change from Baseline P-Value &
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia (Cont.)									
WEEK 48	52	13.64 (2.54)	12.88 (3.63)	14.4	1.7, 16.0	-0.76 (2.66)	0.0	-7.4, 3.8	0.0445*
Low Dose	21	13.59 (2.24)	13.63 (3.15)	15.3	5.9, 16.0	0.03 (2.41)	0.0	-7.4, 3.8	0.9491
High Dose	31	13.68 (2.76)	12.38 (3.88)	13.8	1.7, 16.0	-1.30 (2.72)	-0.3	-6.6, 2.3	0.0125*
WEEK 60	29	12.86 (2.80)	12.82 (2.87)	13.0	5.6, 16.0	-0.04 (2.02)	0.0	-3.9, 5.3	0.9148
Low Dose	16	12.93 (2.26)	13.09 (3.12)	13.8	5.6, 16.0	0.16 (1.70)	0.0	-3.9, 3.0	0.7135
High Dose	13	12.78 (3.45)	12.49 (2.60)	12.9	7.8, 16.0	-0.29 (2.41)	-0.5	-3.9, 5.3	0.6761
WEEK 72	12	13.02 (2.85)	12.04 (3.79)	13.2	5.6, 16.0	-0.98 (3.98)	0.0	-10.4, 5.1	0.4138
Low Dose	6	13.84 (2.50)	14.31 (1.66)	14.7	12.3, 16.0	0.47 (1.03)	0.2	-0.8, 2.2	0.3183
High Dose	6	12.20 (3.15)	9.78 (4.07)	9.5	5.6, 14.3	-2.42 (5.37)	-3.2	-10.4, 5.1	0.3201
WEEK 84	2	12.94 (4.33)	10.29 (8.08)	10.3	4.6, 16.0	-2.65 (3.75)	-2.7	-5.3, 0.0	0.5000
Low Dose	1	16.00 (N/A)	16.00 (N/A)	16.0	16.0, 16.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	1	9.87 (N/A)	4.57 (N/A)	4.6	4.6, 4.6	-5.30 (N/A)	-5.3	-5.3, -5.3	

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.1

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based on Parkinson's Disease Diary
(FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit Mean (SD)	Visit Median	Visit Min, Max	Change from Baseline Mean (SD)	Change from Baseline Median	Change from Baseline Min, Max	P-Value &
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia (Cont.)									
WEEK 96	1	16.00 (N/A)	16.00 (N/A)	16.0	16.0, 16.0	0.00 (N/A)	0.0	0.0, 0.0	
Low Dose	1	16.00 (N/A)	16.00 (N/A)	16.0	16.0, 16.0	0.00 (N/A)	0.0	0.0, 0.0	
High Dose	0								

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

表2.7.3.6-21　MDS-UPDRSスコア（FAS）：M15-741試験（更新時）

[redacted]20[redacted] 10:50 <[redacted]>
ABBV-951
STUDY M15-741 - THIRD INTERIM (CUTOFF [redacted]20[redacted])
R&D/22/0153 - CLINICAL/STATISTICAL

TABLE 14.2__2.1

Change from Baseline to Each Planned Visit in Parkinson's Disease Symptoms as Assessed
by The Movement Disorder Society-Unified Parkinson's Disease Rating Scale Score by Part and Total
(FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
MDS-UPDRS Total Score of Parts I-III									
BASELINE	244		50.4 (18.89)	50.0	13, 117				
Low dose	132		49.9 (19.55)	46.5	13, 117				
High dose	112		51.0 (18.15)	51.0	14, 109				
DAY 2	222	51.0 (18.94)	45.9 (20.28)	44.0	4, 100	-5.0 (12.19)	-4.0	-42, 38	<=0.001***
Low dose	121	49.9 (19.43)	43.9 (18.94)	42.0	5, 100	-6.0 (11.67)	-4.0	-42, 28	<=0.001***
High dose	101	52.2 (18.35)	48.3 (21.62)	46.0	4, 100	-3.9 (12.76)	-4.0	-36, 38	0.0028**
WEEK 1	224	50.4 (19.14)	46.4 (22.58)	43.0	3, 114	-4.0 (16.62)	-4.0	-45, 68	<=0.001***
Low dose	119	49.6 (19.70)	45.2 (21.66)	42.0	3, 109	-4.3 (15.85)	-3.0	-45, 68	0.0034**
High dose	105	51.4 (18.53)	47.8 (23.61)	43.0	10, 114	-3.6 (17.53)	-6.0	-41, 51	0.0378*
WEEK 2	211	50.2 (18.40)	47.5 (23.46)	44.0	2, 114	-2.6 (18.19)	-5.0	-39, 60	0.0367*
Low dose	118	50.0 (19.16)	48.6 (23.95)	44.0	2, 111	-1.4 (18.47)	-5.5	-35, 60	0.4011
High dose	93	50.4 (17.47)	46.2 (22.88)	44.0	6, 114	-4.2 (17.81)	-5.0	-39, 49	0.0268*
WEEK 3	203	49.9 (18.72)	46.8 (22.87)	45.0	1, 135	-3.2 (18.50)	-4.0	-50, 94	0.0156*
Low dose	108	49.2 (18.82)	47.2 (23.93)	43.0	1, 135	-2.0 (18.01)	-3.0	-39, 94	0.2531
High dose	95	50.7 (18.66)	46.2 (21.73)	45.0	7, 104	-4.5 (19.06)	-5.0	-50, 58	0.0234*
WEEK 4	201	49.8 (18.65)	45.3 (22.94)	41.0	5, 107	-4.5 (18.42)	-6.0	-53, 63	<=0.001***
Low dose	109	48.9 (18.69)	47.2 (24.53)	40.0	5, 107	-1.7 (19.35)	-4.0	-43, 63	0.3699
High dose	92	50.9 (18.65)	42.9 (20.80)	41.0	6, 106	-7.9 (16.73)	-8.0	-53, 34	<=0.001***

&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 2.1

Change from Baseline to Each Planned Visit in Parkinson's Disease Symptoms as Assessed by The Movement Disorder Society-Unified Parkinson's Disease Rating Scale Score by Part and Total (FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
MDS-UPDRS Total Score of Parts I-III									
WEEK 6	193	50.2 (18.90)	46.5 (22.63)	43.0	3, 118	-3.7 (19.60)	-6.0	-59, 75	0.0099**
Low dose	105	49.5 (18.87)	48.4 (25.11)	43.0	5, 118	-1.0 (21.92)	-5.0	-39, 75	0.6282
High dose	88	51.1 (19.00)	44.2 (19.14)	43.0	3, 93	-6.8 (15.98)	-6.0	-59, 44	<=0.001***
WEEK 13	162	50.0 (18.48)	44.7 (22.63)	39.0	10, 141	-5.3 (19.94)	-6.0	-58, 66	<=0.001***
Low dose	92	48.8 (17.30)	45.6 (23.90)	41.0	11, 141	-3.2 (21.10)	-5.0	-51, 66	0.1470
High dose	70	51.6 (19.94)	43.5 (20.96)	39.0	10, 103	-8.1 (18.09)	-8.0	-58, 34	<=0.001***
WEEK 26	139	50.4 (18.11)	47.3 (21.75)	45.0	7, 122	-3.1 (17.34)	-2.0	-55, 39	0.0364*
Low dose	76	49.2 (17.36)	47.0 (23.65)	44.0	7, 122	-2.2 (16.90)	-2.0	-40, 39	0.2550
High dose	63	51.8 (19.00)	47.7 (19.39)	47.0	11, 95	-4.2 (17.93)	-2.0	-55, 24	0.0695
WEEK 39	125	49.9 (18.23)	49.0 (24.28)	47.0	11, 132	-0.9 (20.16)	-1.0	-58, 60	0.6010
Low dose	73	49.1 (17.49)	48.0 (25.69)	46.0	15, 132	-1.1 (19.34)	-3.0	-42, 60	0.6212
High dose	52	51.1 (19.33)	50.4 (22.33)	47.5	11, 98	-0.7 (21.45)	2.0	-58, 55	0.8159
WEEK 52	120	50.2 (18.32)	48.3 (23.19)	47.0	6, 117	-1.9 (19.58)	-2.5	-50, 47	0.2816
Low dose	68	48.0 (17.18)	47.5 (23.23)	46.0	8, 117	-0.6 (19.33)	-1.5	-50, 47	0.8074
High dose	52	53.1 (19.51)	49.3 (23.31)	47.0	6, 105	-3.7 (19.96)	-3.5	-49, 47	0.1858

&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 2.1

Change from Baseline to Each Planned Visit in Parkinson's Disease Symptoms as Assessed by The Movement Disorder Society-Unified Parkinson's Disease Rating Scale Score by Part and Total (FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
MDS-UPDRS Part I Score									
BASELINE	244		11.1 (6.39)	10.0	0, 37				
Low dose	132		11.0 (6.66)	10.0	0, 31				
High dose	112		11.3 (6.09)	10.0	1, 37				
DAY 2	222	11.2 (6.41)	9.0 (5.86)	8.0	0, 32	-2.3 (4.00)	-1.0	-16, 6	<=0.001***
Low dose	121	11.1 (6.69)	8.5 (5.91)	7.0	0, 32	-2.6 (4.27)	-2.0	-16, 6	<=0.001***
High dose	101	11.4 (6.08)	9.6 (5.76)	9.0	0, 27	-1.9 (3.62)	-1.0	-14, 6	<=0.001***
WEEK 1	225	11.3 (6.48)	8.3 (5.73)	7.0	0, 32	-3.0 (5.62)	-3.0	-29, 18	<=0.001***
Low dose	120	11.2 (6.73)	8.5 (6.05)	7.0	0, 30	-2.6 (5.74)	-2.0	-18, 18	<=0.001***
High dose	105	11.5 (6.20)	8.0 (5.34)	7.0	0, 32	-3.4 (5.48)	-3.0	-29, 11	<=0.001***
WEEK 2	212	11.1 (6.08)	8.8 (5.71)	8.0	0, 27	-2.3 (5.20)	-2.0	-18, 11	<=0.001***
Low dose	118	10.9 (6.52)	8.6 (5.85)	8.0	0, 27	-2.3 (5.42)	-2.0	-18, 11	<=0.001***
High dose	94	11.2 (5.50)	9.0 (5.54)	8.0	0, 26	-2.2 (4.95)	-2.0	-15, 8	<=0.001***
WEEK 3	203	11.1 (6.31)	8.5 (5.58)	7.0	0, 31	-2.6 (5.77)	-2.0	-22, 10	<=0.001***
Low dose	108	11.2 (6.49)	8.9 (6.18)	7.5	0, 31	-2.3 (5.63)	-2.0	-16, 10	<=0.001***
High dose	95	11.1 (6.14)	8.1 (4.82)	7.0	0, 23	-2.9 (5.94)	-2.0	-22, 9	<=0.001***
WEEK 4	203	11.1 (6.31)	8.8 (5.81)	8.0	0, 36	-2.3 (5.88)	-2.0	-21, 27	<=0.001***
Low dose	110	11.0 (6.53)	9.3 (6.71)	8.0	0, 36	-1.7 (6.24)	-2.0	-16, 27	0.0058**
High dose	93	11.2 (6.07)	8.1 (4.47)	8.0	0, 22	-3.1 (5.37)	-2.0	-21, 9	<=0.001***

&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 2.1

Change from Baseline to Each Planned Visit in Parkinson's Disease Symptoms as Assessed by The Movement Disorder Society-Unified Parkinson's Disease Rating Scale Score by Part and Total (FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
MDS-UPDRS Part I Score									
WEEK 6	193	11.1 (6.20)	9.8 (6.42)	9.0	0, 39	-1.4 (6.21)	-2.0	-17, 30	0.0026**
Low dose	105	11.3 (6.52)	10.3 (7.20)	9.0	1, 39	-1.0 (7.07)	-2.0	-17, 30	0.1580
High dose	88	10.9 (5.83)	9.1 (5.30)	9.0	0, 23	-1.8 (5.00)	-2.0	-16, 15	<=0.001***
WEEK 13	170	11.4 (6.24)	9.7 (5.77)	8.0	0, 30	-1.7 (5.69)	-2.0	-18, 16	<=0.001***
Low dose	94	11.3 (6.46)	9.5 (5.68)	8.0	0, 30	-1.8 (5.77)	-2.0	-18, 14	0.0034**
High dose	76	11.5 (5.99)	9.8 (5.92)	8.0	1, 28	-1.7 (5.62)	-2.0	-15, 16	0.0103*
WEEK 26	148	11.6 (6.26)	10.7 (6.24)	10.0	1, 29	-0.9 (5.42)	-1.0	-21, 15	0.0354*
Low dose	80	11.2 (6.17)	10.1 (6.08)	9.0	1, 25	-1.1 (4.99)	-1.0	-12, 15	0.0550
High dose	68	12.2 (6.36)	11.4 (6.39)	10.5	1, 29	-0.8 (5.92)	0.0	-21, 9	0.2813
WEEK 39	130	11.2 (6.23)	11.0 (6.33)	10.0	0, 26	-0.2 (5.84)	-1.0	-14, 14	0.6533
Low dose	73	11.0 (6.25)	10.6 (6.49)	9.0	0, 26	-0.4 (5.83)	-1.0	-14, 14	0.5623
High dose	57	11.6 (6.24)	11.6 (6.13)	11.0	2, 25	-0.0 (5.91)	-1.0	-12, 13	0.9822
WEEK 52	120	11.3 (6.39)	10.5 (5.87)	10.0	0, 27	-0.8 (5.87)	-1.0	-17, 14	0.1379
Low dose	68	10.8 (6.35)	10.3 (5.52)	10.0	0, 27	-0.5 (5.34)	-1.0	-13, 11	0.4837
High dose	52	12.0 (6.44)	10.8 (6.35)	10.0	2, 25	-1.3 (6.52)	-1.0	-17, 14	0.1728

&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 2.1

Change from Baseline to Each Planned Visit in Parkinson's Disease Symptoms as Assessed by The Movement Disorder Society-Unified Parkinson's Disease Rating Scale Score by Part and Total (FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
MDS-UPDRS Part II Score									
BASELINE	244		15.8 (7.38)	15.0	1, 37				
Low dose	132		15.2 (7.48)	14.5	1, 36				
High dose	112		16.4 (7.23)	16.0	2, 37				
DAY 2	222	15.9 (7.52)	13.9 (7.62)	13.0	0, 35	-2.1 (4.47)	-1.0	-19, 12	<=0.001***
Low dose	121	15.1 (7.62)	12.4 (7.12)	11.0	0, 31	-2.7 (4.54)	-1.0	-15, 6	<=0.001***
High dose	101	16.9 (7.33)	15.6 (7.86)	15.0	0, 35	-1.3 (4.26)	-1.0	-19, 12	0.0038**
WEEK 1	225	15.8 (7.39)	12.0 (7.32)	11.0	0, 34	-3.8 (5.39)	-4.0	-18, 14	<=0.001***
Low dose	120	15.0 (7.42)	11.4 (7.16)	10.0	0, 30	-3.7 (4.94)	-3.0	-17, 8	<=0.001***
High dose	105	16.7 (7.29)	12.8 (7.46)	12.0	1, 34	-3.9 (5.88)	-4.0	-18, 14	<=0.001***
WEEK 2	212	15.8 (7.21)	12.5 (7.69)	11.0	0, 37	-3.3 (6.26)	-4.0	-19, 18	<=0.001***
Low dose	118	15.4 (7.35)	12.1 (7.67)	11.0	0, 33	-3.3 (6.03)	-3.5	-19, 16	<=0.001***
High dose	94	16.4 (7.02)	13.1 (7.73)	12.0	0, 37	-3.4 (6.56)	-4.0	-18, 18	<=0.001***
WEEK 3	203	15.9 (7.30)	12.2 (7.47)	12.0	0, 37	-3.7 (6.21)	-3.0	-23, 12	<=0.001***
Low dose	108	15.2 (7.18)	11.7 (7.74)	11.0	0, 37	-3.5 (5.81)	-3.0	-19, 12	<=0.001***
High dose	95	16.6 (7.39)	12.8 (7.15)	12.0	0, 34	-3.8 (6.66)	-2.0	-23, 12	<=0.001***
WEEK 4	203	15.8 (7.26)	12.2 (6.92)	11.0	0, 31	-3.7 (5.98)	-4.0	-29, 12	<=0.001***
Low dose	110	15.2 (7.18)	12.5 (7.40)	11.5	0, 31	-2.7 (5.47)	-3.0	-14, 12	<=0.001***
High dose	93	16.6 (7.31)	11.8 (6.33)	11.0	1, 28	-4.9 (6.36)	-4.0	-29, 7	<=0.001***

&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 2.1

Change from Baseline to Each Planned Visit in Parkinson's Disease Symptoms as Assessed by The Movement Disorder Society-Unified Parkinson's Disease Rating Scale Score by Part and Total (FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
MDS-UPDRS Part II Score									
WEEK 6	193	15.8 (7.15)	12.5 (7.42)	12.0	0, 32	-3.3 (6.41)	-3.0	-22, 17	<=0.001***
Low dose	105	15.1 (7.01)	12.6 (8.00)	12.0	0, 32	-2.5 (6.56)	-3.0	-16, 17	<=0.001***
High dose	88	16.5 (7.29)	12.3 (6.72)	12.0	0, 31	-4.2 (6.12)	-3.0	-22, 10	<=0.001***
WEEK 13	170	15.8 (7.06)	12.1 (7.06)	11.0	0, 35	-3.7 (6.50)	-3.0	-24, 15	<=0.001***
Low dose	94	15.1 (6.89)	11.9 (7.40)	11.0	0, 35	-3.2 (6.41)	-3.5	-19, 15	<=0.001***
High dose	76	16.6 (7.23)	12.3 (6.67)	11.0	2, 31	-4.3 (6.60)	-3.0	-24, 7	<=0.001***
WEEK 26	148	15.9 (7.07)	12.7 (7.55)	12.0	0, 38	-3.2 (6.65)	-3.0	-21, 21	<=0.001***
Low dose	80	15.0 (6.89)	12.4 (7.85)	10.5	0, 38	-2.6 (6.24)	-3.0	-15, 21	<=0.001***
High dose	68	17.0 (7.19)	13.0 (7.22)	13.0	0, 33	-3.9 (7.08)	-3.0	-21, 10	<=0.001***
WEEK 39	130	15.3 (6.76)	12.2 (7.60)	11.0	0, 38	-3.1 (6.70)	-2.0	-21, 19	<=0.001***
Low dose	73	14.6 (6.73)	12.1 (8.36)	11.0	1, 38	-2.5 (6.46)	-3.0	-16, 19	0.0014**
High dose	57	16.1 (6.76)	12.2 (6.58)	12.0	0, 27	-3.9 (6.98)	-2.0	-21, 8	<=0.001***
WEEK 52	120	15.3 (7.03)	12.3 (7.47)	12.0	0, 35	-3.0 (7.17)	-3.0	-19, 18	<=0.001***
Low dose	68	14.1 (6.48)	12.3 (7.93)	11.0	0, 35	-1.8 (6.87)	-2.0	-14, 18	0.0378*
High dose	52	16.8 (7.47)	12.2 (6.88)	12.0	1, 29	-4.6 (7.31)	-4.5	-19, 13	<=0.001***

