被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
妄想	X			X
妄想症	X			X
精神病性障害	X			X

Treatment Group	Age at Study Start	Sex	Race
ABBV-951	5[redacted]	MALE	WHITE

Medical History	Onset Year
MYOPIA	20[redacted]
BACK PAIN	20[redacted]
ANXIETY	20[redacted]
ARTHRITIS, NECK	20[redacted]
VITAMIN B12 DEFICIENCY	20[redacted]
VITAMIN B6 DEFICIENCY	20[redacted]

Indication Disease History, Diagnosis and/or Symptoms	Onset Year
LEVODOPA INDUCED DYSKINESIA	NOT REPORTED
PARKINSON'S DISEASE	20[redacted]
PARKINSON'S DISEASE DIAGNOSIS	20[redacted]
ONSET OF MOTOR FLUCTUATION	20[redacted]

Prior Procedures	Procedure Year
HERNIA REPAIR	19[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	1 CIGARETTE	1	19[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	LESS THAN 2 DRINKS

Study Drug Prescription

Study Drug	New Quadrant for Pump Infusion	Continuous Flow Rate (mL/h)	Infusion Loading Dose Volume (mL)	Oral study drug dose (CAPSULE)	Dose Date/Day
ABBV-951	SITE B1				[redacted]20[redacted]/ 1
ABBV-951		0.57	1.1		[redacted]20[redacted]/ 1
ABBV-951	SITE B10				[redacted]20[redacted]/ 3
ABBV-951	SITE A6				[redacted]20[redacted]/ 4
ABBV-951	SITE A11				[redacted]20[redacted]/ 7
ABBV-951	SITE A3				[redacted]20[redacted]/ 8
ABBV-951	SITE A9				[redacted]20[redacted]/ 11
ABBV-951	SITE B4				[redacted]20[redacted]/ 13
ABBV-951	SITE B2				[redacted]20[redacted]/ 16
ABBV-951	SITE B11				[redacted]20[redacted]/ 16
ABBV-951	SITE A2				[redacted]20[redacted]/ 19
ABBV-951	SITE B5				[redacted]20[redacted]/ 22
ABBV-951	SITE A1				[redacted]20[redacted]/ 25
ABBV-951	SITE A10				[redacted]20[redacted]/ 25
ABBV-951	SITE B8				[redacted]20[redacted]/ 28
ABBV-951		0.60	0.0		[redacted]20[redacted]/ 29
ABBV-951	SITE B12				[redacted]20[redacted]/ 32
ABBV-951	SITE A2				[redacted]20[redacted]/ 35
ABBV-951	SITE A5				[redacted]20[redacted]/ 35
ABBV-951	SITE B9				[redacted]20[redacted]/ 38
ABBV-951	SITE A3				[redacted]20[redacted]/ 41
ABBV-951	SITE A12				[redacted]20[redacted]/ 44
ABBV-951	SITE B4				[redacted]20[redacted]/ 44
ABBV-951	SITE B10				[redacted]20[redacted]/ 47
ABBV-951	SITE B4				[redacted]20[redacted]/ 47
ABBV-951	SITE A9				[redacted]20[redacted]/ 51
ABBV-951	SITE B2				[redacted]20[redacted]/ 54
ABBV-951	SITE B7				[redacted]20[redacted]/ 57
ABBV-951	SITE A4				[redacted]20[redacted]/ 60
ABBV-951	SITE A3				[redacted]20[redacted]/ 63
ABBV-951	SITE B4				[redacted]20[redacted]/ 80

ABBV-951		0.47	0.0	[redacted] / 80
ABBV-951	SITE A9			[redacted] / 83
ABBV-951	SITE B6			[redacted] / 86

Daily Dose by Molecular Weight

Study Drug	CSCI Infusion (mg LD)	Total Oral Dose (mg)	Route (Subcutaneous) / Frequency (Times per Day)	First Dose Date/Day	Last Dose Date/Day
ABBV-951 Loading dose	187.82		SC / CONTINUOUS	[redacted] / 1	
Placebo ORAL CD/LD			ORAL / 5	[redacted] / 1	
ABBV-951	1192.26		SC / CONTINUOUS	[redacted] / 1	[redacted] / 1
Placebo ORAL CD/LD			ORAL / 7	[redacted] / 2	
ABBV-951	2269.67		SC / CONTINUOUS	[redacted] / 2	[redacted] / 2
Placebo ORAL CD/LD			ORAL / 7	[redacted] / 3	
ABBV-951	2255.07		SC / CONTINUOUS	[redacted] / 3	[redacted] / 3
Placebo ORAL CD/LD			ORAL / 9	[redacted] / 4	
ABBV-951	2185.00		SC / CONTINUOUS	[redacted] / 4	[redacted] / 4
Placebo ORAL CD/LD			ORAL / 9	[redacted] / 5	
ABBV-951	2201.54		SC / CONTINUOUS	[redacted] / 5	[redacted] / 5
Placebo ORAL CD/LD			ORAL / 9	[redacted] / 6	
ABBV-951	2281.35		SC / CONTINUOUS	[redacted] / 6	[redacted] / 6
Placebo ORAL CD/LD			ORAL / 9	[redacted] / 7	
ABBV-951	2204.46		SC / CONTINUOUS	[redacted] / 7	[redacted] / 7
Placebo ORAL CD/LD			ORAL / 9	[redacted] / 8	
ABBV-951	2221.01		SC / CONTINUOUS	[redacted] / 8	[redacted] / 8
Placebo ORAL CD/LD			ORAL / 9	[redacted] / 9	
ABBV-951	2255.07		SC / CONTINUOUS	[redacted] / 9	[redacted] / 9
Placebo ORAL CD/LD			ORAL / 9	[redacted] / 10	
ABBV-951	2171.37		SC / CONTINUOUS	[redacted] / 10	[redacted] / 10
Placebo ORAL CD/LD			ORAL / 9	[redacted] / 11	
ABBV-951	2215.17		SC / CONTINUOUS	[redacted] / 11	[redacted] / 11
Placebo ORAL CD/LD			ORAL / 9	[redacted] / 12	
ABBV-951	2304.71		SC / CONTINUOUS	[redacted] / 12	[redacted] / 12
Placebo ORAL CD/LD			ORAL / 9	[redacted] / 13	
ABBV-951	2190.84		SC / CONTINUOUS	[redacted] / 13	[redacted] / 13
Placebo ORAL CD/LD			ORAL / 9	[redacted] / 14	
ABBV-951	2260.91		SC / CONTINUOUS	[redacted] / 14	[redacted] / 14
Placebo ORAL CD/LD			ORAL / 9	[redacted] / 15	

ABBV-951	2248.26	SC / CONTINUOUS	[redacted]20[redacted] / 15	[redacted]20[redacted] / 15
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 16	
ABBV-951	2128.55	SC / CONTINUOUS	[redacted]20[redacted] / 16	[redacted]20[redacted] / 16
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 17	
ABBV-951	2257.02	SC / CONTINUOUS	[redacted]20[redacted] / 17	[redacted]20[redacted] / 17
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 18	
ABBV-951	2225.87	SC / CONTINUOUS	[redacted]20[redacted] / 18	[redacted]20[redacted] / 18
Placebo ORAL CD/LD		ORAL / 10	[redacted]20[redacted] / 19	
ABBV-951	2170.40	SC / CONTINUOUS	[redacted]20[redacted] / 19	[redacted]20[redacted] / 19
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 20	
ABBV-951	2276.49	SC / CONTINUOUS	[redacted]20[redacted] / 20	[redacted]20[redacted] / 20
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 21	
ABBV-951	2199.60	SC / CONTINUOUS	[redacted]20[redacted] / 21	[redacted]20[redacted] / 21
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 22	
ABBV-951	2192.78	SC / CONTINUOUS	[redacted]20[redacted] / 22	[redacted]20[redacted] / 22
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 23	
ABBV-951	2269.67	SC / CONTINUOUS	[redacted]20[redacted] / 23	[redacted]20[redacted] / 23
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 24	
ABBV-951	2306.66	SC / CONTINUOUS	[redacted]20[redacted] / 24	[redacted]20[redacted] / 24
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 25	
ABBV-951	2148.01	SC / CONTINUOUS	[redacted]20[redacted] / 25	[redacted]20[redacted] / 25
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 26	
ABBV-951	2215.17	SC / CONTINUOUS	[redacted]20[redacted] / 26	[redacted]20[redacted] / 26
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 27	
ABBV-951	2233.66	SC / CONTINUOUS	[redacted]20[redacted] / 27	[redacted]20[redacted] / 27
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 28	
ABBV-951	2154.83	SC / CONTINUOUS	[redacted]20[redacted] / 28	[redacted]20[redacted] / 28
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 29	
ABBV-951	2284.63	SC / CONTINUOUS	[redacted]20[redacted] / 29	[redacted]20[redacted] / 29
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 30	
ABBV-951	2419.86	SC / CONTINUOUS	[redacted]20[redacted] / 30	[redacted]20[redacted] / 30
Placebo ORAL CD/LD		ORAL / 8	[redacted]20[redacted] / 31	
ABBV-951	2382.98	SC / CONTINUOUS	[redacted]20[redacted] / 31	[redacted]20[redacted] / 31
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 32	
ABBV-951	2392.20	SC / CONTINUOUS	[redacted]20[redacted] / 32	[redacted]20[redacted] / 32
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 33	
ABBV-951	2444.45	SC / CONTINUOUS	[redacted]20[redacted] / 33	[redacted]20[redacted] / 33

Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 34	
ABBV-951	2400.40	SC / CONTINUOUS	[redacted]20[redacted] / 34	[redacted]20[redacted] / 34
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 35	
ABBV-951	2310.24	SC / CONTINUOUS	[redacted]20[redacted] / 35	[redacted]20[redacted] / 35
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 36	
ABBV-951	2385.03	SC / CONTINUOUS	[redacted]20[redacted] / 36	[redacted]20[redacted] / 36
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 37	
ABBV-951	2391.18	SC / CONTINUOUS	[redacted]20[redacted] / 37	[redacted]20[redacted] / 37
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 38	
ABBV-951	2369.66	SC / CONTINUOUS	[redacted]20[redacted] / 38	[redacted]20[redacted] / 38
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 39	
ABBV-951	2408.59	SC / CONTINUOUS	[redacted]20[redacted] / 39	[redacted]20[redacted] / 39
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 40	
ABBV-951	2390.15	SC / CONTINUOUS	[redacted]20[redacted] / 40	[redacted]20[redacted] / 40
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 41	
ABBV-951	2374.79	SC / CONTINUOUS	[redacted]20[redacted] / 41	[redacted]20[redacted] / 41
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 42	
ABBV-951	2415.77	SC / CONTINUOUS	[redacted]20[redacted] / 42	[redacted]20[redacted] / 42
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 43	
ABBV-951	2281.56	SC / CONTINUOUS	[redacted]20[redacted] / 43	[redacted]20[redacted] / 43
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 44	
ABBV-951	2381.96	SC / CONTINUOUS	[redacted]20[redacted] / 44	[redacted]20[redacted] / 44
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 45	
ABBV-951	2437.28	SC / CONTINUOUS	[redacted]20[redacted] / 45	[redacted]20[redacted] / 45
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 46	
ABBV-951	2400.40	SC / CONTINUOUS	[redacted]20[redacted] / 46	[redacted]20[redacted] / 46
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 47	
ABBV-951	2338.93	SC / CONTINUOUS	[redacted]20[redacted] / 47	[redacted]20[redacted] / 47
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 48	
ABBV-951	2399.37	SC / CONTINUOUS	[redacted]20[redacted] / 48	[redacted]20[redacted] / 48
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 49	
ABBV-951	2424.99	SC / CONTINUOUS	[redacted]20[redacted] / 49	[redacted]20[redacted] / 49
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 50	
ABBV-951	2432.16	SC / CONTINUOUS	[redacted]20[redacted] / 50	[redacted]20[redacted] / 50
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 51	
ABBV-951	2416.79	SC / CONTINUOUS	[redacted]20[redacted] / 51	[redacted]20[redacted] / 51
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 52	

ABBV-951	2358.39	SC / CONTINUOUS	[redacted]20[redacted] / 52	[redacted]20[redacted] / 52
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 53	
ABBV-951	2399.37	SC / CONTINUOUS	[redacted]20[redacted] / 53	[redacted]20[redacted] / 53
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 54	
ABBV-951	2384.01	SC / CONTINUOUS	[redacted]20[redacted] / 54	[redacted]20[redacted] / 54
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 55	
ABBV-951	2384.01	SC / CONTINUOUS	[redacted]20[redacted] / 55	[redacted]20[redacted] / 55
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 56	
ABBV-951	2418.84	SC / CONTINUOUS	[redacted]20[redacted] / 56	[redacted]20[redacted] / 56
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 57	
ABBV-951	2390.15	SC / CONTINUOUS	[redacted]20[redacted] / 57	[redacted]20[redacted] / 57
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 58	
ABBV-951	2426.01	SC / CONTINUOUS	[redacted]20[redacted] / 58	[redacted]20[redacted] / 58
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 59	
ABBV-951	2405.52	SC / CONTINUOUS	[redacted]20[redacted] / 59	[redacted]20[redacted] / 59
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 60	
ABBV-951	2368.64	SC / CONTINUOUS	[redacted]20[redacted] / 60	[redacted]20[redacted] / 60
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 61	
ABBV-951	2429.08	SC / CONTINUOUS	[redacted]20[redacted] / 61	[redacted]20[redacted] / 61
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 62	
ABBV-951	2448.55	SC / CONTINUOUS	[redacted]20[redacted] / 62	[redacted]20[redacted] / 62
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 63	
ABBV-951	2419.86	SC / CONTINUOUS	[redacted]20[redacted] / 63	[redacted]20[redacted] / 63
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 64	
ABBV-951	2410.64	SC / CONTINUOUS	[redacted]20[redacted] / 64	[redacted]20[redacted] / 64
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 65	
ABBV-951	2374.79	SC / CONTINUOUS	[redacted]20[redacted] / 65	[redacted]20[redacted] / 65
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 66	
ABBV-951	2384.01	SC / CONTINUOUS	[redacted]20[redacted] / 66	[redacted]20[redacted] / 66
Placebo ORAL CD/LD		ORAL / 9	[redacted]20[redacted] / 67	
ABBV-951	2411.67	SC / CONTINUOUS	[redacted]20[redacted] / 67	[redacted]20[redacted] / 67
Placebo ORAL CD/LD		ORAL / 2	[redacted]20[redacted] / 68	
ABBV-951	2458.8	SC / CONTINUOUS	[redacted]20[redacted] / 68	[redacted]20[redacted] / 68
INTERRUPTION			[redacted]20[redacted] / 68	[redacted]20[redacted] / 80
ABBV-951	2458.8	SC / CONTINUOUS	[redacted]20[redacted] / 69	[redacted]20[redacted] / 69
ABBV-951	2458.8	SC / CONTINUOUS	[redacted]20[redacted] / 70	[redacted]20[redacted] / 70
ABBV-951	2458.8	SC / CONTINUOUS	[redacted]20[redacted] / 71	[redacted]20[redacted] / 71

ABBV-951	2458.8	SC / CONTINUOUS	[redacted]20[redacted] / 72	[redacted]20[redacted] / 72
ABBV-951	2458.8	SC / CONTINUOUS	[redacted]20[redacted] / 73	[redacted]20[redacted] / 73
ABBV-951	2458.8	SC / CONTINUOUS	[redacted]20[redacted] / 74	[redacted]20[redacted] / 74
ABBV-951	2458.8	SC / CONTINUOUS	[redacted]20[redacted] / 75	[redacted]20[redacted] / 75
ABBV-951	2458.8	SC / CONTINUOUS	[redacted]20[redacted] / 76	[redacted]20[redacted] / 76
ABBV-951	2458.8	SC / CONTINUOUS	[redacted]20[redacted] / 77	[redacted]20[redacted] / 77
ABBV-951	2458.8	SC / CONTINUOUS	[redacted]20[redacted] / 78	[redacted]20[redacted] / 78
ABBV-951	2458.8	SC / CONTINUOUS	[redacted]20[redacted] / 79	[redacted]20[redacted] / 79
Placebo ORAL CD/LD		ORAL / 4	[redacted]20[redacted] / 80	
ABBV-951	2170.76	SC / CONTINUOUS	[redacted]20[redacted] / 80	[redacted]20[redacted] / 80
Placebo ORAL CD/LD		ORAL / 8	[redacted]20[redacted] / 81	
ABBV-951	1897.97	SC / CONTINUOUS	[redacted]20[redacted] / 81	[redacted]20[redacted] / 81
Placebo ORAL CD/LD		ORAL / 7	[redacted]20[redacted] / 82	
ABBV-951	1900.37	SC / CONTINUOUS	[redacted]20[redacted] / 82	[redacted]20[redacted] / 82
Placebo ORAL CD/LD		ORAL / 7	[redacted]20[redacted] / 83	
ABBV-951	1809.69	SC / CONTINUOUS	[redacted]20[redacted] / 83	[redacted]20[redacted] / 83
Placebo ORAL CD/LD		ORAL / 7	[redacted]20[redacted] / 84	
ABBV-951	1899.57	SC / CONTINUOUS	[redacted]20[redacted] / 84	[redacted]20[redacted] / 84
Placebo ORAL CD/LD		ORAL / 6	[redacted]20[redacted] / 85	
ABBV-951	1904.39	SC / CONTINUOUS	[redacted]20[redacted] / 85	[redacted]20[redacted] / 85
Placebo ORAL CD/LD		ORAL / 3	[redacted]20[redacted] / 86	
ABBV-951	1876.30	SC / CONTINUOUS	[redacted]20[redacted] / 86	[redacted]20[redacted] / 86

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
NAPROXEN	220 mg	PRN	Y-M: 20[redacted]
CARBIDOPA MONOHYDRATE;LEVODOPA	100.000 mg	PRN	Y-M: 20[redacted]-[redacted]
CARBIDOPA MONOHYDRATE;LEVODOPA	100.000 mg	QID	Y-M: 20[redacted]-[redacted]
CARBIDOPA MONOHYDRATE;LEVODOPA	150.000 mg	BID	Y-M: 20[redacted]-[redacted]
ROPINIROLE	4.000 mg	6 TIMES PER DAY	Y-M: 20[redacted]-[redacted]
CARBIDOPA MONOHYDRATE;LEVODOPA	200.000 mg	QD	Y-M: 20[redacted]-[redacted]
ENTACAPONE	200.000 mg	6 TIMES PER DAY	Y-M: 20[redacted]-[redacted] / -174
ESCITALOPRAM OXALATE	20 mg	QD	Y-M: 20[redacted]-[redacted] / -133
COLECALCIFEROL	2000 IU	QD	Y-M: 20[redacted]-[redacted] / -68

VITAMIN B12 NOS	1000 ug	QD	Y-M: 20[redacted] / -68
PYRIDOXINE HYDROCHLORIDE	100 mg	QD	Y-M: 20[redacted] / -61

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
NAPROXEN	220 mg	PRN	Y-M: 20[redacted]	ONGOING
ESCITALOPRAM OXALATE	20 mg	QD	Y-M: 20[redacted] / -133	ONGOING
COLECALCIFEROL	2000 IU	QD	Y-M: 20[redacted] / -68	ONGOING
VITAMIN B12 NOS	1000 ug	QD	Y-M: 20[redacted] / -68	ONGOING
PYRIDOXINE HYDROCHLORIDE	100 mg	QD	Y-M: 20[redacted] / -61	ONGOING
QUETIAPINE	12.5 mg	BID	Y-M: 20[redacted] / 65	Y-M: 20[redacted] / 67
QUETIAPINE	25 mg	BID	Y-M: 20[redacted] / 68	Y-M: 20[redacted] / 69
QUETIAPINE	12.5 mg	QD	Y-M: 20[redacted] / 70	ONGOING
QUETIAPINE	25 mg	QD	Y-M: 20[redacted] / 70	ONGOING

Event #1: Serious Adverse Event, Event of Interest - Hallucinations/Psychosis

Event Description	DELUSIONS
Preferred Term	妄想
AE Onset Date / Rx Day	[redacted]20[redacted] / 60
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 69): ALANINE AMINOTRANSFERASE: 5 [8 - 66] U/L; ALBUMIN: 42 [38 - 50] G/L; ALKALINE PHOSPHATASE: 81 [40 - 129] U/L; ASPARTATE AMINOTRANSFERASE: 28 [13 - 44] U/L; BILIRUBIN: 24 [3 - 21] UMOL/L; BLOOD UREA NITROGEN: 5.7 [2.1 - 8.2] MMOL/L; CALCIUM: 2.25 [2.15 - 2.55] MMOL/L; CREATININE: 57 [62 - 115] UMOL/L; ERYTHROCYTES: 4.8 [4.4 - 5.9] 10^12/L; HEMATOCRIT: 0.44 [0.4 - 0.51] FRACTION OF 1; HEMOGLOBIN: 145 [137 - 175] G/L; LEUKOCYTES: 9.3 [3.9 - 11.2] 10^9/L; PLATELETS: 210 [165 - 366] 10^9/L; POTASSIUM: 3.6 [3.4 - 5.1] MMOL/L; PROTEIN: 67 [61 - 82] G/L; SODIUM: 142 [136 - 145] MMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 68): CHEST RADIOGRAPH:HEART, MEDIASTINUM, AND PULMONARY VASCULATURE: THE CARDIOMEDIASTINAL SILHOUETTE IS WITHIN NORMAL LIMITS FOR SIZE AND CONTOUR. NO PULMONARY VASCULAR CONGESTION. LUNGS AND PLEURA: NO PULMONARY CONSOL IDATION OR EDEMA. NO PLEURAL EFFUSION. NO PNEUMOTHORAX. BONES: NO ACUTE ABNORMALITY.; [redacted]20[redacted] (RX DAY 69): 12-LEAD EKG:NORMAL SINUS RHYTHM, VOLTAGE CRITERIA FOR LEFT VENTRICULAR HYPERTROPHY

AE Stopped Rx Day	76
Duration of AE	17 DAYS

Severity	SEVERE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
SAE: Investigator Opinion of Relationship to Infusion Pump	PROBABLE
SAE: Investigator Opinion of Relationship to [redacted] Infusion Pump	NOT REPORTED
Other Cause of Event	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #2: Serious Adverse Event, Event of Interest - Hallucinations/Psychosis

Event Description	PARANOIA
Preferred Term	妄想症
AE Onset Date / Rx Day	[redacted]20[redacted] / 60
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 69): ALANINE AMINOTRANSFERASE: 5 [8 - 66] U/L; ALBUMIN: 42 [38 - 50] G/L; ALKALINE PHOSPHATASE: 81 [40 - 129] U/L; ASPARTATE AMINOTRANSFERASE: 28 [13 - 44] U/L; BILIRUBIN: 24 [3 - 21] UMOL/L; BLOOD UREA NITROGEN: 5.7 [2.1 - 8.2] MMOL/L; CALCIUM: 2.25 [2.15 - 2.55] MMOL/L; CREATININE: 57 [62 - 115] UMOL/L; ERYTHROCYTES: 4.8 [4.4 - 5.9] 10^12/L; HEMATOCRIT: 0.44 [0.4 - 0.51] FRACTION OF 1; HEMOGLOBIN: 145 [137 - 175] G/L; LEUKOCYTES: 9.3 [3.9 - 11.2] 10^9/L; PLATELETS: 210 [165 - 366] 10^9/L; POTASSIUM: 3.6 [3.4 - 5.1] MMOL/L; PROTEIN: 67 [61 - 82] G/L; SODIUM: 142 [136 - 145] MMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 68): CHEST RADIOGRAPH:HEART, MEDIASTINUM, AND PULMONARY VASCULATURE: THE CARDIOMEDIASTINAL SILHOUETTE IS WITHIN NORMAL LIMITS FOR SIZE AND CONTOUR. NO PULMONARY VASCULAR CONGESTION. LUNGS AND PLEURA: NO PULMONARY CONSOL IDATION OR EDEMA. NO PLEURAL EFFUSION. NO PNEUMOTHORAX. BONES: NO ACUTE ABNORMALITY.; [redacted]20[redacted] (RX DAY 69): 12-LEAD EKG:NORMAL SINUS RHYTHM, VOLTAGE CRITERIA FOR LEFT VENTRICULAR HYPERTROPHY

AE Stopped Rx Day	76
Duration of AE	17 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
SAE: Investigator Opinion of Relationship to Infusion Pump	PROBABLE

SAE: Investigator Opinion of Relationship to [redacted] Infusion Pump	NOT REPORTED
Other Cause of Event	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #3: Serious Adverse Event, Event of Interest - Hallucinations/Psychosis

Event Description	PSYCHOSIS
Preferred Term	精神病性障害
AE Onset Date / Rx Day	[redacted]20[redacted] / 60
Age at AE Onset	5[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 69): ALANINE AMINOTRANSFERASE: 5 [8 - 66] U/L; ALBUMIN: 42 [38 - 50] G/L; ALKALINE PHOSPHATASE: 81 [40 - 129] U/L; ASPARTATE AMINOTRANSFERASE: 28 [13 - 44] U/L; BILIRUBIN: 24 [3 - 21] UMOL/L; BLOOD UREA NITROGEN: 5.7 [2.1 - 8.2] MMOL/L; CALCIUM: 2.25 [2.15 - 2.55] MMOL/L; CREATININE: 57 [62 - 115] UMOL/L; ERYTHROCYTES: 4.8 [4.4 - 5.9] 10^12/L; HEMATOCRIT: 0.44 [0.4 - 0.51] FRACTION OF 1; HEMOGLOBIN: 145 [137 - 175] G/L; LEUKOCYTES: 9.3 [3.9 - 11.2] 10^9/L; PLATELETS: 210 [165 - 366] 10^9/L; POTASSIUM: 3.6 [3.4 - 5.1] MMOL/L; PROTEIN: 67 [61 - 82] G/L; SODIUM: 142 [136 - 145] MMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 68): CHEST RADIOGRAPH:HEART, MEDIASTINUM, AND PULMONARY VASCULATURE: THE CARDIOMEDIASTINAL SILHOUETTE IS WITHIN NORMAL LIMITS FOR SIZE AND CONTOUR. NO PULMONARY VASCULAR CONGESTION. LUNGS AND PLEURA: NO PULMONARY CONSOL IDATION OR EDEMA. NO PLEURAL EFFUSION. NO PNEUMOTHORAX. BONES: NO ACUTE ABNORMALITY.; [redacted]20[redacted] (RX DAY 69): 12-LEAD EKG:NORMAL SINUS RHYTHM, VOLTAGE CRITERIA FOR LEFT VENTRICULAR HYPERTROPHY

AE Stopped Rx Day	76
Duration of AE	17 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
SAE: Investigator Opinion of Relationship to Infusion Pump	PROBABLE
SAE: Investigator Opinion of Relationship to [redacted] Infusion Pump	NOT REPORTED
Other Cause of Event	NOT REPORTED
Discontinued Study Drug Due to the Event	NO

SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #4: Event of Interest - Hallucinations/Psychosis

Event Description	DELUSIONS
Preferred Term	妄想
AE Onset Date / Rx Day	[redacted]20[redacted] / 85
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	MODERATE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
SAE: Investigator Opinion of Relationship to Infusion Pump	NOT APPLICABLE
SAE: Investigator Opinion of Relationship to [redacted] Infusion Pump	NOT APPLICABLE
Other Cause of Event	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #5: Event of Interest - Hallucinations/Psychosis

Event Description	PARANOIA
Preferred Term	妄想症
AE Onset Date / Rx Day	[redacted]20[redacted] / 85
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	MODERATE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
SAE: Investigator Opinion of Relationship to Infusion Pump	NOT APPLICABLE
SAE: Investigator Opinion of Relationship to [redacted] Infusion Pump	NOT APPLICABLE
Other Cause of Event	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Generated: [redacted]20[redacted]:10:27
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-736

治験責任医師からの報告。本被験者は米国の 5[redacted] 歳男性であり，アッヴィ社の ABBV-951（Foscarbidopa/Foslevodopa）の治験で盲検下にて治験薬及び CD/LD が投与され，精神病性障害，妄想症，及び妄想を発現した。

Event 1，2 及び 3 の臨床経過：

関連する病歴は，パーキンソン病，ビタミン B12 欠乏症，ビタミン B6 欠乏症，元喫煙者（1 日 1 本を 1 年間）及び飲酒者（1 日 2 杯未満）であった。

ランダム化に先立ち，本被験者は 20[redacted] 年 [redacted] 月 [redacted] 日から 20[redacted] 年 [redacted] 月 [redacted] 日まで本治験の安定化期にて CD/LD を経口投与された。20[redacted] 年 [redacted] 月 [redacted] 日，本被験者はランダム化され，本治験の二重盲検最適化期を開始した。投与 1 日目から 28 日目まで，被験者は本治験の二重盲検最適化期にて最適な臨床反応を達成するための皮下投与製剤の調整を必要とした。本期間を通して被疑薬の用量が調整された可能性がある。投与 29 日目（V11），被験者は維持期に移行した。被疑薬に関する情報は，本事象発現時の皮下投与製剤の用量で示されている。

投与 60 日目，被験者は精神病性障害，妄想症，及び妄想を発現した。投与 76 日目，精神病性障害，妄想症，及び妄想は消失した。

投与 60 日目，被験者は妻に対して妄想及び偏執行動の徴候を示し始めた。被験者は妻の携帯電話，家計状況，及び携帯電話の履歴をチェックすることに執着した。被験者は妻が「夫（被

験者）をやっつけよう」としており，被験者に隠れて様々なことをし，電子的に追跡していると考えた。また，被験者は自分の銀行口座が電子的にハッキング攻撃されると妄想した。投与 64 日目，被験者の妻は治験責任医師に連絡し，被験者に妄想行為があり，薬の服用を拒否していると知らせた。投与 65 日目，被験者は遠隔医療により治験責任医師にかかり，パーキンソン病の治療薬を調整された。しかし，妄想症及び妄想は継続していた。投与 67 日目，被験者の妻が救急サービスに電話し，被験者を救急診療部に連れてきた。被験者は入院せず，帰宅した。

投与 68 日目，治験責任医師の勧めにより被験者の妻は再び救急サービスに電話し，被験者を救急診療部に連れ戻した。被験者は誰も信用せず，服薬を拒否し続けた。同日，被験者は精神病性障害，妄想症，及び妄想のため検査入院した。診断検査に特記すべきことはなかった。翌日，被験者は精神病性障害，妄想症，及び妄想の治療を開始した。投与 70 日目，精神科での評価の結果，被験者は妄想があると確定された。治験責任医師は入院のまま更に投薬を最適化すべきと勧めたが，精神科で被験者の退院が許可された。被験者のパーキンソン病に対する治療は入院中を通して調整された。被験者は帰宅すると譲らなかった。投与 70 日目，被験者はまだ動揺し妄想があったが，退院し帰宅した。退院後，被験者は治験責任医師のスタッフに毎日連絡し，症状は改善した。

治験責任医師によると，被験者のパーキンソン病の病歴及び高用量のロピニロールが本事象と関連するリスク因子であった。

被験者にセロクエル及びクエチアピンが投与された。

The patient's past medications include:

CARBIDOPA/LEVODOPA IMMEDIATE RELEASE for PARKINSON'S DISEASE ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

ENTACAPONE for PARKINSON'S DISEASE ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for ABBV-951 (Blinded)

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1) Psychosis (10037234) (Psychotic disorder (10061920)) [v.24.0] [10037234]

Causality as per reporter (Drug/Vaccine): Reasonable possibility

Causality as per Mfr. (Drug/Vaccine): Reasonable possibility

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

2) Paranoia (10033864) (Paranoia (10033864)) [v.24.0] [10033864]

Causality as per reporter (Drug/Vaccine): Reasonable possibility

Causality as per Mfr. (Drug/Vaccine): Reasonable possibility

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

3) Delusions (10012260) (Delusion (10012239)) [v.24.0] [10012260]

Causality as per reporter (Drug/Vaccine): Reasonable possibility

Causality as per Mfr. (Drug/Vaccine): Reasonable possibility

Dechallenge: Yes

Rechallenge: No rechallenge was done, recurrence is not applicable

Causality for CARBIDOPA/LEVODOPA (Open Label)

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1) Psychosis (10037234) (Psychotic disorder (10061920)) [v.24.0] [10037234]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

2) Paranoia (10033864) (Paranoia (10033864)) [v.24.0] [10033864]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

3) Delusions (10012260) (Delusion (10012239)) [v.24.0] [10012260]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

Alternative Etiology for ABBV-951 (Blinded)

Event of PSYCHOSIS, PARANOIA, DELUSIONS

- Investigator: Not applicable

- AbbVie: Not applicable

Alternative Etiology for CARBIDOPA/LEVODOPA (Open Label)

Event of PSYCHOSIS, PARANOIA, DELUSIONS

- Investigator: More likely related to ABBV-951/Placebo

- AbbVie: Event occurred more than 2 months after last dose of oral Carbidopa/Levodopa. Risk factors include Parkinson disease and use of dopaminergic antiparkinson medications.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CHEST RADIOGRAPH:** Heart, mediastinum, and pulmonary vasculature: The cardiomediastinal silhouette is within normal limits for size and contour. No pulmonary vascular congestion. Lungs and pleura: No pulmonary consolidation or edema. No pleural effusion. No pneumothorax. Bones: No acute abnormality.

[redacted] **20[redacted] EKG:** Normal sinus rhythm, Voltage criteria for left ventricular hypertrophy.