&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 2.1

Change from Baseline to Each Planned Visit in Parkinson's Disease Symptoms as Assessed by The Movement Disorder Society-Unified Parkinson's Disease Rating Scale Score by Part and Total (FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
MDS-UPDRS Part III Score									
BASELINE	244		23.5 (11.47)	23.0	2, 63				
Low dose	132		23.7 (11.85)	22.0	2, 63				
High dose	112		23.2 (11.05)	23.0	3, 55				
DAY 2	222	23.8 (11.44)	23.1 (12.96)	21.0	1, 66	-0.7 (8.78)	-1.0	-24, 30	0.2315
Low dose	121	23.7 (11.69)	23.0 (12.25)	21.0	1, 66	-0.6 (8.43)	-1.0	-24, 30	0.4080
High dose	101	23.9 (11.18)	23.1 (13.83)	21.0	1, 59	-0.8 (9.23)	-1.0	-20, 28	0.3904
WEEK 1	224	23.3 (11.62)	26.1 (14.93)	25.0	0, 76	2.8 (11.31)	1.0	-36, 67	<=0.001***
Low dose	119	23.4 (11.90)	25.4 (14.19)	24.0	0, 76	1.9 (11.53)	1.0	-36, 67	0.0719
High dose	105	23.2 (11.35)	27.0 (15.76)	26.0	1, 70	3.7 (11.04)	2.0	-17, 37	<=0.001***
WEEK 2	211	23.3 (11.41)	26.2 (14.91)	23.0	0, 77	2.9 (12.18)	2.0	-29, 68	<=0.001***
Low dose	118	23.7 (11.66)	27.9 (15.17)	24.0	0, 77	4.2 (12.98)	2.5	-29, 68	<=0.001***
High dose	93	22.8 (11.12)	24.1 (14.38)	23.0	1, 68	1.3 (10.94)	0.0	-24, 35	0.2401
WEEK 3	203	22.9 (11.06)	26.0 (14.64)	24.0	0, 84	3.1 (12.02)	2.0	-24, 75	<=0.001***
Low dose	108	22.9 (11.03)	26.7 (14.66)	24.0	0, 84	3.8 (11.94)	2.0	-20, 75	0.0013**
High dose	95	23.0 (11.15)	25.3 (14.67)	24.0	3, 66	2.3 (12.13)	1.0	-24, 40	0.0707
WEEK 4	200	23.0 (10.97)	24.4 (15.00)	22.0	0, 80	1.5 (12.05)	0.0	-36, 53	0.0891
Low dose	108	22.7 (10.84)	25.5 (15.35)	22.5	0, 80	2.8 (12.80)	1.0	-23, 53	0.0251*
High dose	92	23.2 (11.18)	23.1 (14.55)	21.0	1, 75	-0.1 (10.97)	0.0	-36, 48	0.9170

&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 2.1

Change from Baseline to Each Planned Visit in Parkinson's Disease Symptoms as Assessed by The Movement Disorder Society-Unified Parkinson's Disease Rating Scale Score by Part and Total (FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
MDS-UPDRS Part III Score									
WEEK 6	193	23.3 (11.13)	24.3 (14.12)	23.0	0, 74	0.9 (12.07)	0.0	-36, 60	0.2764
Low dose	105	23.0 (11.12)	25.5 (15.53)	23.0	0, 74	2.4 (13.69)	0.0	-36, 60	0.0719
High dose	88	23.6 (11.20)	22.8 (12.16)	22.5	0, 55	-0.8 (9.57)	0.0	-31, 28	0.4242
WEEK 13	159	22.9 (10.79)	23.0 (14.51)	22.0	0, 82	0.1 (13.01)	0.0	-47, 37	0.9274
Low dose	90	22.5 (9.92)	24.0 (14.61)	23.5	0, 82	1.5 (13.73)	2.0	-38, 37	0.2998
High dose	69	23.4 (11.88)	21.7 (14.39)	20.0	0, 60	-1.8 (11.86)	-1.0	-47, 33	0.2241
WEEK 26	139	22.9 (10.93)	23.7 (14.63)	22.0	0, 83	0.8 (12.19)	0.0	-34, 39	0.4403
Low dose	76	23.4 (10.99)	24.7 (16.04)	22.0	0, 83	1.4 (12.64)	-0.5	-34, 39	0.3483
High dose	63	22.4 (10.91)	22.5 (12.74)	23.0	0, 59	0.1 (11.70)	0.0	-30, 27	0.9380
WEEK 39	125	23.4 (11.23)	25.6 (15.57)	23.0	1, 76	2.1 (13.00)	1.0	-28, 47	0.0693
Low dose	73	23.6 (11.20)	25.4 (16.49)	22.0	4, 76	1.8 (12.84)	0.0	-28, 47	0.2399
High dose	52	23.3 (11.38)	25.9 (14.34)	25.0	1, 63	2.6 (13.34)	2.0	-28, 40	0.1622
WEEK 52	120	23.6 (10.92)	25.5 (15.27)	23.0	1, 66	1.8 (12.86)	1.5	-35, 42	0.1193
Low dose	68	23.1 (11.25)	24.8 (15.64)	22.0	1, 66	1.6 (12.47)	1.5	-35, 35	0.2801
High dose	52	24.3 (10.55)	26.3 (14.87)	26.0	2, 62	2.1 (13.46)	1.5	-26, 42	0.2667

&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 2.1

Change from Baseline to Each Planned Visit in Parkinson's Disease Symptoms as Assessed by The Movement Disorder Society-Unified Parkinson's Disease Rating Scale Score by Part and Total (FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
MDS-UPDRS Part IV Score									
BASELINE	244		9.5 (3.17)	9.0	0, 20				
Low dose	132		9.6 (3.21)	9.0	0, 20				
High dose	112		9.5 (3.13)	9.0	1, 18				
DAY 2	218	9.6 (3.18)	8.2 (4.01)	8.0	0, 20	-1.5 (3.52)	-1.0	-12, 9	<=0.001***
Low dose	118	9.7 (3.27)	8.0 (4.07)	8.0	0, 20	-1.7 (3.56)	-1.0	-12, 9	<=0.001***
High dose	100	9.5 (3.09)	8.4 (3.94)	8.0	0, 19	-1.1 (3.46)	0.0	-11, 8	0.0018**
WEEK 1	221	9.6 (3.21)	7.9 (4.13)	8.0	0, 19	-1.7 (3.97)	-2.0	-17, 10	<=0.001***
Low dose	117	9.6 (3.26)	7.9 (4.12)	8.0	0, 18	-1.7 (3.86)	-2.0	-17, 9	<=0.001***
High dose	104	9.6 (3.16)	7.9 (4.17)	8.0	0, 19	-1.7 (4.11)	-2.0	-14, 10	<=0.001***
WEEK 2	208	9.7 (3.15)	7.3 (3.92)	7.0	0, 17	-2.4 (3.57)	-2.0	-13, 6	<=0.001***
Low dose	116	9.7 (3.19)	7.3 (4.01)	7.0	0, 17	-2.5 (3.57)	-2.0	-11, 6	<=0.001***
High dose	92	9.6 (3.13)	7.3 (3.83)	7.0	0, 16	-2.3 (3.58)	-2.0	-13, 6	<=0.001***
WEEK 3	198	9.5 (3.26)	7.3 (4.03)	7.0	0, 19	-2.2 (3.90)	-2.0	-15, 8	<=0.001***
Low dose	103	9.6 (3.31)	7.4 (4.35)	7.0	0, 19	-2.2 (4.09)	-3.0	-11, 8	<=0.001***
High dose	95	9.5 (3.21)	7.2 (3.67)	7.0	0, 16	-2.3 (3.72)	-2.0	-15, 5	<=0.001***
WEEK 4	200	9.5 (3.23)	6.7 (4.17)	7.0	0, 21	-2.8 (3.73)	-3.0	-15, 7	<=0.001***
Low dose	107	9.6 (3.31)	6.6 (4.50)	7.0	0, 21	-3.0 (3.69)	-3.0	-14, 5	<=0.001***
High dose	93	9.5 (3.15)	6.8 (3.78)	7.0	0, 16	-2.7 (3.78)	-3.0	-15, 7	<=0.001***

&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 2.1

Change from Baseline to Each Planned Visit in Parkinson's Disease Symptoms as Assessed by The Movement Disorder Society-Unified Parkinson's Disease Rating Scale Score by Part and Total (FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
MDS-UPDRS Part IV Score									
WEEK 6	190	9.5 (3.25)	6.8 (4.05)	7.0	0, 17	-2.7 (3.61)	-3.0	-15, 5	<=0.001***
Low dose	102	9.5 (3.35)	7.0 (4.13)	7.0	0, 17	-2.5 (3.37)	-3.0	-9, 5	<=0.001***
High dose	88	9.4 (3.15)	6.6 (3.97)	6.0	0, 17	-2.9 (3.88)	-3.0	-15, 5	<=0.001***
WEEK 13	166	9.5 (3.20)	6.0 (3.85)	6.0	0, 15	-3.5 (3.74)	-3.0	-15, 10	<=0.001***
Low dose	90	9.3 (3.29)	5.6 (3.87)	5.5	0, 15	-3.7 (3.46)	-4.0	-12, 10	<=0.001***
High dose	76	9.7 (3.09)	6.5 (3.78)	6.0	0, 14	-3.2 (4.06)	-3.0	-15, 6	<=0.001***
WEEK 26	146	9.5 (3.29)	6.0 (3.90)	6.0	0, 16	-3.5 (3.76)	-3.0	-15, 6	<=0.001***
Low dose	78	9.3 (3.43)	5.8 (3.87)	6.0	0, 16	-3.5 (3.41)	-3.0	-14, 5	<=0.001***
High dose	68	9.7 (3.13)	6.1 (3.94)	6.0	0, 14	-3.5 (4.15)	-3.0	-15, 6	<=0.001***
WEEK 39	128	9.4 (3.37)	6.0 (4.03)	6.0	0, 17	-3.4 (4.09)	-3.0	-15, 6	<=0.001***
Low dose	72	9.4 (3.54)	6.0 (4.08)	6.0	0, 17	-3.5 (4.07)	-3.5	-14, 6	<=0.001***
High dose	56	9.4 (3.18)	6.0 (4.00)	6.0	0, 17	-3.4 (4.15)	-3.0	-15, 5	<=0.001***
WEEK 52	120	9.3 (3.31)	5.4 (3.94)	5.0	0, 21	-3.8 (4.29)	-3.5	-17, 13	<=0.001***
Low dose	68	9.4 (3.53)	5.5 (3.53)	6.0	0, 16	-3.9 (3.75)	-4.0	-17, 6	<=0.001***
High dose	52	9.1 (3.02)	5.4 (4.45)	5.0	0, 21	-3.7 (4.94)	-3.0	-15, 13	<=0.001***

&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

表2.7.3.6-22　MDS-UPDRSスコア（FAS）：M15-737試験（更新時）

[redacted]20[redacted] 10:45 <[redacted]>
ABBV-951
STUDY M15-737 - THIRD INTERIM (CUTOFF [redacted]20[redacted])
R&D/22/0154 - CLINICAL/STATISTICAL

TABLE 14.2__2.1

Change from Baseline to Each Planned Visit in Parkinson's Disease Symptoms as Assessed
by The Movement Disorder Society-Unified Parkinson's Disease Rating Scale Score by Part and Total
(FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit Mean (SD)	Visit Median	Visit Min, Max	Change from Baseline Mean (SD)	Change from Baseline Median	Change from Baseline Min, Max	P-Value &
MDS-UPDRS Part I Score									
BASELINE	106		10.7 (5.93)	10.5	0, 27				
Low dose	48		10.4 (5.75)	10.0	0, 27				
High dose	58		10.9 (6.12)	11.0	2, 25				
WEEK 24	83	10.7 (5.98)	11.1 (6.41)	11.0	0, 27	0.4 (4.36)	1.0	-11, 12	0.4523
Low dose	36	11.0 (6.08)	11.4 (6.99)	12.0	0, 27	0.4 (4.50)	1.0	-8, 10	0.6331
High dose	47	10.5 (5.95)	10.9 (6.00)	10.0	1, 23	0.4 (4.30)	0.0	-11, 12	0.5670
WEEK 48	64	10.4 (6.09)	10.6 (5.62)	10.0	1, 28	0.2 (5.18)	0.5	-15, 13	0.7730
Low dose	26	11.0 (6.05)	10.0 (5.44)	8.5	3, 23	-1.0 (4.63)	0.0	-11, 8	0.2632
High dose	38	10.0 (6.17)	11.1 (5.77)	11.0	1, 28	1.0 (5.43)	1.0	-15, 13	0.2510
WEEK 72	12	10.5 (7.10)	12.2 (6.86)	11.0	3, 23	1.7 (3.77)	1.0	-5, 9	0.1543
Low dose	5	10.0 (7.58)	10.0 (7.52)	8.0	4, 23	0.0 (3.24)	0.0	-5, 4	>0.999
High dose	7	10.9 (7.34)	13.7 (6.47)	13.0	3, 22	2.9 (3.89)	1.0	-2, 9	0.1001
MDS-UPDRS Part II Score									
BASELINE	106		11.8 (7.04)	11.0	0, 29				
Low dose	48		11.4 (7.56)	10.0	0, 28				
High dose	58		12.1 (6.64)	12.0	1, 29				
WEEK 24	83	11.6 (7.12)	12.4 (7.85)	11.0	0, 38	0.9 (4.16)	0.0	-9, 15	0.0649
Low dose	36	11.5 (8.02)	12.1 (8.34)	10.5	0, 32	0.6 (4.45)	1.0	-9, 11	0.4154
High dose	47	11.6 (6.45)	12.6 (7.54)	12.0	2, 38	1.0 (3.97)	0.0	-7, 15	0.0785

&: P-value is obtained from two-sided paired-sample t-test.
N/A = Not Applicable.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 2.1

Change from Baseline to Each Planned Visit in Parkinson's Disease Symptoms as Assessed by The Movement Disorder Society-Unified Parkinson's Disease Rating Scale Score by Part and Total (FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
MDS-UPDRS Part II Score									
WEEK 48	64	10.9 (6.91)	12.7 (7.04)	13.0	0, 34	1.8 (5.53)	1.5	-13, 21	0.0123*
Low dose	26	11.1 (9.04)	11.3 (7.28)	10.0	1, 29	0.3 (5.45)	1.5	-13, 9	0.8033
High dose	38	10.8 (5.12)	13.6 (6.82)	13.0	0, 34	2.8 (5.41)	1.5	-5, 21	0.0028**
WEEK 72	12	10.3 (6.65)	15.1 (9.37)	14.5	3, 31	4.8 (6.12)	2.5	0, 20	0.0211*
Low dose	5	6.8 (4.44)	11.2 (8.53)	11.0	3, 24	4.4 (8.73)	1.0	0, 20	0.3230
High dose	7	12.9 (7.08)	17.9 (9.53)	18.0	4, 31	5.0 (4.20)	3.0	1, 11	0.0199*
MDS-UPDRS Part III Score									
BASELINE	106		23.6 (13.76)	22.0	1, 62				
Low dose	48		22.1 (13.51)	21.0	1, 58				
High dose	58		24.8 (13.97)	23.0	2, 62				
WEEK 24	79	22.7 (13.58)	24.3 (15.90)	24.0	0, 92	1.6 (9.23)	1.0	-21, 40	0.1333
Low dose	35	19.5 (11.73)	24.2 (15.37)	25.0	0, 65	4.7 (7.71)	3.0	-6, 26	0.0011**
High dose	44	25.2 (14.53)	24.3 (16.48)	23.5	0, 92	-0.9 (9.69)	-1.5	-21, 40	0.5516
WEEK 48	56	22.5 (13.68)	22.9 (13.27)	23.0	0, 59	0.4 (7.96)	0.0	-17, 16	0.7259
Low dose	22	21.5 (14.78)	24.1 (15.17)	25.0	0, 59	2.7 (9.20)	3.0	-17, 16	0.1862
High dose	34	23.2 (13.11)	22.1 (12.05)	23.0	2, 45	-1.1 (6.78)	-0.5	-16, 13	0.3435
WEEK 72	12	21.1 (18.60)	24.5 (17.10)	24.0	1, 55	3.4 (11.73)	2.1	-18, 30	0.3334
Low dose	5	15.8 (12.44)	25.0 (16.55)	23.0	1, 45	9.2 (13.33)	2.0	-2, 30	0.1976
High dose	7	24.9 (22.17)	24.2 (18.79)	25.0	4, 55	-0.7 (9.29)	2.1	-18, 8	0.8494

&: P-value is obtained from two-sided paired-sample t-test.
N/A = Not Applicable.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 2.1

Change from Baseline to Each Planned Visit in Parkinson's Disease Symptoms as Assessed by The Movement Disorder Society-Unified Parkinson's Disease Rating Scale Score by Part and Total (FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
MDS-UPDRS Part IV Score									
BASELINE	106		5.4 (4.04)	5.0	0, 21				
Low dose	48		5.2 (3.74)	5.0	0, 16				
High dose	58		5.6 (4.28)	5.0	0, 21				
WEEK 24	83	5.0 (3.74)	5.8 (4.09)	6.0	0, 18	0.8 (3.16)	0.0	-10, 14	0.0189*
Low dose	36	4.8 (4.02)	5.4 (3.98)	5.5	0, 14	0.6 (2.44)	0.0	-3, 10	0.1420
High dose	47	5.1 (3.54)	6.1 (4.19)	6.0	0, 18	1.0 (3.64)	0.0	-10, 14	0.0657
WEEK 48	63	4.6 (3.50)	5.4 (4.18)	5.0	0, 15	0.8 (3.34)	0.0	-11, 10	0.0641
Low dose	25	4.2 (3.54)	5.0 (4.58)	5.0	0, 15	0.8 (3.33)	0.0	-5, 10	0.2654
High dose	38	4.8 (3.50)	5.6 (3.94)	6.5	0, 14	0.8 (3.39)	1.0	-11, 7	0.1467
WEEK 72	12	4.0 (2.56)	5.7 (3.42)	6.0	0, 10	1.7 (2.90)	2.0	-5, 7	0.0721
Low dose	5	3.4 (3.44)	5.8 (4.15)	8.0	0, 10	2.4 (2.70)	2.0	0, 7	0.1180
High dose	7	4.4 (1.90)	5.6 (3.15)	6.0	0, 10	1.1 (3.13)	2.0	-5, 5	0.3716
MDS-UPDRS Total Score of Parts I-III									
BASELINE	106		46.1 (21.59)	45.0	6, 105				
Low dose	48		44.0 (21.55)	39.0	8, 94				
High dose	58		47.9 (21.65)	47.0	6, 105				
WEEK 24	79	44.9 (22.09)	47.6 (26.02)	46.0	1, 148	2.7 (13.05)	2.0	-24, 64	0.0687
Low dose	35	41.7 (21.73)	47.4 (25.83)	49.0	1, 114	5.7 (11.38)	6.0	-12, 39	0.0053**
High dose	44	47.5 (22.28)	47.8 (26.46)	46.0	7, 148	0.3 (13.90)	0.0	-24, 64	0.8840

&: P-value is obtained from two-sided paired-sample t-test.
N/A = Not Applicable.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 2.1

Change from Baseline to Each Planned Visit in Parkinson's Disease Symptoms as Assessed
by The Movement Disorder Society-Unified Parkinson's Disease Rating Scale Score by Part and Total
(FAS)

Parameter Time Point Dose Category	N	Baseline Mean (SD)	Visit Mean (SD)	Visit Median	Visit Min, Max	Change from Baseline Mean (SD)	Change from Baseline Median	Change from Baseline Min, Max	P-Value &
MDS-UPDRS Total Score of Parts I-III									
WEEK 48	57	43.6 (22.85)	46.5 (21.31)	43.0	11, 95	2.9 (15.27)	2.0	-29, 64	0.1558
Low dose	22	43.7 (26.15)	45.5 (23.17)	41.5	11, 88	1.7 (13.64)	2.5	-29, 22	0.5588
High dose	35	43.5 (20.91)	47.1 (20.39)	47.0	13, 95	3.7 (16.36)	2.0	-23, 64	0.1953
WEEK 72	12	41.9 (27.68)	51.8 (27.88)	57.0	11, 95	9.8 (17.28)	7.1	-15, 54	0.0740
Low dose	5	32.6 (22.28)	46.2 (26.61)	54.0	11, 78	13.6 (23.69)	4.0	-3, 54	0.2686
High dose	7	48.6 (30.82)	55.7 (30.14)	66.0	11, 95	7.2 (12.38)	9.0	-15, 24	0.1764

&: P-value is obtained from two-sided paired-sample t-test.
N/A = Not Applicable.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

表2.7.3.6-23　PDSS-2スコア（FAS）：M15-741試験（更新時）

[redacted]20[redacted] 10:50 <[redacted]>
ABBV-951
STUDY M15-741 - THIRD INTERIM (CUTOFF [redacted]20[redacted])
R&D/22/0153 - CLINICAL/STATISTICAL

TABLE 14.2__3

Change from Baseline to Each Planned Visit in Sleep Symptoms as Assessed
by The Parkinson's Disease Sleep Scale - 2
(FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
PDSS-2 Total Score									
BASELINE	243		20.4 (9.64)	19.0	0.0, 56.0				
Low dose	132		19.6 (9.41)	18.0	2.0, 56.0				
High dose	111		21.3 (9.87)	20.0	0.0, 47.0				
WEEK 6	196	20.2 (9.42)	14.2 (8.54)	12.5	0.0, 45.0	-6.1 (10.31)	-6.0	-50.0, 27.0	<=0.001***
Low dose	106	19.8 (9.40)	14.8 (8.84)	13.0	1.0, 45.0	-5.0 (11.35)	-4.0	-50.0, 27.0	<=0.001***
High dose	90	20.7 (9.47)	13.5 (8.15)	12.0	0.0, 43.0	-7.3 (8.85)	-7.0	-27.0, 14.0	<=0.001***
WEEK 13	170	20.7 (9.61)	13.2 (8.37)	11.0	0.0, 45.0	-7.5 (9.94)	-6.0	-48.0, 21.0	<=0.001***
Low dose	94	19.8 (9.49)	12.9 (8.67)	9.5	0.0, 45.0	-6.9 (10.70)	-6.0	-48.0, 17.0	<=0.001***
High dose	76	21.8 (9.70)	13.6 (8.02)	13.0	2.0, 43.0	-8.2 (8.94)	-8.0	-27.0, 21.0	<=0.001***
WEEK 26	148	20.5 (9.61)	13.9 (9.24)	12.0	0.0, 51.0	-6.6 (11.14)	-7.0	-48.0, 40.0	<=0.001***
Low dose	80	19.2 (9.44)	14.0 (9.80)	11.0	0.0, 51.0	-5.2 (13.07)	-6.0	-48.0, 40.0	<=0.001***
High dose	68	22.1 (9.66)	13.8 (8.59)	12.5	0.0, 35.0	-8.3 (8.11)	-8.0	-34.0, 10.0	<=0.001***
WEEK 39	132	20.2 (9.51)	13.4 (8.36)	12.0	1.0, 53.0	-6.8 (10.34)	-6.0	-53.0, 18.0	<=0.001***
Low dose	74	19.5 (9.52)	12.9 (7.63)	12.0	2.0, 43.0	-6.6 (11.10)	-5.5	-53.0, 18.0	<=0.001***
High dose	58	21.2 (9.48)	14.1 (9.23)	12.0	1.0, 53.0	-7.1 (9.37)	-7.0	-30.0, 16.0	<=0.001***
WEEK 52	118	20.5 (9.92)	13.4 (8.45)	11.5	0.0, 47.0	-7.1 (10.55)	-7.5	-53.0, 21.0	<=0.001***
Low dose	67	19.6 (9.79)	13.4 (7.98)	12.0	2.0, 44.0	-6.2 (11.88)	-6.0	-53.0, 21.0	<=0.001***
High dose	51	21.8 (10.05)	13.4 (9.11)	11.0	0.0, 47.0	-8.4 (8.45)	-8.0	-33.0, 7.0	<=0.001***

&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 3

Change from Baseline to Each Planned Visit in Sleep Symptoms as Assessed
by The Parkinson's Disease Sleep Scale - 2
(FAS)

Parameter Time Point Dose Category	N	Baseline Mean (SD)	Visit Mean (SD)	Visit Median	Visit Min, Max	Change from Baseline Mean (SD)	Change from Baseline Median	Change from Baseline Min, Max	Change from Baseline P-Value &
PDSS-2 Motor Symptoms at Night Score									
BASELINE	243		5.2 (4.10)	5.0	0.0, 20.0				
Low dose	132		5.1 (4.06)	4.5	0.0, 20.0				
High dose	111		5.3 (4.16)	5.0	0.0, 16.0				
WEEK 6	196	5.2 (3.99)	3.5 (3.59)	2.0	0.0, 15.0	-1.7 (4.61)	-2.0	-19.0, 12.0	<=0.001***
Low dose	106	5.2 (4.08)	3.7 (3.63)	3.0	0.0, 14.0	-1.5 (4.95)	-1.0	-19.0, 12.0	0.0025**
High dose	90	5.1 (3.90)	3.1 (3.53)	2.0	0.0, 15.0	-2.0 (4.18)	-2.0	-11.0, 10.0	<=0.001***
WEEK 13	170	5.5 (4.20)	3.1 (3.47)	2.0	0.0, 16.0	-2.3 (4.41)	-2.0	-19.0, 11.0	<=0.001***
Low dose	94	5.3 (4.22)	3.0 (3.61)	2.0	0.0, 16.0	-2.3 (4.59)	-2.0	-19.0, 9.0	<=0.001***
High dose	76	5.7 (4.18)	3.3 (3.31)	2.0	0.0, 15.0	-2.4 (4.22)	-2.5	-13.0, 11.0	<=0.001***
WEEK 26	148	5.3 (4.15)	3.5 (3.94)	2.0	0.0, 20.0	-1.8 (5.07)	-2.0	-20.0, 20.0	<=0.001***
Low dose	80	4.9 (4.09)	3.7 (4.18)	2.0	0.0, 20.0	-1.2 (5.90)	-2.0	-20.0, 20.0	0.0725
High dose	68	5.8 (4.20)	3.3 (3.65)	2.0	0.0, 16.0	-2.5 (3.81)	-2.0	-12.0, 11.0	<=0.001***
WEEK 39	132	5.2 (4.20)	3.4 (3.67)	2.0	0.0, 20.0	-1.9 (4.54)	-1.0	-18.0, 12.0	<=0.001***
Low dose	74	5.1 (4.12)	3.2 (3.49)	2.0	0.0, 16.0	-1.9 (4.73)	-1.5	-18.0, 12.0	<=0.001***
High dose	58	5.4 (4.33)	3.6 (3.89)	3.0	0.0, 20.0	-1.8 (4.32)	-1.0	-12.0, 12.0	0.0021**
WEEK 52	118	5.4 (4.30)	3.3 (3.59)	2.0	0.0, 16.0	-2.1 (4.73)	-2.0	-19.0, 14.0	<=0.001***
Low dose	67	5.1 (4.17)	3.3 (3.58)	2.0	0.0, 14.0	-1.8 (5.42)	-2.0	-19.0, 14.0	0.0098**
High dose	51	5.7 (4.48)	3.3 (3.64)	2.0	0.0, 16.0	-2.5 (3.66)	-2.0	-13.0, 6.0	<=0.001***

&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 3

Change from Baseline to Each Planned Visit in Sleep Symptoms as Assessed
by The Parkinson's Disease Sleep Scale - 2
(FAS)

Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
PDSS-2 PD Symptoms at Night Score									
BASELINE	243		5.0 (3.99)	4.0	0.0, 20.0				
Low dose	132		4.7 (3.88)	4.0	0.0, 20.0				
High dose	111		5.4 (4.11)	5.0	0.0, 16.0				
WEEK 6	196	4.9 (3.81)	2.9 (3.41)	2.0	0.0, 18.0	-2.0 (3.81)	-2.0	-19.0, 12.0	<=0.001***
Low dose	106	4.8 (3.79)	2.9 (3.59)	2.0	0.0, 18.0	-1.8 (4.04)	-1.5	-19.0, 12.0	<=0.001***
High dose	90	5.2 (3.85)	2.9 (3.21)	2.0	0.0, 15.0	-2.3 (3.51)	-2.0	-12.0, 5.0	<=0.001***
WEEK 13	170	5.0 (3.86)	2.7 (3.17)	2.0	0.0, 18.0	-2.2 (3.98)	-2.0	-16.0, 11.0	<=0.001***
Low dose	94	4.7 (3.69)	2.7 (3.22)	2.0	0.0, 18.0	-2.0 (3.98)	-2.0	-16.0, 10.0	<=0.001***
High dose	76	5.3 (4.07)	2.8 (3.14)	2.0	0.0, 16.0	-2.5 (3.98)	-2.0	-11.0, 11.0	<=0.001***
WEEK 26	148	4.9 (3.91)	3.0 (3.63)	2.0	0.0, 19.0	-2.0 (4.27)	-2.0	-16.0, 17.0	<=0.001***
Low dose	80	4.5 (3.69)	3.2 (3.95)	2.0	0.0, 19.0	-1.4 (4.63)	-1.0	-16.0, 17.0	0.0108*
High dose	68	5.4 (4.14)	2.7 (3.21)	1.5	0.0, 12.0	-2.7 (3.72)	-3.0	-14.0, 5.0	<=0.001***
WEEK 39	132	4.7 (3.86)	2.4 (3.11)	1.0	0.0, 20.0	-2.3 (3.95)	-2.0	-19.0, 8.0	<=0.001***
Low dose	74	4.5 (3.80)	2.4 (2.81)	1.0	0.0, 13.0	-2.1 (4.31)	-2.0	-19.0, 7.0	<=0.001***
High dose	58	5.0 (3.96)	2.5 (3.48)	1.5	0.0, 20.0	-2.5 (3.47)	-2.0	-12.0, 8.0	<=0.001***
WEEK 52	118	4.8 (4.05)	2.5 (3.06)	2.0	0.0, 15.0	-2.4 (4.25)	-2.0	-19.0, 14.0	<=0.001***
Low dose	67	4.5 (3.91)	2.6 (3.06)	2.0	0.0, 15.0	-2.0 (4.50)	-2.0	-19.0, 14.0	<=0.001***
High dose	51	5.3 (4.24)	2.4 (3.10)	1.0	0.0, 14.0	-2.9 (3.86)	-3.0	-12.0, 5.0	<=0.001***

&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 3

Change from Baseline to Each Planned Visit in Sleep Symptoms as Assessed
by The Parkinson's Disease Sleep Scale - 2
(FAS)

Parameter Time Point Dose Category	N	Baseline Mean (SD)	Visit Mean (SD)	Visit Median	Visit Min, Max	Change from Baseline Mean (SD)	Change from Baseline Median	Change from Baseline Min, Max	Change from Baseline P-Value &
PDSS-2 Disturbed Sleep Score									
BASELINE	243		10.2 (3.71)	10.0	0.0, 19.0				
Low dose	132		9.8 (3.66)	10.0	1.0, 19.0				
High dose	111		10.6 (3.73)	11.0	0.0, 19.0				
WEEK 6	196	10.1 (3.72)	7.8 (3.63)	8.0	0.0, 19.0	-2.3 (4.56)	-2.0	-12.0, 17.0	<=0.001***
Low dose	106	9.8 (3.76)	8.1 (3.75)	8.0	1.0, 19.0	-1.7 (4.78)	-2.0	-12.0, 17.0	<=0.001***
High dose	90	10.4 (3.66)	7.4 (3.47)	8.0	0.0, 16.0	-3.0 (4.20)	-2.0	-11.0, 8.0	<=0.001***
WEEK 13	170	10.3 (3.78)	7.4 (4.01)	7.0	0.0, 20.0	-2.9 (4.51)	-3.0	-13.0, 11.0	<=0.001***
Low dose	94	9.9 (3.82)	7.2 (3.96)	7.0	0.0, 17.0	-2.6 (4.60)	-2.0	-13.0, 11.0	<=0.001***
High dose	76	10.9 (3.68)	7.6 (4.09)	8.0	0.0, 20.0	-3.3 (4.42)	-3.0	-13.0, 6.0	<=0.001***
WEEK 26	148	10.3 (3.79)	7.4 (3.70)	7.0	0.0, 17.0	-2.9 (4.42)	-2.0	-14.0, 10.0	<=0.001***
Low dose	80	9.8 (3.76)	7.1 (3.49)	7.0	0.0, 14.0	-2.6 (4.56)	-2.0	-12.0, 10.0	<=0.001***
High dose	68	10.9 (3.76)	7.8 (3.95)	7.0	0.0, 17.0	-3.1 (4.27)	-2.5	-14.0, 7.0	<=0.001***
WEEK 39	132	10.3 (3.71)	7.6 (3.68)	7.0	0.0, 16.0	-2.7 (4.57)	-2.0	-16.0, 7.0	<=0.001***
Low dose	74	9.9 (3.66)	7.3 (3.69)	7.0	0.0, 16.0	-2.6 (4.67)	-2.0	-16.0, 7.0	<=0.001***
High dose	58	10.8 (3.76)	7.9 (3.67)	8.0	0.0, 15.0	-2.8 (4.47)	-2.0	-13.0, 5.0	<=0.001***
WEEK 52	118	10.3 (3.74)	7.6 (3.85)	7.0	0.0, 17.0	-2.7 (4.61)	-3.0	-15.0, 10.0	<=0.001***
Low dose	67	10.0 (3.65)	7.5 (3.70)	7.0	0.0, 15.0	-2.5 (4.63)	-2.0	-15.0, 10.0	<=0.001***
High dose	51	10.7 (3.86)	7.8 (4.07)	8.0	0.0, 17.0	-3.0 (4.62)	-3.0	-11.0, 7.0	<=0.001***

&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

表2.7.3.6-24　PD日誌に基づく，標準化した1日あたりの平均「オフ」時間及び「オン」時間の要約（FAS，部分集団別）：M15-741試験（更新時）

TABLE 14.2__1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Gender:Female									
Average Daily Normalized 'Off' Time									
BASELINE	95		5.99 (2.28)	6.1	0.0, 10.3				
Low Dose	64		6.02 (2.32)	6.2	0.0, 10.3				
High Dose	31		5.93 (2.23)	5.7	1.5, 9.5				
WEEK 1	92	5.96 (2.29)	4.44 (3.75)	3.8	0.0, 14.8	-1.52 (4.10)	-1.7	-10.2, 10.4	<=0.001***
Low Dose	62	6.03 (2.35)	3.83 (3.54)	2.9	0.0, 13.8	-2.20 (3.89)	-2.3	-10.2, 5.9	<=0.001***
High Dose	30	5.82 (2.19)	5.71 (3.91)	5.5	0.0, 14.8	-0.11 (4.24)	-0.3	-7.5, 10.4	0.8888
WEEK 6	83	5.90 (2.30)	4.20 (3.40)	3.8	0.0, 14.9	-1.70 (3.91)	-2.0	-10.2, 8.1	<=0.001***
Low Dose	55	5.87 (2.32)	3.67 (3.34)	3.3	0.0, 14.9	-2.21 (3.75)	-2.7	-10.2, 8.1	<=0.001***
High Dose	28	5.96 (2.31)	5.25 (3.34)	5.2	0.0, 12.5	-0.71 (4.09)	-1.1	-7.5, 6.8	0.3659
WEEK 13	45	5.68 (2.47)	3.38 (3.34)	2.0	0.0, 12.1	-2.30 (4.20)	-3.3	-9.9, 8.1	<=0.001***
Low Dose	32	5.68 (2.54)	3.06 (3.39)	1.6	0.0, 12.1	-2.62 (4.31)	-3.3	-9.9, 8.1	0.0017**
High Dose	13	5.68 (2.40)	4.15 (3.20)	4.2	0.0, 10.3	-1.53 (3.99)	-2.4	-7.5, 6.3	0.1930

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours
(i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Gender:Female (Cont.)									
Average Daily Normalized 'Off' Time (Cont.)									
WEEK 26	51	6.14 (2.13)	2.22 (2.66)	1.0	0.0, 9.8	-3.92 (3.32)	-4.0	-10.2, 5.5	<=0.001***
Low Dose	35	6.06 (2.09)	1.74 (2.25)	0.8	0.0, 7.9	-4.32 (3.04)	-4.0	-10.2, 2.7	<=0.001***
High Dose	16	6.30 (2.28)	3.26 (3.22)	2.2	0.0, 9.8	-3.04 (3.83)	-3.4	-9.2, 5.5	0.0062**
WEEK 39	49	6.09 (2.15)	2.54 (2.32)	1.8	0.0, 7.7	-3.55 (3.16)	-2.9	-9.9, 2.9	<=0.001***
Low Dose	34	5.91 (2.07)	2.05 (1.95)	1.4	0.0, 6.2	-3.87 (2.83)	-3.1	-9.9, 1.1	<=0.001***
High Dose	15	6.49 (2.34)	3.65 (2.76)	4.2	0.0, 7.7	-2.84 (3.82)	-2.3	-9.2, 2.9	0.0121*
WEEK 52	38	6.27 (1.96)	1.84 (2.23)	1.0	0.0, 8.8	-4.43 (3.05)	-4.3	-10.2, 3.1	<=0.001***
Low Dose	29	6.29 (1.96)	2.03 (2.43)	1.1	0.0, 8.8	-4.26 (3.02)	-4.1	-10.2, 3.1	<=0.001***
High Dose	9	6.21 (2.07)	1.21 (1.35)	0.8	0.0, 3.6	-4.99 (3.27)	-4.8	-9.2, -0.3	0.0018**
Average Daily Normalized 'On' Time Without Dyskinesia									
BASELINE	95		6.26 (3.20)	6.5	0.0, 14.0				
Low Dose	64		5.95 (3.11)	5.8	0.0, 14.0				
High Dose	31		6.90 (3.32)	6.9	0.9, 12.0				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit Mean (SD)	Visit Median	Visit Min, Max	Change from Baseline Mean (SD)	Change from Baseline Median	Change from Baseline Min, Max	P-Value &
Gender:Female (Cont.)									
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 1	92	6.17 (3.19)	8.03 (4.47)	7.8	0.0, 16.0	1.86 (4.29)	1.9	-8.9, 10.4	<=0.001***
Low Dose	62	5.82 (3.06)	7.75 (4.68)	7.3	0.0, 16.0	1.93 (4.17)	1.9	-8.9, 10.4	<=0.001***
High Dose	30	6.89 (3.38)	8.61 (4.01)	8.2	0.5, 16.0	1.72 (4.59)	1.9	-8.1, 8.7	0.0497*
WEEK 6	83	6.31 (3.15)	9.75 (4.05)	9.9	0.0, 16.0	3.45 (4.32)	4.1	-8.3, 12.7	<=0.001***
Low Dose	55	6.00 (3.10)	9.91 (4.20)	10.2	0.0, 16.0	3.91 (4.11)	4.3	-8.3, 12.7	<=0.001***
High Dose	28	6.91 (3.20)	9.45 (3.80)	9.8	2.4, 16.0	2.54 (4.65)	2.7	-6.7, 9.5	0.0074**
WEEK 13	45	6.64 (3.14)	11.16 (4.42)	13.1	0.0, 16.0	4.52 (4.27)	5.6	-9.0, 11.0	<=0.001***
Low Dose	32	6.43 (2.94)	11.35 (4.66)	13.2	0.0, 16.0	4.92 (4.17)	5.6	-9.0, 11.0	<=0.001***
High Dose	13	7.17 (3.66)	10.69 (3.88)	10.6	3.8, 16.0	3.52 (4.53)	4.3	-6.3, 9.5	0.0159*
WEEK 26	51	6.38 (3.40)	12.11 (3.58)	13.1	0.6, 16.0	5.73 (4.34)	6.6	-11.0, 11.5	<=0.001***
Low Dose	35	6.29 (3.28)	12.97 (2.64)	13.5	7.5, 16.0	6.68 (2.95)	6.8	-1.2, 11.5	<=0.001***
High Dose	16	6.58 (3.74)	10.23 (4.63)	9.9	0.6, 16.0	3.65 (6.03)	5.2	-11.0, 9.5	0.0286*
WEEK 39	49	6.53 (3.27)	11.37 (3.93)	11.8	1.2, 16.0	4.84 (3.91)	5.2	-5.0, 12.4	<=0.001***
Low Dose	34	6.49 (3.04)	11.93 (3.65)	13.0	5.0, 16.0	5.43 (3.67)	5.7	-5.0, 11.4	<=0.001***
High Dose	15	6.60 (3.86)	10.10 (4.36)	11.3	1.2, 16.0	3.50 (4.22)	2.7	-2.9, 12.4	0.0063**