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
挫傷	X			X
転倒	X			X

Treatment Group	Age at Study Start	Sex	Race
ORAL CD/LD	7[redacted]	MALE	WHITE

Medical History	Onset Year
CHRONIC LEFT HIP PAIN	19[redacted]
CHRONIC LOW BACK PAIN	19[redacted]
KYPHOSIS	19[redacted]
SCOLIOSIS	19[redacted]
ALLERGY TO DILANTIN (RASH)	19[redacted]
CEREBRAL INFARCTION	19[redacted]
LEFT VERTEBRAL ARTERY DISSECTION	19[redacted]
SEIZURES RELATED TO STROKE	19[redacted]
MIDDLE INSOMNIA	20[redacted]
REM SLEEP BEHAVIOR DISORDER	20[redacted]
ENVIRONMENTAL ALLERGIES	20[redacted]
SEASONAL ALLERGIES	20[redacted]
RESTLESS LEG SYNDROME	20[redacted]
HYPERLIPIDEMIA	20[redacted]
SLEEP APNEA	20[redacted]
ORTHOSTATIC HYPOTENSION	20[redacted]
DAYTIME SLEEPINESS RELATED TO PARKINSON'S DISEASE	20[redacted]
CONSTIPATION	20[redacted]
URINARY DYSFUNCTION	20[redacted]

Indication Disease History, Diagnosis and/or Symptoms	Onset Year
LEVODOPA INDUCED DYSKINESIA	NOT REPORTED
PARKINSON'S DISEASE	20[redacted]
ONSET OF MOTOR FLUCTUATION	20[redacted]

PARKINSON'S DISEASE DIAGNOSIS 20[redacted]

Prior Procedures	Procedure Year
SPINAL FUSION L-3, L-4	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	20 CIGARETTE	10	19[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	LESS THAN 2 DRINKS

Study Drug Prescription

Study Drug	New Quadrant for Pump Infusion	Continuous Flow Rate (mL/h)	Infusion Loading Dose Volume (mL)	Oral study drug dose (CAPSULE)	Dose Date/Day
ORAL CD/LD				14	[redacted]20[redacted]/ 1
Placebo for ABBV-951	SITE A2				[redacted]20[redacted]/ 1
Placebo for ABBV-951		0.47	1.1		[redacted]20[redacted]/ 1
Placebo for ABBV-951		0.50	0.0		[redacted]20[redacted]/ 2
Placebo for ABBV-951	SITE A12				[redacted]20[redacted]/ 3
Placebo for ABBV-951		0.57	0.0		[redacted]20[redacted]/ 4
Placebo for ABBV-951	SITE B11				[redacted]20[redacted]/ 6
Placebo for ABBV-951		0.64	0.0		[redacted]20[redacted]/ 7
Placebo for ABBV-951	SITE A10				[redacted]20[redacted]/ 9
Placebo for ABBV-951	SITE B6				[redacted]20[redacted]/ 9
Placebo for ABBV-951		0.74	0.0		[redacted]20[redacted]/ 9
Placebo for ABBV-951		0.64	0.0		[redacted]20[redacted]/ 10
Placebo for ABBV-951	SITE B10				[redacted]20[redacted]/ 12
Placebo for ABBV-951	SITE A7				[redacted]20[redacted]/ 13
Placebo for ABBV-951	SITE B9				[redacted]20[redacted]/ 15

Placebo for ABBV-951	SITE B4	[redacted]20[redacted]/ 18
Placebo for ABBV-951	SITE B9	[redacted]20[redacted]/ 21
Placebo for ABBV-951	SITE A10	[redacted]20[redacted]/ 25
Placebo for ABBV-951	SITE B5	[redacted]20[redacted]/ 25
Placebo for ABBV-951	SITE A2	[redacted]20[redacted]/ 26
Placebo for ABBV-951	SITE A12	[redacted]20[redacted]/ 29
Placebo for ABBV-951	SITE A12	[redacted]20[redacted]/ 29
Placebo for ABBV-951	SITE B2	[redacted]20[redacted]/ 32
Placebo for ABBV-951	SITE A11	[redacted]20[redacted]/ 38
Placebo for ABBV-951	SITE A2	[redacted]20[redacted]/ 41
Placebo for ABBV-951	SITE A1	[redacted]20[redacted]/ 49
Placebo for ABBV-951	SITE A4	[redacted]20[redacted]/ 57
Placebo for ABBV-951	SITE B7	[redacted]20[redacted]/ 64
Placebo for ABBV-951	SITE A9	[redacted]20[redacted]/ 67
Placebo for ABBV-951	SITE A12	[redacted]20[redacted]/ 68
Placebo for ABBV-951	SITE B3	[redacted]20[redacted]/ 70
Placebo for ABBV-951	SITE A3	[redacted]20[redacted]/ 73
Placebo for ABBV-951	SITE B6	[redacted]20[redacted]/ 76
Placebo for ABBV-951	SITE A10	[redacted]20[redacted]/ 79
Placebo for ABBV-951	SITE B6	[redacted]20[redacted]/ 81
Placebo for ABBV-951	SITE B5	[redacted]20[redacted]/ 84

Daily Dose by Molecular Weight

Study Drug	CSCI Infusion (mg LD)	Total Oral Dose (mg)	Route (Subcutaneous) / Frequency (Times per Day)	First Dose Date/Day	Last Dose Date/Day
Placebo for ABBV-951 Loading dose			SC / CONTINUOUS	[redacted]20[redacted] / 1	
Placebo for ABBV-951			SC / CONTINUOUS	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1
Placebo for ABBV-951			SC / CONTINUOUS	[redacted]20[redacted] / 2	[redacted]20[redacted] / 2

Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 3	[redacted]20[redacted] / 3
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 4	[redacted]20[redacted] / 4
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 5	[redacted]20[redacted] / 5
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 6	[redacted]20[redacted] / 6
ORAL CD/LD	1200	ORAL / 6	[redacted]20[redacted] / 7	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 7	[redacted]20[redacted] / 7
ORAL CD/LD	1400	ORAL / 7	[redacted]20[redacted] / 8	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 8	[redacted]20[redacted] / 8
ORAL CD/LD	1200	ORAL / 6	[redacted]20[redacted] / 9	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 9	[redacted]20[redacted] / 9
ORAL CD/LD	200	ORAL / 1	[redacted]20[redacted] / 10	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 10	[redacted]20[redacted] / 10
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 11	[redacted]20[redacted] / 11
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 12	[redacted]20[redacted] / 12
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 13	[redacted]20[redacted] / 13
ORAL CD/LD	1400	ORAL / 7	[redacted]20[redacted] / 14	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 14	[redacted]20[redacted] / 14
ORAL CD/LD	1400	ORAL / 7	[redacted]20[redacted] / 15	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 15	[redacted]20[redacted] / 15
ORAL CD/LD	1200	ORAL / 6	[redacted]20[redacted] / 16	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 16	[redacted]20[redacted] / 16
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 17	[redacted]20[redacted] / 17
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 18	[redacted]20[redacted] / 18
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 19	[redacted]20[redacted] / 19
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 20	[redacted]20[redacted] / 20
ORAL CD/LD	1400	ORAL / 7	[redacted]20[redacted] / 21	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 21	[redacted]20[redacted] / 21
ORAL CD/LD	1600	ORAL / 8	[redacted]20[redacted] / 22	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 22	[redacted]20[redacted] / 22
ORAL CD/LD	1400	ORAL / 7	[redacted]20[redacted] / 23	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 23	[redacted]20[redacted] / 23
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 24	[redacted]20[redacted] / 24
ORAL CD/LD	1400	ORAL / 7	[redacted]20[redacted] / 25	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 25	[redacted]20[redacted] / 25
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 26	[redacted]20[redacted] / 26
ORAL CD/LD	1400	ORAL / 7	[redacted]20[redacted] / 27	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 27	[redacted]20[redacted] / 27

ORAL CD/LD	1400	ORAL / 7	[redacted]20[redacted] / 28	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 28	[redacted]20[redacted] / 28
ORAL CD/LD	1400	ORAL / 7	[redacted]20[redacted] / 29	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 29	[redacted]20[redacted] / 29
ORAL CD/LD	1000	ORAL / 5	[redacted]20[redacted] / 30	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 30	[redacted]20[redacted] / 30
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 31	[redacted]20[redacted] / 31
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 32	[redacted]20[redacted] / 32
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 33	[redacted]20[redacted] / 33
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 34	[redacted]20[redacted] / 34
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 35	[redacted]20[redacted] / 35
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 36	[redacted]20[redacted] / 36
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 37	[redacted]20[redacted] / 37
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 38	[redacted]20[redacted] / 38
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 39	[redacted]20[redacted] / 39
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 40	[redacted]20[redacted] / 40
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 41	[redacted]20[redacted] / 41
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 42	[redacted]20[redacted] / 42
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 43	[redacted]20[redacted] / 43
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 44	[redacted]20[redacted] / 44
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 45	[redacted]20[redacted] / 45
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 46	[redacted]20[redacted] / 46
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 47	[redacted]20[redacted] / 47
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 48	[redacted]20[redacted] / 48
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 49	[redacted]20[redacted] / 49
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 50	[redacted]20[redacted] / 50
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 51	[redacted]20[redacted] / 51
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 52	[redacted]20[redacted] / 52
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 53	[redacted]20[redacted] / 53
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 54	[redacted]20[redacted] / 54
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 55	[redacted]20[redacted] / 55
ORAL CD/LD	1200	ORAL / 6	[redacted]20[redacted] / 56	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 56	[redacted]20[redacted] / 56
ORAL CD/LD	1200	ORAL / 6	[redacted]20[redacted] / 57	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 57	[redacted]20[redacted] / 57
ORAL CD/LD	1400	ORAL / 7	[redacted]20[redacted] / 58	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 58	[redacted]20[redacted] / 58

ORAL CD/LD	200	ORAL / 1	[redacted]20[redacted] / 59	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 59	[redacted]20[redacted] / 59
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 60	[redacted]20[redacted] / 60
INTERRUPTION			[redacted]20[redacted] / 61	[redacted]20[redacted] / 61
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 61	[redacted]20[redacted] / 61
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 62	[redacted]20[redacted] / 62
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 63	[redacted]20[redacted] / 63
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 64	[redacted]20[redacted] / 64
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 65	[redacted]20[redacted] / 65
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 66	[redacted]20[redacted] / 66
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 67	[redacted]20[redacted] / 67
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 68	[redacted]20[redacted] / 68
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 69	[redacted]20[redacted] / 69
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 70	[redacted]20[redacted] / 70
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 71	[redacted]20[redacted] / 71
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 72	[redacted]20[redacted] / 72
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 73	[redacted]20[redacted] / 73
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 74	[redacted]20[redacted] / 74
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 75	[redacted]20[redacted] / 75
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 76	[redacted]20[redacted] / 76
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 77	[redacted]20[redacted] / 77
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 78	[redacted]20[redacted] / 78
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 79	[redacted]20[redacted] / 79
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 80	[redacted]20[redacted] / 80
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 81	[redacted]20[redacted] / 81
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 82	[redacted]20[redacted] / 82
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 83	[redacted]20[redacted] / 83
ORAL CD/LD	1400	ORAL / 7	[redacted]20[redacted] / 84	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 84	[redacted]20[redacted] / 84
ORAL CD/LD	1400	ORAL / 7	[redacted]20[redacted] / 85	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 85	[redacted]20[redacted] / 85
ORAL CD/LD	1400	ORAL / 7	[redacted]20[redacted] / 86	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 86	[redacted]20[redacted] / 86

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
VITAMINS NOS	1 OTHER: TABLET	QD	Y-M: 19[redacted]
CLOPIDOGREL BISULFATE	75 mg	QD	Y-M: 20[redacted]
CLONAZEPAM	1 mg	QD	Y-M: 20[redacted]
LORATADINE	10 mg	QD	Y-M: 20[redacted]
PRAMIPEXOLE DIHYDROCHLORIDE MONOHYDRATE	0.5 mg	QD	Y-M: 20[redacted]
PRAMIPEXOLE DIHYDROCHLORIDE MONOHYDRATE	1.0 mg	QD	Y-M: 20[redacted]
ATORVASTATIN CALCIUM	10 mg	QD	Y-M: 20[redacted]
GABAPENTIN	300 mg	BID	Y-M: 20[redacted]
CARBIDOPA MONOHYDRATE;LEVODOPA	200.000 mg	6 TIMES PER DAY	Y-M: 20[redacted]
COLECALCIFEROL	1000 IU	BID	Y-M: 20[redacted]
MELATONIN	10 mg	QD	Y-M: 20[redacted]
DOCUSATE	100 OTHER: MG	TID	Y-M: 20[redacted]
OXYBUTYNIN HYDROCHLORIDE	10 mg	QD	Y-M: 20[redacted]
VITAMIN B12 NOS	1000 ug	QD	Y-M: 20[redacted]
PARACETAMOL	1000 mg	PRN	Y-M: 20[redacted]-[redacted]
TRAMADOL HYDROCHLORIDE	50 mg	PRN	Y-M: 20[redacted]-[redacted]
METHYLPHENIDATE HYDROCHLORIDE	10 mg	BID	Y-M: 20[redacted]-[redacted] / -237
CARBIDOPA MONOHYDRATE;LEVODOPA	100.000 mg	PRN	Y-M: 20[redacted]-[redacted] / -162
CARBIDOPA MONOHYDRATE;LEVODOPA	200.000 mg	PRN	Y-M: 20[redacted]-[redacted] / -162
MIDODRINE HYDROCHLORIDE	2.5 mg	BID	Y-M: 20[redacted]-[redacted] / -64

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
VITAMINS NOS	1 OTHER: TABLET	QD	Y-M: 19[redacted]	ONGOING
CLOPIDOGREL BISULFATE	75 mg	QD	Y-M: 20[redacted]	ONGOING
CLONAZEPAM	1 mg	QD	Y-M: 20[redacted]	ONGOING
LORATADINE	10 mg	QD	Y-M: 20[redacted]	ONGOING
PRAMIPEXOLE DIHYDROCHLORIDE MONOHYDRATE	0.5 mg	QD	Y-M: 20[redacted]	ONGOING
PRAMIPEXOLE DIHYDROCHLORIDE MONOHYDRATE	1.0 mg	QD	Y-M: 20[redacted]	ONGOING

ATORVASTATIN CALCIUM	10 mg	QD	Y-M: 20[redacted]	ONGOING
GABAPENTIN	300 mg	BID	Y-M: 20[redacted]	ONGOING
COLECALCIFEROL	1000 IU	BID	Y-M: 20[redacted]	ONGOING
MELATONIN	10 mg	QD	Y-M: 20[redacted]	ONGOING
DOCUSATE	100 OTHER: MG	TID	Y-M: 20[redacted]	ONGOING
VITAMIN B12 NOS	1000 ug	QD	Y-M: 20[redacted]	ONGOING
OXYBUTYNIN HYDROCHLORIDE	10 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 37
PARACETAMOL	1000 mg	PRN	Y-M: 20[redacted]	ONGOING
TRAMADOL HYDROCHLORIDE	50 mg	PRN	Y-M: 20[redacted]	ONGOING
METHYLPHENIDATE HYDROCHLORIDE	10 mg	BID	Y-M: 20[redacted] / -237	ONGOING
MIDODRINE HYDROCHLORIDE	2.5 mg	BID	Y-M: 20[redacted] / -64	ONGOING
OXYBUTYNIN HYDROCHLORIDE	20 mg	QD	Y-M: 20[redacted] / 38	Y-M: 20[redacted] / 49
MIRABEGRON	50 mg	QD	Y-M: 20[redacted] / 50	Y-M: 20[redacted] / 90
TOZINAMERAN		ONCE	Y-M: 20[redacted] / 58	NOT REPORTED
SERTRALINE HYDROCHLORIDE	25 mg	QD	Y-M: 20[redacted] / 59	Y-M: 20[redacted] / 65
SERTRALINE HYDROCHLORIDE	50 mg	QD	Y-M: 20[redacted] / 66	ONGOING

Event #1: Serious Adverse Event, Event of Interest - Falls and Associated Injuries

Event Description	CONTUSION TO BACK (THORACIC-JUST BELOW LEFT SCAPULA).
Preferred Term	挫傷
AE Onset Date / Rx Day	[redacted]20[redacted] / 59
Age at AE Onset	7[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 63): X-RAY LEFT RIBS (2 VIEWS):NEGATIVE. NO DISPLACED RIB FRACTURE.

AE Stopped Rx Day	72
Duration of AE	14 DAYS
Severity	MODERATE

Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
SAE: Investigator Opinion of Relationship to Infusion Pump	NOT RELATED
SAE: Investigator Opinion of Relationship to [redacted] Infusion Pump	NOT REPORTED
Other Cause of Event	ACCIDENTAL FALL DUE TO PARKINSON'S DISEASE. SUBJECT LOST HIS BALANCE AND FELL WHILE CARRYING A LARGE, CUMBERSOME AND FAIRLY HEAVY BAG OF STUDY SUPPLIES UP THE GARAGE STAIRS AND INTO THE HOUSE.
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #2: Serious Adverse Event, Event of Interest - Falls and Associated Injuries

Event Description	CONTUSION RIGHT HIP
Preferred Term	挫傷
AE Onset Date / Rx Day	[redacted]20[redacted] / 59
Age at AE Onset	7[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 60): CT OF THE RIGHT HIP:MULTIPLE FEMORAL NECK HEAD JUNCTION CYSTS, SMALL. THEY DO NOT APPEAR TO BE IMPENDING FRACTURES. THE CYSTS ARE WELL ROUNDED AND SCLEROTIC BORDER CONSISTENT WITH BENIGN PRESENTATION.

AE Stopped Rx Day	72
Duration of AE	14 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
SAE: Investigator Opinion of Relationship to Infusion Pump	NOT RELATED
SAE: Investigator Opinion of Relationship to [redacted] Infusion Pump	NOT REPORTED
Other Cause of Event	SUBJECT LOST HIS BALANCE AND FELL WHILE CARRYING A LARGE, CUMBERSOME AND FAIRLY HEAVY BAG OF STUDY SUPPLIES UP THE GARAGE STAIRS AND INTO THE HOUSE.
Discontinued Study Drug Due to the Event	NO

SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #3: Event of Interest - Falls and Associated Injuries

Event Description	CONTUSION TO HEAD
Preferred Term	挫傷
AE Onset Date / Rx Day	[redacted]20[redacted] / 59
Age at AE Onset	7[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	62
Duration of AE	4 DAYS
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
SAE: Investigator Opinion of Relationship to Infusion Pump	NOT APPLICABLE
SAE: Investigator Opinion of Relationship to [redacted] Infusion Pump	NOT APPLICABLE
Other Cause of Event	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #4: Serious Adverse Event, Event of Interest - Falls and Associated Injuries

Event Description	ACCIDENTAL FALL
Preferred Term	転倒
AE Onset Date / Rx Day	[redacted]20[redacted] / 59
Age at AE Onset	7[redacted]
Laboratory Testing	

[redacted]20[redacted] (RX DAY 60): BLOOD UREA NITROGEN: 7.9 [2.5 - 8.2] MMOL/L; CREATININE: 44 [62 - 115] UMOL/L; GLUCOSE: 3.8 [3.9 - 5.6] MMOL/L; NPTST015-CHLORIDE: 104 [97 - 110] MMOL/L; POTASSIUM: 3.6 [3.5 - 5.2] MMOL/L; SODIUM: 136 [135 - 145] MMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	59
Duration of AE	1 DAY
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
SAE: Investigator Opinion of Relationship to Infusion Pump	NOT RELATED
SAE: Investigator Opinion of Relationship to [redacted] Infusion Pump	NOT REPORTED
Other Cause of Event	UNSTEADINESS AND POOR BALANCE DUE TO PARKINSON'S DISEASE.
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted]20[redacted]:10:27
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-736

治験責任医師からの報告。本被験者は米国の 7[redacted] 歳男性であり，アッヴィ社の ABBV-951（Foscarbidopa/Foslevodopa）の治験で盲検下にて治験薬及び CD/LD が投与され，偶発的な転倒，背部挫傷（胸部－左肩甲骨直下）及び右臀部挫傷を発現した。

Event 1 及び 2 の臨床経過：

関連する病歴は，慢性左股関節痛，慢性腰痛，高脂血症，起立性低血圧，パーキンソン病，L3 及び L4 の脊椎固定術，元喫煙者（1 日 20 本を 10 年間）及び飲酒者（1 日 2 杯未満）であった。

被験者が COVID-19 ワクチンの治験に組み入れられているかは不明であった。

投与 58 日目，被験者はファイザー製の COVID-19 ワクチン（1 回目）を接種された。製造番号，有効期限は不明であった。

投与 79 日目，被験者はファイザー製の COVID-19 ワクチン（2 回目）を接種された。製造番号，有効期限は不明であった。

投与 59 日目，被験者は転倒，背部挫傷（胸部－左肩甲骨直下）及び右臀部挫傷を発現した。投与 59 日目，転倒の事象は消失した。投与 72 日目，背部挫傷（胸部－左肩甲骨直下）及び右臀部挫傷は消失した。

投与 59 日目，被験者は家で転倒し頭部，背部及び右臀部を打ち付けた。同日，被験者は右臀部及び肩甲骨直下の背部全体の痛み（左側より右側の方が強い）のため入院した。その他の症状は，背部の挫傷，右臀部の挫傷，及び頭部の挫傷（非重篤）であった。X 線及びスキャンでは骨折や裂傷は認められなかった。投与 63 日目，被験者は退院した。

治験責任医師によると，パーキンソン病に関連する不安定及び平衡障害がリスク因子に含まれた。

The patient's past medications include:

CARBIDOPA/LEVODOPA IMMEDIATE RELEASE (SINEMET IR) for PARKINSON'S DISEASE (20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

DILANTIN for UNKNOWN INDICATION

Causality for ABBV-951 (Blinded)

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1) Fall (10016173) (Fall (10016173)) [v.24.0] [10016173]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

2) Contusion of back (10010841) (Contusion (10050584)) [v.24.0] [10010841]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

3) Contusion of hip (10010858) (Contusion (10050584)) [v.24.0] [10010858]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

Causality for CARBIDOPA/LEVODOPA (Open Label)

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1) Fall (10016173) (Fall (10016173)) [v.24.0] [10016173]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

2) Contusion of back (10010841) (Contusion (10050584)) [v.24.0] [10010841]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

3) Contusion of hip (10010858) (Contusion (10050584)) [v.24.0] [10010858]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

Alternative Etiology for ABBV-951 (Blinded)

Event of ACCIDENTAL FALL

- Investigator: Unsteadiness and poor balance due to Parkinson's Disease.

- AbbVie: More likely related to an incidental accident in an advanced aged patient with a history of Parkinson's disease

Event of CONTUSION TO BACK (THORACIC-JUST BELOW LEFT SCAPULAE)

- Investigator: Accidental fall due to Parkinson's Disease. Subject lost his balance and fell while carrying a large, cumbersome and fairly heavy bag of study supplies up the garage stairs and into the house.

- AbbVie: More likely related to a traumatic injury due to the concurrent event of fall in an advanced aged patient with a history of Parkinson's disease

Event of CONTUSION TO RIGHT HIP

- Investigator: Subject lost his balance and fell while carrying a large, cumbersome and fairly heavy bag of study supplies up the garage stairs and into the house.

- AbbVie: More likely related to a traumatic injury due to the concurrent event of fall in an advanced aged patient with a history of Parkinson's disease

Alternative Etiology for CARBIDOPA/LEVODOPA (Open Label)

Event of ACCIDENTAL FALL

- Investigator: Unsteadiness and poor balance due to Parkinson's Disease.

- AbbVie: More likely related to an incidental accident in an advanced aged patient with a history of Parkinson's disease

Event of CONTUSION TO BACK (THORACIC-JUST BELOW LEFT SCAPULAE)

- Investigator: Accidental fall due to Parkinson's Disease. Subject lost his balance and fell while carrying a large, cumbersome and fairly heavy bag of study supplies up the garage stairs and into the house.

- AbbVie: More likely related to a traumatic injury due to the concurrent event of fall in an advanced aged patient with a history of Parkinson's disease

Event of CONTUSION TO RIGHT HIP

- Investigator: Subject lost his balance and fell while carrying a large, cumbersome and fairly heavy bag of study supplies up the garage stairs and into the house.

- AbbVie: More likely related to a traumatic injury due to the concurrent event of fall in an advanced aged patient with a history of Parkinson's disease

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALBUMIN:** 3.6 MEQ/L (normal 3.5 to 5.2)

[redacted] **20[redacted] BUN:** 22 mg/dL (normal 7 to 23)

[redacted] **20[redacted] CHLORIDE:** 104 MMOL/L (normal 97 to 110)

[redacted] **20[redacted] CREATININE:** 0.5 mg/dL (normal 0.7 to 1.3)

[redacted] **20[redacted] CT OF THE RIGHT HIP:** Multiple femoral neck head junction cysts, small. They do not appear to be impending fractures. The cysts are well rounded and sclerotic border consistent with benign presentation.

[redacted] **20[redacted] GLUCOSE:** 69 mg/dL (normal 70 to 100)

[redacted] **20[redacted] POTASSIUM:** 3.6 no unit

[redacted] **20[redacted] SODIUM:** 136 MEQ/L (normal 135 to 145)

[redacted] **20[redacted] VITAMIN D LEVEL:** 73.8 no unit

[redacted] **20[redacted] X-RAY LEFT RIBS (2 VIEWS):** Negative. No displaced rib fracture.

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
COVID-19 肺炎	X			
** Disc. due to withdrawal by subject				X

Disc = Discontinued.

Treatment Group	Age at Study Start	Sex	Race
ORAL CD/LD	6[redacted]	FEMALE	WHITE

Medical History	Onset Year
HYSTERECTOMY	20[redacted]
UTERINE FIBROIDS	20[redacted]
APPENDICITIS	20[redacted]
GALLSTONES	20[redacted]
CONSTIPATION	20[redacted]
INSOMNIA	20[redacted]
CONTROLLED DEPRESSION	20[redacted]
HYPOPARATHYROIDISM	20[redacted]
VITAMIN B6 DEFICIENCY	20[redacted]

Indication Disease History, Diagnosis and/or Symptoms	Onset Year
LEVODOPA INDUCED DYSKINESIA	NOT REPORTED
PARKINSON'S DISEASE	20[redacted]
PARKINSON'S DISEASE DIAGNOSIS	20[redacted]
ONSET OF MOTOR FLUCTUATION	20[redacted]

Prior Procedures	Procedure Year
HYSTERECTOMY	20[redacted]
APPENDECTOMY	20[redacted]
CHOLECYSTECTOMY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	NEVER			
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	LESS THAN 2 DRINKS

Study Drug Prescription

Study Drug	New Quadrant for Pump Infusion	Continuous Flow Rate (mL/h)	Infusion Loading Dose Volume (mL)	Oral study drug dose (CAPSULE)	Dose Date/Day
ORAL CD/LD				7	[redacted]20[redacted] / 1
Placebo for ABBV-951	SITE B3				[redacted]20[redacted] / 1
Placebo for ABBV-951		0.24	1.1		[redacted]20[redacted] / 1
Placebo for ABBV-951	SITE B4				[redacted]20[redacted] / 4

Daily Dose by Molecular Weight

Study Drug	CSCI Infusion (mg LD)	Total Oral Dose (mg)	Route (Subcutaneous) / Frequency (Times per Day)	First Dose Date/Day	Last Dose Date/Day
Placebo for ABBV-951 Loading dose			SC / CONTINUOUS	[redacted]20[redacted] / 1	
ORAL CD/LD		700	ORAL / 5	[redacted]20[redacted] / 2	
Placebo for ABBV-951			SC / CONTINUOUS	[redacted]20[redacted] / 2	[redacted]20[redacted] / 2
ORAL CD/LD		700	ORAL / 5	[redacted]20[redacted] / 3	
Placebo for ABBV-951			SC / CONTINUOUS	[redacted]20[redacted] / 3	[redacted]20[redacted] / 3
ORAL CD/LD		700	ORAL / 5	[redacted]20[redacted] / 4	
Placebo for ABBV-951			SC / CONTINUOUS	[redacted]20[redacted] / 4	[redacted]20[redacted] / 4
ORAL CD/LD		100	ORAL / 1	[redacted]20[redacted] / 5	

Placebo for ABBV-951	SC / CONTINUOUS	[redacted]20[redacted] / 5	[redacted]20[redacted] / 5
INTERRUPTION		[redacted]20[redacted] / 18	
INTERRUPTION		[redacted]20[redacted] / 19	

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
AMANTADINE	100.000 mg	BID	Y-M: 20[redacted]
MELATONIN	5 mg	QD	Y-M: 20[redacted]
BENZATROPINE	2.000 mg	BID	Y-M: 20[redacted]
CARBIDOPA MONOHYDRATE;LEVODOPA	200.000 mg	QID	Y-M: 20[redacted]
BISACODYL	1 OTHER: TABLET	QD	Y-M: 20[redacted]
MAGNESIUM	400 mg	QD	Y-M: 20[redacted]
ERGOCALCIFEROL	50,000 IU	OTHER: ONCE PER WEEK	Y-M: 20[redacted]
RASAGILINE	1.000 mg	QD	Y-M: 20[redacted]-[redacted] / -278
ESCITALOPRAM	5 mg	QD	Y-M: 20[redacted]-[redacted] / -186
VITAMIN B COMPLEX	100 mg	BID	Y-M: 20[redacted]-[redacted] / -38

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MELATONIN	5 mg	QD	Y-M: 20[redacted]	ONGOING
BISACODYL	1 OTHER: TABLET	QD	Y-M: 20[redacted]	ONGOING
MAGNESIUM	400 mg	QD	Y-M: 20[redacted]	ONGOING
ERGOCALCIFEROL	50,000 IU	OTHER: ONCE PER WEEK	Y-M: 20[redacted]	ONGOING
ESCITALOPRAM	5 mg	QD	Y-M: 20[redacted]-[redacted] / -186	ONGOING
VITAMIN B COMPLEX	100 mg	BID	Y-M: 20[redacted]-[redacted] / -38	ONGOING
TOZINAMERAN		ONCE	Y-M: 20[redacted]-[redacted] / 2	NOT REPORTED
IBUPROFEN	800 mg	QD	Y-M: 20[redacted]-[redacted] / 11	ONGOING
REMDESIVIR	200 mg	OTHER: ONCE	Y-M: 20[redacted]-[redacted] / 20	Y-M: 20[redacted]-[redacted] / 20
PARACETAMOL	650 mg	PRN	Y-M: 20[redacted]-[redacted] / 20	Y-M: 20[redacted]-[redacted] / 25
RASAGILINE	1 mg	QD	Y-M: 20[redacted]-[redacted] / 20	Y-M: 20[redacted]-[redacted] / 25
PANTOPRAZOLE SODIUM SESQUIHYDRATE	40 mg	QD	Y-M: 20[redacted]-[redacted] / 20	Y-M: 20[redacted]-[redacted] / 50
ENOXAPARIN SODIUM	40 mg	QD	Y-M: 20[redacted]-[redacted] / 21	Y-M: 20[redacted]-[redacted] / 22
REMDESIVIR	100 mg	QD	Y-M: 20[redacted]-[redacted] / 21	Y-M: 20[redacted]-[redacted] / 25

DEXAMETHASONE	6 mg	QD	Y-M: 20[redacted]-[redacted] / 21	Y-M: 20[redacted]-[redacted] / 31

Event #1: Serious Adverse Event

Event Description	COVID-19 PNEUMONIA INFECTION
Preferred Term	COVID-19 肺炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 9
Age at AE Onset	6[redacted]

Laboratory Testing

NOT REPORTED

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 20): CHEST CT PE PROTOCOL W/ CONTRAST:NO EVIDENCE OF PULMONARY EMBOLISM. ATYPICAL PNEUMONIA IS A PREDOMINANT CONCERN.; CHEST SINGLE VIEW XR:PATCHY GROUNDGLASS INFILTRATION THE LUNG PARENCHYMA BILATERALLY THAT MAY REPRESENT ATYPICAL PNEUMONIA/VIRAL PNEUMONIA COVID PNEUMONIA; ECG:SINUS RHYTHM LEFT AXIS DEVIATION. NO ST ELEVATION/DEPRESSION

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
SAE: Investigator Opinion of Relationship to Infusion Pump	NOT RELATED
SAE: Investigator Opinion of Relationship to [redacted] Infusion Pump	NOT REPORTED
Other Cause of Event	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted]20[redacted]:10:27

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-736

治験責任医師からの報告。本被験者は米国の 6[redacted] 歳女性であり，アッヴィ社の ABBV-951（Foscarbidopa/Foslevodopa）の治験で盲検下にて治験薬及び CD/LD が投与され，COVID-19 肺炎感染症を発現した。

Event 1 の臨床経過：

関連する病歴は，パーキンソン病，副甲状腺機能低下症，非喫煙者，及び飲酒者（1 日 2 杯未満）であった。

ランダム化に先立ち，本被験者は 20[redacted] 年 [redacted] 月 [redacted] 日から 20[redacted] 年 [redacted] 月 [redacted] 日まで本治験の安定化期にて CD/LD を経口投与された。20[redacted] 年 [redacted] 月 [redacted] 日，本被験者はランダム化され，本治験の二重盲検最適化期を開始した。本事象は本治験の二重盲検最適化期中に発現した。

投与 9 日目，被験者は COVID-19 肺炎感染症を発現した。

本事象の発現前に，被験者は投与 2 日目に 1 回目の COVID-19 ワクチンを接種された。投与 4 日目，被験者の COVID-19 検査が陽性であった。

投与 9 日目，被験者は発熱，頭痛，筋肉痛，及び咳嗽を認めた。投与 20 日目，被験者は息切れ，上背部痛，及び COVID-19 のため入院した。投与 25 日目，被験者は COVID-19 肺炎と診断され退院した。

本事象により治験薬の投与が中止された。

被験者に LOVENOX，PROTONIX，ラサギリン，レムデシビル，イブプロフェン，アセトアミノフェン，及びデキサメタゾンが投与された。

Causality for ABBV-951 (Blinded)

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1) COVID-19 pneumonia (10084380) (COVID-19 pneumonia (10084380)) [v.24.0] [10084380]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: No

Causality for CARBIDOPA/LEVODOPA (Open Label)

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1) COVID-19 pneumonia (10084380) (COVID-19 pneumonia (10084380)) [v.24.0] [10084380]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

Alternative Etiology for ABBV-951 (Blinded)

Event of COVID19 PNEUMONIA INFECTION

- Investigator: Not related

- AbbVie: More likely related to SARS CoV-2 pandemic in a 6[redacted] year old subject.

Alternative Etiology for CARBIDOPA/LEVODOPA (Open Label)

Event of COVID19 PNEUMONIA INFECTION

- Investigator: Not related

- AbbVie: More likely related to SARS CoV-2 pandemic in a 6[redacted] year old subject.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] BMI:** 27.4 Kg/m2

[redacted] **20[redacted] BODY WEIGHT:** 6[redacted] KG

[redacted] **20[redacted] COVID-19 VIRUS TEST:** Nasopharyngeal swab-Tested positive

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
腎結石症	X			

Treatment Group	Age at Study Start	Sex	Race
ORAL CD/LD	5[redacted]	MALE	WHITE

Medical History	Onset Year
HYPERTENSION	19[redacted]
INTERMITTENT HEADACHES	20[redacted]
OBESITY	20[redacted]
BACK PAIN	20[redacted]
GABAPENTIN ALLERGY	20[redacted]
HERNIATED DISC	20[redacted]
MORPHINE ALLERGY	20[redacted]
SLEEP APNEA	20[redacted]
FATIGUE	20[redacted]
HYPOTHYROIDISM	20[redacted]
SEXUAL DYSFUNCTION	20[redacted]
INTERMITTENT CHEST PAIN	20[redacted]
BRUISING OF UPPER ABDOMEN	20[redacted]

Indication Disease History, Diagnosis and/or Symptoms	Onset Year
LEVODOPA INDUCED DYSKINESIA	NOT REPORTED
ONSET OF MOTOR FLUCTUATION	20[redacted]
PARKINSON'S DISEASE	20[redacted]
PARKINSON'S DISEASE DIAGNOSIS	20[redacted]

Prior Procedures	Procedure Year
GASTRIC BYPASS SURGERY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			

CIGARETTES	NEVER
CIGARS	NEVER
E-CIGARETTES	NEVER
PIPES	NEVER

Alcohol Use	Status	Number/Day
ALCOHOL	FORMER	MORE THAN 4 DRINKS

Study Drug Prescription

Study Drug	New Quadrant for Pump Infusion	Continuous Flow Rate (mL/h)	Infusion Loading Dose Volume (mL)	Oral study drug dose (CAPSULE)	Dose Date/Day
ORAL CD/LD				11	[redacted]
Placebo for ABBV-951	SITE B11				[redacted]
Placebo for ABBV-951	SITE B11				[redacted]
Placebo for ABBV-951		0.74	1.1		[redacted]
ORAL CD/LD				22	[redacted]
Placebo for ABBV-951		0.80	0.0		[redacted]
Placebo for ABBV-951	SITE B4				[redacted]
Placebo for ABBV-951	SITE B10				[redacted]
Placebo for ABBV-951	SITE B11				[redacted]
Placebo for ABBV-951	SITE B12				[redacted]
Placebo for ABBV-951	SITE B3				[redacted]
Placebo for ABBV-951	SITE B4				[redacted]
Placebo for ABBV-951		0.86	0.0		[redacted]
Placebo for ABBV-951		0.92	0.0		[redacted]
Placebo for ABBV-951	SITE B5				[redacted]
Placebo for ABBV-951	SITE A9				[redacted]
Placebo for ABBV-951	SITE B1				[redacted]
Placebo for ABBV-951	SITE A10				[redacted]
Placebo for ABBV-951		1.02	0.0		[redacted]
Placebo for ABBV-951		1.04	0.0		[redacted]
Placebo for ABBV-951	SITE A1				[redacted]
Placebo for ABBV-951	SITE A8				[redacted]
Placebo for ABBV-951	SITE B9				[redacted]
Placebo for ABBV-951	SITE A3				[redacted]
Placebo for ABBV-951	SITE B12				[redacted]
Placebo for ABBV-951	SITE A6				[redacted]

Placebo for ABBV-951	SITE A1	[redacted]20[redacted]/ 39
Placebo for ABBV-951	SITE A9	[redacted]20[redacted]/ 42
Placebo for ABBV-951	SITE A4	[redacted]20[redacted]/ 45
Placebo for ABBV-951	SITE A10	[redacted]20[redacted]/ 53
Placebo for ABBV-951	SITE A5	[redacted]20[redacted]/ 56
Placebo for ABBV-951	SITE A1	[redacted]20[redacted]/ 58
Placebo for ABBV-951	SITE B3	[redacted]20[redacted]/ 61
Placebo for ABBV-951	SITE A1	[redacted]20[redacted]/ 61
Placebo for ABBV-951	SITE A7	[redacted]20[redacted]/ 63
Placebo for ABBV-951	SITE A5	[redacted]20[redacted]/ 66
Placebo for ABBV-951	SITE A11	[redacted]20[redacted]/ 69
Placebo for ABBV-951	SITE A3	[redacted]20[redacted]/ 73
Placebo for ABBV-951	SITE A10	[redacted]20[redacted]/ 76
Placebo for ABBV-951	SITE B2	[redacted]20[redacted]/ 78
Placebo for ABBV-951	SITE B3	[redacted]20[redacted]/ 82
Placebo for ABBV-951	SITE A2	[redacted]20[redacted]/ 84

Daily Dose by Molecular Weight

Study Drug	CSCI Infusion (mg LD)	Total Oral Dose (mg)	Route (Subcutaneous) / Frequency (Times per Day)	First Dose Date/Day	Last Dose Date/Day
Placebo for ABBV-951 Loading dose			SC / CONTINUOUS	[redacted]20[redacted] / 1	
ORAL CD/LD		200	ORAL / 3	[redacted]20[redacted] / 3	
Placebo for ABBV-951			SC / CONTINUOUS	[redacted]20[redacted] / 3	[redacted]20[redacted] / 3
Placebo for ABBV-951			SC / CONTINUOUS	[redacted]20[redacted] / 4	[redacted]20[redacted] / 4
ORAL CD/LD		1200	ORAL / 7	[redacted]20[redacted] / 5	
Placebo for ABBV-951			SC / CONTINUOUS	[redacted]20[redacted] / 5	[redacted]20[redacted] / 5
ORAL CD/LD		1600	ORAL / 8	[redacted]20[redacted] / 6	
Placebo for ABBV-951			SC / CONTINUOUS	[redacted]20[redacted] / 6	[redacted]20[redacted] / 6

ORAL CD/LD	1800	ORAL / 9	[redacted] / 7
Placebo for ABBV-951		SC / CONTINUOUS	[redacted] / 7 [redacted] / 7
ORAL CD/LD	1400	ORAL / 7	[redacted] / 8
Placebo for ABBV-951		SC / CONTINUOUS	[redacted] / 8 [redacted] / 8
ORAL CD/LD	200	ORAL / 1	[redacted] / 9
Placebo for ABBV-951		SC / CONTINUOUS	[redacted] / 9 [redacted] / 9
ORAL CD/LD	2000	ORAL / 10	[redacted] / 10
Placebo for ABBV-951		SC / CONTINUOUS	[redacted] / 10 [redacted] / 10
ORAL CD/LD	2200	ORAL / 11	[redacted] / 11
Placebo for ABBV-951		SC / CONTINUOUS	[redacted] / 11 [redacted] / 11
ORAL CD/LD	1800	ORAL / 9	[redacted] / 12
Placebo for ABBV-951		SC / CONTINUOUS	[redacted] / 12 [redacted] / 12
ORAL CD/LD	1000	ORAL / 5	[redacted] / 13
Placebo for ABBV-951		SC / CONTINUOUS	[redacted] / 13 [redacted] / 13
ORAL CD/LD	1600	ORAL / 8	[redacted] / 14
Placebo for ABBV-951		SC / CONTINUOUS	[redacted] / 14 [redacted] / 14
ORAL CD/LD	1000	ORAL / 5	[redacted] / 15
Placebo for ABBV-951		SC / CONTINUOUS	[redacted] / 15 [redacted] / 15
Placebo for ABBV-951		SC / CONTINUOUS	[redacted] / 16 [redacted] / 16
Placebo for ABBV-951		SC / CONTINUOUS	[redacted] / 17 [redacted] / 17
Placebo for ABBV-951		SC / CONTINUOUS	[redacted] / 18 [redacted] / 18
Placebo for ABBV-951		SC / CONTINUOUS	[redacted] / 19 [redacted] / 19
ORAL CD/LD	1600	ORAL / 8	[redacted] / 20
Placebo for ABBV-951		SC / CONTINUOUS	[redacted] / 20 [redacted] / 20
ORAL CD/LD	1600	ORAL / 8	[redacted] / 21
Placebo for ABBV-951		SC / CONTINUOUS	[redacted] / 21 [redacted] / 21
ORAL CD/LD	600	ORAL / 3	[redacted] / 22
Placebo for ABBV-951		SC / CONTINUOUS	[redacted] / 22 [redacted] / 22
Placebo for ABBV-951		SC / CONTINUOUS	[redacted] / 23 [redacted] / 23
Placebo for ABBV-951		SC / CONTINUOUS	[redacted] / 24 [redacted] / 24
Placebo for ABBV-951		SC / CONTINUOUS	[redacted] / 25 [redacted] / 25
ORAL CD/LD	2000	ORAL / 10	[redacted] / 26
Placebo for ABBV-951		SC / CONTINUOUS	[redacted] / 26 [redacted] / 26
ORAL CD/LD	1800	ORAL / 9	[redacted] / 27
Placebo for ABBV-951		SC / CONTINUOUS	[redacted] / 27 [redacted] / 27
ORAL CD/LD	1600	ORAL / 8	[redacted] / 28
Placebo for ABBV-951		SC / CONTINUOUS	[redacted] / 28 [redacted] / 28

Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 29	[redacted]20[redacted] / 29
ORAL CD/LD	1800	ORAL / 9	[redacted]20[redacted] / 30	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 30	[redacted]20[redacted] / 30
ORAL CD/LD	1400	ORAL / 7	[redacted]20[redacted] / 32	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 32	[redacted]20[redacted] / 32
ORAL CD/LD	2000	ORAL / 10	[redacted]20[redacted] / 33	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 33	[redacted]20[redacted] / 33
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 34	[redacted]20[redacted] / 34
ORAL CD/LD	800	ORAL / 4	[redacted]20[redacted] / 35	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 35	[redacted]20[redacted] / 35
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 36	[redacted]20[redacted] / 36
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 37	[redacted]20[redacted] / 37
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 38	[redacted]20[redacted] / 38
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 39	[redacted]20[redacted] / 39
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 40	[redacted]20[redacted] / 40
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 41	[redacted]20[redacted] / 41
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 42	[redacted]20[redacted] / 42
ORAL CD/LD	1900	ORAL / 9	[redacted]20[redacted] / 43	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 43	[redacted]20[redacted] / 43
ORAL CD/LD	2200	ORAL / 11	[redacted]20[redacted] / 44	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 44	[redacted]20[redacted] / 44
ORAL CD/LD	2000	ORAL / 10	[redacted]20[redacted] / 45	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 45	[redacted]20[redacted] / 45
ORAL CD/LD	1400	ORAL / 7	[redacted]20[redacted] / 46	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 46	[redacted]20[redacted] / 46
ORAL CD/LD	1800	ORAL / 9	[redacted]20[redacted] / 47	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 47	[redacted]20[redacted] / 47
ORAL CD/LD	1600	ORAL / 8	[redacted]20[redacted] / 48	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 48	[redacted]20[redacted] / 48
ORAL CD/LD	1800	ORAL / 9	[redacted]20[redacted] / 49	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 49	[redacted]20[redacted] / 49
ORAL CD/LD	1800	ORAL / 9	[redacted]20[redacted] / 50	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 50	[redacted]20[redacted] / 50
ORAL CD/LD	1800	ORAL / 9	[redacted]20[redacted] / 51	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 51	[redacted]20[redacted] / 51
ORAL CD/LD	1200	ORAL / 6	[redacted]20[redacted] / 52	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 52	[redacted]20[redacted] / 52

ORAL CD/LD	200	ORAL / 1	[redacted]20[redacted] / 53
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 53 [redacted]20[redacted] / 53
ORAL CD/LD	2000	ORAL / 10	[redacted]20[redacted] / 54
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 54 [redacted]20[redacted] / 54
ORAL CD/LD	1800	ORAL / 9	[redacted]20[redacted] / 55
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 55 [redacted]20[redacted] / 55
ORAL CD/LD	1800	ORAL / 9	[redacted]20[redacted] / 56
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 56 [redacted]20[redacted] / 56
ORAL CD/LD	1600	ORAL / 8	[redacted]20[redacted] / 57
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 57 [redacted]20[redacted] / 57
ORAL CD/LD	1800	ORAL / 9	[redacted]20[redacted] / 58
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 58 [redacted]20[redacted] / 58
ORAL CD/LD	1600	ORAL / 8	[redacted]20[redacted] / 59
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 59 [redacted]20[redacted] / 59
ORAL CD/LD	1800	ORAL / 9	[redacted]20[redacted] / 60
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 60 [redacted]20[redacted] / 60
ORAL CD/LD	1800	ORAL / 9	[redacted]20[redacted] / 61
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 61 [redacted]20[redacted] / 61
ORAL CD/LD	1600	ORAL / 8	[redacted]20[redacted] / 62
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 62 [redacted]20[redacted] / 62
ORAL CD/LD	2000	ORAL / 10	[redacted]20[redacted] / 63
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 63 [redacted]20[redacted] / 63
ORAL CD/LD	1400	ORAL / 7	[redacted]20[redacted] / 64
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 64 [redacted]20[redacted] / 64
ORAL CD/LD	1800	ORAL / 9	[redacted]20[redacted] / 65
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 65 [redacted]20[redacted] / 65
ORAL CD/LD	1400	ORAL / 7	[redacted]20[redacted] / 66
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 66 [redacted]20[redacted] / 66
ORAL CD/LD	1600	ORAL / 8	[redacted]20[redacted] / 67
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 67 [redacted]20[redacted] / 67
ORAL CD/LD	1600	ORAL / 8	[redacted]20[redacted] / 68
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 68 [redacted]20[redacted] / 68
ORAL CD/LD	2000	ORAL / 10	[redacted]20[redacted] / 69
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 69 [redacted]20[redacted] / 69
ORAL CD/LD	1800	ORAL / 9	[redacted]20[redacted] / 70
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 70 [redacted]20[redacted] / 70
ORAL CD/LD	1600	ORAL / 8	[redacted]20[redacted] / 71

Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 71	[redacted]20[redacted] / 71
ORAL CD/LD	1600	ORAL / 8	[redacted]20[redacted] / 72	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 72	[redacted]20[redacted] / 72
ORAL CD/LD	1400	ORAL / 7	[redacted]20[redacted] / 73	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 73	[redacted]20[redacted] / 73
ORAL CD/LD	1600	ORAL / 8	[redacted]20[redacted] / 74	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 74	[redacted]20[redacted] / 74
ORAL CD/LD	1600	ORAL / 8	[redacted]20[redacted] / 75	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 75	[redacted]20[redacted] / 75
ORAL CD/LD	2000	ORAL / 10	[redacted]20[redacted] / 76	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 76	[redacted]20[redacted] / 76
ORAL CD/LD	1800	ORAL / 9	[redacted]20[redacted] / 77	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 77	[redacted]20[redacted] / 77
ORAL CD/LD	1800	ORAL / 9	[redacted]20[redacted] / 78	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 78	[redacted]20[redacted] / 78
ORAL CD/LD	1800	ORAL / 9	[redacted]20[redacted] / 79	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 79	[redacted]20[redacted] / 79
ORAL CD/LD	2000	ORAL / 10	[redacted]20[redacted] / 80	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 80	[redacted]20[redacted] / 80
ORAL CD/LD	1600	ORAL / 8	[redacted]20[redacted] / 81	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 81	[redacted]20[redacted] / 81
ORAL CD/LD	1000	ORAL / 5	[redacted]20[redacted] / 82	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 82	[redacted]20[redacted] / 82
ORAL CD/LD	1600	ORAL / 8	[redacted]20[redacted] / 83	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 83	[redacted]20[redacted] / 83
ORAL CD/LD	1200	ORAL / 6	[redacted]20[redacted] / 84	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 84	[redacted]20[redacted] / 84
ORAL CD/LD	1000	ORAL / 5	[redacted]20[redacted] / 85	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 85	[redacted]20[redacted] / 85

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
LEVOTHYROXINE	.05 mg	QD	Y-M: 20[redacted]
OXYCODONE HYDROCHLORIDE;PARACETAMOL	10/325 mg	QID	Y-M: 20[redacted]
PRAMIPEXOLE	0.500 mg	QD	Y-M: 20[redacted]-[redacted]
LISINOPRIL	20 mg	QD	Y-M: 20[redacted]-[redacted] / -357

AMANTADINE	100.000 mg	BID	Y-M: 20[redacted] / -336
AMITRIPTYLINE	25 mg	QD	Y-M: 20[redacted] / -235
ATENOLOL	100 mg	QD	Y-M: 20[redacted] / -174
CARBIDOPA MONOHYDRATE;LEVODOPA	200.000 mg	10 TIMES PER DAY	Y-M: 20[redacted] / -152
CYANOCOBALAMIN	1000 mg	QD	Y-M: 20[redacted] / -36
POTASSIUM CHLORIDE	1 OTHER: TABLET	QD	Y-M: 20[redacted] / -36

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
LEVOTHYROXINE	.05 mg	QD	Y-M: 20[redacted]	ONGOING
OXYCODONE HYDROCHLORIDE;PARACETAMOL	10/325 mg	QID	Y-M: 20[redacted]	ONGOING
LISINOPRIL	20 mg	QD	Y-M: 20[redacted] / -357	ONGOING
AMITRIPTYLINE	25 mg	QD	Y-M: 20[redacted] / -235	ONGOING
CYANOCOBALAMIN	1000 mg	QD	Y-M: 20[redacted] / -36	ONGOING
POTASSIUM CHLORIDE	1 OTHER: TABLET	QD	Y-M: 20[redacted] / -36	ONGOING
AMLODIPINE BESILATE	5 mg	QD	Y-M: 20[redacted] / 2	ONGOING

Event #1: Serious Adverse Event

Event Description	KIDNEY STONES
Preferred Term	腎結石症
AE Onset Date / Rx Day	[redacted]20[redacted] / 28
Age at AE Onset	5[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	31
Duration of AE	4 DAYS
Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY

SAE: Investigator Opinion of Relationship to Infusion Pump	NOT RELATED
SAE: Investigator Opinion of Relationship to [redacted] Infusion Pump	NOT REPORTED
Other Cause of Event	NATURAL CAUSES POSSIBLY DUE TO OBESITY
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted]20[redacted]:10:27
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-736

治験責任医師からの報告。本被験者は米国の 5[redacted] 歳男性であり，アッヴィ社の ABBV-951（Foscarbidopa/Foslevodopa）の治験で盲検下にて治験薬及び即放性 CD/LD が投与され，腎結石を発現した。

Event 1 の臨床経過：

関連する病歴は，高血圧，肥満，背部痛，パーキンソン病，甲状腺機能低下症，非喫煙者，及び元飲酒者（1 日 4 杯超）であった。

投与 28 日目，被験者は腎結石を発現した。投与 31 日目，腎結石は消失した。

投与 28 日目，被験者は腰痛のため入院した。被験者はその後，泌尿器科医にかかり体外衝撃波結石破砕術について話し合うことを勧められた。投与 31 日目，被験者は退院した。

被験者に認められた本事象に関連するリスク因子は肥満であった。

The patient's past medications include:

GABAPENTIN for UNKNOWN INDICATION (20[redacted] - 20[redacted])

MORPHINE for UNKNOWN INDICATION (20[redacted] - 20[redacted])

Causality for ABBV-951 (Blinded)

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1) Kidney stones (10023437) (Nephrolithiasis (10029148)) [v.24.0] [10023437]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

Causality for CARBIDOPA/LEVODOPA IR (Open Label)

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1) Kidney stones (10023437) (Nephrolithiasis (10029148)) [v.24.0] [10023437]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

Alternative Etiology for ABBV-951 (Blinded)

Event of KIDNEY STONES

- Investigator: Natural causes possibly due to obesity

- AbbVie: More likely related to underlying risk factors in an obese subject with history of gastric bypass surgery, and hypertension.

Alternative Etiology for CARBIDOPA/LEVODOPA IR (Open Label)

Event of KIDNEY STONES

- Investigator: Natural causes possibly due to obesity.

- AbbVie: Temporally implausible, event occurred 27 days after the administration of last dose of carbidopa/levodopa IR.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20**[redacted] **BMI:** 38.6 kg/mm2

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
片頭痛	X			

Treatment Group	Age at Study Start	Sex	Race
ABBV-951	5[redacted]	MALE	WHITE

Medical History	Onset Year
INFLAMMATION OF TONSILS	19[redacted]
NASAL FRACTURE	19[redacted]
ELEVATED HEPATIC ENZYME	20[redacted]
INSOMNIA	20[redacted]
SYNCOPE	20[redacted]

Indication Disease History, Diagnosis and/or Symptoms	Onset Year
PARKINSON'S DISEASE	20[redacted]
ONSET OF MOTOR FLUCTUATION	20[redacted]
PARKINSON'S DISEASE DIAGNOSIS	20[redacted]

Prior Procedures	Procedure Year
TONSILECTOMY	19[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	NEVER			
CIGARS	CURRENT			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	2 - 4 DRINKS

Study Drug Prescription

Study Drug	New Quadrant for Pump Infusion	Continuous Flow Rate (mL/h)	Infusion Loading Dose Volume (mL)	Oral study drug dose (CAPSULE)	Dose Date/Day
ABBV-951		0.50	1.6		[redacted] / 1
ABBV-951	SITE A10				[redacted] / 2
ABBV-951	SITE A1				[redacted] / 2
ABBV-951	SITE B8				[redacted] / 3
ABBV-951	SITE A1				[redacted] / 4
ABBV-951	SITE A11				[redacted] / 6
ABBV-951	SITE A11				[redacted] / 11
ABBV-951	SITE A3				[redacted] / 13
ABBV-951	SITE A3				[redacted] / 27
ABBV-951	SITE A11				[redacted] / 29
ABBV-951	SITE A2				[redacted] / 57
ABBV-951	SITE A11				[redacted] / 59
ABBV-951	SITE A4				[redacted] / 84

Daily Dose by Molecular Weight

Study Drug	CSCI Infusion (mg LD)	Total Oral Dose (mg)	Route (Subcutaneous) / Frequency (Times per Day)	First Dose Date/Day	Last Dose Date/Day
ABBV-951 Loading dose	273.2		SC / CONTINUOUS	[redacted] / 1	
ABBV-951	298.81		SC / CONTINUOUS	[redacted] / 3	[redacted] / 3
Placebo ORAL CD/LD			ORAL / 5	[redacted] / 4	
ABBV-951	2049		SC / CONTINUOUS	[redacted] / 4	[redacted] / 4
Placebo ORAL CD/LD			ORAL / 6	[redacted] / 5	
ABBV-951	1515.40		SC / CONTINUOUS	[redacted] / 5	[redacted] / 5
Placebo ORAL CD/LD			ORAL / 5	[redacted] / 6	
ABBV-951	1458.20		SC / CONTINUOUS	[redacted] / 6	[redacted] / 6
Placebo ORAL CD/LD			ORAL / 6	[redacted] / 7	
ABBV-951	2037.90		SC / CONTINUOUS	[redacted] / 7	[redacted] / 7
ABBV-951	2049		SC / CONTINUOUS	[redacted] / 8	[redacted] / 8
ABBV-951	2049		SC / CONTINUOUS	[redacted] / 9	[redacted] / 9
ABBV-951	2049		SC / CONTINUOUS	[redacted] / 10	[redacted] / 10
ABBV-951	2049		SC / CONTINUOUS	[redacted] / 11	[redacted] / 11
Placebo ORAL CD/LD			ORAL / 5	[redacted] / 12	

ABBV-951	2032.77	SC / CONTINUOUS	[redacted]20[redacted] / 12	[redacted]20[redacted] / 12
Placebo ORAL CD/LD		ORAL / 5	[redacted]20[redacted] / 13	
ABBV-951	2020.82	SC / CONTINUOUS	[redacted]20[redacted] / 13	[redacted]20[redacted] / 13
ABBV-951	2031.07	SC / CONTINUOUS	[redacted]20[redacted] / 14	[redacted]20[redacted] / 14
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 15	[redacted]20[redacted] / 15
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 16	[redacted]20[redacted] / 16
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 17	[redacted]20[redacted] / 17
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 18	[redacted]20[redacted] / 18
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 19	[redacted]20[redacted] / 19
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 20	[redacted]20[redacted] / 20
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 21	[redacted]20[redacted] / 21
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 22	[redacted]20[redacted] / 22
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 23	[redacted]20[redacted] / 23
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 24	[redacted]20[redacted] / 24
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 25	[redacted]20[redacted] / 25
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 26	[redacted]20[redacted] / 26
Placebo ORAL CD/LD		ORAL / 6	[redacted]20[redacted] / 27	
ABBV-951	2047.29	SC / CONTINUOUS	[redacted]20[redacted] / 27	[redacted]20[redacted] / 27
Placebo ORAL CD/LD		ORAL / 5	[redacted]20[redacted] / 28	
ABBV-951	2043.87	SC / CONTINUOUS	[redacted]20[redacted] / 28	[redacted]20[redacted] / 28
Placebo ORAL CD/LD		ORAL / 6	[redacted]20[redacted] / 29	
ABBV-951	2038.75	SC / CONTINUOUS	[redacted]20[redacted] / 29	[redacted]20[redacted] / 29
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 30	[redacted]20[redacted] / 30
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 31	[redacted]20[redacted] / 31
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 32	[redacted]20[redacted] / 32
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 33	[redacted]20[redacted] / 33
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 34	[redacted]20[redacted] / 34
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 35	[redacted]20[redacted] / 35
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 36	[redacted]20[redacted] / 36
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 37	[redacted]20[redacted] / 37
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 38	[redacted]20[redacted] / 38
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 39	[redacted]20[redacted] / 39
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 40	[redacted]20[redacted] / 40
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 41	[redacted]20[redacted] / 41
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 42	[redacted]20[redacted] / 42
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 43	[redacted]20[redacted] / 43
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 44	[redacted]20[redacted] / 44

ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 45	[redacted]20[redacted] / 45
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 46	[redacted]20[redacted] / 46
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 47	[redacted]20[redacted] / 47
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 48	[redacted]20[redacted] / 48
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 49	[redacted]20[redacted] / 49
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 50	[redacted]20[redacted] / 50
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 51	[redacted]20[redacted] / 51
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 52	[redacted]20[redacted] / 52
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 53	[redacted]20[redacted] / 53
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 54	[redacted]20[redacted] / 54
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 55	[redacted]20[redacted] / 55
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 56	[redacted]20[redacted] / 56
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 57	[redacted]20[redacted] / 57
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 58	[redacted]20[redacted] / 58
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 59	[redacted]20[redacted] / 59
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 60	[redacted]20[redacted] / 60
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 61	[redacted]20[redacted] / 61
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 62	[redacted]20[redacted] / 62
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 63	[redacted]20[redacted] / 63
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 64	[redacted]20[redacted] / 64
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 65	[redacted]20[redacted] / 65
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 66	[redacted]20[redacted] / 66
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 67	[redacted]20[redacted] / 67
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 68	[redacted]20[redacted] / 68
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 69	[redacted]20[redacted] / 69
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 70	[redacted]20[redacted] / 70
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 71	[redacted]20[redacted] / 71
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 72	[redacted]20[redacted] / 72
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 73	[redacted]20[redacted] / 73
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 74	[redacted]20[redacted] / 74
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 75	[redacted]20[redacted] / 75
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 76	[redacted]20[redacted] / 76
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 77	[redacted]20[redacted] / 77
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 78	[redacted]20[redacted] / 78
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 79	[redacted]20[redacted] / 79
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 80	[redacted]20[redacted] / 80
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 81	[redacted]20[redacted] / 81

ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 82	[redacted]20[redacted] / 82
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 83	[redacted]20[redacted] / 83
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 84	[redacted]20[redacted] / 84
Placebo ORAL CD/LD		ORAL / 6	[redacted]20[redacted] / 85	
ABBV-951	2030.21	SC / CONTINUOUS	[redacted]20[redacted] / 85	[redacted]20[redacted] / 85
Placebo ORAL CD/LD		ORAL / 5	[redacted]20[redacted] / 86	
ABBV-951	2046.43	SC / CONTINUOUS	[redacted]20[redacted] / 86	[redacted]20[redacted] / 86
Placebo ORAL CD/LD		ORAL / 1	[redacted]20[redacted] / 87	
ABBV-951	2043.02	SC / CONTINUOUS	[redacted]20[redacted] / 87	[redacted]20[redacted] / 87
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 88	[redacted]20[redacted] / 88
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 89	[redacted]20[redacted] / 89
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 90	[redacted]20[redacted] / 90
ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 91	[redacted]20[redacted] / 91
ABBV-951	937.41	SC / CONTINUOUS	[redacted]20[redacted] / 92	[redacted]20[redacted] / 92

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
CARBIDOPA MONOHYDRATE;LEVODOPA	200.000 mg	6 TIMES PER DAY	Y-M: 20[redacted]-[redacted]
MELATONIN	10 mg	QD	Y-M: 20[redacted]-[redacted]
ROTIGOTINE	4.000 mg	QD	Y-M: 20[redacted]-[redacted]
VITAMINS NOS	1 OTHER: CAPSULE	QD	Y-M: 20[redacted]
CARBIDOPA MONOHYDRATE;LEVODOPA	200.000 mg	QD	Y-M: 20[redacted]-[redacted]
ENTACAPONE	200.000 mg	TID	Y-M: 20[redacted]-[redacted]

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
MELATONIN	10 mg	QD	Y-M: 20[redacted]-[redacted]	ONGOING
VITAMINS NOS	1 OTHER: CAPSULE	QD	Y-M: 20[redacted]	ONGOING
FLUDROCORTISONE	0.1 mg	QD	Y-M: 20[redacted]-[redacted] / 46	ONGOING

Event #1: Serious Adverse Event

Event Description	ATYPICAL MIGRAINE
Preferred Term	片頭痛
AE Onset Date / Rx Day	[redacted]20[redacted] / 87

Age at AE Onset	5[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
[redacted]20[redacted] (RX DAY 87): CT OF HEAD WITH AND WITHOUT CONTRAST:NORMAL; ECHOCARDIOGRAM:NORMAL; EEG:NORMAL; MRA WITH AND WITHOUT CONTRAST:NORMAL	
AE Stopped Rx Day	88
Duration of AE	2 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
SAE: Investigator Opinion of Relationship to Infusion Pump	NOT RELATED
SAE: Investigator Opinion of Relationship to [redacted] Infusion Pump	NOT REPORTED
Other Cause of Event	UNDETERMINED AT THIS TIME
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted]20[redacted]:10:27
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-736

治験責任医師からの報告。本被験者は米国の 5[redacted] 歳男性であり，アッヴィ社の ABBV-951（Foscarbidopa/Foslevodopa）の治験で盲検下にて治験薬及び CD/LD が投与され，非定型片頭痛を発現した。

Event 1 の臨床経過：

関連する病歴は，鼻骨骨折，パーキンソン病，失神，起立性低血圧，現飲酒者（1 日 2 杯未満），及び非喫煙者であった。

ランダム化に先立ち，本被験者は 20[redacted] 年 [redacted] 月 [redacted] 日から 20[redacted] 年 [redacted] 月 [redacted] 日まで本治験の安定化期にて CD/LD を経口投与された。20[redacted] 年 [redacted] 月 [redacted] 日，本被験者はランダム化され，本治験の二重

盲検最適化期を開始した。投与 1 日目から 28 日目まで，被験者は本治験の二重盲検最適化期にて最適な臨床反応を達成するための皮下投与製剤の調整を必要とした。本期間を通して被疑薬の用量が調整された可能性がある。投与 29 日目（V11），被験者は維持期に移行した。被疑薬に関する情報は，本事象発現時の皮下投与製剤の用量で示されている。

投与日 87 目，被験者は非定型片頭痛を発現した。投与 88 日目，非定型片頭痛は消失した。

投与 83 日目，被験者は左側の頭部に鋭い痛みを発現し，不明瞭な発語及び浮動性めまいを伴った。徐々に症状は軽減し，被験者は正常な健康状態に戻った。

投与 86 日目，被験者は浮動性めまい及び左眼の下垂を伴う痛みが再発したため救急処置室に行った。投与 87 日目，被験者は入院し，非定型片頭痛と診断された。投与 88 日目，被験者は退院した。

The patient's past medications include:

CARBIDOPA LEVODOPA IMMEDIATE RELEASE for PARKINSON'S DISEASE ([redacted] 20[redacted] - [redacted] 20[redacted])

ENTACAPONE for PARKINSON'S DISEASE ([redacted] 20[redacted] - [redacted] 20[redacted])

SINEMET PLUS for PARKINSON'S DISEASE ([redacted] 20[redacted] - [redacted] 20[redacted])

Causality for ABBV-951 (Blinded)

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1) Migraine (10027599) (Migraine (10027599)) [v.24.0] [10027599]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

Causality for CARBIDOPA/LEVODOPA (Open Label)

---

1) Migraine (10027599) (Migraine (10027599)) [v.24.0] [10027599]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

Alternative Etiology for ABBV-951 (Blinded)

Event of ATYPICAL MIGRAINE

- Investigator: UNDETERMINED AT THIS TIME

- AbbVie: More likely related to genetics and environment in a patient with a history of insomnia.