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit Mean (SD)	Visit Median	Visit Min, Max	Change from Baseline Mean (SD)	Change from Baseline Median	Change from Baseline Min, Max	P-Value &
Gender:Female (Cont.)									
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 52	38	6.67 (3.06)	11.59 (4.70)	13.2	0.0, 16.0	4.91 (4.81)	6.0	-12.0, 11.3	<=0.001***
Low Dose	29	6.13 (2.95)	11.97 (4.34)	13.3	1.3, 16.0	5.84 (3.97)	6.7	-6.5, 11.3	<=0.001***
High Dose	9	8.44 (2.84)	10.35 (5.81)	12.4	0.0, 16.0	1.91 (6.20)	2.2	-12.0, 9.5	0.3817
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia									
BASELINE	95		2.52 (2.11)	2.6	0.0, 8.5				
Low Dose	64		2.55 (2.18)	2.6	0.0, 8.5				
High Dose	31		2.44 (1.98)	2.4	0.0, 7.6				
WEEK 1	92	2.59 (2.10)	2.45 (3.11)	1.1	0.0, 13.6	-0.15 (3.39)	-0.3	-8.5, 13.6	0.6809
Low Dose	62	2.63 (2.17)	3.01 (3.35)	2.2	0.0, 13.6	0.38 (3.77)	0.0	-8.5, 13.6	0.4338
High Dose	30	2.52 (1.96)	1.29 (2.15)	0.4	0.0, 8.1	-1.23 (2.09)	-0.7	-5.1, 5.0	0.0032**
WEEK 6	83	2.60 (2.16)	1.58 (2.67)	0.5	0.0, 15.4	-1.02 (2.73)	-0.8	-7.6, 11.6	0.0010**
Low Dose	55	2.67 (2.25)	1.90 (2.99)	0.8	0.0, 15.4	-0.76 (2.90)	-0.8	-7.6, 11.6	0.0562
High Dose	28	2.48 (2.02)	0.95 (1.80)	0.0	0.0, 6.2	-1.53 (2.33)	-0.8	-7.6, 4.0	0.0018**

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Gender:Female (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 13	45	2.79 (2.35)	1.10 (2.41)	0.0	0.0, 14.0	-1.70 (2.65)	-2.0	-6.5, 7.9	<=0.001***
Low Dose	32	2.79 (2.35)	1.18 (2.60)	0.0	0.0, 14.0	-1.61 (2.83)	-1.6	-6.5, 7.9	0.0031**
High Dose	13	2.81 (2.47)	0.90 (1.93)	0.0	0.0, 6.4	-1.92 (2.22)	-2.0	-5.3, 1.9	0.0091**
WEEK 26	51	2.55 (2.22)	1.54 (2.62)	0.0	0.0, 15.2	-1.01 (3.24)	-1.0	-6.7, 12.0	0.0304*
Low Dose	35	2.61 (2.29)	1.24 (1.71)	0.0	0.0, 7.3	-1.37 (2.79)	-1.0	-6.7, 4.3	0.0063**
High Dose	16	2.43 (2.13)	2.20 (3.94)	0.0	0.0, 15.2	-0.23 (4.06)	-1.0	-5.3, 12.0	0.8255
WEEK 39	49	2.61 (2.42)	1.64 (2.57)	0.0	0.0, 8.8	-0.96 (3.16)	-0.6	-7.8, 7.2	0.0377*
Low Dose	34	2.76 (2.50)	1.73 (2.58)	0.0	0.0, 7.7	-1.03 (2.95)	0.0	-7.8, 5.0	0.0505
High Dose	15	2.25 (2.27)	1.43 (2.62)	0.0	0.0, 8.8	-0.82 (3.69)	-2.0	-6.4, 7.2	0.4039
WEEK 52	38	2.31 (2.14)	1.92 (3.55)	0.0	0.0, 12.9	-0.40 (3.94)	-0.4	-6.7, 12.9	0.5374
Low Dose	29	2.65 (2.26)	1.83 (3.32)	0.0	0.0, 12.0	-0.82 (3.63)	-0.4	-6.7, 9.2	0.2332
High Dose	9	1.24 (1.28)	2.21 (4.42)	0.0	0.0, 12.9	0.97 (4.76)	-0.4	-2.7, 12.9	0.5572

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Gender:Female (Cont.)									
Average Daily Normalized 'On' Time With Troublesome Dyskinesia									
BASELINE	95		1.24 (2.06)	0.0	0.0, 10.5				
Low Dose	64		1.48 (2.30)	0.0	0.0, 10.5				
High Dose	31		0.74 (1.33)	0.0	0.0, 5.3				
WEEK 1	92	1.28 (2.08)	1.08 (2.15)	0.0	0.0, 10.5	-0.20 (1.99)	0.0	-6.0, 10.5	0.3434
Low Dose	62	1.52 (2.32)	1.41 (2.49)	0.2	0.0, 10.5	-0.11 (2.25)	0.0	-6.0, 10.5	0.7022
High Dose	30	0.77 (1.34)	0.39 (0.89)	0.0	0.0, 4.2	-0.38 (1.33)	0.0	-4.9, 3.4	0.1286
WEEK 6	83	1.19 (2.10)	0.46 (1.30)	0.0	0.0, 5.8	-0.72 (1.79)	0.0	-9.2, 4.1	<=0.001***
Low Dose	55	1.46 (2.39)	0.52 (1.43)	0.0	0.0, 5.8	-0.94 (2.10)	0.0	-9.2, 4.1	0.0016**
High Dose	28	0.66 (1.24)	0.35 (1.01)	0.0	0.0, 4.3	-0.30 (0.82)	0.0	-2.5, 1.4	0.0583
WEEK 13	45	0.88 (1.57)	0.36 (1.37)	0.0	0.0, 8.0	-0.52 (1.90)	0.0	-7.2, 6.0	0.0735
Low Dose	32	1.10 (1.78)	0.41 (1.53)	0.0	0.0, 8.0	-0.70 (2.14)	0.0	-7.2, 6.0	0.0757
High Dose	13	0.34 (0.64)	0.26 (0.93)	0.0	0.0, 3.4	-0.08 (1.02)	0.0	-2.2, 2.6	0.7786

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit Mean (SD)	Visit Median	Visit Min, Max	Change from Baseline Mean (SD)	Change from Baseline Median	Change from Baseline Min, Max	P-Value &
Gender:Female (Cont.)									
Average Daily Normalized 'On' Time With Troublesome Dyskinesia (Cont.)									
WEEK 26	51	0.93 (1.77)	0.13 (0.45)	0.0	0.0, 2.4	-0.80 (1.83)	0.0	-9.2, 1.6	0.0032**
Low Dose	35	1.04 (1.93)	0.05 (0.22)	0.0	0.0, 1.3	-0.99 (1.97)	0.0	-9.2, 1.3	0.0056**
High Dose	16	0.69 (1.37)	0.31 (0.73)	0.0	0.0, 2.4	-0.38 (1.46)	0.0	-4.9, 1.6	0.3172
WEEK 39	49	0.78 (1.36)	0.45 (1.43)	0.0	0.0, 8.1	-0.33 (1.50)	0.0	-5.1, 7.3	0.1339
Low Dose	34	0.83 (1.36)	0.29 (0.91)	0.0	0.0, 3.8	-0.54 (1.10)	0.0	-5.1, 0.5	0.0070**
High Dose	15	0.67 (1.41)	0.82 (2.20)	0.0	0.0, 8.1	0.16 (2.13)	0.0	-2.2, 7.3	0.7770
WEEK 52	38	0.74 (1.31)	0.66 (2.41)	0.0	0.0, 13.5	-0.08 (2.74)	0.0	-5.1, 13.0	0.8508
Low Dose	29	0.94 (1.44)	0.18 (0.56)	0.0	0.0, 2.7	-0.76 (1.38)	0.0	-5.1, 1.8	0.0059**
High Dose	9	0.11 (0.23)	2.22 (4.71)	0.0	0.0, 13.5	2.11 (4.59)	0.0	-0.5, 13.0	0.2053
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia									
BASELINE	95		8.78 (2.72)	8.9	0.3, 15.0				
Low Dose	64		8.51 (2.70)	8.8	0.3, 15.0				
High Dose	31		9.33 (2.70)	9.8	2.6, 14.5				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit Mean (SD)	Visit Median	Visit Min, Max	Change from Baseline Mean (SD)	Change from Baseline Median	Change from Baseline Min, Max	P-Value &
Gender:Female (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia (Cont.)									
WEEK 1	92	8.76 (2.74)	10.48 (3.82)	10.5	1.2, 16.0	1.71 (4.08)	1.5	-10.4, 11.3	<=0.001***
Low Dose	62	8.45 (2.72)	10.76 (3.81)	11.0	2.2, 16.0	2.31 (3.68)	2.1	-5.9, 11.3	<=0.001***
High Dose	30	9.41 (2.71)	9.90 (3.84)	9.9	1.2, 16.0	0.49 (4.64)	0.8	-10.4, 8.3	0.5679
WEEK 6	83	8.91 (2.65)	11.34 (3.49)	11.7	1.1, 16.0	2.43 (3.99)	2.8	-6.8, 10.5	<=0.001***
Low Dose	55	8.67 (2.64)	11.81 (3.50)	12.3	1.1, 16.0	3.15 (3.69)	3.0	-5.7, 10.5	<=0.001***
High Dose	28	9.38 (2.66)	10.40 (3.35)	10.2	3.5, 16.0	1.02 (4.26)	1.2	-6.8, 8.4	0.2180
WEEK 13	45	9.44 (2.42)	12.26 (3.63)	14.0	3.9, 16.0	2.82 (3.88)	3.5	-6.3, 9.9	<=0.001***
Low Dose	32	9.22 (2.36)	12.53 (3.73)	14.4	3.9, 16.0	3.32 (3.63)	3.6	-5.0, 9.9	<=0.001***
High Dose	13	9.98 (2.57)	11.59 (3.43)	11.8	5.7, 16.0	1.61 (4.33)	2.4	-6.3, 7.5	0.2057
WEEK 26	51	8.93 (2.85)	13.65 (2.68)	14.8	6.2, 16.0	4.71 (3.83)	5.2	-5.5, 12.5	<=0.001***
Low Dose	35	8.90 (2.88)	14.21 (2.30)	15.2	8.1, 16.0	5.31 (3.47)	5.2	-2.7, 12.5	<=0.001***
High Dose	16	9.01 (2.88)	12.43 (3.11)	12.9	6.2, 16.0	3.42 (4.36)	4.1	-5.5, 10.2	0.0067**
WEEK 39	49	9.13 (2.63)	13.01 (2.79)	13.7	2.4, 16.0	3.88 (3.75)	3.1	-9.2, 9.9	<=0.001***
Low Dose	34	9.26 (2.49)	13.66 (2.04)	14.1	9.8, 16.0	4.41 (3.00)	3.4	-1.1, 9.9	<=0.001***
High Dose	15	8.85 (2.98)	11.53 (3.68)	11.8	2.4, 16.0	2.68 (4.98)	2.6	-9.2, 9.7	0.0560

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Gender:Female (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia (Cont.)									
WEEK 52	38	8.99 (2.38)	13.50 (3.00)	14.7	2.5, 16.0	4.52 (3.22)	4.7	-3.8, 10.2	<=0.001***
Low Dose	29	8.77 (2.44)	13.80 (2.48)	14.7	7.2, 16.0	5.02 (3.00)	5.0	-3.1, 10.2	<=0.001***
High Dose	9	9.68 (2.15)	12.56 (4.34)	13.8	2.5, 16.0	2.88 (3.54)	2.3	-3.8, 7.5	0.0404*
Gender:Male									
Average Daily Normalized 'Off' Time									
BASELINE	141		5.85 (2.22)	5.8	0.0, 12.6				
Low Dose	63		5.34 (2.01)	5.4	0.0, 10.0				
High Dose	78		6.26 (2.31)	6.4	0.0, 12.6				
WEEK 1	133	5.88 (2.23)	3.64 (3.16)	2.7	0.0, 16.0	-2.24 (3.34)	-2.7	-9.7, 8.0	<=0.001***
Low Dose	59	5.42 (2.02)	3.54 (2.81)	2.8	0.0, 11.2	-1.88 (3.05)	-2.2	-9.7, 5.6	<=0.001***
High Dose	74	6.24 (2.33)	3.72 (3.43)	2.7	0.0, 16.0	-2.53 (3.54)	-3.4	-8.9, 8.0	<=0.001***
WEEK 6	122	5.97 (2.20)	3.10 (3.09)	2.5	0.0, 16.0	-2.86 (3.32)	-3.4	-10.6, 9.9	<=0.001***
Low Dose	56	5.59 (1.92)	2.98 (3.33)	2.3	0.0, 16.0	-2.62 (3.57)	-3.4	-8.6, 9.9	<=0.001***
High Dose	66	6.29 (2.39)	3.21 (2.90)	2.7	0.0, 11.3	-3.07 (3.09)	-3.3	-10.6, 5.6	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Gender:Male (Cont.)									
Average Daily Normalized 'Off' Time (Cont.)									
WEEK 13	69	5.41 (2.15)	2.90 (3.55)	1.7	0.0, 13.4	-2.51 (3.36)	-3.2	-9.2, 7.8	<=0.001***
Low Dose	32	5.13 (1.85)	2.71 (3.70)	1.2	0.0, 13.4	-2.43 (3.29)	-3.4	-6.6, 7.8	<=0.001***
High Dose	37	5.65 (2.38)	3.07 (3.46)	1.7	0.0, 10.7	-2.59 (3.46)	-3.2	-9.2, 5.2	<=0.001***
WEEK 26	80	5.83 (2.30)	2.86 (3.22)	1.7	0.0, 14.3	-2.97 (3.17)	-2.9	-10.6, 7.1	<=0.001***
Low Dose	34	5.46 (1.79)	3.19 (3.79)	1.5	0.0, 14.3	-2.28 (3.40)	-3.0	-6.6, 7.1	<=0.001***
High Dose	46	6.10 (2.60)	2.62 (2.75)	1.8	0.0, 8.9	-3.48 (2.92)	-2.9	-10.6, 4.4	<=0.001***
WEEK 39	70	5.75 (2.26)	2.73 (3.08)	2.1	0.0, 13.3	-3.02 (3.12)	-3.4	-8.1, 9.6	<=0.001***
Low Dose	33	5.33 (1.80)	3.06 (3.61)	2.5	0.0, 13.3	-2.27 (3.58)	-2.9	-7.1, 9.6	<=0.001***
High Dose	37	6.12 (2.57)	2.44 (2.53)	2.1	0.0, 7.2	-3.68 (2.52)	-3.6	-8.1, 4.0	<=0.001***
WEEK 52	66	5.65 (2.41)	2.91 (3.14)	2.2	0.0, 11.5	-2.74 (3.02)	-2.9	-11.2, 5.9	<=0.001***
Low Dose	27	5.28 (1.99)	3.27 (3.09)	2.6	0.0, 10.9	-2.02 (2.84)	-2.4	-5.9, 5.9	0.0010**
High Dose	39	5.90 (2.66)	2.66 (3.19)	0.7	0.0, 11.5	-3.24 (3.07)	-3.4	-11.2, 2.8	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Gender:Male (Cont.)									
Average Daily Normalized 'On' Time Without Dyskinesia									
BASELINE	141		6.68 (3.45)	6.7	0.0, 15.4				
Low Dose	63		6.76 (3.77)	7.5	0.0, 15.4				
High Dose	78		6.62 (3.20)	6.6	0.0, 13.8				
WEEK 1	133	6.70 (3.39)	8.70 (4.55)	8.9	0.0, 16.0	2.00 (3.96)	1.2	-6.1, 12.0	<=0.001***
Low Dose	59	6.62 (3.67)	8.24 (4.40)	8.6	0.0, 16.0	1.62 (3.70)	1.0	-6.0, 10.7	0.0014**
High Dose	74	6.77 (3.17)	9.08 (4.66)	9.1	0.0, 16.0	2.31 (4.16)	1.8	-6.1, 12.0	<=0.001***
WEEK 6	122	6.70 (3.50)	10.03 (4.77)	11.4	0.0, 16.0	3.33 (4.45)	3.0	-9.1, 13.8	<=0.001***
Low Dose	56	6.74 (3.75)	9.81 (4.90)	11.3	0.0, 16.0	3.07 (4.85)	2.9	-9.1, 13.8	<=0.001***
High Dose	66	6.67 (3.30)	10.22 (4.68)	11.6	0.0, 16.0	3.55 (4.11)	3.4	-6.4, 12.0	<=0.001***
WEEK 13	69	6.69 (3.61)	10.56 (4.75)	10.9	0.0, 16.0	3.87 (4.43)	3.7	-6.5, 15.2	<=0.001***
Low Dose	32	6.88 (3.94)	9.96 (5.15)	10.1	0.0, 16.0	3.08 (4.51)	2.5	-6.5, 15.2	<=0.001***
High Dose	37	6.53 (3.35)	11.08 (4.39)	11.3	0.9, 16.0	4.55 (4.30)	4.7	-4.7, 14.1	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Gender:Male (Cont.)									
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 26	80	7.15 (3.33)	10.77 (4.69)	11.4	0.0, 16.0	3.62 (4.38)	4.0	-10.1, 14.1	<=0.001***
Low Dose	34	7.29 (3.61)	10.38 (5.03)	10.8	0.0, 16.0	3.09 (4.14)	3.6	-10.1, 11.2	<=0.001***
High Dose	46	7.05 (3.15)	11.06 (4.45)	12.4	0.0, 16.0	4.01 (4.56)	4.3	-9.6, 14.1	<=0.001***
WEEK 39	70	7.27 (3.28)	10.68 (4.67)	11.3	0.0, 16.0	3.42 (4.15)	3.1	-10.6, 13.5	<=0.001***
Low Dose	33	7.31 (3.51)	10.54 (5.11)	11.3	0.3, 16.0	3.23 (4.52)	3.1	-10.6, 11.2	<=0.001***
High Dose	37	7.23 (3.11)	10.81 (4.30)	11.3	0.0, 16.0	3.58 (3.85)	3.3	-3.8, 13.5	<=0.001***
WEEK 52	66	7.24 (3.43)	10.39 (4.64)	11.2	0.0, 16.0	3.15 (3.71)	3.2	-3.1, 13.8	<=0.001***
Low Dose	27	7.47 (3.53)	10.62 (4.29)	11.8	0.0, 16.0	3.15 (3.23)	3.4	-2.9, 8.1	<=0.001***
High Dose	39	7.08 (3.40)	10.23 (4.91)	11.2	0.0, 16.0	3.14 (4.05)	2.5	-3.1, 13.8	<=0.001***
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia									
BASELINE	141		2.70 (2.82)	2.1	0.0, 12.2				
Low Dose	63		2.83 (2.60)	2.7	0.0, 10.3				
High Dose	78		2.60 (2.99)	1.4	0.0, 12.2				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Gender:Male (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 1	133	2.71 (2.84)	2.73 (3.20)	1.5	0.0, 14.9	0.02 (2.78)	0.0	-8.2, 8.8	0.9435
Low Dose	59	2.91 (2.64)	3.07 (3.22)	2.4	0.0, 14.9	0.17 (2.73)	0.0	-5.3, 8.6	0.6419
High Dose	74	2.55 (3.01)	2.45 (3.17)	1.0	0.0, 12.8	-0.10 (2.83)	0.0	-8.2, 8.8	0.7582
WEEK 6	122	2.72 (2.89)	2.44 (3.62)	0.5	0.0, 14.6	-0.28 (3.16)	0.0	-7.8, 9.6	0.3320
Low Dose	56	2.82 (2.59)	2.55 (3.34)	0.9	0.0, 12.2	-0.27 (3.20)	0.0	-6.8, 9.6	0.5296
High Dose	66	2.63 (3.14)	2.34 (3.86)	0.1	0.0, 14.6	-0.29 (3.15)	-0.1	-7.8, 9.6	0.4642
WEEK 13	69	3.10 (2.99)	2.23 (3.73)	0.0	0.0, 16.0	-0.87 (3.96)	-0.5	-12.2, 13.2	0.0733
Low Dose	32	3.09 (2.82)	2.96 (4.40)	0.5	0.0, 16.0	-0.13 (4.12)	-0.5	-8.0, 13.2	0.8590
High Dose	37	3.11 (3.17)	1.60 (2.95)	0.0	0.0, 14.4	-1.50 (3.75)	-0.5	-12.2, 7.2	0.0198*
WEEK 26	80	2.36 (2.63)	1.93 (3.11)	0.6	0.0, 14.9	-0.42 (3.24)	0.0	-12.2, 7.8	0.2457
Low Dose	34	2.47 (2.27)	1.88 (2.91)	0.7	0.0, 12.1	-0.59 (2.72)	0.0	-6.8, 5.4	0.2141
High Dose	46	2.27 (2.88)	1.97 (3.28)	0.2	0.0, 14.9	-0.30 (3.60)	0.0	-12.2, 7.8	0.5750
WEEK 39	70	2.31 (2.63)	2.31 (4.06)	0.0	0.0, 16.0	-0.00 (3.65)	0.0	-7.8, 15.4	0.9959
Low Dose	33	2.59 (2.29)	2.16 (4.23)	0.0	0.0, 15.4	-0.43 (4.12)	-0.6	-6.8, 15.4	0.5491
High Dose	37	2.06 (2.90)	2.44 (3.97)	0.0	0.0, 16.0	0.38 (3.19)	0.0	-7.8, 9.9	0.4699