Alternative Etiology for CARBIDOPA/LEVODOPA (Open Label)

Event of ATYPICAL MIGRAINE

- Investigator: UNDETERMINED AT THIS TIME

- AbbVie: More likely related to genetics and environment in a patient with a history of insomnia.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] CT OF HEAD WITH AND WITHOUT CONTRAST:** Normal

[redacted] **20[redacted] ECHOCARDIOGRAM:** Normal

[redacted] **20[redacted] EEG:** Normal

[redacted] **20[redacted] MRA WITH AND WITHOUT CONTRAST:** Normal

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
カテーテル留置部位蜂巣炎	X			X
半月板損傷				X

Treatment Group	Age at Study Start	Sex	Race
ABBV-951	6[redacted]	MALE	WHITE

Medical History	Onset Year
HIGH CHOLESTEROL	20[redacted]
HYPERTENSION	20[redacted]
PSORIATIC ARTHRITIS	20[redacted]
RHEUMATOID ARTHRITIS	20[redacted]
OBESITY	20[redacted]
ENLARGED PROSTATE	20[redacted]
PERFORATED NASAL SEPTUM	20[redacted]
LEFT THUMB MCP JOINT HYPEREXTENSION	20[redacted]

Indication Disease History, Diagnosis and/or Symptoms	Onset Year
PARKINSON'S DISEASE	20[redacted]
PARKINSON'S DISEASE DIAGNOSIS	20[redacted]
ONSET OF MOTOR FLUCTUATION	20[redacted]

Prior Procedures	Procedure Year
LAP BAN SURGERY	20[redacted]
PERFORATED SEPTUM REPAIR	20[redacted]
THUMB CMC ARTHROPLASTY	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	FORMER	10 CIGARETTE	5	19[redacted]
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	NEVER	

Study Drug Prescription

Study Drug	New Quadrant for Pump Infusion	Continuous Flow Rate (mL/h)	Infusion Loading Dose Volume (mL)	Oral study drug dose (CAPSULE)	Dose Date/Day
ABBV-951	SITE B9				[redacted]
ABBV-951		0.16	0.6		[redacted]
ABBV-951		0.18	0.0		[redacted]
ABBV-951		0.20	0.0		[redacted]
ABBV-951	SITE A1				[redacted]
ABBV-951	SITE B10				[redacted]
ABBV-951		0.22	0.0		[redacted]
ABBV-951	SITE B3				[redacted]
ABBV-951	SITE A5				[redacted]
ABBV-951	SITE A9				[redacted]
ABBV-951	SITE B4				[redacted]
ABBV-951	SITE A10				[redacted]
ABBV-951	SITE B12				[redacted]
ABBV-951	SITE A4				[redacted]
ABBV-951	SITE B11				[redacted]
ABBV-951	SITE A4				[redacted]
ABBV-951	SITE B3				[redacted]
ABBV-951	SITE B9				[redacted]
ABBV-951	SITE A1				[redacted]
ABBV-951	SITE A10				[redacted]
ABBV-951	SITE A10				[redacted]
ABBV-951	SITE A6				[redacted]
ABBV-951	SITE A5				[redacted]
ABBV-951	SITE A3				[redacted]

ABBV-951	SITE A4	[redacted]20[redacted]/ 77
ABBV-951	SITE A1	[redacted]20[redacted]/ 80

Daily Dose by Molecular Weight

Study Drug	CSCI Infusion (mg LD)	Total Oral Dose (mg)	Route (Subcutaneous) / Frequency (Times per Day)	First Dose Date/Day	Last Dose Date/Day
ABBV-951 Loading dose	85.37		SC / CONTINUOUS	[redacted]20[redacted] / 1	
Placebo ORAL CD/LD			ORAL / 1	[redacted]20[redacted] / 1	
ABBV-951	361.99		SC / CONTINUOUS	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
ACETYLSALICYLIC ACID	81 mg	QD	Y-M: 20[redacted]
SIMVASTATIN	40 mg	QD	Y-M: 20[redacted]
LISINOPRIL	20 mg	QD	Y-M: 20[redacted]
GUSELKUMAB	100 mg	QD	Y-M: 20[redacted]
FINASTERIDE	5 mg	QD	Y-M: 20[redacted]
PRAMIPEXOLE	1.500 mg	QD	Y-M: 20[redacted]
RASAGILINE	1.000 mg	QD	Y-M: 20[redacted]
ROTIGOTINE	4.000 mg	QD	Y-M: 20[redacted]
CARBIDOPA MONOHYDRATE;LEVODOPA	100.000 mg	TID	Y-M: 20[redacted]-[redacted]
CARBIDOPA MONOHYDRATE;LEVODOPA	100.000 mg	QID	Y-M: 20[redacted]-[redacted] / -163
IXEKIZUMAB	80 mg	OTHER: Q 4WEEKS	Y-M: 20[redacted]-[redacted] / -27

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
ACETYLSALICYLIC ACID	81 mg	QD	Y-M: 20[redacted]	ONGOING
SIMVASTATIN	40 mg	QD	Y-M: 20[redacted]	ONGOING
LISINOPRIL	20 mg	QD	Y-M: 20[redacted]	ONGOING
GUSELKUMAB	100 mg	QD	Y-M: 20[redacted]	ONGOING
FINASTERIDE	5 mg	QD	Y-M: 20[redacted]	ONGOING
IXEKIZUMAB	80 mg	OTHER: Q 4WEEKS	Y-M: 20[redacted]-[redacted] / -27	Y-M: 20[redacted]-[redacted] / 69

TOZINAMERAN		ONCE	Y-M: 20[redacted]-[redacted] / 30	NOT REPORTED
IBUPROFEN	200 mg	PRN	Y-M: 20[redacted]-[redacted] / 47	ONGOING
TOZINAMERAN		ONCE	Y-M: 20[redacted]-[redacted] / 54	NOT REPORTED
HYDROMORPHONE HYDROCHLORIDE	0.5 mg	QD	Y-M: 20[redacted]-[redacted] / 59	Y-M: 20[redacted]-[redacted] / 59
VANCOMYCIN	100 mg	BID	Y-M: 20[redacted]-[redacted] / 59	Y-M: 20[redacted]-[redacted] / 60
OXYCODONE HYDROCHLORIDE;PARACETAMOL	5-325 mg	PRN	Y-M: 20[redacted]-[redacted] / 59	Y-M: 20[redacted]-[redacted] / 64
TRAMADOL	50 mg	PRN	Y-M: 20[redacted]-[redacted] / 60	Y-M: 20[redacted]-[redacted] / 64
VANCOMYCIN	2000 mg	QD	Y-M: 20[redacted]-[redacted] / 61	Y-M: 20[redacted]-[redacted] / 61
VANCOMYCIN	1500 mg	BID	Y-M: 20[redacted]-[redacted] / 61	Y-M: 20[redacted]-[redacted] / 64
IBUPROFEN	600 mg	PRN	Y-M: 20[redacted]-[redacted] / 63	Y-M: 20[redacted]-[redacted] / 93
DOXYCYCLINE	100 mg	BID	Y-M: 20[redacted]-[redacted] / 64	Y-M: 20[redacted]-[redacted] / 69
SULFAMETHOXAZOLE	4000 mg	BID	Y-M: 20[redacted]-[redacted] / 69	Y-M: 20[redacted]-[redacted] / 82
TRIMETHOPRIM	80 mg	BID	Y-M: 20[redacted]-[redacted] / 69	Y-M: 20[redacted]-[redacted] / 82

Event #1: Event of Interest - Falls and Associated Injuries

Event Description	MENISCUS TEAR
Preferred Term	半月板損傷
AE Onset Date / Rx Day	[redacted]20[redacted] / 47
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING

Severity	MODERATE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
SAE: Investigator Opinion of Relationship to Infusion Pump	NOT APPLICABLE
SAE: Investigator Opinion of Relationship to [redacted] Infusion Pump	NOT APPLICABLE
Other Cause of Event	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #2: Serious Adverse Event, Event of Interest - Infusion Site Related Infections

Event Description	CELLULITIS OF THE ABDOMEN AT CANULA SITE
Preferred Term	カテーテル留置部位蜂巣炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 59
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 50): HEMOGLOBIN: 129 [135 - 175] G/L; [redacted]20[redacted] (RX DAY 60): BLOOD UREA NITROGEN: 5.4 [2.9 - 7.1] MMOL/L; CALCIUM: 2.02 [2.22 - 2.57] MMOL/L; CREATININE: 80 [53 - 115] UMOL/L; ERYTHROCYTES: 4.6 [4.3 - 5.7] 10^12/L; GLUCOSE: 6.2 [3.9 - 5.5] MMOL/L; HEMATOCRIT: 0.41 [0.39 - 0.49] FRACTION OF 1; HEMOGLOBIN: 141 [135 - 175] G/L; LEUKOCYTES: 13.6 [4.6 - 10.2] 10^9/L; NPTST004-ANION GAP: 4 [6 - 18] MMOL/L; NPTST013-CARBON DIOXIDE: 28 [22 - 32] MMOL/L; NPTST015-CHLORIDE: 101 [98 - 107] MMOL/L; NPTST030-GRF: >60 [NOT REPORTED - NOT REPORTED] ML/MIN; NPTST037-LACTATE LEVEL: 0.8 [0.5 - 2] MMOL/L; PLATELETS: 182 [142 - 424] 10^9/L; POTASSIUM: 3.4 [3.6 - 5.1] MMOL/L; SODIUM: 133 [136 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 61): BLOOD UREA NITROGEN: 5 [2.9 - 7.1] MMOL/L; CALCIUM: 1.92 [2.22 - 2.57] MMOL/L; CREATININE: 67 [53 - 115] UMOL/L; ERYTHROCYTES: 4.2 [4.3 - 5.7] 10^12/L; GLUCOSE: 5.5 [3.9 - 5.5] MMOL/L; HEMATOCRIT: 0.38 [0.39 - 0.49] FRACTION OF 1; HEMOGLOBIN: 127 [135 - 175] G/L; LEUKOCYTES: 12.1 [4.6 - 10.2] 10^9/L; NPTST004-ANION GAP: 4 [6 - 18] MMOL/L; NPTST013-CARBON DIOXIDE: 26 [22 - 32] MMOL/L; NPTST015-CHLORIDE: 107 [98 - 107] MMOL/L; PLATELETS: 158 [142 - 424] 10^9/L; SODIUM: 137 [136 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 62): BLOOD UREA NITROGEN: 4.3 [2.9 - 7.1] MMOL/L; CALCIUM: 2.05 [2.22 - 2.57] MMOL/L; CREATININE: 69 [53 - 115] UMOL/L; ERYTHROCYTES: 4.2 [4.3 - 5.7] 10^12/L; GLUCOSE: 5.4 [3.9 - 5.5] MMOL/L; HEMATOCRIT: 0.37 [0.39 - 0.49] FRACTION OF 1; HEMOGLOBIN: 127 [135 - 175] G/L; LEUKOCYTES: 9.9 [4.6 - 10.2] 10^9/L; NPTST004-ANION GAP: 5 [6 - 18] MMOL/L; NPTST013-CARBON DIOXIDE: 27 [22 - 32] MMOL/L; NPTST015-CHLORIDE: 103 [98 - 107] MMOL/L; PLATELETS: 181 [142 - 424] 10^9/L; POTASSIUM: 3.5 [3.6 - 5.1] MMOL/L; SODIUM: 135 [136 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 63): BLOOD UREA NITROGEN: 3.6 [2.9 - 7.1] MMOL/L; CALCIUM: 2.05 [2.22 - 2.57] MMOL/L; CREATININE: 65 [53 - 115] UMOL/L; ERYTHROCYTES: 4.2 [4.3 - 5.7] 10^12/L; GLUCOSE: 5.2 [3.9 - 5.5] MMOL/L; HEMATOCRIT: 0.38 [0.39 - 0.49] FRACTION OF 1; LEUKOCYTES: 8.2 [4.6 - 10.2] 10^9/L; NPTST004-ANION GAP: 5 [6 - 18] MMOL/L; NPTST013-CARBON DIOXIDE: 26 [22 - 32] MMOL/L; NPTST015-CHLORIDE: 106 [98 - 107] MMOL/L; PLATELETS: 196 [142 - 424] 10^9/L; POTASSIUM: 3.7 [3.6 - 5.1] MMOL/L; SODIUM: 137 [136 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 64): BLOOD UREA NITROGEN: 4.6 [2.9 - 7.1] MMOL/L; CALCIUM: 2.12 [2.22 - 2.57] MMOL/L; CREATININE: 68 [53 - 115] UMOL/L; GLUCOSE: 4.8 [3.9 - 5.5] MMOL/L; HEMATOCRIT: 0.39 [0.39 - 0.49] FRACTION OF 1; HEMOGLOBIN: 130 [135 - 175] G/L; LEUKOCYTES: 9.0 [4.6 - 10.2] THOU/MCL; NPTST004-ANION GAP: 5 [6 - 18] MMOL/L; NPTST013-CARBON DIOXIDE: 28 [22 - 32]

MMOL/L; NPTST015-CHLORIDE: 106 [98 - 107] MMOL/L; PLATELETS: 217 [142 - 424] 10^9/L; POTASSIUM: 3.7 [3.6 - 5.1] MMOL/L; SODIUM: 139 [136 - 145] MMOL/L

Microbiology

[redacted]20[redacted] (RX DAY 69): BLOOD WOUND AEROBIC CULTURE: NEGATIVE; [redacted]20[redacted] (RX DAY 124): OTHER NASOPHARYNGEAL MRSA CULTURE/SCREEN: NEGATIVE-NO MRSA ISOLATED. LIGHT GROWTH STAPHYLOCOCCUS AUREUS

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 61): CT OF THE ABDOMEN:DISPLAYED ABDOMINAL WALL CELLULITIS WITHOUT AN ABSCESS AND SOME FLUID IN THE DISTAL ESOPHAGUS; [redacted]20[redacted] (RX DAY 63): ABDOMINAL ULTRASOUND:PERSISTENCE OF INDURATION WITH CELLULITIS WAS NEGATIVE FOR FLUID COLLECTION.

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	MODERATE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
SAE: Investigator Opinion of Relationship to Infusion Pump	CAUSAL RELATIONSHIP
SAE: Investigator Opinion of Relationship to [redacted] Infusion Pump	[redacted] INFUSION SET 9 MM
Other Cause of Event	NOT REPORTED
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted]20[redacted]:10:27

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-736

治験責任医師からの報告。本被験者は米国の 6[redacted] 歳男性であり，アッヴィ社の ABBV-951（Foscarbidopa/Foslevodopa）の治験で盲検下にて治験薬及び CD/LD が投与され，カニューレ部位の腹部蜂巣炎を発現した。

Event 2 の臨床経過：

関連する病歴は，乾癬性関節炎，肥満，パーキンソン病，元喫煙者（1 日 10 本を 5 年間）及び非飲酒者であった。

ランダム化に先立ち，本被験者は20[redacted]年[redacted]月[redacted]日から20[redacted]年[redacted]月[redacted]日まで本治験の安定化期にてCD/LDを経口投与された。20[redacted]年[redacted]月[redacted]日（投与1日目，V6），本被験者はランダム化され，本治験の二重盲検最適化期を開始した。投与1日目から28日目まで，被験者は本治験の二重盲検最適化期にて最適な臨床反応を達成するための皮下投与製剤の調整を必要とした。本期間を通して被疑薬の用量が調整された可能性がある。投与29日目（V11），被験者は維持期に移行した。被疑薬に関する情報は，本事象発現時の皮下投与製剤の用量で示されている。

投与59日目，被験者はカニューレ部位の腹部蜂巣炎を発現した。投与97日目，カニューレ部位の腹部蜂巣炎は消失した。

投与59日目，被験者は腹壁の蜂巣炎のため救急処置室に行った。被験者の腹部はカニューレ部位が赤く，圧痛があり，熱を帯びていた。被験者は経口抗生物質の服用を開始した。投与60日目，被験者は薬剤を2回投与した後，腹部の紅斑が若干悪化したため救急処置室に戻ってきた。被験者は入院し，静注の抗生物質及び鎮痛剤を投与された。被験者に対するポンプでの注入は，別の非感染部位で継続した。投与65日目，被験者は退院した。

被験者にドキシサイクリン，トラマドール，DILAUDID，PERCOCET，スルファメトキサゾール，イブプロフェン，及びバンコマイシンが投与された。

The patient's past medications include:

CARBIDOPA/LEVODOPA IMMEDIATE RELEASE for PARKINSON'S DISEASE (20[redacted] - [redacted] 20[redacted])

Causality for ABBV-951 (Blinded)

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1) Catheter site cellulitis (10053183) (Catheter site cellulitis (10053183)) [v.24.0] [10053183]

Causality as per reporter (Drug/Vaccine): Reasonable possibility

Causality as per Mfr. (Drug/Vaccine): Reasonable possibility

Dechallenge: Not Applicable

Causality for CARBIDOPA/LEVODOPA (Open Label)

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1) Catheter site cellulitis (10053183) (Catheter site cellulitis (10053183)) [v.24.0] [10053183]

Causality as per reporter (Drug/Vaccine): Reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

Alternative Etiology for ABBV-951 (Blinded)

Event of CELLULITIS OF THE ABDOMEN AT CANULA SITE

- Investigator: Causal relationship

- AbbVie: Not Applicable

Alternative Etiology for CARBIDOPA/LEVODOPA (Open Label)

Event of CELLULITIS OF THE ABDOMEN AT CANULA SITE

- Investigator: Causal relationship

- AbbVie: Temporally implausible, event occurred 2 months post administration of oral carbidopa/levodopa during the stabilization period.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ABDOMINAL CT:** Abdominal wall cellulitis without an abscess and some fluid in the distal esophagus

[redacted] **20[redacted] ABDOMINAL ULTRASOUND:** Persistence of induration with cellulitis. Negative for fluid colltion.

[redacted] **20[redacted] AEROBIC CULTURE:** Wound Aerobic Culture - negative

[redacted] **20[redacted] BMI:** 34 kg/m2

[redacted] **20[redacted] HCT:** 41.3% (normal 39.0 to 49)

[redacted] **20[redacted] HGB:** 14.1 G/DL (normal 13.5 to 17.5)

[redacted] **20[redacted] WBC:** 13.6 throu/mcL (normal 4.6 to 10.2)

[redacted] **20[redacted] WBC:** 9.0 throu/mcL

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
急性呼吸不全	X		X	
蜂巣炎	X	X		
** Disc. due to adverse event				X

Disc = Discontinued.

Treatment Group	Age at Study Start	Sex	Race
ORAL CD/LD	8[redacted]	FEMALE	WHITE

Medical History	Onset Year
GALLSTONES	19[redacted]
UTERINE FYBROIDS	19[redacted]
CARPAL TUNNEL SYNDROM	19[redacted]
STERILIZATION	19[redacted]
BREAST CANCER	19[redacted]
CHRONIC OBSTRUCTIVE PULMONARY DISEASE	19[redacted]
HIGH CHOLESTEROL	20[redacted]
HYPERTENSION	20[redacted]
ATRIAL FIBRILLATION	20[redacted]
OSTEOPOROSIS	20[redacted]
COMMON COLD	20[redacted]
UPPER RESPIRATORY INFECTION	20[redacted]

Indication Disease History, Diagnosis and/or Symptoms	Onset Year
PARKINSON'S DISEASE	20[redacted]
PARKINSON'S DISEASE DIAGNOSIS	20[redacted]
ONSET OF MOTOR FLUCTUATION	20[redacted]

Prior Procedures	Procedure Year
LAPAROSCOPIC GALLBLADDER	19[redacted]
CARPAL TUNNEL RELEASE SURGERY	19[redacted]
HYSTERECTOMY	19[redacted]
MASTECTOMY (LEFT)	19[redacted]
PACEMAKER	20[redacted]

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	CURRENT	8 CIGARETTE	60	
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	LESS THAN 2 DRINKS

Study Drug Prescription

Study Drug	New Quadrant for Pump Infusion	Continuous Flow Rate (mL/h)	Infusion Loading Dose Volume (mL)	Oral study drug dose (CAPSULE)	Dose Date/Day
ORAL CD/LD				7	[redacted]20[redacted]/ 1
Placebo for ABBV-951	SITE A1				[redacted]20[redacted]/ 1
Placebo for ABBV-951		0.24	1.1		[redacted]20[redacted]/ 1
Placebo for ABBV-951	SITE A2				[redacted]20[redacted]/ 7
Placebo for ABBV-951		0.26	1.1		[redacted]20[redacted]/ 8
Placebo for ABBV-951	SITE B4				[redacted]20[redacted]/ 10
Placebo for ABBV-951	SITE B7				[redacted]20[redacted]/ 13
Placebo for ABBV-951		0.28	0.0		[redacted]20[redacted]/ 13
Placebo for ABBV-951	SITE B9				[redacted]20[redacted]/ 16
Placebo for ABBV-951	SITE B10				[redacted]20[redacted]/ 19

Placebo for ABBV-951	SITE A12	[redacted]20[redacted] / 24
Placebo for ABBV-951	SITE B1	[redacted]20[redacted] / 27
Placebo for ABBV-951	SITE B2	[redacted]20[redacted] / 30
Placebo for ABBV-951	SITE B2	[redacted]20[redacted] / 33
Placebo for ABBV-951	SITE B5	[redacted]20[redacted] / 36
Placebo for ABBV-951	SITE B9	[redacted]20[redacted] / 39
Placebo for ABBV-951	SITE B12	[redacted]20[redacted] / 45
Placebo for ABBV-951	SITE B1	[redacted]20[redacted] / 48
Placebo for ABBV-951	SITE B1	[redacted]20[redacted] / 50
Placebo for ABBV-951	SITE B4	[redacted]20[redacted] / 53
Placebo for ABBV-951	SITE B6	[redacted]20[redacted] / 56
Placebo for ABBV-951	SITE B7	[redacted]20[redacted] / 61
Placebo for ABBV-951	SITE B10	[redacted]20[redacted] / 66

Daily Dose by Molecular Weight

Study Drug	CSCI Infusion (mg LD)	Total Oral Dose (mg)	Route (Subcutaneous) / Frequency (Times per Day)	First Dose Date/Day	Last Dose Date/Day
Placebo for ABBV-951 Loading dose			SC / CONTINUOUS	[redacted]20[redacted] / 1	
Placebo for ABBV-951			SC / CONTINUOUS	[redacted]20[redacted] / 2	[redacted]20[redacted] / 2
Placebo for ABBV-951			SC / CONTINUOUS	[redacted]20[redacted] / 3	[redacted]20[redacted] / 3
Placebo for ABBV-951			SC / CONTINUOUS	[redacted]20[redacted] / 4	[redacted]20[redacted] / 4
Placebo for ABBV-951			SC / CONTINUOUS	[redacted]20[redacted] / 5	[redacted]20[redacted] / 5
Placebo for ABBV-951			SC / CONTINUOUS	[redacted]20[redacted] / 6	[redacted]20[redacted] / 6
Placebo for ABBV-951			SC / CONTINUOUS	[redacted]20[redacted] / 7	[redacted]20[redacted] / 7
ORAL CD/LD		1100	ORAL / 4	[redacted]20[redacted] / 8	

Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 8	[redacted]20[redacted] / 8
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 9	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 9	[redacted]20[redacted] / 9
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 10	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 10	[redacted]20[redacted] / 10
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 11	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 11	[redacted]20[redacted] / 11
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 12	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 12	[redacted]20[redacted] / 12
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 13	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 13	[redacted]20[redacted] / 13
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 14	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 14	[redacted]20[redacted] / 14
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 15	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 15	[redacted]20[redacted] / 15
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 16	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 16	[redacted]20[redacted] / 16
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 17	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 17	[redacted]20[redacted] / 17
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 18	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 18	[redacted]20[redacted] / 18
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 19	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 19	[redacted]20[redacted] / 19
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 20	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 20	[redacted]20[redacted] / 20
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 21	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 21	[redacted]20[redacted] / 21
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 22	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 22	[redacted]20[redacted] / 22
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 23	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 23	[redacted]20[redacted] / 23
ORAL CD/LD	900	ORAL / 2	[redacted]20[redacted] / 24	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 24	[redacted]20[redacted] / 24
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 25	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 25	[redacted]20[redacted] / 25
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 26	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 26	[redacted]20[redacted] / 26

ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 27	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 27	[redacted]20[redacted] / 27
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 28	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 28	[redacted]20[redacted] / 28
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 29	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 29	[redacted]20[redacted] / 29
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 30	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 30	[redacted]20[redacted] / 30
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 31	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 31	[redacted]20[redacted] / 31
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 32	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 32	[redacted]20[redacted] / 32
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 33	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 33	[redacted]20[redacted] / 33
ORAL CD/LD	1900	ORAL / 5	[redacted]20[redacted] / 34	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 34	[redacted]20[redacted] / 34
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 35	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 35	[redacted]20[redacted] / 35
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 36	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 36	[redacted]20[redacted] / 36
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 37	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 37	[redacted]20[redacted] / 37
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 38	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 38	[redacted]20[redacted] / 38
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 39	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 39	[redacted]20[redacted] / 39
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 40	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 40	[redacted]20[redacted] / 40
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 41	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 41	[redacted]20[redacted] / 41
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 42	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 42	[redacted]20[redacted] / 42
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 43	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 43	[redacted]20[redacted] / 43
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 44	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 44	[redacted]20[redacted] / 44
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 45	

Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 45	[redacted]20[redacted] / 45
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 46	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 46	[redacted]20[redacted] / 46
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 47	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 47	[redacted]20[redacted] / 47
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 48	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 48	[redacted]20[redacted] / 48
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 49	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 49	[redacted]20[redacted] / 49
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 50	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 50	[redacted]20[redacted] / 50
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 51	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 51	[redacted]20[redacted] / 51
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 52	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 52	[redacted]20[redacted] / 52
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 53	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 53	[redacted]20[redacted] / 53
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 54	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 54	[redacted]20[redacted] / 54
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 55	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 55	[redacted]20[redacted] / 55
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 56	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 56	[redacted]20[redacted] / 56
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 57	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 57	[redacted]20[redacted] / 57
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 58	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 58	[redacted]20[redacted] / 58
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 59	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 59	[redacted]20[redacted] / 59
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 60	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 60	[redacted]20[redacted] / 60
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 61	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 61	[redacted]20[redacted] / 61
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 62	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 62	[redacted]20[redacted] / 62
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 63	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 63	[redacted]20[redacted] / 63

ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 64	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 64	[redacted]20[redacted] / 64
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 65	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 65	[redacted]20[redacted] / 65
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 66	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 66	[redacted]20[redacted] / 66
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 67	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 67	[redacted]20[redacted] / 67
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 68	
Placebo for ABBV-951		SC / CONTINUOUS	[redacted]20[redacted] / 68	[redacted]20[redacted] / 68
ORAL CD/LD	1200	ORAL / 3	[redacted]20[redacted] / 69	

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
OMEGA-3 FATTY ACIDS	UNKNOWN OTHER: UNKNOWN	QD	Y-M: 20[redacted]
ROSUVASTATIN	5 mg	QD	Y-M: 20[redacted]
CALCIUM	UNKNOWN IU	OTHER: UNKNOWN	Y-M: 20[redacted]
MAGNESIUM	UNKNOWN OTHER: UNKNOWN	QD	Y-M: 20[redacted]
METOPROLOL SUCCINATE	25 mg	QD	Y-M: 20[redacted]
VITAMIN D NOS	UNKNOWN OTHER: UNKNOWN	QD	Y-M: 20[redacted]
ZINC	UNKNOWN OTHER: UNKNOWN	QD	Y-M: 20[redacted]
WARFARIN	2.5 mg	QD	Y-M: 20[redacted]
BUDESONIDE;FORMOTEROL	2 OTHER: PUFFS	BID	Y-M: 20[redacted]
FUROSEMIDE	60 mg	QD	Y-M: 20[redacted]
HYDROCHLOROTHIAZIDE;TRIAMTERENE	37.5-25 mg	QD	Y-M: 20[redacted]
POTASSIUM CHLORIDE	30 mEq	QD	Y-M: 20[redacted]
MINERALS NOS;VITAMINS NOS	UNKNOWN OTHER: UNKNOWN	QD	Y-M: 20[redacted]
PRAMIPEXOLE	1.000 mg	TID	Y-M: 20[redacted]
CARBIDOPA MONOHYDRATE;LEVODOPA	100.000 mg	TID	Y-M: 20[redacted]-[redacted]
SELEGILINE	1.000 mg	BID	Y-M: 20[redacted]
CARBIDOPA MONOHYDRATE;LEVODOPA	100.000 mg	TID	Y-M: 20[redacted]-[redacted]
CARBIDOPA MONOHYDRATE;LEVODOPA	200.000 mg	TID	Y-M: 20[redacted]-[redacted]

DENOSUMAB	60 mg	OTHER: 6 MONTHS	Y-M: 20[redacted]
PARACETAMOL;PSEUDOEPHEDRINE	2 OTHER: UNKNOWN	PRN	Y-M: 20[redacted] / -47
AMOXICILLIN	500 mg	TID	Y-M: 20[redacted] / -45
AZITHROMYCIN	500 mg	QD	Y-M: 20[redacted] / -31
AZITHROMYCIN	250 mg	QD	Y-M: 20[redacted] / -29

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
OMEGA-3 FATTY ACIDS	UNKNOWN OTHER: UNKNOWN	QD	Y-M: 20[redacted]	ONGOING
ROSUVASTATIN	5 mg	QD	Y-M: 20[redacted]	ONGOING
CALCIUM	UNKNOWN IU	OTHER: UNKNOWN	Y-M: 20[redacted]	ONGOING
MAGNESIUM	UNKNOWN OTHER: UNKNOWN	QD	Y-M: 20[redacted]	ONGOING
METOPROLOL SUCCINATE	25 mg	QD	Y-M: 20[redacted]	ONGOING
VITAMIN D NOS	UNKNOWN OTHER: UNKNOWN	QD	Y-M: 20[redacted]	ONGOING
ZINC	UNKNOWN OTHER: UNKNOWN	QD	Y-M: 20[redacted]	ONGOING
WARFARIN	2.5 mg	QD	Y-M: 20[redacted]	Y-M: 20[redacted] / 98
FUROSEMIDE	60 mg	QD	Y-M: 20[redacted]	ONGOING
HYDROCHLOROTHIAZIDE;TRIAMTERENE	37.5-25 mg	QD	Y-M: 20[redacted]	ONGOING
POTASSIUM CHLORIDE	30 mEq	QD	Y-M: 20[redacted]	ONGOING
BUDESONIDE;FORMOTEROL	2 OTHER: PUFFS	BID	Y-M: 20[redacted]	Y-M: 20[redacted] / 98
MINERALS NOS;VITAMINS NOS	UNKNOWN OTHER: UNKNOWN	QD	Y-M: 20[redacted]	ONGOING
DENOSUMAB	60 mg	OTHER: 6 MONTHS	Y-M: 20[redacted]	ONGOING
HYDROCODONE BITARTRATE;PARACETAMOL	5 mg	PRN	Y-M: 20[redacted] / 72	Y-M: 20[redacted] / 76
MORPHINE	2 mg	PRN	Y-M: 20[redacted] / 72	Y-M: 20[redacted] / 76
VANCOMYCIN	1500/250 ML/ HR/IVPB mg	OTHER: ONCE	Y-M: 20[redacted] / 72	Y-M: 20[redacted] / 76

Event #1: Serious Adverse Event, AE Leading to Discontinuation of Study Drug

Event Description	CELLULITIS OF THE RIGHT LEG
Preferred Term	蜂巣炎
AE Onset Date / Rx Day	[redacted]20[redacted] / 68
Age at AE Onset	8[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 69): BLOOD UREA NITROGEN: 29.3 [2.9 - 7.1] MMOL/L; CALCIUM: 2.37 [2.22 - 2.57] MMOL/L; CREATININE: 157 [53 - 115] UMOL/L; GLUCOSE: 6.2 [3.9 - 5.5] MMOL/L; NPTST004-ANION GAP: 8 [6 - 18] MMOL/L; NPTST014-CARBON DIOXIDE LEVEL: 41 [22 - 32] MMOL/L; NPTST015-CHLORIDE: 89 [98 - 107] MMOL/L; NPTST037-LACTATE LEVEL: 1.2 [0.5 - 2] MMOL/L; POTASSIUM: 4.2 [3.6 - 5.1] MMOL/L; SODIUM: 138 [136 - 145] MMOL/L; [redacted]20[redacted] (RX DAY 70): BLOOD UREA NITROGEN: 28.2 [2.9 - 7.1] MMOL/L; CREATININE: 142 [53 - 115] UMOL/L; GLUCOSE: 7.4 [3.9 - 5.5] MMOL/L; NPTST013-CARBON DIOXIDE: 40 [22 - 32] MMOL/L; NPTST015-CHLORIDE: 93 [98 - 107] MMOL/L; POTASSIUM: 3.9 [3.6 - 5.1] MMOL/L; [redacted]20[redacted] (RX DAY 71): BLOOD UREA NITROGEN: 29.6 [2.9 - 7.1] MMOL/L; GLUCOSE: 5.8 [3.9 - 5.5] MMOL/L; POTASSIUM: 5 [3.6 - 5.1] MMOL/L; SODIUM: 135 [136 - 145] MMOL/L

Microbiology

[redacted]20[redacted] (RX DAY 70): OTHER CULTURE DRAINAGE CULTURE: NEGATIVE-NO POLYS SEEN, RARE EPIS, NO ORGANISM SEEN

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 69): CHEST X-RAY:THE HEART REMAINS ENLARGED WITH A 3-LEAD CARDIAC PACER ENTERING FROM THE RIGHT SUBCLAVIAN. SOME SMALL AREAS OF MORE FOCAL DENSITY IN THE UPPER RIGHT LUNG AND LEFT LOWER LUNG ON THE PRIOR EXAM ARE NO LONGER IDENTIFIED. THERE ARE SURGICAL STAPLES IN THE RIGHT LUNG SURGICAL CLIPS OVER THE LEFT AXILLARY REGION. BILATERAL INTERSTITIAL LUNG OPACITY PERSISTS. THERE IS A SMALL RIGHT PLEURAL EFFUSION. NO P NEUMOTHORAX IDENTIFIED.; RIGHT LOWER EXTREMITY VENOUS DUPLEX EXAM:NORMAL OF THE DEEP AND SUPERFICIAL VEINS IN THE RIGHT LOWER EXTREMITY

AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
SAE: Investigator Opinion of Relationship to Infusion Pump	NOT RELATED
SAE: Investigator Opinion of Relationship to [redacted] Infusion Pump	NOT REPORTED
Other Cause of Event	SUBJECT BUMPED HER KNEE RESULTING IN INFECTION
Discontinued Study Drug Due to the Event	YES
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #2: Serious Adverse Event, Death

Event Description	ACUTE RESPIRATORY FAILURE
Preferred Term	急性呼吸不全
AE Onset Date / Rx Day	[redacted]20[redacted] / 91 (21 DAYS AFTER LAST TREATMENT)
Age at AE Onset	8[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	98 (28 DAYS AFTER LAST TREATMENT)
Duration of AE	8 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
SAE: Investigator Opinion of Relationship to Infusion Pump	NOT RELATED
SAE: Investigator Opinion of Relationship to [redacted] Infusion Pump	NOT REPORTED
Other Cause of Event	SEPSIS
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION, LIFE THREATENING, RESULTS IN DEATH

Generated: [redacted]20[redacted]:10:27
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-736

治験責任医師からの報告。本被験者は米国の 8[redacted] 歳女性であり，アッヴィ社の ABBV-951（Foscarbidopa/Foslevodopa）の治験で盲検下にて治験薬及び CD/LD が投与され，右下肢の蜂巣炎を発現した。

Event 1 の臨床経過：

関連する病歴は，慢性閉塞性肺疾患，高コレステロール，高血圧，パーキンソン病，喫煙者（1 日 8 本を 60 年間），及び飲酒者（1 日 2 杯未満）であった。

ランダム化に先立ち，本被験者は 20[redacted] 年 [redacted] 月 [redacted] 日から 20[redacted] 年 [redacted] 月 [redacted] 日まで本治験の安定化期にて CD/LD を経口投与された。20[redacted] 年 [redacted] 月 [redacted] 日（投与 1 日目，V6），本被験者はランダム化され，本治験の二重盲検最適化期を開始した。投与 1 日目から 28 日目まで，被験者は本治験の二重盲検最適化期にて最適な臨床反応を達成するための皮下投与製剤の調整を必要とした。本期間を通して被疑薬の用量が調整された可能性がある。投与 29 日目（V11），被験者は維持期に移行した。被疑薬に関する情報は，本事象発現時の皮下投与製剤の用量で示されている。

投与 68 日目，被験者は右下肢の蜂巣炎を発現した。

入院前に，被験者は膝の疼痛及び圧痛のため救急処置室に行った。被験者は膝の蜂巣炎と診断された。投与 69 日目，被験者は顕著な腫脹，水泡，及び創傷部からの滲出を伴う右膝から下方への疼痛及び紅斑の伸展のため入院した。蜂巣炎の治療のため，バンコマイシン及び静脈内輸液を開始した。その時点で深部静脈血栓症又は敗血症の疑いはなかった。投与 76 日目，被験者は退院した。

本事象により治験薬の投与が中止された。

被験者にモルヒネ，NORCO，及びバンコマイシンが投与された。

The patient's past medications include:

SINEMET IR for PARKINSON'S DISEASE ([redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted], [redacted] 20[redacted] - [redacted] 20[redacted])

Causality for ABBV-951 (Blinded)

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1) Cellulitis of leg (10007912) (Cellulitis (10007882)) [v.24.0] [10007912]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: No

Causality for CARBIDOPA/LEVODOPA (Open Label)

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1) Cellulitis of leg (10007912) (Cellulitis (10007882)) [v.24.0] [10007912]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

Alternative Etiology for ABBV-951 (Blinded)

Event of CELLULITIS OF THE RIGHT LEG

- Investigator: Subject bumped her knee, resulting in infection.

- AbbVie: More likely related to incidental injury from a bumped knee resulting in leg infection (per PI). Elderly patients are at increased risk for developing skin break down and cellulitis.

Alternative Etiology for CARBIDOPA/LEVODOPA (Open Label)

Event of CELLULITIS OF THE RIGHT LEG

- Investigator: Subject bumped her knee, resulting in infection.

- AbbVie: Elderly patients are at increased risk for developing skin break down and cellulitis. Event occurred 68 days after administration of last dose of oral carbidopa/levodopa.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ANION GAP:** 8.0 MMOL/L (normal 6.0 to 18.0)

[redacted] **20[redacted] CARBON DIOXIDE:** 41 MMOL/L (normal 22 to 32)

[redacted] **20[redacted] CHEST X-RAY:** The heart remains enlarged with a 3-lead cardiac pacer entering from the right subclavian. Some small areas of more focal density in the upper right lung and left lower lung on the prior exam are no longer identified. There are surgical staples in the right lung surgical clips over the left axillary region. Bilateral interstitial lung opacity persists. There is a small right pleural effusion. No

pneumothorax identified.

[redacted] **20[redacted] CHLORIDE:** 89 MMOL/L (normal 98 to 107)

[redacted] **20[redacted] DRAINAGE** CULTURE: Negative

[redacted] **20[redacted] POTASSIUM:** 4.2 MMOL/L (normal 3.6 to 5.1)

[redacted] **20[redacted] SODIUM:** 138 MMOL/L (normal 136 to 145)

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-736

治験責任医師からの報告。本被験者は米国の 8[redacted] 歳女性であり，アッヴィ社の ABBV-951（Foscarbidopa/Foslevodopa）の治験で盲検下にて治験薬及び CD/LD が投与され，死亡に至った Grade 5 の急性呼吸不全を発現した。

Event 2 の臨床経過：

関連する病歴は，慢性閉塞性肺疾患，高コレステロール，高血圧，パーキンソン病，上気道感染，喫煙者（1 日 8 本を 60 年間），及び飲酒者（1 日 2 杯未満）であった。

ランダム化に先立ち，本被験者は 20[redacted] 年 [redacted] 月 [redacted] 日から 20[redacted] 年 [redacted] 月 [redacted] 日まで本治験の安定化期にて CD/LD を経口投与された。20[redacted] 年 [redacted] 月 [redacted] 日（投与 1 日目，V6），本被験者はランダム化され，本治験の二重盲検最適化期を開始した。投与 1 日目から 28 日目まで，被験者は本治験の二重盲検最適化期にて最適な臨床反応を達成するための皮下投与製剤の調整を必要とした。本期間を通して被疑薬の用量が調整された可能性がある。投与 29 日目（V11），被験者は維持期に移行した。被疑薬に関する情報は，本事象発現時の皮下投与製剤の用量で示されている。

投与 91 日目，被験者は急性呼吸不全を発現した。投与 98 日目，被験者は死亡した。死因は急性呼吸不全と報告された。剖検は行われなかった。

投与 91 日目，被験者は意識不明で発見され，救急車で病院に搬送された。発見時，被験者の呼吸は浅く，低血圧であった。被験者に対し胸骨圧迫が行われ，広域スペクトラム抗生物質が投与された後，直接集中治療室に入院し，挿管された。家族の要望で被験者は一般運動病棟に移送された。投与 97 日目，被験者は退院した。

治験責任医師によると，被験者には慢性呼吸不全の病歴があり，ベースライン時点で 4 L の酸素吸入を行っていた。

Causality for ABBV-951 (Blinded)

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1) Acute respiratory failure (10001053) (Acute respiratory failure (10001053)) [v.24.0] [10001053]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

Causality for CARBIDOPA/LEVODOPA (Open Label)

---

1) Acute respiratory failure (10001053) (Acute respiratory failure (10001053)) [v.24.0] [10001053]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

Alternative Etiology for ABBV-951 (Blinded)

Event of ACUTE RESPIRATORY FAILURE

- Investigator: Sepsis

- AbbVie: More likely related to reported sepsis in an elderly aged subject with history of Parkinson disease, chronic obstructive pulmonary disease and smoking.

Alternative Etiology for CARBIDOPA/LEVODOPA (Open Label)

Event of ACUTE RESPIRATORY FAILURE

- Investigator: Sepsis

- AbbVie: More likely related to reported sepsis in an elderly aged subject with history of Parkinson disease, chronic obstructive pulmonary disease and smoking.

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
脱水	X			
幻覚		X		X
** Disc. due to adverse event				X

Disc = Discontinued.

Treatment Group	Age at Study Start	Sex	Race
ABBV-951	7[redacted]	MALE	WHITE

Medical History	Onset Year
HEMANGIOMA	19[redacted]
SEASONAL ALLERGIES	19[redacted]
ACTINIC KERATOSIS	19[redacted]
POLLEN EXTRACT ALLERGY	19[redacted]
LOW TESTOSTERONE	20[redacted]
ANXIETY	20[redacted]
INTERMITTENT HALLUCINATIONS	20[redacted]
LEFT EYE GLAUCOMA	20[redacted]
PERNICIOUS ANEMIA	20[redacted]
RIGHT EYE GLAUCOMA	20[redacted]
CHRONIC KIDNEY DISEASE MILD	20[redacted]
DEPRESSION	20[redacted]
VITAMIN B 12 DEFICIENCY	20[redacted]
VITAMIN D DEFICIENCY	20[redacted]
BILATERAL LOWER EXTREMITY EDEMA	20[redacted]
CONSTIPATION	20[redacted]
OSTEOPENIA	20[redacted]
URINARY INCONTINENCE	20[redacted]
VENOUS INSUFFICIENCY	20[redacted]

Indication Disease History, Diagnosis and/or Symptoms	Onset Year
LEVODOPA INDUCED DYSKINESIA	NOT REPORTED
PARKINSON'S DISEASE	20[redacted]
ONSET OF MOTOR FLUCTUATION	20[redacted]
PARKINSON'S DISEASE DIAGNOSIS	20[redacted]

Prior Procedures	Procedure Year
NOT REPORTED	

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	NEVER			
CIGARETTES	NEVER			
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	CURRENT	LESS THAN 2 DRINKS

Study Drug Prescription

Study Drug	New Quadrant for Pump Infusion	Continuous Flow Rate (mL/h)	Infusion Loading Dose Volume (mL)	Oral study drug dose (CAPSULE)	Dose Date/Day
ABBV-951	SITE A1				[redacted]20[redacted] / 1
ABBV-951		0.30	0.5		[redacted]20[redacted] / 1
ABBV-951	SITE B1				[redacted]20[redacted] / 4
ABBV-951	SITE A2				[redacted]20[redacted] / 7
ABBV-951		0.4	0.0		[redacted]20[redacted] / 8
ABBV-951	SITE B10				[redacted]20[redacted] / 12
ABBV-951	SITE A9				[redacted]20[redacted] / 15
ABBV-951		0.47	0.0		[redacted]20[redacted] / 15
ABBV-951	SITE B3				[redacted]20[redacted] / 17
ABBV-951	SITE A12				[redacted]20[redacted] / 20
ABBV-951	SITE B11				[redacted]20[redacted] / 23
ABBV-951		0.5	0.0		[redacted]20[redacted] / 24
ABBV-951	SITE B12				[redacted]20[redacted] / 26

Daily Dose by Molecular Weight

Study Drug	CSCI Infusion (mg LD)	Total Oral Dose (mg)	Route (Subcutaneous) / Frequency (Times per Day)	First Dose Date/Day	Last Dose Date/Day
ABBV-951 Loading dose	85.37		SC / CONTINUOUS	[redacted] / 1	
ABBV-951	668.48		SC / CONTINUOUS	[redacted] / 1	[redacted] / 1
ABBV-951	1229.4		SC / CONTINUOUS	[redacted] / 2	[redacted] / 2
ABBV-951	1229.4		SC / CONTINUOUS	[redacted] / 3	[redacted] / 3
ABBV-951	1216.59		SC / CONTINUOUS	[redacted] / 4	[redacted] / 4
ABBV-951	1201.22		SC / CONTINUOUS	[redacted] / 5	[redacted] / 5
ABBV-951	1229.4		SC / CONTINUOUS	[redacted] / 6	[redacted] / 6
ABBV-951	1229.4		SC / CONTINUOUS	[redacted] / 7	[redacted] / 7
ABBV-951	1205.32		SC / CONTINUOUS	[redacted] / 8	[redacted] / 8
ABBV-951	1633.73		SC / CONTINUOUS	[redacted] / 9	[redacted] / 9
ABBV-951	1628.95		SC / CONTINUOUS	[redacted] / 10	[redacted] / 10
ABBV-951	1625.54		SC / CONTINUOUS	[redacted] / 11	[redacted] / 11
Placebo ORAL CD/LD			ORAL / 9	[redacted] / 12	
ABBV-951	1622.12		SC / CONTINUOUS	[redacted] / 12	[redacted] / 12
Placebo ORAL CD/LD			ORAL / 9	[redacted] / 13	
ABBV-951	1603.00		SC / CONTINUOUS	[redacted] / 13	[redacted] / 13
Placebo ORAL CD/LD			ORAL / 9	[redacted] / 14	
ABBV-951	1623.49		SC / CONTINUOUS	[redacted] / 14	[redacted] / 14
Placebo ORAL CD/LD			ORAL / 1	[redacted] / 15	
ABBV-951	1609.14		SC / CONTINUOUS	[redacted] / 15	[redacted] / 15
ABBV-951	1926.06		SC / CONTINUOUS	[redacted] / 16	[redacted] / 16
ABBV-951	1883.52		SC / CONTINUOUS	[redacted] / 17	[redacted] / 17
ABBV-951	1915.62		SC / CONTINUOUS	[redacted] / 18	[redacted] / 18
ABBV-951	1881.92		SC / CONTINUOUS	[redacted] / 19	[redacted] / 19
Placebo ORAL CD/LD			ORAL / 10	[redacted] / 20	
ABBV-951	1895.56		SC / CONTINUOUS	[redacted] / 20	[redacted] / 20
Placebo ORAL CD/LD			ORAL / 9	[redacted] / 21	
ABBV-951	1915.62		SC / CONTINUOUS	[redacted] / 21	[redacted] / 21
Placebo ORAL CD/LD			ORAL / 10	[redacted] / 22	
ABBV-951	1912.41		SC / CONTINUOUS	[redacted] / 22	[redacted] / 22
Placebo ORAL CD/LD			ORAL / 8	[redacted] / 23	
ABBV-951	1926.06		SC / CONTINUOUS	[redacted] / 23	[redacted] / 23
Placebo ORAL CD/LD			ORAL / 1	[redacted] / 24	
ABBV-951	1905.99		SC / CONTINUOUS	[redacted] / 24	[redacted] / 24

ABBV-951	2049	SC / CONTINUOUS	[redacted]20[redacted] / 25	[redacted]20[redacted] / 25
ABBV-951	1349.77	SC / CONTINUOUS	[redacted]20[redacted] / 26	[redacted]20[redacted] / 26

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
PRAMIPEXOLE DIHYDROCHLORIDE MONOHYDRATE	1.500 mg	TID	Y-M: 20[redacted]
RASAGILINE MESYLATE	1.000 mg	QD	Y-M: 20[redacted]
LACTOBACILLUS NOS	1 OTHER: CAPSULE	QD	Y-M: 20[redacted]
TESTOSTERONE	2 g	QD	Y-M: 20[redacted]
BRIMONIDINE TARTRATE	1%	BID	Y-M: 20[redacted]
CARBIDOPA MONOHYDRATE;LEVODOPA	100.000 mg	8 TIMES PER DAY	Y-M: 20[redacted]
COLECALCIFEROL	2000 IU	QD	Y-M: 20[redacted]
VITAMIN B12 NOS	1000 ug	QD	Y-M: 20[redacted]
ALPRAZOLAM	0.5 mg	PRN	Y-M: 20[redacted]
DENOSUMAB	60 mg	PRN	Y-M: 20[redacted]
MENAQUINONE	100 ug	QD	Y-M: 20[redacted]
MINERALS NOS;VITAMINS NOS	1 OTHER: CAPSULE	QD	Y-M: 20[redacted]
ALKA 4-COMPLEX;DIOSMIN	630 mg	QD	Y-M: 20[redacted]-[redacted] / -279

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
LACTOBACILLUS NOS	1 OTHER: CAPSULE	QD	Y-M: 20[redacted]	ONGOING
TESTOSTERONE	2 g	QD	Y-M: 20[redacted]	ONGOING
BRIMONIDINE TARTRATE	1%	BID	Y-M: 20[redacted]	ONGOING
COLECALCIFEROL	2000 IU	QD	Y-M: 20[redacted]	ONGOING
VITAMIN B12 NOS	1000 ug	QD	Y-M: 20[redacted]	ONGOING
ALPRAZOLAM	0.5 mg	PRN	Y-M: 20[redacted]	ONGOING
DENOSUMAB	60 mg	PRN	Y-M: 20[redacted]	ONGOING
MENAQUINONE	100 ug	QD	Y-M: 20[redacted]	ONGOING
MINERALS NOS;VITAMINS NOS	1 OTHER: CAPSULE	QD	Y-M: 20[redacted]	ONGOING
ALKA 4-COMPLEX;DIOSMIN	630 mg	QD	Y-M: 20[redacted]-[redacted] / -279	ONGOING
SODIUM CHLORIDE	2-10 mL	PRN	Y-M: 20[redacted]-[redacted] / 26	Y-M: 20[redacted]-[redacted] / 26

Event #1: AE Leading to Discontinuation of Study Drug, Event of Interest - Hallucinations/Psychosis

Event Description	WORSENING OF HALLUCINATIONS
Preferred Term	幻覚
AE Onset Date / Rx Day	[redacted]20[redacted] / 12
Age at AE Onset	7[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	ONGOING
Duration of AE	ONGOING
Severity	SEVERE
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
SAE: Investigator Opinion of Relationship to Infusion Pump	NOT APPLICABLE
SAE: Investigator Opinion of Relationship to [redacted] Infusion Pump	NOT APPLICABLE
Other Cause of Event	NOT APPLICABLE
Discontinued Study Drug Due to the Event	YES
SAE Criteria	NONE

Event #2: Serious Adverse Event

Event Description	WORSENING OF DEHYDRATION
Preferred Term	脱水
AE Onset Date / Rx Day	[redacted]20[redacted] / 26
Age at AE Onset	7[redacted]
Laboratory Testing	
NOT REPORTED	
Microbiology	
NOT REPORTED	
SAE Supplemental Procedure	
NOT REPORTED	
AE Stopped Rx Day	27 (1 DAY AFTER LAST TREATMENT)

Duration of AE	2 DAYS
Severity	SEVERE
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
SAE: Investigator Opinion of Relationship to Infusion Pump	UNLIKELY
SAE: Investigator Opinion of Relationship to [redacted] Infusion Pump	NOT REPORTED
Other Cause of Event	LOSS OF AUTONOMIC FUNCTION LEADING TO DEHYDRATION, NO SENSE OF THIRST
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Generated: [redacted]20[redacted]:10:27
Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-736

治験責任医師からの報告。本被験者は米国の 7[redacted] 歳男性であり，アッヴィ社の ABBV-951（Foscarbidopa/Foslevodopa）の治験で盲検下にて治験薬及び CD/LD が投与され，脱水の悪化を発現した。

Event 2 の臨床経過：

関連する病歴は，パーキンソン病，軽度の慢性腎疾患，尿失禁，非喫煙者，及び飲酒者（1 日 2 杯未満）であった。

ランダム化に先立ち，本被験者は 20[redacted] 年 [redacted] 月 [redacted] 日から 20[redacted] 年 [redacted] 月 [redacted] 日まで本治験の安定化期にて CD/LD を経口投与された。20[redacted] 年 [redacted] 月 [redacted] 日（投与 1 日目，V6），本被験者はランダム化され，本治験の二重盲検最適化期を開始した。投与 1 日目から 28 日目まで，被験者は本治験の二重盲検最適化期にて最適な臨床反応を達成するための皮下投与製剤の調整を必要とした。本期間を通して被疑薬の用量が調整された可能性がある。投与 29 日目（V11），被験者は維持期に移行した。被疑薬に関する情報は，本事象発現時の皮下投与製剤の用量で示されている。

投与 26 日目，被験者は脱水の悪化を発現した。投与 27 日目，脱水の悪化は消失した。

投与 5 日前，被験者は非重篤な有害事象として脱水を発現した。投与 12 日目，被験者は非重篤な有害事象として幻覚の悪化を発現した。

投与 26 日目，被験者は運動症状の悪化のために入院した。また，被験者は精神状態の変化及び妄想症を発現した。被験者が会話の途中で寝てしまったため，ソーシャルワーカーは発現時に被験者の精神状態を完全に評価することができなかった。同日，脱水の悪化の治療のために被験者に 0.9%塩化ナトリウムが静脈内投与された。投与 27 日目，被験者は退院した。
治験責任医師によると，口渇感のない自律神経機能の消失がリスク因子に含まれた。
被験者に 0.9%塩化ナトリウムが投与された。

The patient's past medications include:

CARBIDOPA/LEVODOPA for PARKINSON'S DISEASE (Started 20[redacted])

Causality for ABBV-951 (Blinded)

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1) Dehydration (10012174) (Dehydration (10012174)) [v.24.0] [10012174]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

Causality for CARBIDOPA/LEVODOPA (Open Label)

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1) Dehydration (10012174) (Dehydration (10012174)) [v.24.0] [10012174]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

Alternative Etiology for ABBV-951 (Blinded)

Event of WORSENING OF DEHYDRATION

- Investigator: Loss of autonomic function leading to dehydration, no sense of thirst

- AbbVie: More likely related to a reported loss of thirst sensation with Parkinson Disease in an elderly patient with history of chronic kidney disease.

Alternative Etiology for CARBIDOPA/LEVODOPA (Open Label)

Event of WORSENING OF DEHYDRATION

- Investigator: Loss of autonomic function leading to dehydration, no sense of thirst

- AbbVie: More likely related to a history of chronic kidney disease, urinary incontinence and Parkinson's disease in an elderly patient.

被験者番号 [redacted] (Investigator [redacted])

Reason for Narrative

Adverse Event Preferred Term(s)	Serious Adverse Event	Adverse Event Leading to Discontinuation of Study Drug	Death	Event of Interest
注入部位内出血				X
注入部位紅斑				X
注入部位出血				X
注入部位疼痛				X
前立腺腫大	X			

Treatment Group	Age at Study Start	Sex	Race
ABBV-951	6[redacted]	MALE	WHITE

Medical History	Onset Year
PERICARDITIS	19[redacted]
HYPERTENSION	20[redacted]
ATRIAL FIBRILLATION	20[redacted]
BRADYKINESIA	20[redacted]
LEFT RESTING HAND TREMOR	20[redacted]
MIXED ANXIETY AND DEPRESSIVE DISORDER	20[redacted]

Indication Disease History, Diagnosis and/or Symptoms	Onset Year
ONSET OF MOTOR FLUCTUATION	20[redacted]
PARKINSON'S DISEASE	20[redacted]
PARKINSON'S DISEASE DIAGNOSIS	20[redacted]

Prior Procedures	Procedure Year
NOT REPORTED	

Tobacco Use	Status	Number/Day	Number of Years	Year Stopped
CHEWING TOBACCO	FORMER			
CIGARETTES	NEVER			
CIGARS	NEVER			
E-CIGARETTES	NEVER			
PIPES	NEVER			

Alcohol Use	Status	Number/Day
ALCOHOL	FORMER	LESS THAN 2 DRINKS

Study Drug Prescription

Study Drug	New Quadrant for Pump Infusion	Continuous Flow Rate (mL/h)	Infusion Loading Dose Volume (mL)	Oral study drug dose (CAPSULE)	Dose Date/Day
ABBV-951	SITE A1				[redacted]
ABBV-951		0.27	1.1		[redacted]
ABBV-951	SITE B12				[redacted]
ABBV-951	SITE B2				[redacted]
ABBV-951	SITE B10				[redacted]
ABBV-951	SITE B4				[redacted]
ABBV-951		0.34	0.0		[redacted]
ABBV-951	SITE A4				[redacted]
ABBV-951	SITE A10				[redacted]
ABBV-951	SITE A11				[redacted]
ABBV-951	SITE A2				[redacted]
ABBV-951	SITE A3				[redacted]
ABBV-951	SITE B3				[redacted]
ABBV-951		0.37	0.0		[redacted]
ABBV-951	SITE B9				[redacted]
ABBV-951	SITE B4				[redacted]
ABBV-951	SITE B1				[redacted]
ABBV-951	SITE A9				[redacted]
ABBV-951	SITE A3				[redacted]
ABBV-951	SITE B10				[redacted]
ABBV-951	SITE B2				[redacted]
ABBV-951	SITE B8				[redacted]
ABBV-951	SITE A9				[redacted]
ABBV-951	SITE B10				[redacted]
ABBV-951	SITE B5				[redacted]
ABBV-951	SITE B11				[redacted]
ABBV-951	SITE A10				[redacted]
ABBV-951	SITE A9				[redacted]
ABBV-951	SITE B3				[redacted]
ABBV-951	SITE A3				[redacted]

ABBV-951	SITE A11	[redacted]20[redacted] / 76
ABBV-951	SITE B4	[redacted]20[redacted] / 78
ABBV-951	SITE B9	[redacted]20[redacted] / 80
ABBV-951	SITE A4	[redacted]20[redacted] / 81
ABBV-951	SITE B10	[redacted]20[redacted] / 83

Daily Dose by Molecular Weight

Study Drug	CSCI Infusion (mg LD)	Total Oral Dose (mg)	Route (Subcutaneous) / Frequency (Times per Day)	First Dose Date/Day	Last Dose Date/Day
ABBV-951 Loading dose	187.82		SC / CONTINUOUS	[redacted]20[redacted] / 1	
ABBV-951	437.97		SC / CONTINUOUS	[redacted]20[redacted] / 1	[redacted]20[redacted] / 1
ABBV-951	1106.46		SC / CONTINUOUS	[redacted]20[redacted] / 2	[redacted]20[redacted] / 2
ABBV-951	344.84		SC / CONTINUOUS	[redacted]20[redacted] / 3	[redacted]20[redacted] / 3
Placebo ORAL CD/LD			ORAL / 4	[redacted]20[redacted] / 5	
ABBV-951	134.61		SC / CONTINUOUS	[redacted]20[redacted] / 5	[redacted]20[redacted] / 5
Placebo ORAL CD/LD			ORAL / 4	[redacted]20[redacted] / 6	
ABBV-951	34.57		SC / CONTINUOUS	[redacted]20[redacted] / 6	[redacted]20[redacted] / 6
Placebo ORAL CD/LD			ORAL / 4	[redacted]20[redacted] / 7	
ABBV-951	794.34		SC / CONTINUOUS	[redacted]20[redacted] / 7	[redacted]20[redacted] / 7
Placebo ORAL CD/LD			ORAL / 4	[redacted]20[redacted] / 8	
ABBV-951	1066.35		SC / CONTINUOUS	[redacted]20[redacted] / 8	[redacted]20[redacted] / 8
Placebo ORAL CD/LD			ORAL / 5	[redacted]20[redacted] / 9	
ABBV-951	1106.46		SC / CONTINUOUS	[redacted]20[redacted] / 9	[redacted]20[redacted] / 9
Placebo ORAL CD/LD			ORAL / 4	[redacted]20[redacted] / 10	
ABBV-951	1105.07		SC / CONTINUOUS	[redacted]20[redacted] / 10	[redacted]20[redacted] / 10
Placebo ORAL CD/LD			ORAL / 4	[redacted]20[redacted] / 11	
ABBV-951	1086.17		SC / CONTINUOUS	[redacted]20[redacted] / 11	[redacted]20[redacted] / 11
Placebo ORAL CD/LD			ORAL / 3	[redacted]20[redacted] / 12	
ABBV-951	1104.15		SC / CONTINUOUS	[redacted]20[redacted] / 12	[redacted]20[redacted] / 12
Placebo ORAL CD/LD			ORAL / 4	[redacted]20[redacted] / 13	
ABBV-951	1104.61		SC / CONTINUOUS	[redacted]20[redacted] / 13	[redacted]20[redacted] / 13
Placebo ORAL CD/LD			ORAL / 4	[redacted]20[redacted] / 14	
ABBV-951	1091.24		SC / CONTINUOUS	[redacted]20[redacted] / 14	[redacted]20[redacted] / 14
Placebo ORAL CD/LD			ORAL / 4	[redacted]20[redacted] / 15	
ABBV-951	1105.07		SC / CONTINUOUS	[redacted]20[redacted] / 15	[redacted]20[redacted] / 15
Placebo ORAL CD/LD			ORAL / 5	[redacted]20[redacted] / 16	
ABBV-951	1353.26		SC / CONTINUOUS	[redacted]20[redacted] / 16	[redacted]20[redacted] / 16

Placebo ORAL CD/LD		ORAL / 3	[redacted] / 17	
ABBV-951	1390.41	SC / CONTINUOUS	[redacted] / 17	[redacted] / 17
Placebo ORAL CD/LD		ORAL / 4	[redacted] / 18	
ABBV-951	1368.93	SC / CONTINUOUS	[redacted] / 18	[redacted] / 18
Placebo ORAL CD/LD		ORAL / 4	[redacted] / 19	
ABBV-951	1390.99	SC / CONTINUOUS	[redacted] / 19	[redacted] / 19
Placebo ORAL CD/LD		ORAL / 3	[redacted] / 20	
ABBV-951	1366.61	SC / CONTINUOUS	[redacted] / 20	[redacted] / 20
Placebo ORAL CD/LD		ORAL / 4	[redacted] / 21	
ABBV-951	1390.99	SC / CONTINUOUS	[redacted] / 21	[redacted] / 21
Placebo ORAL CD/LD		ORAL / 4	[redacted] / 22	
ABBV-951	1368.93	SC / CONTINUOUS	[redacted] / 22	[redacted] / 22
Placebo ORAL CD/LD		ORAL / 4	[redacted] / 23	
ABBV-951	1390.41	SC / CONTINUOUS	[redacted] / 23	[redacted] / 23
Placebo ORAL CD/LD		ORAL / 4	[redacted] / 24	
ABBV-951	1370.67	SC / CONTINUOUS	[redacted] / 24	[redacted] / 24
Placebo ORAL CD/LD		ORAL / 4	[redacted] / 25	
ABBV-951	1372.42	SC / CONTINUOUS	[redacted] / 25	[redacted] / 25
Placebo ORAL CD/LD		ORAL / 4	[redacted] / 26	
ABBV-951	1376.48	SC / CONTINUOUS	[redacted] / 26	[redacted] / 26
Placebo ORAL CD/LD		ORAL / 4	[redacted] / 27	
ABBV-951	1393.32	SC / CONTINUOUS	[redacted] / 27	[redacted] / 27
Placebo ORAL CD/LD		ORAL / 4	[redacted] / 28	
ABBV-951	1383.45	SC / CONTINUOUS	[redacted] / 28	[redacted] / 28
ABBV-951	1393.32	SC / CONTINUOUS	[redacted] / 29	[redacted] / 29
ABBV-951	1516.26	SC / CONTINUOUS	[redacted] / 30	[redacted] / 30
ABBV-951	1516.26	SC / CONTINUOUS	[redacted] / 31	[redacted] / 31
ABBV-951	1500.46	SC / CONTINUOUS	[redacted] / 32	[redacted] / 32
ABBV-951	1516.26	SC / CONTINUOUS	[redacted] / 33	[redacted] / 33
ABBV-951	1516.26	SC / CONTINUOUS	[redacted] / 34	[redacted] / 34
ABBV-951	1516.26	SC / CONTINUOUS	[redacted] / 35	[redacted] / 35
ABBV-951	1502.36	SC / CONTINUOUS	[redacted] / 36	[redacted] / 36
ABBV-951	1516.26	SC / CONTINUOUS	[redacted] / 37	[redacted] / 37
ABBV-951	1516.26	SC / CONTINUOUS	[redacted] / 38	[redacted] / 38
ABBV-951	1496.04	SC / CONTINUOUS	[redacted] / 39	[redacted] / 39
ABBV-951	1516.26	SC / CONTINUOUS	[redacted] / 40	[redacted] / 40
ABBV-951	1516.26	SC / CONTINUOUS	[redacted] / 41	[redacted] / 41

ABBV-951	1516.26	SC / CONTINUOUS	[redacted]20[redacted] / 42	[redacted]20[redacted] / 42
ABBV-951	1484.67	SC / CONTINUOUS	[redacted]20[redacted] / 43	[redacted]20[redacted] / 43
ABBV-951	1516.26	SC / CONTINUOUS	[redacted]20[redacted] / 44	[redacted]20[redacted] / 44
ABBV-951	1516.26	SC / CONTINUOUS	[redacted]20[redacted] / 45	[redacted]20[redacted] / 45
ABBV-951	1485.30	SC / CONTINUOUS	[redacted]20[redacted] / 46	[redacted]20[redacted] / 46
ABBV-951	1516.26	SC / CONTINUOUS	[redacted]20[redacted] / 47	[redacted]20[redacted] / 47
ABBV-951	1516.26	SC / CONTINUOUS	[redacted]20[redacted] / 48	[redacted]20[redacted] / 48
ABBV-951	1500.46	SC / CONTINUOUS	[redacted]20[redacted] / 49	[redacted]20[redacted] / 49
ABBV-951	1516.26	SC / CONTINUOUS	[redacted]20[redacted] / 50	[redacted]20[redacted] / 50
Placebo ORAL CD/LD		ORAL / 4	[redacted]20[redacted] / 51	
ABBV-951	1514.36	SC / CONTINUOUS	[redacted]20[redacted] / 51	[redacted]20[redacted] / 51
Placebo ORAL CD/LD		ORAL / 4	[redacted]20[redacted] / 52	
ABBV-951	1500.46	SC / CONTINUOUS	[redacted]20[redacted] / 52	[redacted]20[redacted] / 52
Placebo ORAL CD/LD		ORAL / 4	[redacted]20[redacted] / 53	
ABBV-951	1485.93	SC / CONTINUOUS	[redacted]20[redacted] / 53	[redacted]20[redacted] / 53
ABBV-951	1516.26	SC / CONTINUOUS	[redacted]20[redacted] / 54	[redacted]20[redacted] / 54
ABBV-951	1496.04	SC / CONTINUOUS	[redacted]20[redacted] / 55	[redacted]20[redacted] / 55
ABBV-951	1516.26	SC / CONTINUOUS	[redacted]20[redacted] / 56	[redacted]20[redacted] / 56
ABBV-951	1489.72	SC / CONTINUOUS	[redacted]20[redacted] / 57	[redacted]20[redacted] / 57
ABBV-951	1516.26	SC / CONTINUOUS	[redacted]20[redacted] / 58	[redacted]20[redacted] / 58
ABBV-951	1516.26	SC / CONTINUOUS	[redacted]20[redacted] / 59	[redacted]20[redacted] / 59
ABBV-951	1490.98	SC / CONTINUOUS	[redacted]20[redacted] / 60	[redacted]20[redacted] / 60
ABBV-951	1516.26	SC / CONTINUOUS	[redacted]20[redacted] / 61	[redacted]20[redacted] / 61
ABBV-951	1501.72	SC / CONTINUOUS	[redacted]20[redacted] / 62	[redacted]20[redacted] / 62
ABBV-951	1516.26	SC / CONTINUOUS	[redacted]20[redacted] / 63	[redacted]20[redacted] / 63
ABBV-951	1497.93	SC / CONTINUOUS	[redacted]20[redacted] / 64	[redacted]20[redacted] / 64
ABBV-951	1516.26	SC / CONTINUOUS	[redacted]20[redacted] / 65	[redacted]20[redacted] / 65
ABBV-951	1496.67	SC / CONTINUOUS	[redacted]20[redacted] / 66	[redacted]20[redacted] / 66
ABBV-951	1516.26	SC / CONTINUOUS	[redacted]20[redacted] / 67	[redacted]20[redacted] / 67
ABBV-951	1516.26	SC / CONTINUOUS	[redacted]20[redacted] / 68	[redacted]20[redacted] / 68
ABBV-951	1492.88	SC / CONTINUOUS	[redacted]20[redacted] / 69	[redacted]20[redacted] / 69
INTERRUPTION			[redacted]20[redacted] / 69	[redacted]20[redacted] / 70
ABBV-951	1496.04	SC / CONTINUOUS	[redacted]20[redacted] / 70	[redacted]20[redacted] / 70
ABBV-951	1503.62	SC / CONTINUOUS	[redacted]20[redacted] / 71	[redacted]20[redacted] / 71
ABBV-951	1516.26	SC / CONTINUOUS	[redacted]20[redacted] / 72	[redacted]20[redacted] / 72
ABBV-951	1516.26	SC / CONTINUOUS	[redacted]20[redacted] / 73	[redacted]20[redacted] / 73
ABBV-951	1501.09	SC / CONTINUOUS	[redacted]20[redacted] / 74	[redacted]20[redacted] / 74