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit Mean (SD)	Visit Median	Visit Min, Max	Change from Baseline Mean (SD)	Change from Baseline Median	Change from Baseline Min, Max	P-Value &
Gender:Male (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 52	66	2.59 (3.00)	2.30 (4.03)	0.3	0.0, 16.0	-0.29 (3.04)	0.0	-7.3, 7.5	0.4414
Low Dose	27	2.79 (2.82)	1.89 (3.79)	0.3	0.0, 16.0	-0.91 (3.15)	-0.6	-6.8, 6.0	0.1458
High Dose	39	2.45 (3.14)	2.59 (4.21)	0.5	0.0, 16.0	0.14 (2.93)	0.0	-7.3, 7.5	0.7694
Average Daily Normalized 'On' Time With Troublesome Dyskinesia									
BASELINE	141		0.77 (1.44)	0.0	0.0, 8.8				
Low Dose	63		1.07 (1.69)	0.2	0.0, 8.8				
High Dose	78		0.52 (1.16)	0.0	0.0, 5.0				
WEEK 1	133	0.71 (1.36)	0.93 (2.05)	0.0	0.0, 11.7	0.22 (1.81)	0.0	-5.7, 7.9	0.1624
Low Dose	59	1.05 (1.66)	1.14 (2.20)	0.0	0.0, 11.7	0.10 (1.92)	0.0	-5.7, 7.9	0.6962
High Dose	74	0.44 (1.00)	0.75 (1.91)	0.0	0.0, 9.8	0.32 (1.72)	0.0	-3.7, 7.0	0.1167
WEEK 6	122	0.61 (1.12)	0.42 (1.31)	0.0	0.0, 9.0	-0.19 (1.43)	0.0	-4.9, 6.9	0.1425
Low Dose	56	0.85 (1.26)	0.66 (1.75)	0.0	0.0, 9.0	-0.19 (1.71)	0.0	-3.4, 6.9	0.4157
High Dose	66	0.41 (0.96)	0.22 (0.71)	0.0	0.0, 4.4	-0.19 (1.15)	0.0	-4.9, 4.4	0.1753

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Gender:Male (Cont.)									
Average Daily Normalized 'On' Time With Troublesome Dyskinesia (Cont.)									
WEEK 13	69	0.80 (1.35)	0.31 (0.93)	0.0	0.0, 5.5	-0.49 (1.08)	0.0	-4.9, 1.7	<=0.001***
Low Dose	32	0.90 (1.35)	0.38 (1.09)	0.0	0.0, 5.5	-0.52 (1.14)	0.0	-3.4, 1.7	0.0148*
High Dose	37	0.71 (1.36)	0.25 (0.78)	0.0	0.0, 3.7	-0.46 (1.05)	0.0	-4.9, 0.9	0.0112*
WEEK 26	80	0.66 (1.32)	0.44 (1.73)	0.0	0.0, 12.1	-0.23 (1.84)	0.0	-4.9, 8.8	0.2712
Low Dose	34	0.77 (1.32)	0.55 (2.15)	0.0	0.0, 12.1	-0.22 (1.88)	0.0	-3.6, 7.2	0.5054
High Dose	46	0.58 (1.32)	0.35 (1.35)	0.0	0.0, 8.8	-0.24 (1.83)	0.0	-4.9, 8.8	0.3868
WEEK 39	70	0.67 (1.26)	0.28 (0.71)	0.0	0.0, 2.9	-0.40 (1.22)	0.0	-5.0, 2.7	0.0084**
Low Dose	33	0.77 (1.29)	0.25 (0.64)	0.0	0.0, 2.6	-0.52 (1.03)	0.0	-3.6, 0.8	0.0069**
High Dose	37	0.59 (1.26)	0.31 (0.78)	0.0	0.0, 2.9	-0.29 (1.37)	0.0	-5.0, 2.7	0.2118
WEEK 52	66	0.52 (1.08)	0.40 (1.04)	0.0	0.0, 5.3	-0.11 (1.42)	0.0	-5.0, 5.3	0.5157
Low Dose	27	0.45 (0.85)	0.23 (0.70)	0.0	0.0, 3.3	-0.22 (1.13)	0.0	-3.4, 3.3	0.3177
High Dose	39	0.56 (1.23)	0.52 (1.21)	0.0	0.0, 5.3	-0.04 (1.60)	0.0	-5.0, 5.3	0.8792

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Gender:Male (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia									
BASELINE	141		9.39 (2.33)	9.6	3.1, 16.0				
Low Dose	63		9.59 (2.54)	10.1	3.1, 16.0				
High Dose	78		9.22 (2.14)	9.3	3.4, 16.0				
WEEK 1	133	9.41 (2.30)	11.43 (3.55)	11.7	0.0, 16.0	2.02 (3.56)	2.5	-8.0, 9.7	<=0.001***
Low Dose	59	9.53 (2.50)	11.31 (3.46)	11.2	1.6, 16.0	1.78 (3.39)	2.2	-5.6, 9.7	<=0.001***
High Dose	74	9.32 (2.14)	11.53 (3.63)	11.9	0.0, 16.0	2.21 (3.70)	2.6	-8.0, 8.9	<=0.001***
WEEK 6	122	9.42 (2.27)	12.47 (3.21)	13.0	0.0, 16.0	3.05 (3.27)	3.5	-9.9, 10.6	<=0.001***
Low Dose	56	9.56 (2.37)	12.37 (3.56)	12.9	0.0, 16.0	2.80 (3.50)	3.7	-9.9, 9.2	<=0.001***
High Dose	66	9.30 (2.19)	12.57 (2.90)	13.1	4.7, 16.0	3.27 (3.07)	3.5	-2.6, 10.6	<=0.001***
WEEK 13	69	9.79 (2.31)	12.79 (3.61)	13.9	2.6, 16.0	3.00 (3.22)	3.2	-5.2, 9.2	<=0.001***
Low Dose	32	9.97 (2.37)	12.92 (3.75)	13.9	2.6, 16.0	2.95 (2.99)	3.7	-4.9, 7.2	<=0.001***
High Dose	37	9.63 (2.27)	12.68 (3.53)	13.9	5.3, 16.0	3.05 (3.44)	3.2	-5.2, 9.2	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit Mean (SD)	Visit Median	Visit Min, Max	Change from Baseline Mean (SD)	Change from Baseline Median	Change from Baseline Min, Max	P-Value &
Gender:Male (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia (Cont.)									
WEEK 26	80	9.51 (2.41)	12.70 (3.51)	14.1	1.5, 16.0	3.20 (3.24)	2.9	-5.5, 10.6	<=0.001***
Low Dose	34	9.77 (2.37)	12.26 (4.23)	13.8	1.5, 16.0	2.50 (3.56)	3.0	-5.5, 9.4	<=0.001***
High Dose	46	9.32 (2.45)	13.03 (2.88)	14.1	7.1, 16.0	3.71 (2.91)	2.9	-2.5, 10.6	<=0.001***
WEEK 39	70	9.58 (2.36)	12.99 (3.17)	13.2	2.7, 16.0	3.41 (2.99)	3.4	-9.1, 9.4	<=0.001***
Low Dose	33	9.90 (2.33)	12.69 (3.64)	12.9	2.7, 16.0	2.79 (3.48)	3.0	-9.1, 9.4	<=0.001***
High Dose	37	9.28 (2.38)	13.25 (2.71)	13.8	6.6, 16.0	3.97 (2.39)	4.1	-1.3, 8.9	<=0.001***
WEEK 52	66	9.83 (2.43)	12.69 (3.20)	13.4	4.5, 16.0	2.86 (2.90)	2.9	-5.4, 11.2	<=0.001***
Low Dose	27	10.27 (2.23)	12.51 (3.03)	13.4	5.1, 16.0	2.24 (2.46)	2.8	-5.4, 5.9	<=0.001***
High Dose	39	9.53 (2.54)	12.82 (3.35)	14.2	4.5, 16.0	3.28 (3.13)	3.4	-2.8, 11.2	<=0.001***
Race:WHITE									
Average Daily Normalized 'Off' Time									
BASELINE	199		5.75 (2.25)	5.8	0.0, 12.6				
Low Dose	98		5.46 (2.16)	5.6	0.0, 10.2				
High Dose	101		6.04 (2.30)	6.1	0.0, 12.6				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:WHITE (Cont.)									
Average Daily Normalized 'Off' Time (Cont.)									
WEEK 1	190	5.76 (2.25)	3.86 (3.46)	2.9	0.0, 16.0	-1.91 (3.68)	-2.1	-10.2, 10.4	<=0.001***
Low Dose	93	5.53 (2.18)	3.45 (3.17)	2.7	0.0, 11.2	-2.08 (3.45)	-2.4	-10.2, 5.9	<=0.001***
High Dose	97	5.99 (2.29)	4.24 (3.70)	3.1	0.0, 16.0	-1.75 (3.90)	-2.0	-8.9, 10.4	<=0.001***
WEEK 6	173	5.82 (2.27)	3.25 (3.08)	2.9	0.0, 16.0	-2.57 (3.52)	-2.9	-10.6, 9.9	<=0.001***
Low Dose	86	5.59 (2.15)	2.93 (3.16)	2.6	0.0, 16.0	-2.66 (3.54)	-2.9	-10.2, 9.9	<=0.001***
High Dose	87	6.05 (2.37)	3.57 (2.98)	3.0	0.0, 10.7	-2.48 (3.51)	-2.9	-10.6, 6.8	<=0.001***
WEEK 13	99	5.45 (2.30)	2.69 (3.11)	1.7	0.0, 12.6	-2.76 (3.45)	-3.2	-9.9, 7.8	<=0.001***
Low Dose	51	5.31 (2.24)	2.22 (2.81)	1.1	0.0, 12.6	-3.09 (3.26)	-3.4	-9.9, 7.8	<=0.001***
High Dose	48	5.60 (2.38)	3.18 (3.36)	2.0	0.0, 10.7	-2.41 (3.64)	-3.2	-9.2, 6.3	<=0.001***
WEEK 26	112	5.86 (2.33)	2.17 (2.53)	1.2	0.0, 9.8	-3.69 (2.91)	-3.9	-10.6, 5.5	<=0.001***
Low Dose	54	5.68 (2.11)	1.69 (2.21)	0.6	0.0, 7.4	-3.99 (2.64)	-4.2	-10.2, 3.3	<=0.001***
High Dose	58	6.03 (2.51)	2.61 (2.74)	1.7	0.0, 9.8	-3.41 (3.14)	-3.1	-10.6, 5.5	<=0.001***
WEEK 39	100	5.75 (2.29)	2.29 (2.46)	1.5	0.0, 11.4	-3.46 (2.81)	-3.3	-9.9, 6.4	<=0.001***
Low Dose	52	5.44 (2.04)	1.92 (2.28)	1.0	0.0, 11.4	-3.52 (2.72)	-3.1	-9.9, 6.4	<=0.001***
High Dose	48	6.08 (2.51)	2.69 (2.61)	2.1	0.0, 7.7	-3.40 (2.92)	-3.4	-9.2, 4.0	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:WHITE (Cont.)									
Average Daily Normalized 'Off' Time (Cont.)									
WEEK 52	88	5.70 (2.34)	2.18 (2.77)	0.9	0.0, 11.5	-3.51 (3.04)	-3.7	-11.2, 5.9	<=0.001***
Low Dose	44	5.62 (2.13)	2.16 (2.61)	1.2	0.0, 10.9	-3.46 (2.93)	-3.7	-10.2, 5.9	<=0.001***
High Dose	44	5.78 (2.55)	2.20 (2.94)	0.6	0.0, 11.5	-3.57 (3.18)	-3.7	-11.2, 2.8	<=0.001***
Average Daily Normalized 'On' Time Without Dyskinesia									
BASELINE	199		6.63 (3.42)	6.7	0.0, 15.4				
Low Dose	98		6.52 (3.59)	6.6	0.0, 15.4				
High Dose	101		6.74 (3.27)	6.7	0.0, 13.8				
WEEK 1	190	6.61 (3.37)	8.80 (4.52)	8.8	0.0, 16.0	2.19 (4.09)	1.9	-8.8, 12.0	<=0.001***
Low Dose	93	6.37 (3.49)	8.61 (4.59)	8.6	0.0, 16.0	2.24 (3.85)	1.9	-8.8, 10.7	<=0.001***
High Dose	97	6.83 (3.26)	8.98 (4.47)	9.0	0.0, 16.0	2.14 (4.34)	2.1	-8.1, 12.0	<=0.001***
WEEK 6	173	6.62 (3.43)	10.28 (4.42)	11.2	0.0, 16.0	3.67 (4.16)	3.9	-8.3, 12.7	<=0.001***
Low Dose	86	6.46 (3.56)	10.22 (4.60)	10.9	0.0, 16.0	3.75 (4.20)	4.0	-8.3, 12.7	<=0.001***
High Dose	87	6.77 (3.31)	10.34 (4.25)	11.2	0.0, 16.0	3.58 (4.14)	3.5	-6.7, 12.0	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit Mean (SD)	Visit Median	Visit Min, Max	Change from Baseline Mean (SD)	Change from Baseline Median	Change from Baseline Min, Max	P-Value &
Race:WHITE (Cont.)									
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 13	99	6.80 (3.52)	11.41 (4.26)	12.6	0.0, 16.0	4.61 (4.10)	4.9	-6.3, 15.2	<=0.001***
Low Dose	51	6.86 (3.61)	11.62 (4.38)	13.2	0.0, 16.0	4.76 (3.90)	4.9	-3.9, 15.2	<=0.001***
High Dose	48	6.73 (3.46)	11.19 (4.16)	11.5	0.9, 16.0	4.46 (4.34)	5.1	-6.3, 14.1	<=0.001***
WEEK 26	112	6.98 (3.46)	11.74 (4.04)	13.1	0.0, 16.0	4.76 (4.38)	5.3	-11.0, 14.1	<=0.001***
Low Dose	54	7.01 (3.58)	12.58 (3.36)	13.4	0.5, 16.0	5.57 (3.44)	5.6	-2.4, 11.5	<=0.001***
High Dose	58	6.95 (3.37)	10.95 (4.48)	11.9	0.0, 16.0	4.00 (5.02)	4.6	-11.0, 14.1	<=0.001***
WEEK 39	100	7.18 (3.32)	11.29 (4.33)	11.8	0.0, 16.0	4.11 (4.17)	4.2	-10.6, 13.5	<=0.001***
Low Dose	52	7.26 (3.26)	11.86 (4.32)	13.1	0.6, 16.0	4.60 (4.30)	5.1	-10.6, 11.4	<=0.001***
High Dose	48	7.09 (3.42)	10.67 (4.30)	11.3	0.0, 16.0	3.58 (4.00)	3.2	-3.8, 13.5	<=0.001***
WEEK 52	88	7.24 (3.34)	11.00 (4.78)	12.4	0.0, 16.0	3.75 (4.45)	4.3	-12.0, 13.8	<=0.001***
Low Dose	44	7.08 (3.28)	11.67 (4.42)	13.3	0.0, 16.0	4.59 (4.20)	5.0	-6.5, 11.3	<=0.001***
High Dose	44	7.41 (3.43)	10.33 (5.08)	11.5	0.0, 16.0	2.91 (4.58)	2.6	-12.0, 13.8	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:WHITE (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia									
BASELINE	199		2.64 (2.52)	2.4	0.0, 12.2				
Low Dose	98		2.64 (2.31)	2.6	0.0, 10.3				
High Dose	101		2.64 (2.71)	2.0	0.0, 12.2				
WEEK 1	190	2.67 (2.52)	2.37 (2.90)	1.1	0.0, 13.6	-0.29 (2.89)	0.0	-8.5, 13.6	0.1648
Low Dose	93	2.71 (2.33)	2.67 (2.96)	2.0	0.0, 13.6	-0.04 (3.06)	0.0	-8.5, 13.6	0.9055
High Dose	97	2.63 (2.70)	2.09 (2.83)	0.7	0.0, 11.9	-0.54 (2.71)	0.0	-8.2, 8.8	0.0541
WEEK 6	173	2.69 (2.60)	2.03 (3.21)	0.5	0.0, 15.4	-0.66 (2.85)	-0.4	-7.8, 11.6	0.0026**
Low Dose	86	2.71 (2.37)	2.26 (3.18)	1.0	0.0, 15.4	-0.45 (2.89)	-0.3	-7.6, 11.6	0.1497
High Dose	87	2.68 (2.82)	1.81 (3.25)	0.0	0.0, 14.6	-0.87 (2.82)	-0.6	-7.8, 7.5	0.0051**
WEEK 13	99	2.99 (2.78)	1.56 (2.99)	0.0	0.0, 15.5	-1.43 (3.25)	-1.1	-12.2, 7.9	<=0.001***
Low Dose	51	2.88 (2.56)	1.70 (3.21)	0.2	0.0, 15.5	-1.18 (3.07)	-1.2	-8.0, 7.9	0.0083**
High Dose	48	3.10 (3.01)	1.42 (2.77)	0.0	0.0, 14.4	-1.68 (3.45)	-0.9	-12.2, 7.2	0.0015**

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:WHITE (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 26	112	2.36 (2.41)	1.76 (2.93)	0.4	0.0, 15.2	-0.61 (3.31)	-0.2	-12.2, 12.0	0.0550
Low Dose	54	2.29 (2.04)	1.39 (2.10)	0.7	0.0, 10.8	-0.91 (2.68)	-0.6	-6.8, 5.4	0.0159*
High Dose	58	2.43 (2.73)	2.10 (3.52)	0.0	0.0, 15.2	-0.33 (3.81)	-0.1	-12.2, 12.0	0.5172
WEEK 39	100	2.37 (2.48)	2.07 (3.59)	0.0	0.0, 16.0	-0.31 (3.54)	0.0	-7.8, 15.4	0.3869
Low Dose	52	2.50 (2.20)	1.96 (3.48)	0.0	0.0, 15.4	-0.54 (3.62)	-0.1	-7.8, 15.4	0.2854
High Dose	48	2.23 (2.78)	2.18 (3.75)	0.0	0.0, 16.0	-0.05 (3.46)	0.0	-7.8, 9.9	0.9163
WEEK 52	88	2.49 (2.67)	2.29 (4.08)	0.1	0.0, 16.0	-0.20 (3.46)	-0.2	-7.3, 12.9	0.5836
Low Dose	44	2.61 (2.33)	1.97 (3.82)	0.0	0.0, 16.0	-0.64 (3.48)	-0.5	-6.8, 9.2	0.2302
High Dose	44	2.37 (2.99)	2.60 (4.35)	0.4	0.0, 16.0	0.23 (3.43)	0.0	-7.3, 12.9	0.6552
Average Daily Normalized 'On' Time With Troublesome Dyskinesia									
BASELINE	199		0.97 (1.73)	0.0	0.0, 10.5				
Low Dose	98		1.38 (2.08)	0.2	0.0, 10.5				
High Dose	101		0.58 (1.21)	0.0	0.0, 5.3				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:WHITE (Cont.)									
Average Daily Normalized 'On' Time With Troublesome Dyskinesia (Cont.)									
WEEK 1	190	0.96 (1.72)	0.97 (2.05)	0.0	0.0, 11.7	0.01 (1.78)	0.0	-5.7, 10.5	0.9551
Low Dose	93	1.39 (2.08)	1.26 (2.31)	0.0	0.0, 11.7	-0.13 (1.86)	0.0	-5.7, 10.5	0.5025
High Dose	97	0.55 (1.14)	0.69 (1.73)	0.0	0.0, 9.8	0.14 (1.70)	0.0	-4.9, 7.0	0.4237
WEEK 6	173	0.87 (1.61)	0.44 (1.28)	0.0	0.0, 9.0	-0.43 (1.48)	0.0	-9.2, 5.3	<=0.001***
Low Dose	86	1.23 (1.95)	0.60 (1.60)	0.0	0.0, 9.0	-0.64 (1.77)	0.0	-9.2, 5.3	0.0012**
High Dose	87	0.51 (1.08)	0.28 (0.84)	0.0	0.0, 4.4	-0.23 (1.09)	0.0	-4.9, 4.4	0.0564
WEEK 13	99	0.76 (1.27)	0.34 (1.17)	0.0	0.0, 8.0	-0.43 (1.30)	0.0	-5.2, 6.0	0.0015**
Low Dose	51	0.95 (1.35)	0.46 (1.45)	0.0	0.0, 8.0	-0.49 (1.49)	0.0	-5.2, 6.0	0.0236*
High Dose	48	0.57 (1.17)	0.20 (0.74)	0.0	0.0, 3.7	-0.36 (1.07)	0.0	-4.9, 2.6	0.0229*
WEEK 26	112	0.79 (1.55)	0.33 (1.48)	0.0	0.0, 12.1	-0.46 (1.95)	0.0	-9.2, 8.8	0.0140*
Low Dose	54	1.01 (1.77)	0.34 (1.72)	0.0	0.0, 12.1	-0.67 (2.12)	0.0	-9.2, 7.2	0.0231*
High Dose	58	0.59 (1.30)	0.33 (1.24)	0.0	0.0, 8.8	-0.26 (1.78)	0.0	-4.9, 8.8	0.2683
WEEK 39	100	0.70 (1.27)	0.35 (1.10)	0.0	0.0, 8.1	-0.34 (1.40)	0.0	-5.1, 7.3	0.0163*
Low Dose	52	0.79 (1.27)	0.26 (0.76)	0.0	0.0, 3.8	-0.53 (1.08)	0.0	-5.1, 0.8	<=0.001***
High Dose	48	0.59 (1.26)	0.46 (1.38)	0.0	0.0, 8.1	-0.13 (1.66)	0.0	-5.0, 7.3	0.5842

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit Mean (SD)	Visit Median	Visit Min, Max	Change from Baseline Mean (SD)	Change from Baseline Median	Change from Baseline Min, Max	P-Value &
Race:WHITE (Cont.)									
Average Daily Normalized 'On' Time With Troublesome Dyskinesia (Cont.)									
WEEK 52	88	0.57 (1.10)	0.53 (1.79)	0.0	0.0, 13.5	-0.03 (2.11)	0.0	-5.1, 13.0	0.8798
Low Dose	44	0.69 (1.13)	0.20 (0.67)	0.0	0.0, 3.3	-0.49 (1.31)	0.0	-5.1, 3.3	0.0159*
High Dose	44	0.44 (1.07)	0.87 (2.41)	0.0	0.0, 13.5	0.43 (2.62)	0.0	-5.0, 13.0	0.2867
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia									
BASELINE	199		9.27 (2.55)	9.6	0.3, 16.0				
Low Dose	98		9.16 (2.77)	9.8	0.3, 16.0				
High Dose	101		9.38 (2.33)	9.5	2.6, 16.0				
WEEK 1	190	9.27 (2.55)	11.17 (3.73)	11.7	0.0, 16.0	1.90 (3.81)	2.0	-10.4, 11.3	<=0.001***
Low Dose	93	9.08 (2.76)	11.29 (3.69)	12.0	1.6, 16.0	2.21 (3.52)	2.6	-5.9, 11.3	<=0.001***
High Dose	97	9.46 (2.33)	11.06 (3.78)	11.7	0.0, 16.0	1.61 (4.07)	1.5	-10.4, 8.9	<=0.001***
WEEK 6	173	9.31 (2.53)	12.31 (3.23)	12.8	0.0, 16.0	3.00 (3.54)	3.3	-9.9, 10.6	<=0.001***
Low Dose	86	9.17 (2.70)	12.47 (3.43)	12.8	0.0, 16.0	3.30 (3.49)	3.3	-9.9, 10.5	<=0.001***
High Dose	87	9.45 (2.35)	12.15 (3.04)	12.6	5.1, 16.0	2.71 (3.57)	3.3	-6.8, 10.6	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:WHITE (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia (Cont.)									
WEEK 13	99	9.79 (2.36)	12.98 (3.30)	14.1	3.4, 16.0	3.19 (3.41)	3.5	-6.3, 9.9	<=0.001***
Low Dose	51	9.74 (2.43)	13.32 (3.19)	14.5	3.4, 16.0	3.58 (3.05)	4.0	-4.9, 9.9	<=0.001***
High Dose	48	9.84 (2.31)	12.61 (3.41)	13.7	5.3, 16.0	2.78 (3.75)	3.2	-6.3, 9.2	<=0.001***
WEEK 26	112	9.35 (2.71)	13.50 (2.84)	14.5	1.5, 16.0	4.15 (3.35)	4.1	-5.5, 12.5	<=0.001***
Low Dose	54	9.31 (2.88)	13.97 (2.84)	15.3	1.5, 16.0	4.66 (3.34)	4.7	-4.5, 12.5	<=0.001***
High Dose	58	9.38 (2.57)	13.06 (2.80)	14.0	6.2, 16.0	3.67 (3.33)	3.4	-5.5, 10.6	<=0.001***
WEEK 39	100	9.55 (2.47)	13.36 (2.78)	14.0	2.4, 16.0	3.80 (3.12)	3.4	-9.2, 9.9	<=0.001***
Low Dose	52	9.76 (2.38)	13.82 (2.41)	14.6	4.6, 16.0	4.06 (2.86)	3.2	-5.9, 9.9	<=0.001***
High Dose	48	9.33 (2.57)	12.86 (3.08)	13.2	2.4, 16.0	3.53 (3.39)	3.4	-9.2, 9.7	<=0.001***
WEEK 52	88	9.73 (2.42)	13.28 (3.08)	14.1	2.5, 16.0	3.55 (3.09)	3.6	-5.4, 11.2	<=0.001***
Low Dose	44	9.69 (2.42)	13.64 (2.57)	14.0	5.1, 16.0	3.95 (2.93)	3.9	-5.4, 10.2	<=0.001***
High Dose	44	9.78 (2.44)	12.93 (3.51)	14.4	2.5, 16.0	3.15 (3.22)	3.2	-3.8, 11.2	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:ASIAN									
Average Daily Normalized 'Off' Time									
BASELINE	34		6.68 (2.04)	6.8	0.0, 10.3				
Low Dose	27		6.45 (2.13)	6.6	0.0, 10.3				
High Dose	7		7.60 (1.44)	8.1	5.7, 9.6				
WEEK 1	32	6.70 (2.10)	4.78 (3.25)	4.7	0.0, 13.8	-1.92 (3.79)	-2.2	-9.7, 4.7	0.0074**
Low Dose	26	6.43 (2.17)	4.72 (3.18)	4.6	0.0, 13.8	-1.71 (3.75)	-2.0	-9.7, 4.7	0.0283*
High Dose	6	7.89 (1.34)	5.05 (3.84)	5.1	0.0, 10.9	-2.83 (4.22)	-3.9	-8.3, 2.8	0.1613
WEEK 6	29	6.56 (1.96)	5.41 (3.69)	4.3	0.0, 13.4	-1.15 (3.98)	-2.7	-7.5, 6.8	0.1319
Low Dose	23	6.21 (1.97)	5.00 (3.55)	3.8	0.0, 13.4	-1.21 (3.90)	-2.4	-7.5, 6.2	0.1520
High Dose	6	7.89 (1.34)	6.96 (4.16)	5.8	1.6, 12.5	-0.92 (4.67)	-3.1	-5.4, 6.8	0.6493
WEEK 13	13	5.95 (2.10)	5.96 (4.52)	6.2	0.0, 13.4	0.01 (4.89)	0.3	-7.0, 8.1	0.9927
Low Dose	12	5.96 (2.19)	5.94 (4.72)	5.0	0.0, 13.4	-0.01 (5.10)	-0.3	-7.0, 8.1	0.9930
High Dose	1	5.87 (N/A)	6.20 (N/A)	6.2	6.2, 6.2	0.32 (N/A)	0.3	0.3, 0.3	

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:ASIAN (Cont.)									
Average Daily Normalized 'Off' Time (Cont.)									
WEEK 26	18	6.63 (1.39)	5.50 (4.17)	5.4	0.0, 14.3	-1.13 (4.40)	-0.7	-8.1, 7.1	0.2919
Low Dose	14	6.25 (1.12)	5.56 (4.41)	5.4	0.0, 14.3	-0.69 (4.62)	-0.4	-7.8, 7.1	0.5870
High Dose	4	7.98 (1.56)	5.31 (3.81)	6.2	0.0, 8.9	-2.67 (3.64)	-1.1	-8.1, -0.4	0.2388
WEEK 39	18	6.78 (1.52)	4.08 (2.97)	4.2	0.0, 12.3	-2.70 (3.48)	-1.7	-8.1, 5.1	0.0043**
Low Dose	14	6.44 (1.38)	4.09 (3.09)	4.2	0.0, 12.3	-2.35 (3.51)	-1.6	-8.1, 5.1	0.0266*
High Dose	4	7.98 (1.56)	4.03 (2.93)	4.6	0.0, 6.8	-3.95 (3.53)	-3.6	-8.1, -0.6	0.1110
WEEK 52	16	6.85 (1.56)	4.34 (2.88)	5.2	0.0, 10.1	-2.51 (3.54)	-2.7	-8.7, 4.1	0.0126*
Low Dose	12	6.47 (1.43)	4.32 (2.97)	4.5	0.0, 10.1	-2.16 (3.70)	-2.7	-8.7, 4.1	0.0688
High Dose	4	7.98 (1.56)	4.41 (2.99)	5.6	0.0, 6.4	-3.57 (3.23)	-2.7	-8.1, -0.7	0.1143
Average Daily Normalized 'On' Time Without Dyskinesia									
BASELINE	34		5.67 (2.94)	5.8	0.0, 11.8				
Low Dose	27		5.61 (3.03)	5.1	0.0, 11.8				
High Dose	7		5.91 (2.79)	6.5	0.5, 8.4				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit Mean (SD)	Visit Median	Visit Min, Max	Change from Baseline Mean (SD)	Change from Baseline Median	Change from Baseline Min, Max	P-Value &
Race:ASIAN (Cont.)									
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 1	32	5.62 (2.96)	6.34 (4.03)	6.8	0.3, 16.0	0.72 (3.85)	0.7	-8.9, 10.2	0.2970
Low Dose	26	5.48 (3.01)	5.96 (3.81)	6.4	0.3, 14.9	0.48 (3.90)	0.6	-8.9, 10.2	0.5371
High Dose	6	6.22 (2.93)	8.00 (4.92)	8.0	1.2, 16.0	1.78 (3.78)	1.0	-2.8, 8.3	0.3018
WEEK 6	29	5.95 (3.05)	8.38 (4.29)	8.6	0.0, 14.4	2.43 (4.98)	3.5	-6.4, 13.8	0.0137*
Low Dose	23	5.88 (3.14)	9.25 (3.81)	9.3	2.1, 14.4	3.37 (4.78)	3.9	-6.1, 13.8	0.0027**
High Dose	6	6.22 (2.93)	5.06 (4.74)	3.1	0.0, 11.2	-1.16 (4.33)	-1.0	-6.4, 3.5	0.5391
WEEK 13	13	5.47 (2.59)	6.53 (5.28)	5.9	0.0, 14.7	1.06 (5.15)	1.1	-9.0, 9.6	0.4744
Low Dose	12	5.59 (2.67)	6.72 (5.47)	6.1	0.0, 14.7	1.13 (5.38)	1.4	-9.0, 9.6	0.4812
High Dose	1	4.05 (N/A)	4.20 (N/A)	4.2	4.2, 4.2	0.15 (N/A)	0.1	0.1, 0.1	
WEEK 26	18	5.90 (2.66)	8.42 (5.13)	7.8	0.0, 16.0	2.52 (4.76)	2.3	-10.1, 9.5	0.0385*
Low Dose	14	5.73 (2.90)	8.18 (5.36)	7.8	0.0, 16.0	2.45 (5.16)	3.2	-10.1, 9.5	0.0986
High Dose	4	6.50 (1.77)	9.24 (4.80)	7.9	5.1, 16.0	2.74 (3.60)	1.2	0.4, 8.1	0.2257
WEEK 39	18	5.64 (2.83)	9.62 (4.13)	10.3	0.3, 16.0	3.98 (3.01)	4.7	-1.9, 8.1	<=0.001***
Low Dose	14	5.39 (3.08)	9.56 (4.16)	10.5	0.3, 16.0	4.17 (3.02)	4.9	-1.9, 8.0	<=0.001***
High Dose	4	6.50 (1.77)	9.82 (4.67)	9.3	4.7, 16.0	3.32 (3.35)	2.3	0.6, 8.1	0.1414

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:ASIAN (Cont.)									
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 52	16	5.88 (2.89)	9.89 (4.02)	9.4	4.0, 16.0	4.01 (2.56)	3.1	-0.1, 8.7	<=0.001***
Low Dose	12	5.67 (3.21)	10.05 (3.89)	10.0	4.2, 16.0	4.38 (2.21)	3.8	1.9, 8.7	<=0.001***
High Dose	4	6.50 (1.77)	9.42 (4.99)	8.8	4.0, 16.0	2.91 (3.57)	1.8	-0.1, 8.1	0.2009
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia									
BASELINE	34		2.72 (2.80)	2.4	0.0, 8.5				
Low Dose	27		2.97 (2.73)	2.8	0.0, 8.0				
High Dose	7		1.75 (3.10)	0.3	0.0, 8.5				
WEEK 1	32	2.81 (2.85)	3.85 (4.13)	2.5	0.0, 14.9	1.04 (3.49)	0.1	-5.4, 13.2	0.1021
Low Dose	26	3.08 (2.71)	4.07 (4.00)	2.7	0.0, 14.9	0.99 (3.80)	0.1	-5.4, 13.2	0.1978
High Dose	6	1.63 (3.38)	2.90 (4.95)	1.0	0.0, 12.8	1.27 (1.81)	0.7	-0.4, 4.3	0.1459
WEEK 6	29	2.72 (2.83)	2.09 (3.35)	0.5	0.0, 12.3	-0.63 (3.34)	0.0	-6.7, 9.6	0.3169
Low Dose	23	3.01 (2.68)	1.60 (2.46)	0.5	0.0, 9.0	-1.41 (2.76)	0.0	-6.7, 4.4	0.0227*
High Dose	6	1.63 (3.38)	3.98 (5.53)	1.0	0.0, 12.3	2.35 (3.95)	0.8	-1.0, 9.6	0.2048

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:ASIAN (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 13	13	3.15 (2.75)	3.18 (4.95)	1.2	0.0, 16.0	0.03 (4.96)	0.0	-6.5, 13.2	0.9809
Low Dose	12	3.20 (2.86)	3.21 (5.17)	0.7	0.0, 16.0	0.01 (5.18)	-0.3	-6.5, 13.2	0.9947
High Dose	1	2.48 (N/A)	2.80 (N/A)	2.8	2.8, 2.8	0.32 (N/A)	0.3	0.3, 0.3	
WEEK 26	18	2.86 (2.90)	1.84 (3.04)	0.2	0.0, 12.1	-1.01 (2.90)	0.0	-6.7, 4.6	0.1559
Low Dose	14	3.50 (2.95)	2.09 (3.33)	0.2	0.0, 12.1	-1.41 (3.19)	-2.3	-6.7, 4.6	0.1218
High Dose	4	0.62 (1.24)	0.99 (1.76)	0.2	0.0, 3.6	0.37 (0.54)	0.2	0.0, 1.1	0.2625
WEEK 39	18	2.73 (2.96)	1.95 (3.32)	0.0	0.0, 13.2	-0.78 (3.26)	0.0	-6.7, 5.2	0.3235
Low Dose	14	3.33 (3.05)	2.01 (3.65)	0.0	0.0, 13.2	-1.32 (3.48)	-0.9	-6.7, 5.2	0.1800
High Dose	4	0.62 (1.24)	1.72 (2.12)	1.3	0.0, 4.3	1.10 (1.30)	0.9	0.0, 2.5	0.1889
WEEK 52	16	2.49 (3.02)	1.47 (2.08)	0.5	0.0, 6.7	-1.02 (2.84)	0.0	-6.7, 3.9	0.1707
Low Dose	12	3.12 (3.22)	1.43 (2.15)	0.5	0.0, 6.7	-1.69 (2.95)	-0.6	-6.7, 3.9	0.0731
High Dose	4	0.62 (1.24)	1.60 (2.16)	0.9	0.0, 4.6	0.98 (1.13)	0.9	0.0, 2.1	0.1832

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:ASIAN (Cont.)									
Average Daily Normalized 'On' Time With Troublesome Dyskinesia									
BASELINE	34		0.93 (1.77)	0.0	0.0, 7.2				
Low Dose	27		0.98 (1.89)	0.0	0.0, 7.2				
High Dose	7		0.74 (1.31)	0.0	0.0, 3.6				
WEEK 1	32	0.87 (1.75)	1.03 (2.27)	0.0	0.0, 10.3	0.16 (2.39)	0.0	-6.0, 7.9	0.7122
Low Dose	26	1.01 (1.91)	1.26 (2.47)	0.1	0.0, 10.3	0.24 (2.65)	0.0	-6.0, 7.9	0.6420
High Dose	6	0.26 (0.41)	0.04 (0.10)	0.0	0.0, 0.3	-0.22 (0.35)	0.0	-0.8, 0.0	0.1861
WEEK 6	29	0.77 (1.70)	0.12 (0.52)	0.0	0.0, 2.7	-0.65 (1.69)	0.0	-7.2, 1.0	0.0473*
Low Dose	23	0.91 (1.88)	0.16 (0.58)	0.0	0.0, 2.7	-0.75 (1.88)	0.0	-7.2, 1.0	0.0684
High Dose	6	0.26 (0.41)	0.00 (0.00)	0.0	0.0, 0.0	-0.26 (0.41)	0.0	-0.8, 0.0	0.1748
WEEK 13	13	1.43 (2.39)	0.33 (0.85)	0.0	0.0, 2.8	-1.10 (2.39)	0.0	-7.2, 1.3	0.1220
Low Dose	12	1.25 (2.40)	0.13 (0.43)	0.0	0.0, 1.5	-1.13 (2.49)	0.0	-7.2, 1.3	0.1451
High Dose	1	3.59 (N/A)	2.81 (N/A)	2.8	2.8, 2.8	-0.79 (N/A)	-0.8	-0.8, -0.8	