ABBV-951	1516.26	SC / CONTINUOUS	[redacted]20[redacted] / 75	[redacted]20[redacted] / 75
ABBV-951	1503.62	SC / CONTINUOUS	[redacted]20[redacted] / 76	[redacted]20[redacted] / 76
ABBV-951	1516.26	SC / CONTINUOUS	[redacted]20[redacted] / 77	[redacted]20[redacted] / 77
ABBV-951	1501.72	SC / CONTINUOUS	[redacted]20[redacted] / 78	[redacted]20[redacted] / 78
ABBV-951	1516.26	SC / CONTINUOUS	[redacted]20[redacted] / 79	[redacted]20[redacted] / 79
ABBV-951	1489.09	SC / CONTINUOUS	[redacted]20[redacted] / 80	[redacted]20[redacted] / 80
Placebo ORAL CD/LD		ORAL / 4	[redacted]20[redacted] / 81	
ABBV-951	1472.66	SC / CONTINUOUS	[redacted]20[redacted] / 81	[redacted]20[redacted] / 81
Placebo ORAL CD/LD		ORAL / 4	[redacted]20[redacted] / 82	
ABBV-951	1513.10	SC / CONTINUOUS	[redacted]20[redacted] / 82	[redacted]20[redacted] / 82
Placebo ORAL CD/LD		ORAL / 5	[redacted]20[redacted] / 83	
ABBV-951	1479.61	SC / CONTINUOUS	[redacted]20[redacted] / 83	[redacted]20[redacted] / 83

Previous Therapy - Prior to baseline/enrollment

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day
APIXABAN	5 mg	BID	Y-M: 20[redacted]-[redacted]
DILTIAZEM HYDROCHLORIDE	180 mg	BID	Y-M: 20[redacted]-[redacted]
METOPROLOL SUCCINATE	25 mg	QD	Y-M: 20[redacted]-[redacted]
ATROPA BELLADONNA;EUPHRASIA SPP.;SULFURATED POTASH	10 mg	QD	Y-M: 20[redacted]
GENERAL NUTRIENTS	10 mg	QD	Y-M: 20[redacted]
COLECALCIFEROL	50 OTHER: MCG	QD	Y-M: 20[redacted]-[redacted]
RASAGILINE	1.000 mg	QD	Y-M: 20[redacted]-[redacted] / -296
PAROXETINE HYDROCHLORIDE	10 mg	OTHER: QPM	Y-M: 20[redacted]-[redacted] / -196
CARBIDOPA MONOHYDRATE;LEVODOPA	150.000 mg	TID	Y-M: 20[redacted]-[redacted] / -131
PRAMIPEXOLE	0.500 mg	QD	Y-M: 20[redacted]-[redacted] / -114
CARBIDOPA MONOHYDRATE;LEVODOPA	200.000 mg	QD	Y-M: 20[redacted]-[redacted] / -72
COVID-19 VACCINE MRNA (MRNA 1273)	NOT REPORTED	ONCE	Y-M: 20[redacted]-[redacted] / -57
COVID-19 VACCINE MRNA (MRNA 1273)	NOT REPORTED	ONCE	Y-M: 20[redacted]-[redacted] / -29

Other Medications - Medications taken within 30 days prior to each narrative event until AE stopped or end of study

Medication Name (WHO Drug)	Dose/Units	Frequency	Start Year-Month / RX Day	Stop Year-Month / RX Day
APIXABAN	5 mg	BID	Y-M: 20[redacted]-[redacted]	ONGOING
DILTIAZEM HYDROCHLORIDE	180 mg	BID	Y-M: 20[redacted]-[redacted]	ONGOING
METOPROLOL SUCCINATE	25 mg	QD	Y-M: 20[redacted]-[redacted]	ONGOING
ATROPA BELLADONNA;EUPHRASIA	10 mg	QD	Y-M: 20[redacted]	ONGOING

SPP.;SULFURATED POTASH				
GENERAL NUTRIENTS	10 mg	QD	Y-M: 20[redacted]	ONGOING
COLECALCIFEROL	50 OTHER: MCG	QD	Y-M: 20[redacted]-[redacted]	ONGOING
PAROXETINE HYDROCHLORIDE	10 mg	OTHER: QPM	Y-M: 20[redacted]-[redacted] / -196	ONGOING
COVID-19 VACCINE MRNA (MRNA 1273)		ONCE	Y-M: 20[redacted]-[redacted] / -57	NOT REPORTED
COVID-19 VACCINE MRNA (MRNA 1273)		ONCE	Y-M: 20[redacted]-[redacted] / -29	NOT REPORTED
TAMSULOSIN HYDROCHLORIDE	0.4 mg	QD	Y-M: 20[redacted]-[redacted] / 8	Y-M: 20[redacted]-[redacted] / 8
MIRABEGRON	25 mg	QD	Y-M: 20[redacted]-[redacted] / 9	ONGOING

Event #1: Event of Interest - Infusion Site Reaction (Non-Infection)

Event Description	INFUSION SITE BURNING
Preferred Term	注入部位疼痛
AE Onset Date / Rx Day	[redacted]20[redacted] / 1
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	1
Duration of AE	1 DAY
Severity	MILD
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
SAE: Investigator Opinion of Relationship to Infusion Pump	NOT APPLICABLE
SAE: Investigator Opinion of Relationship to [redacted] Infusion Pump	NOT APPLICABLE
Other Cause of Event	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #2: Serious Adverse Event

Event Description	ENLARGED PROSTATE
Preferred Term	前立腺腫大
AE Onset Date / Rx Day	[redacted]20[redacted] / 8
Age at AE Onset	6[redacted]

Laboratory Testing

[redacted]20[redacted] (RX DAY 8): ALBUMIN: 49 [33 - 52] G/L; ALKALINE PHOSPHATASE: 136 [40 - 129] U/L; BASOPHILS: 0.02 [0 - 0.1] 10^9/L; BASOPHILS/LEUKOCYTES: 0.2 [0 - 1] %; BILIRUBIN: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; BILIRUBIN: 17 [3 - 21] UMOL/L; BLOOD: 2+ [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; BLOOD UREA NITROGEN: 5.7 [2.1 - 6.8] MMOL/L; CALCIUM: 2.55 [2.12 - 2.62] MMOL/L; CREATININE: 80 [35 - 106] UMOL/L; EOSINOPHILS: 0.02 [0 - 0.5] 10^9/L; EOSINOPHILS/LEUKOCYTES: 0.2 [1 - 6] %; ERYTHROCYTES: 4.9 [4.7 - 6.1] 10^12/L; ERYTHROCYTES: 31-50 [0 - 3] HPF; GLUCOSE: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; GLUCOSE: 7.3 [3.9 - 5.6] MMOL/L; HEMATOCRIT: 0.45 [0.42 - 0.52] FRACTION OF 1; HEMOGLOBIN: 157 [140 - 180] G/L; KETONES: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; LEUKOCYTES: 10.2 [4.5 - 10.8] 10^9/L; LEUKOCYTES: 1-2 [0 - 2] HPF; LYMPHOCYTES: 0.54 [1 - 3] 10^9/L; LYMPHOCYTES/LEUKOCYTES: 5.3 [20 - 40] %; MONOCYTES: 0.69 [0.2 - 1] 10^9/L; MONOCYTES/LEUKOCYTES: 6.8 [2 - 10] %; NPTST001-ABSOLUTE IMMATURE GRANULOCYTE: 0.03 [0 - 0.09] K/MM3; NPTST003-ALT (SGPT): 14 [0 - 40] U/L; NPTST004-ANION GAP: 14 [6 - 12] MMOL/L; NPTST006-AST: 41 [0 - 37] U/L; NPTST008-BACTERIA: NONE SEEN [NOT REPORTED - NOT REPORTED] HPF; NPTST015-CHLORIDE: 99 [98 - 109] MMOL/L; NPTST016-CLARITY: CLEAR [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST018-CO2: 23 [24 - 32] MMOL/L; NPTST019-COLOR: YELLOW [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST023-EGFR: > 60.00 [60 - NOT REPORTED] ML/MIN/1.73M*2; NPTST033-IMMATURE GRANULOCYTE %: 0.3 [0 - 0.9] %; NPTST034-INR: 1.3 [0.8 - 1.4] UNIT NOT REPORTED; NPTST038-LEUKOCYTES: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST040-MCH: 32 [25.4 - 39] PG; NPTST041-MCHC: 35.1 [31 - 37] G/DL; NPTST042-MCV: 91 [80 - 95] FL; NPTST049-MPV: 8.8 [7 - 11] FL; NPTST051-MUCUS: 1+ [NOT REPORTED - NOT REPORTED] HPF; NPTST052-NITRITE: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; NPTST061-PROTIME: 15.6 [11.9 - 14.8] SEC; NPTST064-RDW: 12.4 [11.5 - 14.5] %; NPTST066-SQUAMOUS EPITHELIAL: NONE SEEN [NOT REPORTED - NOT REPORTED] HPF; NEUTROPHILS: 8.92 [2 - 7] 10^9/L; NEUTROPHILS/LEUKOCYTES: 87.2 [40 - 80] %; PLATELETS: 156 [150 - 450] 10^9/L; POTASSIUM: 4 [3.3 - 4.5] MMOL/L; PROTEIN: NEGATIVE [NOT REPORTED - NOT REPORTED] UNIT NOT REPORTED; PROTEIN: 81 [60 - 85] G/L; SODIUM: 136 [135 - 145] MMOL/L; SPECIFIC GRAVITY: 1.008 [1.002 - 1.03] UNIT NOT REPORTED; PH: 7.0 [5 - 8] UNIT NOT REPORTED; [redacted]20[redacted] (RX DAY 9): BASOPHILS: 0.02 [0 - 0.1] 10^9/L; BASOPHILS/LEUKOCYTES: 0.2 [0 - 1] %; BLOOD UREA NITROGEN: 6.1 [2.1 - 6.8] MMOL/L; CALCIUM: 2.4 [2.12 - 2.62] MMOL/L; CREATININE: 80 [35 - 106] UMOL/L; EOSINOPHILS: 0.01 [0 - 0.5] 10^9/L; EOSINOPHILS/LEUKOCYTES: 0.1 [1 - 6] %; ERYTHROCYTES: 4.8 [4.7 - 6.1] 10^12/L; GLUCOSE: 6.8 [3.9 - 5.6] MMOL/L; HEMATOCRIT: 0.44 [0.42 - 0.52] FRACTION OF 1; HEMOGLOBIN: 157 [140 - 180] G/L; LEUKOCYTES: 9.3 [4.5 - 10.8] 10^9/L; LYMPHOCYTES: 0.93 [1 - 3] 10^9/L; LYMPHOCYTES/LEUKOCYTES: 10 [20 - 40] %; MONOCYTES: 1.01 [0.2 - 1] 10^9/L; MONOCYTES/LEUKOCYTES: 10.9 [2 - 10] %; NPTST001-ABSOLUTE IMMATURE GRANULOCYTE: 0.03 [0 - 0.09] K/MM3; NPTST004-ANION GAP: 13 [6 - 12] MMOL/L; NPTST015-CHLORIDE: 100 [98 - 109] MMOL/L; NPTST018-CO2: 24 [24 - 32] MMOL/L; NPTST026-ESTIMATED GLOMERULAR FILTRATION: > 60.00 [NOT REPORTED - NOT REPORTED] ML/MIN/1.73M*2; NPTST033-IMMATURE GRANULOCYTE %: 0.3 [0 - 0.9] %; NPTST040-MCH: 32.8 [25.4 - 39] PG; NPTST041-MCHC: 35.4 [31 - 37] G/DL; NPTST042-MCV: 93 [80 - 95] FL; NPTST049-MPV: 9.1 [7 - 11] FL; NPTST064-RDW: 12.6 [11.5 - 14.5] %; NEUTROPHILS: 7.28 [2 - 7] 10^9/L; NEUTROPHILS/LEUKOCYTES: 78.5 [40 - 80] %; PLATELETS: 166 [150 - 450] 10^9/L; POTASSIUM: 3.8 [3.3 - 4.5] MMOL/L; SODIUM: 137 [135 - 145] MMOL/L

Microbiology

NOT REPORTED

SAE Supplemental Procedure

[redacted]20[redacted] (RX DAY 8): FOLEY CATHETER INSERTION:SUCCESSFUL INSERTION. SUBJECT WENT HOME WITH FOLEY CATHETER AND FOLLOWED UP WITH UROLOGY.; [redacted]20[redacted] (RX DAY 9): CT ABDOMEN PELVIS W WO CONTRAST:GENITOURINARY: MULTIPLE LEFT PARAPELVIC CYSTS. SUBCENTIMETER HYPODENSE FOCI ARE SEEN IN THE KIDNEYS BILATERALLY WHICH ARE TOO SMALL TO CHARACTERIZE BY CT CRITERIA BUT ARE STATISTICALLY LIKELY TO REPRESENT CYSTS. THE PROSTATE IS MARKEDLY ENLARGED AND CONTAINS COARSE CALCIFICATIONS. THE BLADDER IS RELATIVELY DECOMPRESSED, HOWEVER, THERE IS APPARENT CIRCUMFERENTIAL BLADDER WALL THICKENING WHICH IS LI KELY DUE TO CHRONIC BLADDER OUTLET OBSTRUCTION. BONES AND SOFT TISSUES: DEGENERATIVE CHANGES OF THE LUMBAR SPINE. SCLEROTIC FOCUS ALONG RIGHT ACETABULUM CONSISTENT WITH A BONE ISLAND.

AE Stopped Rx Day	9
Duration of AE	2 DAYS
Severity	MILD
Relation to Study Drug by Investigator	NO REASONABLE POSSIBILITY
SAE: Investigator Opinion of Relationship to Infusion Pump	UNLIKELY
SAE: Investigator Opinion of Relationship to [redacted] Infusion Pump	NOT REPORTED
Other Cause of Event	PARKINSON'S DISEASE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	REQUIRES OR PROLONGS HOSPITALIZATION

Event #3: Event of Interest - Infusion Site Reaction (Non-Infection)

Event Description	INFUSION SITE REDNESS
Preferred Term	注入部位紅斑
AE Onset Date / Rx Day	[redacted]20[redacted] / 11
Age at AE Onset	6[redacted]

Laboratory Testing

NOT APPLICABLE

Microbiology

NOT APPLICABLE

SAE Supplemental Procedure

NOT APPLICABLE

AE Stopped Rx Day	34
Duration of AE	24 DAYS
Severity	MILD

Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
SAE: Investigator Opinion of Relationship to Infusion Pump	NOT APPLICABLE
SAE: Investigator Opinion of Relationship to [redacted] Infusion Pump	NOT APPLICABLE
Other Cause of Event	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #4: Event of Interest - Infusion Site Reaction (Non-Infection)

Event Description	INFUSION SITE BLEEDING
Preferred Term	注入部位出血
AE Onset Date / Rx Day	[redacted]20[redacted] / 22
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	22
Duration of AE	1 DAY
Severity	MILD
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
SAE: Investigator Opinion of Relationship to Infusion Pump	NOT APPLICABLE
SAE: Investigator Opinion of Relationship to [redacted] Infusion Pump	[redacted] INFUSION SET 9 MM
Other Cause of Event	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #5: Event of Interest - Infusion Site Reaction (Non-Infection)

Event Description	INFUSION SITE STINGING
Preferred Term	注入部位疼痛
AE Onset Date / Rx Day	[redacted]20[redacted] / 22
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	22
Duration of AE	1 DAY
Severity	MILD
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
SAE: Investigator Opinion of Relationship to Infusion Pump	NOT APPLICABLE
SAE: Investigator Opinion of Relationship to [redacted] Infusion Pump	[redacted] INFUSION SET 9 MM
Other Cause of Event	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #6: Event of Interest - Infusion Site Reaction (Non-Infection)

Event Description	INFUSION SITE BRUISING
Preferred Term	注入部位内出血
AE Onset Date / Rx Day	[redacted]20[redacted] / 23
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	31
Duration of AE	9 DAYS

Severity	MILD
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
SAE: Investigator Opinion of Relationship to Infusion Pump	NOT APPLICABLE
SAE: Investigator Opinion of Relationship to [redacted] Infusion Pump	[redacted] INFUSION SET 9 MM
Other Cause of Event	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Event #7: Event of Interest - Infusion Site Reaction (Non-Infection)

Event Description	INFUSION SITE REDNESS
Preferred Term	注入部位紅斑
AE Onset Date / Rx Day	[redacted]20[redacted] / 54
Age at AE Onset	6[redacted]
Laboratory Testing	
NOT APPLICABLE	
Microbiology	
NOT APPLICABLE	
SAE Supplemental Procedure	
NOT APPLICABLE	
AE Stopped Rx Day	61
Duration of AE	8 DAYS
Severity	MILD
Relation to Study Drug by Investigator	REASONABLE POSSIBILITY
SAE: Investigator Opinion of Relationship to Infusion Pump	NOT APPLICABLE
SAE: Investigator Opinion of Relationship to [redacted] Infusion Pump	NOT APPLICABLE
Other Cause of Event	NOT APPLICABLE
Discontinued Study Drug Due to the Event	NO
SAE Criteria	NONE

Generated: [redacted]20[redacted]:10:27

Program Source Code: [redacted]

Investigator No.: [redacted]

Subject Number: [redacted]

Protocol Number: M15-736

治験責任医師からの報告。本被験者は米国の 6[redacted] 歳男性であり，アッヴィ社の ABBV-951（Foscarbidopa/Foslevodopa）の治験で盲検下にて治験薬及び CD/LD が投与され，前立腺腫大を発現した。

Event 2 の臨床経過：

関連する病歴は，心膜炎，高血圧，心房細動，運動緩慢，パーキンソン病，非喫煙者，及び元飲酒者（1 日 2 杯未満）であった。

ランダム化に先立ち，本被験者は 20[redacted] 年 [redacted] 月 [redacted] 日から 20[redacted] 年 [redacted] 月 [redacted] 日まで本治験の安定化期にて CD/LD を経口投与された。20[redacted] 年 [redacted] 月 [redacted] 日，本被験者はランダム化され，本治験の二重盲検最適化期を開始した。本事象は本治験の二重盲検最適化期中に発現した。

投与 8 日目，被験者は前立腺腫大を発現した。投与 9 日目，前立腺腫大は消失した。

本事象の発現前に併用薬は使用していなかった。被験者は交通渋滞に巻き込まれたため非常にストレスを感じており，排尿したかったが我慢していた。帰宅時，被験者は引き続き非常にストレスを感じており，おそらくアドレナリン作動性反応が刺激されたものとみられる。被験者は前立腺が肥大していることに気付き，それにより尿閉，高血圧，及び頻脈が引き起こされていた。被験者には尿路感染の基礎疾患はなく，時々尿意切迫が認められた。

投与 8 日目，被験者は尿閉及び血尿のため入院した。被験者には経口カプセルの服用忘れはなく，注入ポンプの停止もなかった。被験者は入院中にシリンジの交換を進めた。フォーリーカテーテルが問題なく挿入され，Flomax の投与を開始した。投与 9 日目，被験者はフォーリーカテーテルを留置したまま退院し，その後泌尿器科で経過観察された。

被験者に FLOMAX が投与された。

Causality for ABBV-951 (Blinded)

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1) Enlarged prostate (10049240) (Prostatomegaly (10051482)) [v.24.0] [10049240]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

Causality for CARBIDOPA/LEVODOPA (Open Label)

---

1) Enlarged prostate (10049240) (Prostatomegaly (10051482)) [v.24.0] [10049240]

Causality as per reporter (Drug/Vaccine): No reasonable possibility

Causality as per Mfr. (Drug/Vaccine): No reasonable possibility

Dechallenge: Not Applicable

Alternative Etiology for ABBV-951 (Blinded)

Event of ENLARGED PROSTATE

- Investigator: Parkinson's disease

- AbbVie: More likely a preexisting condition in a 6[redacted] year old male subject with underlying Parkinson's disease. Event resolved with Foley assisted drainage and treatment with flomax.

Alternative Etiology for CARBIDOPA/LEVODOPA (Open Label)

Event of ENLARGED PROSTATE

- Investigator: Urinary retention may be due to Parkinson's disease. The subject also has a history of atrial fibrillation and hypertension.

- AbbVie: More likely a preexisting condition in a 6[redacted] year old male subject with underlying Parkinson's disease. Event resolved with Foley assisted drainage and treatment with flomax.

Relevant Laboratory & Other Diagnostic Tests

[redacted] **20[redacted] ALBUMIN:** 4.9 G/DL (normal 3.3 to 5.2)

[redacted] 20[redacted] **ALKALINE PHOSPHATASE:** 136 U/L (normal 40 to 129)

[redacted] 20[redacted] **ANION GAP:** 13 MMOL/L (normal 6 to 12)

[redacted] 20[redacted] **AST:** 41 U/L (normal 0 to 37)

[redacted] 20[redacted] **BASOPHILS:** 0.2% (normal 0.0 to 1.0)

[redacted] 20[redacted] **BASOPHILS ABS:** 0.02 K/MM3

[redacted] 20[redacted] **BLOOD HEMATOCRIT:** 44.4% (normal 42.0 to 52.0)

[redacted] 20[redacted] **BLOOD UREA NITROGEN:** 17 mg/dL (normal 6 to 19)

[redacted] 20[redacted] **CALCIUM:** 10.2 mg/dL (normal 8.5 to 10.5)

[redacted] 20[redacted] **CHLORIDE:** 99 MMOL/L (normal 98 to 109)

[redacted] 20[redacted] **CO2:** 24 MMOL/L (normal 24 to 32)

[redacted] 20[redacted] **CREATININE:** 0.9 mg/dL (normal 0.4 to 1.2)

[redacted] 20[redacted] **CT ABDOMEN PELVIS:** W WO CONTRAST - GENITOURINARY: MULTIPLE LEFT PARAPELVIC CYSTS. SUBCENTIMETER HYPODENSE FOCI ARE SEEN IN THE KIDNEYS BILATERALLY WHICH ARE TOO SMALL TO CHARACTERIZE BY CT CRITERIA BUT ARE STATISTICALLY LIKELY TO REPRESENT CYSTS. THE PROSTATE IS MARKEDLY ENLARGED AND CONTAINS COARSE CALCIFICATIONS. THE BLADDER IS RELATIVELY DECOMPRESSED, HOWEVER, THERE IS APPARENT CIRCUMFERENTIAL BLADDER WALL THICKENING WHICH IS LIKELY DUE TO CHRONIC BLADDER OUTLET OBSTRUCTION. BONES AND SOFT TISSUES: DEGENERATIVE CHANGES OF THE LUMBAR SPINE. SCLEROTIC FOCUS ALONG RIGHT ACETABULUM CONSISTENT WITH A BONE ISLAND.

[redacted] 20[redacted] **EGFR:** >60.00 ML/MIN/1.73M*2

[redacted] 20[redacted] **EOSINOPHILS:** 0.1% (normal 1.0 to 6.0)

[redacted] 20[redacted] **EOSINOPHILS ABS:** 0.01 K/MM3

[redacted] 20[redacted] **ESTIMATED GLOMERULAR FILTRATION RATE:** > 60.00 ML/MIN/1.73M*2

[redacted] 20[redacted] **GLUCOSE:** 132 mg/dL (normal 70 to 100)

[redacted] 20[redacted] **GLUCOSE:** 122 mg/dL (normal 70 to 100)

[redacted] 20[redacted] **HEMOGLOBIN:** 15.7 G/DL (normal 14.0 to 18.0)

[redacted] 20[redacted] **IMMATURE GRANULOCYTE:** ABSOLUTE: 0.03 K/MM3

[redacted]20[redacted] **IMMATURE GRANULOCYTE:** 0.3% (normal 0.0 to 0.9)

[redacted]20[redacted] **INR:** 1.3 No units (normal 0.8 to 1.4)

[redacted]20[redacted] **LEUKOCYTES:** NEGATIVE

[redacted]20[redacted] **LYMPHOCYTES:** 5.3% (normal 20.00 to 40.0)

[redacted]20[redacted] **LYMPHOCYTES:** 10.00% (normal 20.0 to 40.0)

[redacted]20[redacted] **LYMPHOCYTES ABS:** 0.93 K/MM3

[redacted]20[redacted] **LYMPHOCYTES ABS:** 0.54 K/MM3

[redacted]20[redacted] **MCH:** 32.8 PG (normal 25.4 to 39.0)

[redacted]20[redacted] **MCHC:** 35.4 G/DL (normal 31.0 to 37.0)

[redacted]20[redacted] **MCV:** 91 FL (normal 80 to 95)

[redacted]20[redacted] **MONOCYTE:** 10.9% (normal 2.0 to 10.0)

[redacted]20[redacted] **MONOCYTE:** 6.8% (normal 2.0 to 10.0)

[redacted]20[redacted] **MONOCYTES ABS:** 0.69 K/MM3

[redacted]20[redacted] **MONOCYTES ABS:** 1.01 K/MM3

[redacted]20[redacted] **MPV:** 8.8 FL (normal 7.0 to 11.0)

[redacted]20[redacted] **NEUTROPHILS:** 87.2% (normal 40.00 to 80.00)

[redacted]20[redacted] **NEUTROPHILS:** 78.5% (normal 40.00 to 80.00)

[redacted]20[redacted] **NEUTROPHILS ABS:** 8.92 K/MM3

[redacted]20[redacted] **NEUTROPHILS ABS:** 7.28 K/MM3

[redacted]20[redacted] **PLATELET COUNT:** 156X10**3/uL

[redacted]20[redacted] **PLATELET COUNT:** 166 X10**3/uL

[redacted]20[redacted] **POTASSIUM:** 3.8 MMOL/L (normal 3.3 to 4.5)

[redacted]20[redacted] **RDW:** 12.4% (normal 11.5 to 14.5)

[redacted]20[redacted] **RED BLOOD CELLS:** 4.78 X10**6/uL

[redacted]20[redacted] **SGPT:** 14 U/L (normal 0 to 40)

[redacted]20[redacted] **SODIUM:** 137 MMOL/L (normal 135 to 145)

[redacted]20[redacted] **SQUAMOUS EPITHELIAL:** URINE: NONE SEEN

[redacted]20[redacted] **TOTAL BILIRUBIN:** 1.0 mg/dL (normal 0.2 to 1.2)

[redacted]20[redacted] **TOTAL PROTEIN:** 8.1 G/DL (normal 6.0 to 8.5)

[redacted]20[redacted] **URINE BACTERIA:** NONE SEEN

[redacted]20[redacted] **URINE BILIRUBIN:** NEGATIVE

[redacted]20[redacted] **BLOOD URINE:** 2+

[redacted]20[redacted] **URINE CLARITY:** CLEAR

[redacted]20[redacted] **URINE COLOR:** YELLOW

[redacted]20[redacted] **URINE KETONES:** NEGATIVE

[redacted]20[redacted] **URINE MUCUS:** 1+HPF

[redacted]20[redacted] **URINE NITRITE:** NEGATIVE

[redacted]20[redacted] **URINE PH:** 7.0 No units (normal 5.0 to 8.0)

[redacted]20[redacted] **URINE PROTEIN:** NEGATIVE

[redacted]20[redacted] **URINE RBC:** 31-50 HPF

[redacted]20[redacted] **URINE SPECIFIC GRAVITY:** 1.008 No units (normal 1.002 to 1.030)

[redacted]20[redacted] **URINE WHITE BLOOD CELLS:** 1-2 HPF

[redacted]20[redacted] **WHITE BLOOD CELLS:** 9.3 X10**3/uL

[redacted]20[redacted] **WHITE BLOOD CELLS:** 10.2 X10**3/uL

M15-741 試験

治験の標題： パーキンソン病患者を対象とした ABBV-951 の持続皮下注入による 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	
施設数 / 実施国名： 60 施設 / 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，イギリス及び米国	
治験責任医師： [redacted], MD，他	
公表文献 (参考資料) ： 2 件の抄録	
治験期間： 最初の被験者の初回来院日：20[redacted] 年 [redacted] 月 [redacted] 日 最後の被験者の最終来院日：20[redacted] 年 [redacted] 月 [redacted] 日（データカットオフ日）	開発のフェーズ：III
目的： 主要目的： 最大 52 週間，1 日 24 時間持続皮下注入（以下「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。 副次目的： 患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。	
被験者数 (計画時と解析時) ： 計画時：約 240 例，解析時：244 例	
診断と主要な組入れ基準： レボドパ反応性の特発性パーキンソン病と診断され，経口治療薬では運動症状の日内変動を十分にコントロールできない 30 歳以上の患者。 識別可能なオフとオンの状態（運動症状の日内変動）があり，本試験登録前のパーキンソン病日誌により 1 日あたりのオフ時間が 2.5 時間以上ある患者。	
治験方法： 本試験は，パーキンソン病の被験者に 1 日 24 時間 CSCI 投与した ABBV-951 の安全性及び忍容性を評価するためにデザインされた，非盲検，単群試験であった。 被験者は，10 日から 42 日間のスクリーニング期を経て 52 週間の投与期に移行した。投与期は，4 週間の最適化期と，48 週間の維持期で構成された。最適化期には，治験責任医師は，個々の被験者に最適な臨床効果が得られるよう，治験薬の標準注入速度の他に事前に設定された追加の低い注入速度及び追加の高い注入速度を被験者が使用できるようにすることを含め，各被験者の ABBV-951 用量について必要な調節を行った。最適な臨床効果とは，1 日あたりのオン時間を最大にし，オフ症状の発現数と日常生活に支障のあるジスキネジアを伴うオン時間を最小にすることと定義した。被験者の併用パーキンソン病治療薬（ドパミンアゴニスト，選択的モノアミン酸化酵素 B 阻害薬，アマンタジン，サフィナミド）は，治験責任医師の判断で被験者の症状コントロールに最善な治療法が提供できるよう，添付文書に従った漸減又は休薬が可能であった。維持期には，ABBV-951 の最適治療用量を投与した。ABBV-951 の投与量は，投与期間を通して調節可能であったが，併用パーキンソン病治療薬は，治験責任医師が医学的に必要と判断した場合を除き，安定して使用することとした。 M15-741 試験で 52 週間の投与期を完了し，適格基準を満たし続けていた被験者は，別の継続試験（M15-737 試験）に移行し，ABBV-951 を更に 96 週間継続投与することが可能であった。	

被験薬，用量，投与方法及びバッチ番号：

ABBV-951 12/240 mg/mL（カルビドパ-4′-リン酸塩 / レボドパ-4′-リン酸塩）注入用溶液を，携帯式ポンプに接続した注入セットを介して 1 日 24 時間 CSCI により投与した。用量は，最適化期に必要な調節を行った後，維持期に最適治療用量を投与した。なお，維持期の投与開始前に，経口レボドパ + ドパ脱炭酸酵素阻害薬（以下「DDCI」）の負荷投与を行った。

バルクロット番号：[redacted] delivery system

治療期間：最大 52 週間

対照薬，用量，投与方法及びバッチ番号：

該当なし

評価基準：

有効性：

有効性評価項目は本試験の副次評価項目であり，パーキンソン病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，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」）の Part I から IV により評価したパーキンソン病症状，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，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，並びに 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について，ベースラインから治験終了時までの変化量により評価した。

安全性：

安全性評価項目は本試験の主要評価項目であり，有害事象を発現した被験者の割合，並びに臨床検査値，バイタルサイン測定値及び心電図のベースラインから治験終了時までの変化量を評価した。局所安全性を注入部位評価尺度（Infusion Site Evaluation Scale）により評価した。更に，自殺傾向及び衝動的強迫行動を，コロンビア自殺評価スケール（以下「C-SSRS」）及びパーキンソン病における衝動制御障害の評価尺度（以下「QUIP-RS」）によりそれぞれ評価した。

統計手法：

有効性：

最大の解析対象集団（以下「FAS」）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 つ以上の観測値が得られたすべての被験者からなり，すべての有効性解析についてこれを用いた。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。

すべての有効性評価項目について，各用量群及び被験者全体におけるベースラインから各規定来院時までの変化量を記述的に要約した。要約統計量には，観察回数，平均値，標準偏差，最小値，中央値及び最大値を含めた。

安全性：

安全性解析対象集団は，ABBV-951 の注入を受けたすべての被験者からなり，すべての安全性解析についてこれを用いた。有害事象は，ABBV-951 の CSCI 投与開始日以降，最終注入後 30 日までに発現又は悪化したすべての事象と定義した。安全性評価項目に関するすべての解析は，有害事象と注入部位評価尺度を除いて，ABBV-951 の最終投与後 1 日目までに収集されたデータを用いて実施した。すべての有害事象は ICH 国際医薬用語集（以下「MedDRA」）version 24.0 を用いて要約した。

安全性に関して，評価項目が連続変数の場合は，各用量群及び被験者全体におけるベースラインからの変化量を，評価時点ごとに記述的に要約した。評価項目がカテゴリー変数の場合は，各用量群及び被験者全体における各カテゴリーの被験者数及び被験者の割合を評価時点ごとに要約した。仮説検定は実施しなかった。

表 1. 治験実施スケジュール

治験の実施項目	スクリーニング (V1)	スクリーニング (V2)	投与期 最適化期 4 週間 登録 投与 1 日目 (V3)	投与 2 日目 (V4)	投与 1 週時 (V5)	投与 2 週時 (V6)	投与 3 週時 (V7)	投与 4 週時 (V8)	維持期 48 週間 投与 6 週時 (V9)	投与 13 週時 (V10)	投与 26 週時 (V11)	投与 39 週時 (V12)	投与 52 週 (V13) / 早期中止	試験終了後 / 早期中止時の電話による追跡調査[d]	交付来院[c]
問診及び質問票															
被験者情報及び同意取得	√														
適格基準	√	√	√ (投与前)												
病歴	√														
臨床評価	√														
進行期パーキンソン病の臨床医による評価	√														
注入部位の評価 (該当する場合は皮膚科学的評価)			√ (投与後)	√	√	√	√	√	√	√	√	√	√		
薬物及びアルコールスクリーニング	√														

表 1. 治験実施スケジュール（続き）

治験の実施項目	スクリーニング (V1)	スクリーニング (V2)	投与期											試験終了後 / 早期中止時の電話による追跡調査[d]	交付来院[c]
			最適化期 4 週間						維持期 48 週間						
			登録 投与 1 日目 (V3)	投与 2 日目 (V4)	投与 1 週時 (V5)	投与 2 週時 (V6)	投与 3 週時 (V7)	投与 4 週時 (V8)	投与 6 週時 (V9)	投与 13 週時 (V10)	投与 26 週時 (V11)	投与 39 週時 (V12)	投与 52 週 (V13) / 早期中止		
有害事象の確認	√	√	√ (投与後)	√	√	√	√	√	√	√	√	√	√	√	
製品に関する苦情・不具合			√ (投与前後)	√	√	√	√	√	√	√	√	√	√		
前治療 / 併用療法	√	√	√ (投与前後)	√	√	√	√	√	√	√	√	√	√		
患者報告アウトカム															
患者による評価 (既定の時点) :															
被験者投与日誌					来院前 2 日間 √	来院前 2 日間 √	来院前 2 日間 √	来院前 2 日間 √	来院前 2 日間 √	来院前 2 日間 √	来院前 2 日間 √	来院前 2 日間 √	来院前 2 日間 √		