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:ASIAN (Cont.)									
Average Daily Normalized 'On' Time With Troublesome Dyskinesia (Cont.)									
WEEK 26	18	0.61 (1.26)	0.23 (0.52)	0.0	0.0, 1.8	-0.37 (1.16)	0.0	-3.4, 1.3	0.1884
Low Dose	14	0.52 (1.14)	0.17 (0.38)	0.0	0.0, 1.3	-0.36 (1.25)	0.0	-3.4, 1.3	0.3082
High Dose	4	0.90 (1.80)	0.46 (0.92)	0.0	0.0, 1.8	-0.44 (0.87)	0.0	-1.7, 0.0	0.3910
WEEK 39	18	0.86 (1.55)	0.36 (0.89)	0.0	0.0, 3.5	-0.50 (0.99)	0.0	-3.0, 0.0	0.0481*
Low Dose	14	0.85 (1.55)	0.34 (0.93)	0.0	0.0, 3.5	-0.51 (1.04)	0.0	-3.0, 0.0	0.0918
High Dose	4	0.90 (1.80)	0.43 (0.86)	0.0	0.0, 1.7	-0.47 (0.94)	0.0	-1.9, 0.0	0.3910
WEEK 52	16	0.78 (1.54)	0.29 (0.66)	0.0	0.0, 2.3	-0.48 (1.13)	0.0	-3.4, 0.5	0.1067
Low Dose	12	0.74 (1.53)	0.20 (0.45)	0.0	0.0, 1.5	-0.54 (1.27)	0.0	-3.4, 0.5	0.1708
High Dose	4	0.90 (1.80)	0.57 (1.14)	0.0	0.0, 2.3	-0.33 (0.65)	0.0	-1.3, 0.0	0.3910
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia									
BASELINE	34		8.39 (2.10)	8.7	2.2, 11.8				
Low Dose	27		8.57 (2.26)	9.0	2.2, 11.8				
High Dose	7		7.66 (1.21)	7.7	6.4, 9.5				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit Mean (SD)	Visit Median	Visit Min, Max	Change from Baseline Mean (SD)	Change from Baseline Median	Change from Baseline Min, Max	P-Value &
Race:ASIAN (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia (Cont.)									
WEEK 1	32	8.43 (2.14)	10.19 (3.33)	10.2	2.2, 16.0	1.76 (3.75)	1.1	-4.0, 9.7	0.0123*
Low Dose	26	8.56 (2.30)	10.03 (3.27)	9.9	2.2, 16.0	1.47 (3.69)	1.0	-4.0, 9.7	0.0538
High Dose	6	7.85 (1.21)	10.90 (3.85)	10.8	5.1, 16.0	3.05 (4.08)	4.2	-2.8, 8.3	0.1261
WEEK 6	29	8.67 (1.77)	10.47 (3.78)	11.5	2.6, 16.0	1.80 (3.90)	3.1	-6.0, 7.5	0.0193*
Low Dose	23	8.88 (1.85)	10.84 (3.69)	12.2	2.6, 16.0	1.96 (3.88)	3.1	-5.7, 7.5	0.0242*
High Dose	6	7.85 (1.21)	9.04 (4.16)	10.2	3.5, 14.4	1.18 (4.29)	3.1	-6.0, 5.4	0.5288
WEEK 13	13	8.62 (2.05)	9.70 (4.53)	9.4	2.6, 16.0	1.09 (3.71)	0.5	-5.0, 7.0	0.3109
Low Dose	12	8.79 (2.03)	9.93 (4.66)	10.5	2.6, 16.0	1.14 (3.87)	0.8	-5.0, 7.0	0.3291
High Dose	1	6.53 (N/A)	7.00 (N/A)	7.0	7.0, 7.0	0.46 (N/A)	0.5	0.5, 0.5	
WEEK 26	18	8.76 (1.72)	10.26 (4.16)	10.0	1.7, 16.0	1.50 (4.02)	0.7	-5.5, 8.1	0.1315
Low Dose	14	9.23 (1.64)	10.27 (4.37)	10.5	1.7, 16.0	1.04 (4.18)	0.5	-5.5, 7.8	0.3678
High Dose	4	7.12 (0.78)	10.23 (3.94)	8.9	7.1, 16.0	3.11 (3.38)	1.8	0.7, 8.1	0.1633
WEEK 39	18	8.36 (2.30)	11.57 (2.90)	11.6	3.7, 16.0	3.20 (3.15)	2.6	-2.1, 9.1	<=0.001***
Low Dose	14	8.72 (2.49)	11.57 (2.92)	11.6	3.7, 16.0	2.86 (3.20)	2.3	-2.1, 9.1	0.0053**
High Dose	4	7.12 (0.78)	11.54 (3.28)	10.6	9.0, 16.0	4.42 (3.02)	4.0	1.5, 8.1	0.0614

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit Mean (SD)	Visit Median	Visit Min, Max	Change from Baseline Mean (SD)	Change from Baseline Median	Change from Baseline Min, Max	P-Value &
Race:ASIAN (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia (Cont.)									
WEEK 52	16	8.37 (2.27)	11.36 (3.08)	10.3	5.9, 16.0	2.99 (3.31)	2.7	-2.2, 8.7	0.0025**
Low Dose	12	8.79 (2.47)	11.48 (3.13)	11.5	5.9, 16.0	2.69 (3.50)	2.7	-2.2, 8.7	0.0220*
High Dose	4	7.12 (0.78)	11.01 (3.37)	9.7	8.6, 16.0	3.89 (2.90)	2.8	1.9, 8.1	0.0745
Race:OTHER									
Average Daily Normalized 'Off' Time									
BASELINE	3		6.91 (2.75)	8.5	3.7, 8.5				
Low Dose	2		6.13 (3.39)	6.1	3.7, 8.5				
High Dose	1		8.46 (N/A)	8.5	8.5, 8.5				
WEEK 1	3	6.91 (2.75)	2.44 (2.29)	2.8	0.0, 4.5	-4.47 (1.12)	-3.9	-5.8, -3.7	0.0201*
Low Dose	2	6.13 (3.39)	1.39 (1.96)	1.4	0.0, 2.8	-4.74 (1.43)	-4.7	-5.8, -3.7	0.1335
High Dose	1	8.46 (N/A)	4.53 (N/A)	4.5	4.5, 4.5	-3.92 (N/A)	-3.9	-3.9, -3.9	
WEEK 6	3	6.91 (2.75)	2.71 (3.86)	1.0	0.0, 7.1	-4.19 (3.13)	-3.7	-7.5, -1.3	0.1460
Low Dose	2	6.13 (3.39)	0.50 (0.71)	0.5	0.0, 1.0	-5.63 (2.68)	-5.6	-7.5, -3.7	0.2070
High Dose	1	8.46 (N/A)	7.14 (N/A)	7.1	7.1, 7.1	-1.32 (N/A)	-1.3	-1.3, -1.3	

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:OTHER (Cont.)									
Average Daily Normalized 'Off' Time (Cont.)									
WEEK 13	2	6.10 (3.34)	4.24 (5.99)	4.2	0.0, 8.5	-1.86 (2.65)	-1.9	-3.7, 0.0	0.5035
Low Dose	1	3.73 (N/A)	0.00 (N/A)	0.0	0.0, 0.0	-3.73 (N/A)	-3.7	-3.7, -3.7	
High Dose	1	8.46 (N/A)	8.48 (N/A)	8.5	8.5, 8.5	0.02 (N/A)	0.0	0.0, 0.0	
WEEK 26	1	3.73 (N/A)	0.00 (N/A)	0.0	0.0, 0.0	-3.73 (N/A)	-3.7	-3.7, -3.7	
Low Dose	1	3.73 (N/A)	0.00 (N/A)	0.0	0.0, 0.0	-3.73 (N/A)	-3.7	-3.7, -3.7	
High Dose	0								
WEEK 39	1	3.73 (N/A)	13.33 (N/A)	13.3	13.3, 13.3	9.60 (N/A)	9.6	9.6, 9.6	
Low Dose	1	3.73 (N/A)	13.33 (N/A)	13.3	13.3, 13.3	9.60 (N/A)	9.6	9.6, 9.6	
High Dose	0								
Average Daily Normalized 'On' Time Without Dyskinesia									
BASELINE	3		8.03 (0.90)	7.5	7.5, 9.1				
Low Dose	2		8.27 (1.13)	8.3	7.5, 9.1				
High Dose	1		7.54 (N/A)	7.5	7.5, 7.5				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:OTHER (Cont.)									
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 1	3	8.03 (0.90)	7.25 (4.01)	6.8	3.5, 11.5	-0.78 (4.16)	-2.3	-4.0, 3.9	0.7761
Low Dose	2	8.27 (1.13)	5.14 (2.34)	5.1	3.5, 6.8	-3.13 (1.21)	-3.1	-4.0, -2.3	0.1695
High Dose	1	7.54 (N/A)	11.47 (N/A)	11.5	11.5, 11.5	3.92 (N/A)	3.9	3.9, 3.9	
WEEK 6	3	8.03 (0.90)	4.09 (4.47)	3.4	0.0, 8.9	-3.94 (5.20)	-4.1	-9.1, 1.3	0.3194
Low Dose	2	8.27 (1.13)	1.70 (2.40)	1.7	0.0, 3.4	-6.57 (3.53)	-6.6	-9.1, -4.1	0.2310
High Dose	1	7.54 (N/A)	8.86 (N/A)	8.9	8.9, 8.9	1.32 (N/A)	1.3	1.3, 1.3	
WEEK 13	2	8.30 (1.08)	8.15 (0.89)	8.1	7.5, 8.8	-0.16 (0.19)	-0.2	-0.3, -0.0	0.4548
Low Dose	1	9.07 (N/A)	8.77 (N/A)	8.8	8.8, 8.8	-0.29 (N/A)	-0.3	-0.3, -0.3	
High Dose	1	7.54 (N/A)	7.52 (N/A)	7.5	7.5, 7.5	-0.02 (N/A)	-0.0	-0.0, -0.0	
WEEK 26	1	9.07 (N/A)	12.58 (N/A)	12.6	12.6, 12.6	3.52 (N/A)	3.5	3.5, 3.5	
Low Dose	1	9.07 (N/A)	12.58 (N/A)	12.6	12.6, 12.6	3.52 (N/A)	3.5	3.5, 3.5	
High Dose	0								
WEEK 39	1	9.07 (N/A)	2.67 (N/A)	2.7	2.7, 2.7	-6.40 (N/A)	-6.4	-6.4, -6.4	
Low Dose	1	9.07 (N/A)	2.67 (N/A)	2.7	2.7, 2.7	-6.40 (N/A)	-6.4	-6.4, -6.4	
High Dose	0								

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:OTHER (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia									
BASELINE	3		0.89 (1.54)	0.0	0.0, 2.7				
Low Dose	2		1.33 (1.89)	1.3	0.0, 2.7				
High Dose	1		0.00 (N/A)	0.0	0.0, 0.0				
WEEK 1	3	0.89 (1.54)	4.58 (4.61)	4.5	0.0, 9.2	3.69 (3.35)	4.5	0.0, 6.5	0.1969
Low Dose	2	1.33 (1.89)	6.86 (3.32)	6.9	4.5, 9.2	5.53 (1.43)	5.5	4.5, 6.5	0.1154
High Dose	1	0.00 (N/A)	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
WEEK 6	3	0.89 (1.54)	5.65 (6.18)	4.7	0.0, 12.2	4.76 (4.79)	4.7	0.0, 9.6	0.2274
Low Dose	2	1.33 (1.89)	8.47 (5.33)	8.5	4.7, 12.2	7.14 (3.45)	7.1	4.7, 9.6	0.2097
High Dose	1	0.00 (N/A)	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
WEEK 13	2	1.33 (1.89)	3.61 (5.11)	3.6	0.0, 7.2	2.28 (3.22)	2.3	0.0, 4.6	0.5000
Low Dose	1	2.67 (N/A)	7.23 (N/A)	7.2	7.2, 7.2	4.56 (N/A)	4.6	4.6, 4.6	
High Dose	1	0.00 (N/A)	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit Mean (SD)	Visit Median	Visit Min, Max	Change from Baseline Mean (SD)	Change from Baseline Median	Change from Baseline Min, Max	P-Value &
Race:OTHER (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 26	1	2.67 (N/A)	3.42 (N/A)	3.4	3.4, 3.4	0.75 (N/A)	0.7	0.7, 0.7	
Low Dose	1	2.67 (N/A)	3.42 (N/A)	3.4	3.4, 3.4	0.75 (N/A)	0.7	0.7, 0.7	
High Dose	0								
WEEK 39	1	2.67 (N/A)	0.00 (N/A)	0.0	0.0, 0.0	-2.67 (N/A)	-2.7	-2.7, -2.7	
Low Dose	1	2.67 (N/A)	0.00 (N/A)	0.0	0.0, 0.0	-2.67 (N/A)	-2.7	-2.7, -2.7	
High Dose	0								
Average Daily Normalized 'On' Time With Troublesome Dyskinesia									
BASELINE	3		0.18 (0.31)	0.0	0.0, 0.5				
Low Dose	2		0.27 (0.38)	0.3	0.0, 0.5				
High Dose	1		0.00 (N/A)	0.0	0.0, 0.0				
WEEK 1	3	0.18 (0.31)	1.74 (3.02)	0.0	0.0, 5.2	1.56 (3.18)	0.0	-0.5, 5.2	0.4843
Low Dose	2	0.27 (0.38)	2.61 (3.69)	2.6	0.0, 5.2	2.35 (4.07)	2.3	-0.5, 5.2	0.5648
High Dose	1	0.00 (N/A)	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Race:OTHER (Cont.)									
Average Daily Normalized 'On' Time With Troublesome Dyskinesia (Cont.)									
WEEK 6	3	0.18 (0.31)	3.56 (3.46)	3.8	0.0, 6.9	3.38 (3.46)	3.2	0.0, 6.9	0.2326
Low Dose	2	0.27 (0.38)	5.33 (2.23)	5.3	3.8, 6.9	5.07 (2.60)	5.1	3.2, 6.9	0.2220
High Dose	1	0.00 (N/A)	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
WEEK 13	2	0.27 (0.38)	0.00 (0.00)	0.0	0.0, 0.0	-0.27 (0.38)	-0.3	-0.5, 0.0	0.5000
Low Dose	1	0.53 (N/A)	0.00 (N/A)	0.0	0.0, 0.0	-0.53 (N/A)	-0.5	-0.5, -0.5	
High Dose	1	0.00 (N/A)	0.00 (N/A)	0.0	0.0, 0.0	0.00 (N/A)	0.0	0.0, 0.0	
WEEK 26	1	0.53 (N/A)	0.00 (N/A)	0.0	0.0, 0.0	-0.53 (N/A)	-0.5	-0.5, -0.5	
Low Dose	1	0.53 (N/A)	0.00 (N/A)	0.0	0.0, 0.0	-0.53 (N/A)	-0.5	-0.5, -0.5	
High Dose	0								
WEEK 39	1	0.53 (N/A)	0.00 (N/A)	0.0	0.0, 0.0	-0.53 (N/A)	-0.5	-0.5, -0.5	
Low Dose	1	0.53 (N/A)	0.00 (N/A)	0.0	0.0, 0.0	-0.53 (N/A)	-0.5	-0.5, -0.5	
High Dose	0								

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit Mean (SD)	Visit Median	Visit Min, Max	Change from Baseline Mean (SD)	Change from Baseline Median	Change from Baseline Min, Max	P-Value &
Race:OTHER (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia									
BASELINE	3		8.92 (2.44)	7.5	7.5, 11.7				
Low Dose	2		9.60 (3.01)	9.6	7.5, 11.7				
High Dose	1		7.54 (N/A)	7.5	7.5, 7.5				
WEEK 1	3	8.92 (2.44)	11.82 (4.01)	11.5	8.0, 16.0	2.91 (2.07)	3.9	0.5, 4.3	0.1351
Low Dose	2	9.60 (3.01)	12.00 (5.66)	12.0	8.0, 16.0	2.40 (2.64)	2.4	0.5, 4.3	0.4214
High Dose	1	7.54 (N/A)	11.47 (N/A)	11.5	11.5, 11.5	3.92 (N/A)	3.9	3.9, 3.9	
WEEK 6	3	8.92 (2.44)	9.73 (2.21)	8.9	8.1, 12.2	0.82 (0.44)	0.6	0.5, 1.3	0.0850
Low Dose	2	9.60 (3.01)	10.17 (2.93)	10.2	8.1, 12.2	0.56 (0.08)	0.6	0.5, 0.6	0.0631
High Dose	1	7.54 (N/A)	8.86 (N/A)	8.9	8.9, 8.9	1.32 (N/A)	1.3	1.3, 1.3	
WEEK 13	2	9.64 (2.96)	11.76 (5.99)	11.8	7.5, 16.0	2.12 (3.03)	2.1	-0.0, 4.3	0.5031
Low Dose	1	11.73 (N/A)	16.00 (N/A)	16.0	16.0, 16.0	4.27 (N/A)	4.3	4.3, 4.3	
High Dose	1	7.54 (N/A)	7.52 (N/A)	7.5	7.5, 7.5	-0.02 (N/A)	-0.0	-0.0, -0.0	