表 1. 治験実施スケジュール（続き）

治験の実施項目	スクリーニング (V1)	スクリーニング (V2)	投与期											試験終了後 / 早期中止時の電話による追跡調査[d]	交付来院[c]
			最適化期 4 週間						維持期 48 週間						
			登録 投与 1 日目 (V3)	投与 2 日目 (V4)	投与 1 週時 (V5)	投与 2 週時 (V6)	投与 3 週時 (V7)	投与 4 週時 (V8)	投与 6 週時 (V9)	投与 13 週時 (V10)	投与 26 週時 (V11)	投与 39 週時 (V12)	投与 52 週 (V13) / 早期中止		
パーキンソン病日誌	√ (一致評価)		来院前 2 日間 √		来院前 2 日間 √				来院前 2 日間 √		来院前 2 日間 √	来院前 2 日間 √	来院前 2 日間 √		
[redacted]	√[a]	√[a]	√[a]	√	√	√	√	√	√	√	√	任意	任意		
EQ-5D-5L			√ (投与前)						√	√	√	√	√		
評価者による評価 (既定の時点) :															
C-SSRS	√	√	√ (投与前)	√	√	√	√	√	√	√	√	√	√		
PDQ-39			√ (投与前)						√	√	√	√	√		

表 1. 治験実施スケジュール（続き）

治験の実施項目	スクリーニング (V1)	スクリーニング (V2)	投与期											試験終了後 / 早期中止時の電話による追跡調査[d]	交付来院[c]
			最適化期 4 週間						維持期 48 週間						
			登録 投与 1 日目 (V3)	投与 2 日目 (V4)	投与 1 週時 (V5)	投与 2 週時 (V6)	投与 3 週時 (V7)	投与 4 週時 (V8)	投与 6 週時 (V9)	投与 13 週時 (V10)	投与 26 週時 (V11)	投与 39 週時 (V12)	投与 52 週 (V13) / 早期中止		
MDS-UPDRS / UPDRS	√		√ (投与前後)	√	√	√	√	√	√	√	√	√	√		
PDSS-2			√ (投与前)						√	√	√	√	√		
MMSE	√														
QUIP-RS			√ (投与前)						√	√	√	√	√		
検査及び診察															
臨床検査	√		√ (投与前)						√		√	√	√		

表 1. 治験実施スケジュール（続き）

治験の実施項目	スクリーニング (V1)	スクリーニング (V2)	投与期											試験終了後 / 早期中止時の電話による追跡調査[d]	交付来院[c]
			最適化期 4 週間						維持期 48 週間						
			登録 投与 1 日目 (V3)	投与 2 日目 (V4)	投与 1 週時 (V5)	投与 2 週時 (V6)	投与 3 週時 (V7)	投与 4 週時 (V8)	投与 6 週時 (V9)	投与 13 週時 (V10)	投与 26 週時 (V11)	投与 39 週時 (V12)	投与 52 週 (V13) / 早期中止		
特別な臨床検査 (ビタミン B6，ビタミン B12，メチルマロン酸，ホモシステイン)	√		√ (投与前)						√		√		√		
任意のバイオマーカー (薬理遺伝学 DNA)			√ (投与前)								√				
12 誘導心電図	√		√ (投与後)						√				√		
身長 (V1 のみ) 及び体重	√		√ (投与前)						√		√		√		
バイタルサイン (立位)			√ (投与後)		√				√		√		√		
バイタルサイン	√	√		√		√	√	√		√		√			

表 1. 治験実施スケジュール（続き）

治験の実施項目	スクリーニング (V1)	スクリーニング (V2)	投与期											試験終了後 / 早期中止時の電話による追跡調査[d]	交付来院[c]
			最適化期 4 週間						維持期 48 週間						
			登録 投与 1 日目 (V3)	投与 2 日目 (V4)	投与 1 週時 (V5)	投与 2 週時 (V6)	投与 3 週時 (V7)	投与 4 週時 (V8)	投与 6 週時 (V9)	投与 13 週時 (V10)	投与 26 週時 (V11)	投与 39 週時 (V12)	投与 52 週 (V13) / 早期中止		
身体検査	√		√ (投与前)						√		√		√		
神経学的検査	√		√ (投与前)						√	√	√	√	√		
中央検査機関での血清妊娠検査	√														
実施医療機関での尿妊娠検査[b]			√ (投与前)										√		
治療															
治験薬投与システム使用のトレーニング		√	√												
治験薬投与			√	√	√	√	√	√	√	√	√	√			

表 1. 治験実施スケジュール（続き）

治験の実施項目	スクリーニング (V1)	スクリーニング (V2)	投与期											試験終了後 / 早期中止時の電話による追跡調査[d]	交付来院[c]
			最適化期 4 週間						維持期 48 週間						
			登録 投与 1 日目 (V3)	投与 2 日目 (V4)	投与 1 週時 (V5)	投与 2 週時 (V6)	投与 3 週時 (V7)	投与 4 週時 (V8)	投与 6 週時 (V9)	投与 13 週時 (V10)	投与 26 週時 (V11)	投与 39 週時 (V12)	投与 52 週 (V13) / 早期中止		
治験薬，治験用機器及び付属品の供給確認			√	√	√	√	√	√	√	√	√	√			√
薬剤及び治験用機器の照合確認			√	√	√	√	√	√	√	√	√	√	√		√
治験薬投与システムの交付 / 返却			治験薬は投与 1 日目，投与 1 週時，それ以降は投与 51 週時まで 2 週間ごとに交付した。 被験者は前回の来院時に交付されたバイアル (使用済み及び未使用分) を投与 1 週時，それ以降は 2 週間ごとに返却した。 また，被験者は治験薬投与システムのすべての部品を投与 52 週 / 早期中止時に返却した。												
治験薬処方記録			√	√	√	√	√	√	√	√	√	√			

MMSE = ミニメンタルステート検査，[redacted] = [redacted]，V = 来院

a. 各国の規制で許容される場合，[redacted]を受領した実施医療機関は，V1 後から観察期開始前までに本デバイスを被験者に提供した。実施医療機関での[redacted]受領後，V3 までのいずれかの時点で 6 日間の観察期を開始し，6 日以上連日で実施した。また，パーキンソン病日誌もこの 6 日間の観察期に 2 日以上連日で記入した。[redacted]が未承認の国では，パーキンソン病日誌の記入及び注入ポンプのトレーニングを考慮し，観察期を少なくとも 2 日間に短縮可能であった。

b. 妊娠可能な女性の場合，毎月，尿妊娠検査を行った。予定された来院がある場合，実施医療機関にて検査を行った。予定された来院がない場合は，規定外来院時又は自宅にて検査を行ってもよいこととした。
c. 交付来院は，来院の有無に関わらず実施可能であった。
d. 被験者の同意を得た上で，電話による試験終了後 / 早期中止時の追跡調査を，試験中止の 30 日後又は継続試験に参加しない被験者については投与 52 週完了の 30 日後に実施した。

被験者の内訳

被験者の内訳を表 2 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%），投与継続中は 26 例（10.7%），また，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。

日本人部分集団における被験者の内訳を表 3 に示す。
本試験では，27 例の日本人被験者が登録され，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 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%），投与継続中は 1 例（3.7%），また，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撤回であり，各 6 例（22.2%）であった。

治験薬投与開始後 12 週間の登録時期別の被験者の内訳を表 4 に示す。
本試験では，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」）ごとに評価項目を要約した。
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の割合は 49 例（31.2%），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の割合は 17 例（19.5%），投与継続中は 70 例（80.5%）であった。なお，データカットオフ時点の Sample 2 の中止率（11.1%）は，Sample 1 の中止率（31.1%）と比較して低かった（表 2）。

日本人部分集団における治験薬投与開始後 12 週間の登録時期別の被験者の内訳を表 5 に示す。
投与開始後 12 週時点の被験者の治験薬投与状況は，Sample 1（18 例）では，治験薬の投与を中止した被験者の割合は 9 例（50.0%），投与継続中は 9 例（50.0%）であった。一方，Sample 2（9 例）では，治験薬の投与を中止した被験者の割合は 1 例（11.1%），投与継続中は 8 例（88.9%）であった。なお，データカットオフ時点の Sample 2 の中止率（7.4%）は，Sample 1 の中止率（48.1%）と比較して低かった（表 3）。

被験者背景

人口統計学的特性及びその他のベースラインの特性

人口統計学的特性及びその他のベースラインの特性を表 6 に示す。

本試験対象集団は，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%であった。

日本人部分集団における人口統計学的特性及びその他のベースラインの特性を表 7 に示す。

本試験対象集団は，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。

パーキンソン病の病歴を表 8 に示す。

パーキンソン病と診断されて 10 年未満の被験者は 131 例（53.7%），10 年以上の被験者は 113 例（46.3%）であり同程度であった。レボドパによるジスキネジアの既往歴のある被験者は 192 例（78.7%），レボドパ反応性が 5 年を超える期間にわたり認められる被験者は 207 例（84.8%）であった。ベースライン時の Hoehn-Yahr 重症度分類はすべての被験者（欠測を除く）で 2 以上であった。

併用薬

治験実施計画書の規定に基づき，すべての被験者は治験開始時に経口パーキンソン病治療薬を使用していた。ベースライン時，1 種類のパーキンソン病治療薬（ドーパ及びドーパ誘導体，又はドパミンアゴニスト）を使用していた被験者は 34 例（13.9%），2 種類のパーキンソン病治療薬を使用していた被験者は 79 例（32.4%），3 種類のパーキンソン病治療薬を使用していた被験者は 81 例（33.2%），4 種類のパーキンソン病治療薬を使用していた被験者は 43 例（17.6%），5 種類以上のパーキンソン病治療薬を使用していた被験者は 7 例（2.9%）であった（M15-741 試験 CSR Table 14.1__3.2.3）。

ABBV-951 の投与開始後，最適化期終了時点で他のパーキンソン病治療薬を使用していなかった被験者は 50 例（23.4%），他のパーキンソン病治療薬を 1 種類使用していた被験者は 72 例（33.6%），他のパーキンソン病治療薬を 2 種類使用していた被験者は 63 例（29.4%），他のパーキンソン病治療薬を 3 種類使用していた被験者は 25 例（11.7%），他のパーキンソン病治療薬を 4 種類使用していた被験者は 3 例（1.4%），他のパーキンソン病治療薬を 5 種類以上使用していた被験者は 1 例（0.5%）であった（M15-741 試験 CSR Table 14.1__3.2.7）。

曝露状況

各被験者の ABBV-951 開始用量は，平均的な 1 日（覚醒時間 16 時間）に摂取した経口レボドパの総量（又はレボドパ換算投与量），並びにホスレボドパ中のレボドパの分子量，製剤濃度，24 時間曝露時間及び薬物動態データを考慮した換算アルゴリズムに従って算出された。

レボドパの 1 日あたりの規定投与量を表 9 に示す。
最適化期終了時には，デザイン上の意図どおり，標準注入速度を下げた被験者よりも上げた被験者の方が多く，標準注入速度の開始時から最適化期終了時又は維持期終了時の平均変化量は，それぞれわずかレボドパ 10.3 mg/hr 又はレボドパ 13.6 mg/hr に相当し，換算アルゴリズムの正確度が確認された。

日本人部分集団におけるレボドパの 1 日あたりの規定投与量を表 10 に示す。
全体集団と同様に，最適化期終了時には標準注入速度を下げた被験者よりも上げた被験者の方が多く，標準注入速度の開始時から最適化期終了時又は維持期終了時の平均変化量は，それぞれわずかレボドパ 7.6 mg/hr 又はレボドパ 9.0 mg/hr に相当し，換算アルゴリズムの正確度が確認された。

規定注入速度を表 11 に示す。
各被験者の標準及び追加の注入速度で最も頻繁に設定されたものを示した。最も頻繁に設定された注入速度は約 0.30 mL/hr から 0.60 mL/hr の範囲であり，これはレボドパ等価物を 1 日あたり約 1200 mg から 2400 mg 投与するものであった。注入速度の全範囲（0.17 mL/hr～1.01 mL/hr）は，第 I 相試験及び第 III 相試験で観察されたものと同様である。実際の，レボドパの 1 日あたりの投与量は，696.7 mg から 4180.0 mg の範囲であった（表 9）。

レボドパの 1 日あたりの投与量を表 12 に示す。
救済療法が必要になった場合に備えて，すべての被験者は治験責任医師又は一般開業医から，レボドパ＋DDCI 速放性錠又はレボドパ吸入粉末を処方されることとした。ABBV-951 の治療が開始された後の救済療法の使用は，ABBV-951 の追加投与に反応しない運動症状の急激な悪化など，重大な医学的必要性がある場合に限ることとした。
本試験では，救済薬を使用した被験者は少なかった。

日本人部分集団におけるレボドパの 1 日あたりの投与量を表 13 に示す。
救済薬を使用した被験者はほとんどいなかった。

レボドパの 1 日あたりの最頻投与量を表 14 に示す。
被験者ごとに，レボドパ換算で 100 mg 間隔の最頻（最も頻度の高い）1 日投与量を算出した。レボドパ換算投与量は，被験者投与日誌の記録に基づき，各被験者が使用した実際の注入速度

と注入時間から算出した。最頻投与量の用量分布はレボドパ換算で 1 日あたり約 600 mg から約 4100 mg であり，第 I 相試験及び第 III 相試験（ABBV-951 が進行性パーキンソン病患者の運動症状を十分にコントロールするために必要な広範囲のレボドパ用量をカバーできることが確認された）で観察された用量分布と類似していた。

ABBV-951 及び併用薬のレボドパ換算 1 日投与量を表 15 に示す。

治験薬曝露期間を表 16 に示す。
被験者が治験薬に曝露された日数の平均は，投与中断を除いて 223.6 日，投与中断を含めて 229.7 日であった。投与中断を除いた場合と含めた場合のいずれにおいても，274 日以上治験薬に曝露されていた被験者は約 50%，92 日以上治験薬に曝露されていた被験者は約 70%であった。投与中断を含めて 6 ヵ月（180 日）以上治験薬に曝露された被験者は 145 例，投与中断を除いて 6 ヵ月（180 日）以上治験薬に曝露された被験者は 137 例であった。

日本人部分集団における治験薬曝露期間を表 17 に示す。
被験者が治験薬に曝露された日数の平均は，投与中断を除いて 188.3 日，投与中断を含めて 199.2 日であった。投与中断を除いた場合と含めた場合のいずれにおいても，274 日以上治験薬に曝露されていた被験者は 44.4%，92 日以上治験薬に曝露されていた被験者は約 60%であった。投与中断を含めて 6 ヵ月（180 日）以上治験薬に曝露された被験者は 14 例，投与中断を除いて 6 ヵ月（180 日）以上治験薬に曝露された被験者は 12 例であった。

治験薬投与中断理由を表 18 に示す。
1 日以上の投与中断が報告された被験者は 92 例であった（表 20）。そのうち投与中断理由が示された被験者は 89 例であった。投与中断理由は，その他（47 例），新型コロナウイルス感染症（以下「COVID-19」）以外の有害事象（38 例），ポンプの故障（20 例）及び COVID-19 による物流上の制約（3 例）であった。投与中断理由の「その他」の大部分は，個人的な衛生 / シャワー若しくは水泳，偶発的なポンプの停止に気付かなかった，不注意によりポンプの再起動を忘れた，カニューレ / コネクターの問題，又は被験者の体調不良であった。

日本人部分集団における治験薬投与中断理由を表 19 に示す。
治験薬の投与を中断した被験者は 9 例であった。投与中断理由は，その他（6 例），COVID-19 以外の有害事象（3 例）及びポンプの故障（1 例）であった。

治験薬投与中断期間を表 20 に示す。
投与中断期間を，1 日未満から 30 日以上までの日数間隔で分類した。治験薬の投与を中断した 92 例の被験者のうち，63.0%が 2 日未満で投与中断した。なお，経口の負荷投与を必要とした被験者は，いずれの時点においても 10 例以下であった（表 12）。

有効性の結果

パーキンソン病日誌

パーキンソン病日誌に基づく，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を表 21 に示す。

各被験者は起床時及び起きている時間は 30 分ごとに，睡眠，ジスキネジアを伴わないオン，日常生活に支障がないジスキネジアを伴うオン，日常生活に支障のあるジスキネジアを伴うオン，又はオフの時間をパーキンソン病日誌に記録した。パーキンソン病日誌は 24 時間を 1 日と定義し（午前 6 時から翌日の午前 5 時 30 分まで），各被験者は 1 日に 48 回，各記録が 0.5 時間に相当するように各規定日に記入することとした。被験者ごとに睡眠パターンが異なることを考慮して，1 日あたりのオン時間とオフ時間を一般的な覚醒時間（16 時間）に標準化した。本試験では，起床時の朝一番の症状がオフの場合，朝の無動とした。

本試験で ABBV-951 を投与した結果，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（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。投与 52 週時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の平均増加量は 3.58 時間，標準化した 1 日あたりの平均オフ時間の平均減少量は 3.39 時間であった。標準化した 1 日あたりの平均オフ時間及びジスキネジアを伴う標準化した 1 日あたりの平均オン時間（日常生活に支障のあるなしを問わない）はともに減少し，それに伴い，最も望ましい状態で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も増加した。投与 52 週時の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の平均増加量は 3.78 時間であった。未治療の解析対象集団を対象とした解析でも同様の結果が認められた（M15-741 試験 CSR Table 14.2__1.2）。

日本人被験者では，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（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。投与 52 週時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の平均増加量は 3.26 時間，標準化した 1 日あたりの平均オフ時間の平均減少量は 2.92 時間であった。投与 52 週時の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の平均増加量は 4.49 時間であった（表 22）。

パーキンソン病日誌に基づく，標準化した 1 日あたりの平均オフ時間及びオン時間の部分集団解析を表 22 に示す。

パーキンソン病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を以下の部分集団ごとに解析した。

- 性別（男性又は女性）
- 人種（白人，アジア人，又はその他）
- 年齢（65 歳未満又は 65 歳以上）
- 地域（北米，欧州及びオーストラリア，又は日本）
- パーキンソン病罹病期間（診断後経過期間）（10 年未満又は 10 年以上）

部分集団解析の結果，有効性の主要解析結果とおおむね一致したが，白人以外の人種及び一部の地域（日本）の被験者数は少なかった。

パーキンソン病日誌に基づく，早朝覚醒時状態の分布を表 23 に示す。

ABBV-951 の投与開始後，朝の起床時にオフ状態であると回答した被験者の割合はベースラインから大きく減少した。ベースラインでは 77.7%の被験者がオフ状態で起床していたが，投与 1 週時には 31.0%の被験者がオフ状態で起床し，50.0%の被験者がジスキネジアを伴わないオン状態で起床した。これらの改善は投与 26 週時にかけて増加し（オフ状態 19.4%，ジスキネジアを伴わないオン状態 67.3%），その後は安定した。

日本人部分集団における，パーキンソン病日誌に基づく早朝覚醒時状態の分布を表 24 に示す。

ABBV-951 の投与開始後，朝の起床時にオフ状態であると回答した被験者の割合はベースラインから大きく減少した。ベースラインでは 93.3%の被験者がオフ状態で起床していたが，オフ状態で起床した被験者は投与 1 週時 29.4%，投与 26 週時 33.3%，ジスキネジアを伴わないオン状態で起床した被験者は投与 1 週時 41.2%，投与 26 週時 44.4%であった。以降は同程度の改善が継続して認められた。

MDS-UPDRS

MDS-UPDRS スコアを表 25 に示す。

MDS-UPDRS は以下のパートで構成される。

- パート I：日常生活における非運動症状（nM-EDL）
- パート II：日常生活における運動症状（以下「M-EDL」）
- パート III：運動症状の調査（Hoehn-Yahr 重症度分類を含む）
- パート IV：運動合併症

MDS-UPDRS 合計スコア（パート I～III）は 0 から 236 で，236 が最も重症度の高い（合計）障害を示し，0 は障害がないことを示す。MDS-UPDRS は投与 1 日目を除き，被験者の最良のオン状態で評価することとした。投与 1 日目は，治験薬投与開始前の被験者の実質的なオフ状態で評価された。

本試験で ABBV-951 を投与した結果，MDS-UPDRS パート II（M-EDL スコア）に関して，ベースラインと比較してすべての評価時点で改善が認められた（nominal $P < 0.001$）。また，

MDS-UPDRS パート IV（運動合併症スコア）についても，ベースラインと比較してすべての時点で改善が認められた（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 2 日目という早い段階から認められた。

日本人部分集団における MDS-UPDRS スコアを表 26 に示す。
日本人被験者では，MDS-UPDRS のいずれのパートにおいても継続的に統計学的有意差が認められた項目はなかったものの，いくつかの時点でベースラインからの改善が認められた。

MDS-UPDRS スコア（Hoehn-Yahr 重症度分類）を表 27 に示す。

PDSS-2
PDSS-2 スコアを表 28 に示す。
PDSS-2 の目的は，パーキンソン病患者における夜間睡眠障害の様々な側面を明らかにすることである。PDSS-2 評価ツールは信頼性が高く，有効かつ正確であり，パーキンソン病の夜間症状及び睡眠障害の評価において治療に対する反応性を示す有望な評価ツールであることが明らかにされている。PDSS-2 は，夜間及び覚醒時の運動症状及び非運動症状，並びに睡眠障害を評価する 15 項目の質問からなり，これらの質問は夜間の運動症状（5 項目），夜間のパーキンソン病症状（5 項目）及び睡眠障害（5 項目）の 3 つのドメインに分類される。点数が低いほど，夜間の症状が少なく睡眠障害が少ないことを示している。具体的には，これらの質問で全般的な睡眠の質，不眠症，睡眠断片化，下肢静止不能症候群及び睡眠時周期性四肢運動，レム睡眠行動障害，幻覚，夜間頻尿，夜間不動，疼痛及び痙攣，朝の無動，振戦，並びに睡眠時無呼吸を評価する。
本試験で ABBV-951 を投与した結果，PDSS-2 合計スコアに関してすべての時点で改善が認められた（nominal $P < 0.01$）。また，夜間の運動症状スコア，夜間のパーキンソン病症状スコア，及び睡眠障害スコアについても改善が認められた。

日本人部分集団における PDSS-2 スコアを表 29 に示す。
日本人部分集団では，PDSS-2 合計スコア，夜間の運動症状スコア，夜間のパーキンソン病症状スコア，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とほぼ同様であった。

生活の質
PDQ-39 スコアを表 30 に，EQ-5D-5L スコアを表 31 に示す。
PDQ-39 は，パーキンソン病患者に関連する健康面を評価するためにデザインされた 39 項目の疾患別評価ツールである。要約指標スコア及び各ドメインの要約スコアは 0 から 100 までの点数で評価され，スコアが低いほど健康状態が良好であることを意味する。
EQ-5D-5L は，EQ-5D 記述システムと EQ 視覚的評価尺度（以下「EQ VAS」）の 2 部から構成される標準化された測定ツールである。EQ-5D 記述システムは，「移動の程度」「身の回り

の管理」「ふだんの活動」「痛み / 不快感」「不安 / ふさぎ込み」の 5 項目から構成される。5 項目それぞれの障害を 5 段階尺度（1 = 問題はない，2 = 少し問題がある，3 = 中程度の問題がある，4 = かなり問題がある，5 = 極度の問題がある）で評価する。健康状態は，国別に重み付けした評価アルゴリズムを用いて要約指標に変換した。米国の要約指標は最悪値–0.109 から最良値 1 であった。

EQ VAS は，被験者の自己評価による健康状態を視覚的評価尺度（VAS）を用いて記録するものであり，尺度の範囲は「想像できる最高の健康状態」から「想像できる最悪の健康状態」である。

本試験で ABBV-951 を投与した結果，PDQ-39 要約指標（具体的には，運動能力，日常生活動作，恥辱感及び身体的苦痛のドメインスコア），EQ-5D-5L 要約指標及び EQ VAS によって測定されたパーキンソン病及び健康関連の生活の質において改善が認められた（nominal $P < 0.05$）。

日本人部分集団における PDQ-39 スコアを表 32 に，日本人部分集団における EQ-5D-5L スコアを表 33 に示す。

PDQ-39 要約指標では統計学的な有意差は認められなかったが，EQ-5D-5L 要約指標では投与 13 週時以外の全時点及び EQ VAS の全時点において改善が認められた（nominal $P < 0.05$）。

安全性の結果

全体集団の有害事象の発現状況を以下に示す。

有害事象の発現割合は 94.3%（230 / 244 例）であった。発現割合が 10%以上の有害事象は，注入部位紅斑 51.2%（125 / 244 例），注入部位結節 27.9%（68 / 244 例），注入部位蜂巣炎 23.0%（56 / 244 例），注入部位浮腫 19.3%（47 / 244 例），幻覚 16.8%（41 / 244 例），転倒 16.0%（39 / 244 例），注入部位疼痛 15.6%（38 / 244 例），注入部位反応 12.7%（31 / 244 例），不安 11.5%（28 / 244 例），注入部位膿瘍 10.7%（26 / 244 例），及び浮動性めまい 10.2%（25 / 244 例）であった。

治験薬と関連ありの有害事象の発現割合は 91.8%（224/ 244 例）であった。発現割合が 10%以上の治験薬と関連ありの有害事象は，注入部位紅斑 48.4%（118 / 244 例），注入部位結節 27.9%（68 / 244 例），注入部位蜂巣炎 21.3%（52 / 244 例），注入部位浮腫 18.9%（46 / 244 例），幻覚 14.8%（36 / 244 例），注入部位疼痛 13.9%（34 / 244 例），及び注入部位反応 12.7%（31 / 244 例）であった。

ABBV-951 の最終投与 30 日以内に死亡に至った有害事象を発現した被験者は 3 例であった。治験責任（分担）医師により，いずれの事象も治験薬との因果関係はないと判断された。

重篤な有害事象の発現割合は 25.0%（61 / 244 例）であった。3 例以上に発現した重篤な有害事象は，注入部位蜂巣炎 4.1%（10 / 244 例），注入部位膿瘍 3.3%（8 / 244 例），幻覚 2.9%（7 / 244 例），パーキンソン病及び精神病性障害が各 2.5%（6 / 244 例），敗血症及び尿路感染が各 1.6%（4 / 244 例），並びに肺炎 1.2%（3 / 244 例）であった。

中止に至った有害事象の発現割合は 25.4%（62 / 244 例）であった。3 例以上に発現した中止に至った有害事象は，幻覚 4.1%（10 / 244 例），注入部位紅斑及び注入部位蜂巣炎が各 3.7%（9 / 244 例），ジスキネジア 2.0%（5 / 244 例），注入部位結節及び注入部位浮腫が各 1.6%（4 / 244 例），並びに注入部位反応，注入部位膿瘍，オンオフ現象及びパーキンソン病が各 1.2%（3 / 244 例）であった。

発現時期別の有害事象の発現割合は，投与開始後 90 日までが 92.2.%（225 / 244 例）と最も高く，その後，発現割合は減少した。有病割合は，発現時期別の有害事象の発現割合と同様に，投与開始後 90 日までが 92.2.%（225 / 244 例）と最も高く，その後減少した。

日本人部分集団の有害事象の発現状況を以下に示す。

日本人部分集団の有害事象の発現割合は 92.6%（25 / 27 例）であった。発現割合が 10%以上の有害事象は，注入部位紅斑 37.0%（10 / 27 例），幻覚 33.3%（9 / 27 例），転倒 29.6%（8 / 27 例），注入部位硬結及び妄想が各 18.5%（5 / 27 例），下痢，注入部位蜂巣炎及びパーキンソン病が各 14.8%（4 / 27 例），並びに注入部位腫瘤及び浮動性めまいが各 11.1%（3 / 27 例）であった。

治験薬と関連ありの有害事象の発現割合は 92.6%（25 / 27 例）であった。発現割合が 10%以上の有害事象は，注入部位紅斑及び幻覚が各 33.3%（9 / 27 例），注入部位硬結及び妄想が各 18.5%（5 / 27 例），注入部位蜂巣炎 14.8%（4 / 27 例），並びに注入部位腫瘤及び浮動性めまいが各 11.1%（3 / 27 例）であった。

死亡した被験者はいなかった。

重篤な有害事象の発現割合は 25.9%（7 / 27 例）であった。認められた重篤な有害事象は，パーキンソン病及び幻覚が各 11.1%（3 / 27 例），並びに蜂巣炎，横紋筋融解症，意識消失及び妄想が各 3.7%（1 / 27 例）であった。

中止に至った有害事象の発現割合は 25.9%（7 / 27 例）であった。認められた中止に至った有害事象は，パーキンソン病 7.4%（2 / 27 例），並びに注入部位腫瘤，注入部位発疹，横紋筋融解症，パーキンソニズム，幻覚，幻視及び蕁麻疹が各 3.7%（1 / 27 例）であった。

本試験で発現した有害事象を以下のとおり示す。

項目	全体集団	日本人部分集団
有害事象の概要	表 34	表 42
すべての有害事象	表 35	表 43
治験薬との因果関係別の有害事象	表 36	表 44
死亡した被験者一覧	表 37	–
重篤な有害事象	表 38	表 45
中止に至った有害事象	表 39	表 46
有害事象の 90 日間ごとの初回発現割合の推移	表 40	–
有害事象の 90 日間ごとの有病割合の推移	表 41	–

結論

ABBV-951 の投与により，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及びオフ時間において 1 日を通して臨床的に意義のある改善が認められた。これらの改善は主に，最も望ましい状態であるジスキネジアを伴わないオン時間への移行によるものであった。また，MDS-UPDRS パート II（M-EDL スコア）及びパート IV（運動合併症スコア）においても改善が認められた。朝の無動及び睡眠症状で認められた臨床的に意味のある改善は，ABBV-951 の 24 時間使用によって期待される効果と一致するものである。ABBV-951 の投与により，PDQ-39 及び EQ-5D-5L によって測定されたパーキンソン病及び健康関連の生活の質の改善が認められた。

ABBV-951 は全般的に安全であり，忍容性は良好であった。大部分の被験者において，注入部位の有害事象は非重篤であり，重症度は軽度又は中等度，転帰は回復であった。ABBV-951 の全身性安全性プロファイルは，レボドパ / カルビドパ療法の確立した安全性プロファイルとおおむね一致していた。その他の安全性に関する新たな懸念は認められなかった。

表2　被験者の内訳（All Enrolled Subjects）：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 5

TABLE 14.1__1.1.1

Subject Disposition
(All Enrolled Subjects)

	Dose Category		
	Low Dose (N=132) n (%)	High Dose (N=112) n (%)	All Subjects (N=244) n (%)
Total subjects enrolled	132 (100)	112 (100)	244 (100)
Subjects previously received ABBV-951	2 (1.5)	5 (4.5)	7 (2.9)
Analysis population			
Full analysis set	132 (100)	112 (100)	244 (100)
Treatment naive analysis set	130 (98.5)	107 (95.5)	237 (97.1)
Safety analysis set	132 (100)	112 (100)	244 (100)
ABBV-951 ongoing	17 (12.9)	9 (8.0)	26 (10.7)
Sample 1	0	0	0
Sample 2	17 (12.9)	9 (8.0)	26 (10.7)
ABBV-951 completed	62 (47.0)	53 (47.3)	115 (47.1)
Sample 1	42 (31.8)	39 (34.8)	81 (33.2)
Sample 2	20 (15.2)	14 (12.5)	34 (13.9)
ABBV-951 prematurely discontinued	53 (40.2)	50 (44.6)	103 (42.2)
Sample 1	37 (28.0)	39 (34.8)	76 (31.1)
Sample 2	16 (12.1)	11 (9.8)	27 (11.1)

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].
One subject can be only counted once.
$ All reasons that are contributing to the disposition event, including the primary reason. One subject can be counted multiple times.

Program Source Code: [redacted]

TABLE 14.1 1.1.1

Subject Disposition
(All Enrolled Subjects)

	Dose Category: Low Dose (N=132) n (%)	Dose Category: High Dose (N=112) n (%)	All Subjects (N=244) n (%)
Primary reasons for ABBV-951 prematurely discontinuation #			
Adverse event	27 (20.5)	28 (25.0)	55 (22.5)
Infusion site related infections	5 (3.8)	7 (6.3)	12 (4.9)
Infusion site related non infection reactions	11 (8.3)	7 (6.3)	18 (7.4)
Polyneuropathy	0	0	0
Weight loss	0	0	0
Hallucinations/psychosis	7 (5.3)	5 (4.5)	12 (4.9)
Somnolence	0	0	0
Falls and associated injuries	0	0	0
Withdrew consent	18 (13.6)	10 (8.9)	28 (11.5)
Lost to follow-up	0	1 (0.9)	1 (0.4)
Lack of efficacy	4 (3.0)	6 (5.4)	10 (4.1)
COVID-19 infection	0	0	0
COVID-19 logistical restrictions	0	0	0
Difficulty with drug delivery system	2 (1.5)	3 (2.7)	5 (2.0)
Other	2 (1.5)	2 (1.8)	4 (1.6)

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].
One subject can be only counted once.
$ All reasons that are contributing to the disposition event, including the primary reason. One subject can be counted multiple times.