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit Mean (SD)	Visit Median	Visit Min, Max	Change from Baseline Mean (SD)	Change from Baseline Median	Change from Baseline Min, Max	P-Value &
Race:OTHER (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia (Cont.)									
WEEK 26	1	11.73 (N/A)	16.00 (N/A)	16.0	16.0, 16.0	4.27 (N/A)	4.3	4.3, 4.3	
Low Dose	1	11.73 (N/A)	16.00 (N/A)	16.0	16.0, 16.0	4.27 (N/A)	4.3	4.3, 4.3	
High Dose	0								
WEEK 39	1	11.73 (N/A)	2.67 (N/A)	2.7	2.7, 2.7	-9.07 (N/A)	-9.1	-9.1, -9.1	
Low Dose	1	11.73 (N/A)	2.67 (N/A)	2.7	2.7, 2.7	-9.07 (N/A)	-9.1	-9.1, -9.1	
High Dose	0								
Age category:< 65 years									
Average Daily Normalized 'Off' Time									
BASELINE	117		5.78 (2.19)	5.8	0.0, 10.3				
Low Dose	61		5.81 (2.06)	5.8	0.0, 10.3				
High Dose	56		5.74 (2.34)	5.8	0.0, 9.6				
WEEK 1	112	5.80 (2.22)	3.62 (3.29)	2.7	0.0, 14.8	-2.18 (3.35)	-2.4	-10.2, 5.9	<=0.001***
Low Dose	57	5.86 (2.09)	3.92 (3.22)	2.9	0.0, 13.8	-1.94 (3.12)	-1.9	-10.2, 5.2	<=0.001***
High Dose	55	5.74 (2.36)	3.31 (3.37)	2.1	0.0, 14.8	-2.42 (3.59)	-3.3	-8.9, 5.9	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit Mean (SD)	Visit Median	Visit Min, Max	Change from Baseline Mean (SD)	Change from Baseline Median	Change from Baseline Min, Max	P-Value &
Age category:< 65 years (Cont.)									
Average Daily Normalized 'Off' Time (Cont.)									
WEEK 6	99	5.79 (2.18)	3.06 (3.03)	2.6	0.0, 12.3	-2.73 (3.27)	-3.1	-10.2, 6.7	<=0.001***
Low Dose	52	5.84 (1.94)	3.21 (2.97)	3.1	0.0, 12.3	-2.63 (3.37)	-2.9	-10.2, 5.7	<=0.001***
High Dose	47	5.73 (2.44)	2.90 (3.12)	1.9	0.0, 10.7	-2.83 (3.19)	-3.3	-8.2, 6.7	<=0.001***
WEEK 13	57	5.48 (2.32)	3.09 (3.62)	1.7	0.0, 12.1	-2.39 (3.60)	-3.2	-9.9, 6.3	<=0.001***
Low Dose	29	5.83 (2.24)	2.65 (3.44)	1.5	0.0, 12.1	-3.18 (3.41)	-3.4	-9.9, 5.0	<=0.001***
High Dose	28	5.12 (2.38)	3.55 (3.81)	1.8	0.0, 10.7	-1.57 (3.67)	-1.5	-7.5, 6.3	0.0321*
WEEK 26	66	5.62 (2.28)	2.55 (2.94)	1.4	0.0, 11.2	-3.06 (3.18)	-3.2	-10.2, 5.5	<=0.001***
Low Dose	32	5.67 (2.04)	2.51 (3.18)	1.1	0.0, 11.2	-3.15 (3.48)	-3.8	-10.2, 5.5	<=0.001***
High Dose	34	5.57 (2.52)	2.59 (2.75)	1.6	0.0, 8.9	-2.98 (2.93)	-2.7	-9.2, 4.4	<=0.001***
WEEK 39	59	5.62 (2.24)	2.31 (2.55)	1.3	0.0, 11.4	-3.31 (2.92)	-3.2	-9.9, 6.4	<=0.001***
Low Dose	31	5.63 (2.08)	2.21 (2.56)	1.2	0.0, 11.4	-3.42 (3.19)	-2.9	-9.9, 6.4	<=0.001***
High Dose	28	5.61 (2.45)	2.43 (2.59)	1.4	0.0, 7.2	-3.19 (2.64)	-3.4	-9.2, 4.0	<=0.001***
WEEK 52	60	5.60 (2.40)	2.62 (3.19)	1.1	0.0, 11.5	-2.98 (3.22)	-3.4	-10.2, 5.9	<=0.001***
Low Dose	31	5.71 (2.22)	2.81 (3.22)	1.7	0.0, 10.9	-2.90 (3.55)	-3.1	-10.2, 5.9	<=0.001***
High Dose	29	5.49 (2.61)	2.42 (3.20)	0.5	0.0, 11.5	-3.07 (2.89)	-3.4	-9.2, 2.6	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Age category:< 65 years (Cont.)									
Average Daily Normalized 'On' Time Without Dyskinesia									
BASELINE	117		6.82 (3.42)	6.7	0.0, 15.4				
Low Dose	61		6.64 (3.49)	6.7	0.0, 15.4				
High Dose	56		7.01 (3.35)	6.7	0.0, 13.8				
WEEK 1	112	6.78 (3.39)	8.85 (4.57)	8.7	0.0, 16.0	2.07 (3.69)	1.7	-5.4, 12.0	<=0.001***
Low Dose	57	6.51 (3.42)	8.63 (4.42)	8.6	0.0, 16.0	2.13 (3.12)	2.0	-4.0, 10.2	<=0.001***
High Dose	55	7.06 (3.36)	9.07 (4.74)	9.1	0.0, 16.0	2.01 (4.23)	1.5	-5.4, 12.0	<=0.001***
WEEK 6	99	6.93 (3.39)	10.49 (4.57)	11.6	0.0, 16.0	3.56 (4.33)	4.0	-6.7, 12.7	<=0.001***
Low Dose	52	6.75 (3.46)	10.38 (4.45)	11.4	0.0, 16.0	3.63 (4.07)	4.0	-6.1, 12.7	<=0.001***
High Dose	47	7.14 (3.34)	10.62 (4.74)	12.8	0.0, 16.0	3.48 (4.63)	4.2	-6.7, 12.0	<=0.001***
WEEK 13	57	6.97 (3.74)	10.78 (4.80)	12.3	0.0, 16.0	3.82 (4.30)	3.7	-9.0, 14.1	<=0.001***
Low Dose	29	7.12 (3.93)	10.63 (5.25)	12.3	0.0, 16.0	3.51 (4.21)	3.7	-9.0, 9.9	<=0.001***
High Dose	28	6.81 (3.60)	10.94 (4.37)	11.9	2.7, 16.0	4.13 (4.45)	4.1	-6.3, 14.1	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit Mean (SD)	Visit Median	Visit Min, Max	Change from Baseline Mean (SD)	Change from Baseline Median	Change from Baseline Min, Max	P-Value &
Age category:< 65 years (Cont.)									
Average Daily Normalized 'On' Time Without Dyskinesia (Cont.)									
WEEK 26	66	7.30 (3.39)	11.26 (4.51)	12.9	0.0, 16.0	3.95 (4.44)	4.3	-10.1, 14.1	<=0.001***
Low Dose	32	7.17 (3.59)	11.45 (4.94)	13.5	0.0, 16.0	4.28 (4.44)	4.8	-10.1, 11.0	<=0.001***
High Dose	34	7.42 (3.24)	11.07 (4.14)	11.7	0.0, 16.0	3.65 (4.49)	3.8	-9.6, 14.1	<=0.001***
WEEK 39	59	7.26 (3.37)	10.96 (4.60)	11.3	0.0, 16.0	3.70 (4.03)	3.3	-10.6, 12.4	<=0.001***
Low Dose	31	7.27 (3.37)	11.57 (4.74)	12.4	0.3, 16.0	4.30 (4.42)	4.9	-10.6, 10.9	<=0.001***
High Dose	28	7.25 (3.42)	10.29 (4.42)	11.0	0.0, 16.0	3.04 (3.52)	2.8	-2.8, 12.4	<=0.001***
WEEK 52	60	7.22 (3.44)	10.37 (5.27)	11.9	0.0, 16.0	3.15 (4.31)	3.4	-12.0, 11.3	<=0.001***
Low Dose	31	6.79 (3.64)	11.01 (4.86)	12.4	0.0, 16.0	4.22 (4.10)	4.3	-6.5, 11.3	<=0.001***
High Dose	29	7.68 (3.22)	9.68 (5.68)	9.6	0.0, 16.0	2.00 (4.30)	2.2	-12.0, 9.5	0.0183*
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia									
BASELINE	117		2.56 (2.71)	2.1	0.0, 12.2				
Low Dose	61		2.49 (2.48)	2.1	0.0, 10.3				
High Dose	56		2.64 (2.96)	2.2	0.0, 12.2				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit Mean (SD)	Visit Median	Visit Min, Max	Change from Baseline Mean (SD)	Change from Baseline Median	Change from Baseline Min, Max	P-Value &
Age category:< 65 years (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 1	112	2.61 (2.74)	2.59 (2.88)	1.7	0.0, 11.9	-0.02 (2.53)	0.0	-8.2, 8.8	0.9198
Low Dose	57	2.58 (2.50)	2.54 (2.72)	2.1	0.0, 10.7	-0.04 (2.30)	0.0	-5.3, 6.9	0.8870
High Dose	55	2.65 (2.99)	2.64 (3.07)	1.5	0.0, 11.9	-0.00 (2.77)	0.0	-8.2, 8.8	0.9913
WEEK 6	99	2.62 (2.81)	1.98 (3.13)	0.5	0.0, 13.9	-0.64 (2.74)	-0.4	-7.6, 9.6	0.0220*
Low Dose	52	2.56 (2.51)	1.86 (2.77)	0.6	0.0, 10.4	-0.70 (2.43)	-0.3	-5.1, 6.2	0.0431*
High Dose	47	2.67 (3.13)	2.10 (3.52)	0.0	0.0, 13.9	-0.58 (3.07)	-0.4	-7.6, 9.6	0.2049
WEEK 13	57	2.80 (3.07)	1.67 (2.76)	0.6	0.0, 15.5	-1.13 (3.06)	-0.5	-12.2, 5.2	0.0070**
Low Dose	29	2.27 (2.77)	2.21 (3.48)	1.0	0.0, 15.5	-0.07 (2.42)	0.0	-4.2, 5.2	0.8809
High Dose	28	3.35 (3.32)	1.12 (1.62)	0.0	0.0, 5.9	-2.24 (3.29)	-1.3	-12.2, 3.3	0.0013**
WEEK 26	66	2.45 (2.62)	1.70 (2.52)	0.7	0.0, 12.1	-0.75 (3.07)	-0.1	-12.2, 7.2	0.0518
Low Dose	32	2.47 (2.39)	1.55 (2.41)	0.7	0.0, 12.1	-0.93 (2.54)	-0.8	-6.5, 4.6	0.0475*
High Dose	34	2.43 (2.86)	1.85 (2.64)	0.6	0.0, 11.0	-0.58 (3.53)	-0.0	-12.2, 7.2	0.3445
WEEK 39	59	2.41 (2.68)	2.30 (3.80)	0.2	0.0, 16.0	-0.11 (3.30)	-0.2	-6.4, 15.4	0.8051
Low Dose	31	2.38 (2.35)	1.98 (3.76)	0.0	0.0, 15.4	-0.40 (3.72)	-0.7	-4.4, 15.4	0.5587
High Dose	28	2.44 (3.05)	2.65 (3.88)	0.7	0.0, 16.0	0.21 (2.80)	0.0	-6.4, 5.8	0.6896

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit Mean (SD)	Visit Median	Visit Min, Max	Change from Baseline Mean (SD)	Change from Baseline Median	Change from Baseline Min, Max	P-Value &
Age category:< 65 years (Cont.)									
Average Daily Normalized 'On' Time With Non-Troublesome Dyskinesia (Cont.)									
WEEK 52	60	2.51 (2.79)	2.50 (4.43)	0.4	0.0, 16.0	-0.01 (3.58)	-0.2	-6.5, 12.9	0.9799
Low Dose	31	2.82 (2.77)	1.98 (3.96)	0.2	0.0, 16.0	-0.84 (3.43)	-0.6	-6.5, 9.2	0.1818
High Dose	29	2.19 (2.83)	3.06 (4.89)	0.7	0.0, 16.0	0.88 (3.57)	0.0	-3.9, 12.9	0.1963
Average Daily Normalized 'On' Time With Troublesome Dyskinesia									
BASELINE	117		0.85 (1.53)	0.0	0.0, 8.8				
Low Dose	61		1.06 (1.77)	0.0	0.0, 8.8				
High Dose	56		0.61 (1.18)	0.0	0.0, 5.0				
WEEK 1	112	0.81 (1.48)	0.94 (2.17)	0.0	0.0, 11.7	0.13 (1.88)	0.0	-5.7, 7.0	0.4566
Low Dose	57	1.05 (1.74)	0.91 (2.18)	0.0	0.0, 11.7	-0.14 (1.82)	0.0	-5.7, 5.8	0.5637
High Dose	55	0.56 (1.12)	0.97 (2.17)	0.0	0.0, 9.8	0.42 (1.91)	0.0	-2.9, 7.0	0.1130
WEEK 6	99	0.66 (1.13)	0.47 (1.37)	0.0	0.0, 9.0	-0.19 (1.38)	0.0	-4.1, 6.9	0.1716
Low Dose	52	0.84 (1.31)	0.54 (1.64)	0.0	0.0, 9.0	-0.30 (1.64)	0.0	-4.1, 6.9	0.1924
High Dose	47	0.46 (0.86)	0.39 (1.01)	0.0	0.0, 4.4	-0.07 (1.02)	0.0	-3.4, 4.4	0.6423

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit Mean (SD)	Visit Median	Visit Min, Max	Change from Baseline Mean (SD)	Change from Baseline Median	Change from Baseline Min, Max	P-Value &
Age category:< 65 years (Cont.)									
Average Daily Normalized 'On' Time With Troublesome Dyskinesia (Cont.)									
WEEK 13	57	0.75 (1.32)	0.46 (1.45)	0.0	0.0, 8.0	-0.29 (1.31)	0.0	-4.6, 6.0	0.0964
Low Dose	29	0.78 (1.35)	0.52 (1.77)	0.0	0.0, 8.0	-0.26 (1.60)	0.0	-4.6, 6.0	0.3877
High Dose	28	0.72 (1.30)	0.39 (1.05)	0.0	0.0, 3.7	-0.33 (0.94)	0.0	-3.4, 2.6	0.0777
WEEK 26	66	0.63 (1.18)	0.49 (1.86)	0.0	0.0, 12.1	-0.14 (1.77)	0.0	-4.0, 8.8	0.5218
Low Dose	32	0.68 (1.19)	0.49 (2.15)	0.0	0.0, 12.1	-0.19 (1.69)	0.0	-3.4, 7.2	0.5202
High Dose	34	0.58 (1.18)	0.49 (1.58)	0.0	0.0, 8.8	-0.09 (1.87)	0.0	-4.0, 8.8	0.7809
WEEK 39	59	0.71 (1.29)	0.43 (1.26)	0.0	0.0, 8.1	-0.29 (1.47)	0.0	-5.0, 7.3	0.1404
Low Dose	31	0.72 (1.32)	0.24 (0.75)	0.0	0.0, 3.5	-0.48 (0.78)	0.0	-2.8, 0.0	0.0018**
High Dose	28	0.70 (1.27)	0.63 (1.65)	0.0	0.0, 8.1	-0.07 (1.97)	0.0	-5.0, 7.3	0.8528
WEEK 52	60	0.66 (1.20)	0.51 (1.86)	0.0	0.0, 13.5	-0.15 (2.07)	0.0	-5.0, 13.0	0.5705
Low Dose	31	0.67 (1.15)	0.20 (0.59)	0.0	0.0, 2.7	-0.47 (1.13)	0.0	-3.4, 1.8	0.0257*
High Dose	29	0.64 (1.27)	0.83 (2.58)	0.0	0.0, 13.5	0.19 (2.73)	0.0	-5.0, 13.0	0.7090

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Age category:< 65 years (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia									
BASELINE	117		9.38 (2.48)	9.8	2.2, 16.0				
Low Dose	61		9.13 (2.63)	9.9	2.2, 16.0				
High Dose	56		9.65 (2.30)	9.6	4.8, 16.0				
WEEK 1	112	9.39 (2.48)	11.44 (3.65)	11.8	1.2, 16.0	2.04 (3.46)	2.0	-5.9, 8.9	<=0.001***
Low Dose	57	9.09 (2.64)	11.18 (3.62)	11.3	1.6, 16.0	2.08 (3.07)	1.9	-5.2, 8.3	<=0.001***
High Dose	55	9.71 (2.28)	11.71 (3.68)	12.0	1.2, 16.0	2.01 (3.86)	2.1	-5.9, 8.9	<=0.001***
WEEK 6	99	9.55 (2.32)	12.47 (3.22)	13.1	3.7, 16.0	2.92 (3.33)	3.5	-6.7, 9.9	<=0.001***
Low Dose	52	9.31 (2.40)	12.24 (3.24)	12.7	3.7, 16.0	2.93 (3.36)	3.6	-5.7, 9.9	<=0.001***
High Dose	47	9.81 (2.23)	12.71 (3.21)	13.5	5.1, 16.0	2.90 (3.33)	3.5	-6.7, 8.2	<=0.001***
WEEK 13	57	9.77 (2.57)	12.45 (3.86)	13.8	3.9, 16.0	2.68 (3.56)	2.9	-6.3, 9.9	<=0.001***
Low Dose	29	9.39 (2.77)	12.83 (3.82)	14.5	3.9, 16.0	3.44 (3.30)	3.3	-5.0, 9.9	<=0.001***
High Dose	28	10.16 (2.34)	12.06 (3.93)	13.6	5.3, 16.0	1.89 (3.69)	2.3	-6.3, 7.5	0.0115*

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Age category:< 65 years (Cont.)									
Average Daily Normalized 'On' Time Without Troublesome Dyskinesia (Cont.)									
WEEK 26	66	9.76 (2.47)	12.96 (3.39)	14.4	1.5, 16.0	3.20 (3.33)	3.1	-5.5, 10.2	<=0.001***
Low Dose	32	9.65 (2.46)	13.00 (3.86)	14.8	1.5, 16.0	3.35 (3.79)	4.0	-5.5, 10.2	<=0.001***
High Dose	34	9.86 (2.52)	12.92 (2.95)	14.1	7.1, 16.0	3.07 (2.89)	2.7	-2.5, 9.4	<=0.001***
WEEK 39	59	9.67 (2.52)	13.26 (3.01)	14.0	2.4, 16.0	3.60 (3.28)	3.4	-9.2, 9.9	<=0.001***
Low Dose	31	9.64 (2.66)	13.55 (2.69)	14.4	4.6, 16.0	3.90 (3.23)	3.1	-5.9, 9.9	<=0.001***
High Dose	28	9.69 (2.41)	12.94 (3.35)	13.9	2.4, 16.0	3.25 (3.36)	3.4	-9.2, 9.7	<=0.001***
WEEK 52	60	9.74 (2.68)	12.87 (3.55)	14.0	2.5, 16.0	3.13 (3.18)	3.1	-5.4, 10.2	<=0.001***
Low Dose	31	9.61 (2.76)	12.99 (3.21)	13.7	5.1, 16.0	3.37 (3.41)	3.1	-5.4, 10.2	<=0.001***
High Dose	29	9.87 (2.63)	12.75 (3.94)	14.9	2.5, 16.0	2.88 (2.95)	2.9	-3.8, 8.4	<=0.001***
Age category:>= 65 years									
Average Daily Normalized 'Off' Time									
BASELINE	119		6.03 (2.30)	6.1	0.0, 12.6				
Low Dose	66		5.56 (2.32)	5.9	0.0, 10.0				
High Dose	53		6.62 (2.15)	7.0	1.5, 12.6				

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]

TABLE 14.2 1.4

Change from Baseline to Each Planned Visit in Average Daily Normalized Time in Hours
Based On Parkinson's Disease Diary by Subgroups
(FAS)

Variable / Parameter / Time Point / Dose Category	N	Baseline Mean (SD)	Visit: Mean (SD)	Visit: Median	Visit: Min, Max	Change from Baseline: Mean (SD)	Change from Baseline: Median	Change from Baseline: Min, Max	P-Value &
Age category:>= 65 years (Cont.)									
Average Daily Normalized 'Off' Time (Cont.)									
WEEK 1	113	6.02 (2.28)	4.31 (3.54)	3.8	0.0, 16.0	-1.71 (3.97)	-2.1	-9.7, 10.4	<=0.001***
Low Dose	64	5.62 (2.31)	3.49 (3.18)	2.6	0.0, 10.3	-2.13 (3.82)	-2.5	-9.7, 5.9	<=0.001***
High Dose	49	6.55 (2.15)	5.39 (3.73)	5.6	0.0, 16.0	-1.16 (4.15)	-1.4	-8.3, 10.4	0.0551
WEEK 6	106	6.08 (2.29)	4.00 (3.41)	3.7	0.0, 16.0	-2.08 (3.88)	-2.4	-10.6, 9.9	<=0.001***
Low Dose	59	5.63 (2.29)	3.41 (3.65)	2.9	0.0, 16.0	-2.22 (3.90)	-2.4	-8.2, 9.9	<=0.001***
High Dose	47	6.65 (2.20)	4.74 (2.95)	4.5	0.0, 12.5	-1.91 (3.88)	-2.4	-10.6, 6.8	0.0016**
WEEK 13	57	5.56 (2.26)	3.08 (3.33)	1.9	0.0, 13.4	-2.47 (3.83)	-3.2	-9.2, 8.1	<=0.001***
Low Dose	35	5.06 (2.17)	3.08 (3.63)	1.7	0.0, 13.4	-1.98 (4.07)	-2.7	-7.0, 8.1	0.0069**
High Dose	22	6.35 (2.21)	3.09 (2.86)	2.5	0.0, 9.3	-3.26 (3.34)	-3.3	-9.2, 4.0	<=0.001***
WEEK 26	65	6.29 (2.14)	2.67 (3.12)	1.2	0.0, 14.3	-3.62 (3.32)	-3.7	-10.6, 7.1	<=0.001***
Low Dose	37	5.85 (1.91)	2.40 (3.21)	0.8	0.0, 14.3	-3.45 (3.30)	-3.7	-8.2, 7.1	<=0.001***
High Dose	28	6.86 (2.33)	3.03 (3.02)	2.0	0.0, 9.8	-3.83 (3.40)	-3.6	-10.6, 5.5	<=0.001***
WEEK 39	60	6.15 (2.17)	2.98 (2.97)	2.2	0.0, 13.3	-3.17 (3.35)	-3.2	-9.1, 9.6	<=0.001***
Low Dose	36	5.62 (1.86)	2.83 (3.19)	1.9	0.0, 13.3	-2.79 (3.40)	-3.1	-7.5, 9.6	<=0.001***
High Dose	24	6.95 (2.40)	3.21 (2.67)	3.0	0.0, 7.7	-3.73 (3.28)	-3.5	-9.1, 2.9	<=0.001***

Note: A PD diary recording day with no more than 2 hours of missing data (4 or less missing entries) or at least 12 awake hours (i.e., at least 24 'Off' or 'On' time entries) for the entire 24-hour diary is considered as a valid PD diary day.
&: P-value is obtained from two-sided paired-sample t-test.
* P-value <= 0.05; ** P-value <= 0.01; *** P-value <= 0.001.

Program Source Code: [redacted]