Program Source Code: [redacted]

TABLE 14.1 1.1.1

Subject Disposition
(All Enrolled Subjects)

	Dose Category: Low Dose (N=132) n (%)	Dose Category: High Dose (N=112) n (%)	All Subjects (N=244) n (%)
All reasons for ABBV-951 prematurely discontinuation $			
Adverse event	31 (23.5)	31 (27.7)	62 (25.4)
Infusion site related infections	5 (3.8)	7 (6.3)	12 (4.9)
Infusion site related non infection reactions	13 (9.8)	7 (6.3)	20 (8.2)
Polyneuropathy	1 (0.8)	0	1 (0.4)
Weight loss	0	0	0
Hallucinations/psychosis	7 (5.3)	6 (5.4)	13 (5.3)
Somnolence	0	0	0
Falls and associated injuries	0	0	0
Withdrew consent	21 (15.9)	16 (14.3)	37 (15.2)
Lost to follow-up	1 (0.8)	1 (0.9)	2 (0.8)
Lack of efficacy	9 (6.8)	8 (7.1)	17 (7.0)
COVID-19 infection	0	0	0
COVID-19 logistical restrictions	0	0	0
Difficulty with drug delivery system	2 (1.5)	3 (2.7)	5 (2.0)
Other	5 (3.8)	6 (5.4)	11 (4.5)
Study ongoing	22 (16.7)	11 (9.8)	33 (13.5)
Sample 1	0	0	0
Sample 2	22 (16.7)	11 (9.8)	33 (13.5)
Study completed	67 (50.8)	55 (49.1)	122 (50.0)
Sample 1	49 (37.1)	41 (36.6)	90 (36.9)
Sample 2	18 (13.6)	14 (12.5)	32 (13.1)

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].
One subject can be only counted once.
$ All reasons that are contributing to the disposition event, including the primary reason. One subject can be counted multiple times.

Program Source Code: [redacted]

TABLE 14.1 1.1.1

Subject Disposition
(All Enrolled Subjects)

	Dose Category: Low Dose (N=132) n (%)	Dose Category: High Dose (N=112) n (%)	All Subjects (N=244) n (%)
Study prematurely discontinued	43 (32.6)	46 (41.1)	89 (36.5)
Sample 1	30 (22.7)	37 (33.0)	67 (27.5)
Sample 2	13 (9.8)	9 (8.0)	22 (9.0)
Primary reasons for study discontinuation #			
Adverse event	20 (15.2)	25 (22.3)	45 (18.4)
Withdrew consent	15 (11.4)	11 (9.8)	26 (10.7)
Lost to follow-up	0	1 (0.9)	1 (0.4)
Lack of efficacy	4 (3.0)	4 (3.6)	8 (3.3)
COVID-19 infection	0	0	0
COVID-19 logistical restrictions	0	0	0
Difficulty with drug delivery system	2 (1.5)	3 (2.7)	5 (2.0)
Other	2 (1.5)	2 (1.8)	4 (1.6)
All reasons for study discontinuation $			
Adverse event	24 (18.2)	26 (23.2)	50 (20.5)
Withdrew consent	22 (16.7)	19 (17.0)	41 (16.8)
Lost to follow-up	0	2 (1.8)	2 (0.8)
Lack of efficacy	8 (6.1)	5 (4.5)	13 (5.3)
COVID-19 infection	0	0	0
COVID-19 logistical restrictions	0	0	0
Difficulty with drug delivery system	2 (1.5)	5 (4.5)	7 (2.9)
Other	8 (6.1)	7 (6.3)	15 (6.1)
Number of sites that screened at least 1 subject			60

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].
One subject can be only counted once.
$ All reasons that are contributing to the disposition event, including the primary reason. One subject can be counted multiple times.

Program Source Code: [redacted]

TABLE 14.1 1.1.1

Subject Disposition
(All Enrolled Subjects)

	Dose Category		
	Low Dose (N=132) n (%)	High Dose (N=112) n (%)	All Subjects (N=244) n (%)
Number of sites that enrolled at least 1 subject			60
Number of country that screened at least 1 subject			13
Number of country that enrolled at least 1 subject			13

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].
One subject can be only counted once.
$ All reasons that are contributing to the disposition event, including the primary reason. One subject can be counted multiple times.

Program Source Code: [redacted]

表3　被験者の内訳（All Enrolled Subjects，日本人部分集団）：M15-741試験

[redacted]20[redacted] 04:27 <[redacted]>
ABBV-951
STUDY M15-741 - SECOND INTERIM (CUTOFF [redacted]20[redacted])
R&D/20/1632 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 5

TABLE 14.1__1.1.1.J

Subject Disposition
(Enrolled Japan Subjects)

	Dose Category		
	Low Dose (N=22) n (%)	High Dose (N=5) n (%)	All Subjects (N=27) n (%)
Total subjects enrolled	22 (100)	5 (100)	27 (100)
Analysis population			
Full analysis set	22 (100)	5 (100)	27 (100)
Treatment naive analysis set	22 (100)	5 (100)	27 (100)
Safety analysis set	22 (100)	5 (100)	27 (100)
ABBV-951 ongoing	1 (4.5)	0	1 (3.7)
Sample 1	0	0	0
Sample 2	1 (4.5)	0	1 (3.7)
ABBV-951 completed	8 (36.4)	3 (60.0)	11 (40.7)
Sample 1	2 (9.1)	3 (60.0)	5 (18.5)
Sample 2	6 (27.3)	0	6 (22.2)
ABBV-951 prematurely discontinued	13 (59.1)	2 (40.0)	15 (55.6)
Sample 1	11 (50.0)	2 (40.0)	13 (48.1)
Sample 2	2 (9.1)	0	2 (7.4)

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].
One subject can be only counted once.
$ All reasons that are contributing to the disposition event, including the primary reason. One subject can be counted multiple times.

Program Source Code: [redacted]

TABLE 14.1 1.1.1.J

Subject Disposition
(Enrolled Japan Subjects)

	Dose Category: Low Dose (N=22) n (%)	Dose Category: High Dose (N=5) n (%)	All Subjects (N=27) n (%)
Primary reasons for ABBV-951 prematurely discontinuation #			
Adverse event	6 (27.3)	0	6 (22.2)
Infusion site related infections	0	0	0
Infusion site related non infection reactions	2 (9.1)	0	2 (7.4)
Polyneuropathy	0	0	0
Weight loss	0	0	0
Hallucinations/psychosis	2 (9.1)	0	2 (7.4)
Somnolence	0	0	0
Falls and associated injuries	0	0	0
Withdrew consent	5 (22.7)	1 (20.0)	6 (22.2)
Lost to follow-up	0	0	0
Lack of efficacy	1 (4.5)	1 (20.0)	2 (7.4)
COVID-19 infection	0	0	0
COVID-19 logistical restrictions	0	0	0
Difficulty with drug delivery system	0	0	0
Other	1 (4.5)	0	1 (3.7)

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].
One subject can be only counted once.
$ All reasons that are contributing to the disposition event, including the primary reason. One subject can be counted multiple times.

Program Source Code: [redacted]

TABLE 14.1 1.1.1.J

Subject Disposition
(Enrolled Japan Subjects)

	Dose Category: Low Dose (N=22) n (%)	Dose Category: High Dose (N=5) n (%)	All Subjects (N=27) n (%)
All reasons for ABBV-951 prematurely discontinuation $			
Adverse event	6 (27.3)	1 (20.0)	7 (25.9)
Infusion site related infections	0	0	0
Infusion site related non infection reactions	2 (9.1)	0	2 (7.4)
Polyneuropathy	0	0	0
Weight loss	0	0	0
Hallucinations/psychosis	2 (9.1)	0	2 (7.4)
Somnolence	0	0	0
Falls and associated injuries	0	0	0
Withdrew consent	6 (27.3)	1 (20.0)	7 (25.9)
Lost to follow-up	0	0	0
Lack of efficacy	3 (13.6)	1 (20.0)	4 (14.8)
COVID-19 infection	0	0	0
COVID-19 logistical restrictions	0	0	0
Difficulty with drug delivery system	0	0	0
Other	2 (9.1)	0	2 (7.4)
Study ongoing	1 (4.5)	0	1 (3.7)
Sample 1	0	0	0
Sample 2	1 (4.5)	0	1 (3.7)
Study completed	8 (36.4)	3 (60.0)	11 (40.7)
Sample 1	2 (9.1)	3 (60.0)	5 (18.5)
Sample 2	6 (27.3)	0	6 (22.2)

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].
One subject can be only counted once.
$ All reasons that are contributing to the disposition event, including the primary reason. One subject can be counted multiple times.

Program Source Code: [redacted]

TABLE 14.1 1.1.1.J

Subject Disposition
(Enrolled Japan Subjects)

	Dose Category		
	Low Dose (N=22) n (%)	High Dose (N=5) n (%)	All Subjects (N=27) n (%)
Study prematurely discontinued	13 (59.1)	2 (40.0)	15 (55.6)
Sample 1	11 (50.0)	2 (40.0)	13 (48.1)
Sample 2	2 (9.1)	0	2 (7.4)
Primary reasons for study discontinuation #			
Adverse event	6 (27.3)	0	6 (22.2)
Withdrew consent	5 (22.7)	1 (20.0)	6 (22.2)
Lost to follow-up	0	0	0
Lack of efficacy	1 (4.5)	1 (20.0)	2 (7.4)
COVID-19 infection	0	0	0
COVID-19 logistical restrictions	0	0	0
Difficulty with drug delivery system	0	0	0
Other	1 (4.5)	0	1 (3.7)
All reasons for study discontinuation $			
Adverse event	6 (27.3)	0	6 (22.2)
Withdrew consent	8 (36.4)	1 (20.0)	9 (33.3)
Lost to follow-up	0	0	0
Lack of efficacy	3 (13.6)	1 (20.0)	4 (14.8)
COVID-19 infection	0	0	0
COVID-19 logistical restrictions	0	0	0
Difficulty with drug delivery system	0	0	0
Other	2 (9.1)	0	2 (7.4)
Number of sites that screened at least 1 subject			5

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].
One subject can be only counted once.
$ All reasons that are contributing to the disposition event, including the primary reason. One subject can be counted multiple times.

Program Source Code: [redacted]

TABLE 14.1 1.1.1.J

Subject Disposition
(Enrolled Japan Subjects)

	Dose Category		
	Low Dose (N=22) n (%)	High Dose (N=5) n (%)	All Subjects (N=27) n (%)
Number of sites that enrolled at least 1 subject			5
Number of country that screened at least 1 subject			1
Number of country that enrolled at least 1 subject			1

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].
One subject can be only counted once.
$ All reasons that are contributing to the disposition event, including the primary reason. One subject can be counted multiple times.

Program Source Code: [redacted]

表4　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

[redacted]20[redacted] 10:11 <[redacted]>
ABBV-951
STUDY M15-741 - SECOND INTERIM (CUTOFF [redacted]20[redacted])
R&D/20/1632 - CLINICAL/STATISTICAL

TABLE 14.1__1.1.2

Subject Disposition during the First 12 Weeks of Study by Enrollment Sample by Time Interval
(All Enrolled Subjects)

	Sample 1 (N=157) n (%)	Sample 2 (N=87) n (%)	All Subjects (N=244) n (%)
ABBV-951 prematurely discontinued within first 12 weeks of study	49 (31.2)	17 (19.5)	66 (27.0)
ABBV-951 ongoing within first 12 weeks of study	108 (68.8)	70 (80.5)	178 (73.0)
Primary reasons #			
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)
Polyneuropathy	0	0	0
Weight loss	0	0	0
Hallucinations/psychosis	6 (3.8)	2 (2.3)	8 (3.3)
Somnolence	0	0	0
Falls and associated injuries	0	0	0
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)
COVID-19 infection	0	0	0
COVID-19 logistical restrictions	0	0	0
Difficulty with drug delivery system	3 (1.9)	1 (1.1)	4 (1.6)
Other	0	1 (1.1)	1 (0.4)

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].
One subject can be only counted once.
$ All reasons that are contributing to the disposition event, including the primary reason. One subject can be counted multiple times.

Program Source Code: [redacted]

TABLE 14.1 1.1.2

Subject Disposition during the First 12 Weeks of Study by Enrollment Sample by Time Interval
(All Enrolled Subjects)

	Sample 1 (N=157) n (%)	Sample 2 (N=87) n (%)	All Subjects (N=244) n (%)
ABBV-951 prematurely discontinued within first 12 weeks of study (cont'd)			
All reasons $			
Adverse event	29 (18.5)	8 (9.2)	37 (15.2)
Infusion site related infections	8 (5.1)	0	8 (3.3)
Infusion site related non infection reactions	11 (7.0)	1 (1.1)	12 (4.9)
Polyneuropathy	0	1 (1.1)	1 (0.4)
Weight loss	0	0	0
Hallucinations/psychosis	6 (3.8)	2 (2.3)	8 (3.3)
Somnolence	0	0	0
Falls and associated injuries	0	0	0
Withdrew consent	18 (11.5)	7 (8.0)	25 (10.2)
Lost to follow-up	2 (1.3)	0	2 (0.8)
Lack of efficacy	9 (5.7)	5 (5.7)	14 (5.7)
COVID-19 infection	0	0	0
COVID-19 logistical restrictions	0	0	0
Difficulty with drug delivery system	3 (1.9)	1 (1.1)	4 (1.6)
Other	2 (1.3)	3 (3.4)	5 (2.0)

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].
One subject can be only counted once.
$ All reasons that are contributing to the disposition event, including the primary reason. One subject can be counted multiple times.

Program Source Code: [redacted]

TABLE 14.1 1.1.2

Subject Disposition during the First 12 Weeks of Study by Enrollment Sample by Time Interval
(All Enrolled Subjects)

	Sample 1 (N=157) n (%)	Sample 2 (N=87) n (%)	All Subjects (N=244) n (%)
ABBV-951 prematurely discontinued within first 10 weeks of study	49 (31.2)	17 (19.5)	66 (27.0)
ABBV-951 ongoing within first 10 weeks of study	108 (68.8)	70 (80.5)	178 (73.0)
Primary reasons #			
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)
Polyneuropathy	0	0	0
Weight loss	0	0	0
Hallucinations/psychosis	6 (3.8)	2 (2.3)	8 (3.3)
Somnolence	0	0	0
Falls and associated injuries	0	0	0
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)
COVID-19 infection	0	0	0
COVID-19 logistical restrictions	0	0	0
Difficulty with drug delivery system	3 (1.9)	1 (1.1)	4 (1.6)
Other	0	1 (1.1)	1 (0.4)

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].
One subject can be only counted once.
$ All reasons that are contributing to the disposition event, including the primary reason. One subject can be counted multiple times.

Program Source Code: [redacted]

TABLE 14.1 1.1.2

Subject Disposition during the First 12 Weeks of Study by Enrollment Sample by Time Interval
(All Enrolled Subjects)

	Sample 1 (N=157) n (%)	Sample 2 (N=87) n (%)	All Subjects (N=244) n (%)
ABBV-951 prematurely discontinued within first 10 weeks of study (cont'd)			
All reasons $			
Adverse event	29 (18.5)	8 (9.2)	37 (15.2)
Infusion site related infections	8 (5.1)	0	8 (3.3)
Infusion site related non infection reactions	11 (7.0)	1 (1.1)	12 (4.9)
Polyneuropathy	0	1 (1.1)	1 (0.4)
Weight loss	0	0	0
Hallucinations/psychosis	6 (3.8)	2 (2.3)	8 (3.3)
Somnolence	0	0	0
Falls and associated injuries	0	0	0
Withdrew consent	18 (11.5)	7 (8.0)	25 (10.2)
Lost to follow-up	2 (1.3)	0	2 (0.8)
Lack of efficacy	9 (5.7)	5 (5.7)	14 (5.7)
COVID-19 infection	0	0	0
COVID-19 logistical restrictions	0	0	0
Difficulty with drug delivery system	3 (1.9)	1 (1.1)	4 (1.6)
Other	2 (1.3)	3 (3.4)	5 (2.0)

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].
One subject can be only counted once.
$ All reasons that are contributing to the disposition event, including the primary reason. One subject can be counted multiple times.

Program Source Code: [redacted]

TABLE 14.1 1.1.2

Subject Disposition during the First 12 Weeks of Study by Enrollment Sample by Time Interval
(All Enrolled Subjects)

	Sample 1 (N=157) n (%)	Sample 2 (N=87) n (%)	All Subjects (N=244) n (%)
ABBV-951 prematurely discontinued within first 6 weeks of study	36 (22.9)	13 (14.9)	49 (20.1)
ABBV-951 ongoing within first 6 weeks of study	121 (77.1)	74 (85.1)	195 (79.9)
Primary reasons #			
Adverse event	17 (10.8)	5 (5.7)	22 (9.0)
Infusion site related infections	7 (4.5)	0	7 (2.9)
Infusion site related non infection reactions	6 (3.8)	1 (1.1)	7 (2.9)
Polyneuropathy	0	0	0
Weight loss	0	0	0
Hallucinations/psychosis	4 (2.5)	2 (2.3)	6 (2.5)
Somnolence	0	0	0
Falls and associated injuries	0	0	0
Withdrew consent	13 (8.3)	4 (4.6)	17 (7.0)
Lost to follow-up	1 (0.6)	0	1 (0.4)
Lack of efficacy	3 (1.9)	2 (2.3)	5 (2.0)
COVID-19 infection	0	0	0
COVID-19 logistical restrictions	0	0	0
Difficulty with drug delivery system	2 (1.3)	1 (1.1)	3 (1.2)
Other	0	1 (1.1)	1 (0.4)

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].
One subject can be only counted once.
$ All reasons that are contributing to the disposition event, including the primary reason. One subject can be counted multiple times.

Program Source Code: [redacted]

TABLE 14.1 1.1.2

Subject Disposition during the First 12 Weeks of Study by Enrollment Sample by Time Interval
(All Enrolled Subjects)

	Sample 1 (N=157) n (%)	Sample 2 (N=87) n (%)	All Subjects (N=244) n (%)
ABBV-951 prematurely discontinued within first 6 weeks of study (cont'd)			
All reasons $			
Adverse event	20 (12.7)	6 (6.9)	26 (10.7)
Infusion site related infections	7 (4.5)	0	7 (2.9)
Infusion site related non infection reactions	7 (4.5)	1 (1.1)	8 (3.3)
Polyneuropathy	0	1 (1.1)	1 (0.4)
Weight loss	0	0	0
Hallucinations/psychosis	4 (2.5)	2 (2.3)	6 (2.5)
Somnolence	0	0	0
Falls and associated injuries	0	0	0
Withdrew consent	17 (10.8)	5 (5.7)	22 (9.0)
Lost to follow-up	2 (1.3)	0	2 (0.8)
Lack of efficacy	6 (3.8)	2 (2.3)	8 (3.3)
COVID-19 infection	0	0	0
COVID-19 logistical restrictions	0	0	0
Difficulty with drug delivery system	2 (1.3)	1 (1.1)	3 (1.2)
Other	1 (0.6)	2 (2.3)	3 (1.2)

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].
One subject can be only counted once.
$ All reasons that are contributing to the disposition event, including the primary reason. One subject can be counted multiple times.

Program Source Code: [redacted]

TABLE 14.1 1.1.2

Subject Disposition during the First 12 Weeks of Study by Enrollment Sample by Time Interval
(All Enrolled Subjects)

	Sample 1 (N=157) n (%)	Sample 2 (N=87) n (%)	All Subjects (N=244) n (%)
ABBV-951 prematurely discontinued within first 4 weeks of study	28 (17.8)	10 (11.5)	38 (15.6)
ABBV-951 ongoing within first 4 weeks of study	129 (82.2)	77 (88.5)	206 (84.4)
Primary reasons #			
Adverse event	14 (8.9)	2 (2.3)	16 (6.6)
Infusion site related infections	6 (3.8)	0	6 (2.5)
Infusion site related non infection reactions	5 (3.2)	0	5 (2.0)
Polyneuropathy	0	0	0
Weight loss	0	0	0
Hallucinations/psychosis	3 (1.9)	0	3 (1.2)
Somnolence	0	0	0
Falls and associated injuries	0	0	0
Withdrew consent	9 (5.7)	4 (4.6)	13 (5.3)
Lost to follow-up	1 (0.6)	0	1 (0.4)
Lack of efficacy	2 (1.3)	2 (2.3)	4 (1.6)
COVID-19 infection	0	0	0
COVID-19 logistical restrictions	0	0	0
Difficulty with drug delivery system	2 (1.3)	1 (1.1)	3 (1.2)
Other	0	1 (1.1)	1 (0.4)

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].
One subject can be only counted once.
$ All reasons that are contributing to the disposition event, including the primary reason. One subject can be counted multiple times.

Program Source Code: [redacted]

TABLE 14.1 1.1.2

Subject Disposition during the First 12 Weeks of Study by Enrollment Sample by Time Interval
(All Enrolled Subjects)

	Sample 1 (N=157) n (%)	Sample 2 (N=87) n (%)	All Subjects (N=244) n (%)
ABBV-951 prematurely discontinued within first 4 weeks of study (cont'd)			
All reasons $			
Adverse event	17 (10.8)	3 (3.4)	20 (8.2)
Infusion site related infections	6 (3.8)	0	6 (2.5)
Infusion site related non infection reactions	6 (3.8)	0	6 (2.5)
Polyneuropathy	0	1 (1.1)	1 (0.4)
Weight loss	0	0	0
Hallucinations/psychosis	3 (1.9)	0	3 (1.2)
Somnolence	0	0	0
Falls and associated injuries	0	0	0
Withdrew consent	12 (7.6)	5 (5.7)	17 (7.0)
Lost to follow-up	2 (1.3)	0	2 (0.8)
Lack of efficacy	4 (2.5)	2 (2.3)	6 (2.5)
COVID-19 infection	0	0	0
COVID-19 logistical restrictions	0	0	0
Difficulty with drug delivery system	2 (1.3)	1 (1.1)	3 (1.2)
Other	1 (0.6)	2 (2.3)	3 (1.2)

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].
One subject can be only counted once.
$ All reasons that are contributing to the disposition event, including the primary reason. One subject can be counted multiple times.

Program Source Code: [redacted]

TABLE 14.1 1.1.2

Subject Disposition during the First 12 Weeks of Study by Enrollment Sample by Time Interval
(All Enrolled Subjects)

	Sample 1 (N=157) n (%)	Sample 2 (N=87) n (%)	All Subjects (N=244) n (%)
ABBV-951 prematurely discontinued within first 2 weeks of study	9 (5.7)	7 (8.0)	16 (6.6)
ABBV-951 ongoing within first 2 weeks of study	148 (94.3)	80 (92.0)	228 (93.4)
Primary reasons #			
Adverse event	4 (2.5)	2 (2.3)	6 (2.5)
Infusion site related infections	2 (1.3)	0	2 (0.8)
Infusion site related non infection reactions	1 (0.6)	0	1 (0.4)
Polyneuropathy	0	0	0
Weight loss	0	0	0
Hallucinations/psychosis	1 (0.6)	0	1 (0.4)
Somnolence	0	0	0
Falls and associated injuries	0	0	0
Withdrew consent	4 (2.5)	2 (2.3)	6 (2.5)
Lost to follow-up	0	0	0
Lack of efficacy	0	1 (1.1)	1 (0.4)
COVID-19 infection	0	0	0
COVID-19 logistical restrictions	0	0	0
Difficulty with drug delivery system	1 (0.6)	1 (1.1)	2 (0.8)
Other	0	1 (1.1)	1 (0.4)

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].
One subject can be only counted once.
$ All reasons that are contributing to the disposition event, including the primary reason. One subject can be counted multiple times.

Program Source Code: [redacted]

TABLE 14.1 1.1.2

Subject Disposition during the First 12 Weeks of Study by Enrollment Sample by Time Interval
(All Enrolled Subjects)

	Sample 1 (N=157) n (%)	Sample 2 (N=87) n (%)	All Subjects (N=244) n (%)
ABBV-951 prematurely discontinued within first 2 weeks of study (cont'd)			
All reasons $			
Adverse event	4 (2.5)	3 (3.4)	7 (2.9)
Infusion site related infections	2 (1.3)	0	2 (0.8)
Infusion site related non infection reactions	1 (0.6)	0	1 (0.4)
Polyneuropathy	0	1 (1.1)	1 (0.4)
Weight loss	0	0	0
Hallucinations/psychosis	1 (0.6)	0	1 (0.4)
Somnolence	0	0	0
Falls and associated injuries	0	0	0
Withdrew consent	6 (3.8)	3 (3.4)	9 (3.7)
Lost to follow-up	0	0	0
Lack of efficacy	0	1 (1.1)	1 (0.4)
COVID-19 infection	0	0	0
COVID-19 logistical restrictions	0	0	0
Difficulty with drug delivery system	1 (0.6)	1 (1.1)	2 (0.8)
Other	1 (0.6)	2 (2.3)	3 (1.2)

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].
One subject can be only counted once.
$ All reasons that are contributing to the disposition event, including the primary reason. One subject can be counted multiple times.

Program Source Code: [redacted]

TABLE 14.1 1.1.2

Subject Disposition during the First 12 Weeks of Study by Enrollment Sample by Time Interval
(All Enrolled Subjects)

	Sample 1 (N=157) n (%)	Sample 2 (N=87) n (%)	All Subjects (N=244) n (%)
ABBV-951 prematurely discontinued within first 1 week of study	5 (3.2)	2 (2.3)	7 (2.9)
ABBV-951 ongoing within first 1 week of study	152 (96.8)	85 (97.7)	237 (97.1)
Primary reasons #			
Adverse event	1 (0.6)	1 (1.1)	2 (0.8)
Infusion site related infections	1 (0.6)	0	1 (0.4)
Infusion site related non infection reactions	0	0	0
Polyneuropathy	0	0	0
Weight loss	0	0	0
Hallucinations/psychosis	0	0	0
Somnolence	0	0	0
Falls and associated injuries	0	0	0
Withdrew consent	3 (1.9)	0	3 (1.2)
Lost to follow-up	0	0	0
Lack of efficacy	0	0	0
COVID-19 infection	0	0	0
COVID-19 logistical restrictions	0	0	0
Difficulty with drug delivery system	1 (0.6)	1 (1.1)	2 (0.8)
Other	0	0	0

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].
One subject can be only counted once.
$ All reasons that are contributing to the disposition event, including the primary reason. One subject can be counted multiple times.

Program Source Code: [redacted]

TABLE 14.1 1.1.2

Subject Disposition during the First 12 Weeks of Study by Enrollment Sample by Time Interval
(All Enrolled Subjects)

	Sample 1 (N=157) n (%)	Sample 2 (N=87) n (%)	All Subjects (N=244) n (%)
ABBV-951 prematurely discontinued within first 1 week of study (cont'd)			
All reasons $			
Adverse event	1 (0.6)	1 (1.1)	2 (0.8)
Infusion site related infections	1 (0.6)	0	1 (0.4)
Infusion site related non infection reactions	0	0	0
Polyneuropathy	0	0	0
Weight loss	0	0	0
Hallucinations/psychosis	0	0	0
Somnolence	0	0	0
Falls and associated injuries	0	0	0
Withdrew consent	3 (1.9)	0	3 (1.2)
Lost to follow-up	0	0	0
Lack of efficacy	0	0	0
COVID-19 infection	0	0	0
COVID-19 logistical restrictions	0	0	0
Difficulty with drug delivery system	1 (0.6)	1 (1.1)	2 (0.8)
Other	0	0	0

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].
One subject can be only counted once.
$ All reasons that are contributing to the disposition event, including the primary reason. One subject can be counted multiple times.

Program Source Code: [redacted]

表5　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

[redacted]20[redacted] 04:27 <[redacted]>
ABBV-951
STUDY M15-741 - SECOND INTERIM (CUTOFF [redacted]20[redacted])
R&D/20/1632 - CLINICAL/STATISTICAL

TABLE 14.1__1.1.2.J

Subject Disposition During the First 12 Weeks of Study by Enrollment Sample by Time Interval
(Enrolled Japan Subjects)

	Sample 1 (N=18) n (%)	Sample 2 (N=9) n (%)	All Subjects (N=27) n (%)
ABBV-951 prematurely discontinued within first 12 weeks of study	9 (50.0)	1 (11.1)	10 (37.0)
ABBV-951 ongoing within first 12 weeks of study	9 (50.0)	8 (88.9)	17 (63.0)
Primary reasons #			
Adverse event	4 (22.2)	0	4 (14.8)
Infusion site related infections	0	0	0
Infusion site related non infection reactions	2 (11.1)	0	2 (7.4)
Polyneuropathy	0	0	0
Weight loss	0	0	0
Hallucinations/psychosis	1 (5.6)	0	1 (3.7)
Somnolence	0	0	0
Falls and associated injuries	0	0	0
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)
COVID-19 infection	0	0	0
COVID-19 logistical restrictions	0	0	0
Difficulty with drug delivery system	0	0	0
Other	0	0	0

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].
One subject can be only counted once.
$ All reasons that are contributing to the disposition event, including the primary reason. One subject can be counted multiple times.

Program Source Code: [redacted]

TABLE 14.1 1.1.2.J

Subject Disposition During the First 12 Weeks of Study by Enrollment Sample by Time Interval
(Enrolled Japan Subjects)

	Sample 1 (N=18) n (%)	Sample 2 (N=9) n (%)	All Subjects (N=27) n (%)
ABBV-951 prematurely discontinued within first 12 weeks of study (cont'd)			
All reasons $			
Adverse event	5 (27.8)	0	5 (18.5)
Infusion site related infections	0	0	0
Infusion site related non infection reactions	2 (11.1)	0	2 (7.4)
Polyneuropathy	0	0	0
Weight loss	0	0	0
Hallucinations/psychosis	1 (5.6)	0	1 (3.7)
Somnolence	0	0	0
Falls and associated injuries	0	0	0
Withdrew consent	3 (16.7)	1 (11.1)	4 (14.8)
Lost to follow-up	0	0	0
Lack of efficacy	4 (22.2)	0	4 (14.8)
COVID-19 infection	0	0	0
COVID-19 logistical restrictions	0	0	0
Difficulty with drug delivery system	0	0	0
Other	0	0	0

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].
One subject can be only counted once.
$ All reasons that are contributing to the disposition event, including the primary reason. One subject can be counted multiple times.

Program Source Code: [redacted]

TABLE 14.1 1.1.2.J

Subject Disposition During the First 12 Weeks of Study by Enrollment Sample by Time Interval
(Enrolled Japan Subjects)

	Sample 1 (N=18) n (%)	Sample 2 (N=9) n (%)	All Subjects (N=27) n (%)
ABBV-951 prematurely discontinued within first 10 weeks of study	9 (50.0)	1 (11.1)	10 (37.0)
ABBV-951 ongoing within first 10 weeks of study	9 (50.0)	8 (88.9)	17 (63.0)
Primary reasons #			
Adverse event	4 (22.2)	0	4 (14.8)
Infusion site related infections	0	0	0
Infusion site related non infection reactions	2 (11.1)	0	2 (7.4)
Polyneuropathy	0	0	0
Weight loss	0	0	0
Hallucinations/psychosis	1 (5.6)	0	1 (3.7)
Somnolence	0	0	0
Falls and associated injuries	0	0	0
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)
COVID-19 infection	0	0	0
COVID-19 logistical restrictions	0	0	0
Difficulty with drug delivery system	0	0	0
Other	0	0	0

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].
One subject can be only counted once.
$ All reasons that are contributing to the disposition event, including the primary reason. One subject can be counted multiple times.

Program Source Code: [redacted]

TABLE 14.1 1.1.2.J

Subject Disposition During the First 12 Weeks of Study by Enrollment Sample by Time Interval
(Enrolled Japan Subjects)

	Sample 1 (N=18) n (%)	Sample 2 (N=9) n (%)	All Subjects (N=27) n (%)
ABBV-951 prematurely discontinued within first 10 weeks of study (cont'd)			
All reasons $			
Adverse event	5 (27.8)	0	5 (18.5)
Infusion site related infections	0	0	0
Infusion site related non infection reactions	2 (11.1)	0	2 (7.4)
Polyneuropathy	0	0	0
Weight loss	0	0	0
Hallucinations/psychosis	1 (5.6)	0	1 (3.7)
Somnolence	0	0	0
Falls and associated injuries	0	0	0
Withdrew consent	3 (16.7)	1 (11.1)	4 (14.8)
Lost to follow-up	0	0	0
Lack of efficacy	4 (22.2)	0	4 (14.8)
COVID-19 infection	0	0	0
COVID-19 logistical restrictions	0	0	0
Difficulty with drug delivery system	0	0	0
Other	0	0	0

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].
One subject can be only counted once.
$ All reasons that are contributing to the disposition event, including the primary reason. One subject can be counted multiple times.

Program Source Code: [redacted]

TABLE 14.1 1.1.2.J

Subject Disposition During the First 12 Weeks of Study by Enrollment Sample by Time Interval
(Enrolled Japan Subjects)

	Sample 1 (N=18) n (%)	Sample 2 (N=9) n (%)	All Subjects (N=27) n (%)
ABBV-951 prematurely discontinued within first 6 weeks of study	8 (44.4)	1 (11.1)	9 (33.3)
ABBV-951 ongoing within first 6 weeks of study	10 (55.6)	8 (88.9)	18 (66.7)
Primary reasons #			
Adverse event	4 (22.2)	0	4 (14.8)
Infusion site related infections	0	0	0
Infusion site related non infection reactions	2 (11.1)	0	2 (7.4)
Polyneuropathy	0	0	0
Weight loss	0	0	0
Hallucinations/psychosis	1 (5.6)	0	1 (3.7)
Somnolence	0	0	0
Falls and associated injuries	0	0	0
Withdrew consent	3 (16.7)	1 (11.1)	4 (14.8)
Lost to follow-up	0	0	0
Lack of efficacy	1 (5.6)	0	1 (3.7)
COVID-19 infection	0	0	0
COVID-19 logistical restrictions	0	0	0
Difficulty with drug delivery system	0	0	0
Other	0	0	0

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].
One subject can be only counted once.
$ All reasons that are contributing to the disposition event, including the primary reason. One subject can be counted multiple times.

Program Source Code: [redacted]

TABLE 14.1 1.1.2.J

Subject Disposition During the First 12 Weeks of Study by Enrollment Sample by Time Interval
(Enrolled Japan Subjects)

	Sample 1 (N=18) n (%)	Sample 2 (N=9) n (%)	All Subjects (N=27) n (%)
ABBV-951 prematurely discontinued within first 6 weeks of study (cont'd)			
All reasons $			
Adverse event	5 (27.8)	0	5 (18.5)
Infusion site related infections	0	0	0
Infusion site related non infection reactions	2 (11.1)	0	2 (7.4)
Polyneuropathy	0	0	0
Weight loss	0	0	0
Hallucinations/psychosis	1 (5.6)	0	1 (3.7)
Somnolence	0	0	0
Falls and associated injuries	0	0	0
Withdrew consent	3 (16.7)	1 (11.1)	4 (14.8)
Lost to follow-up	0	0	0
Lack of efficacy	3 (16.7)	0	3 (11.1)
COVID-19 infection	0	0	0
COVID-19 logistical restrictions	0	0	0
Difficulty with drug delivery system	0	0	0
Other	0	0	0

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].
One subject can be only counted once.
$ All reasons that are contributing to the disposition event, including the primary reason. One subject can be counted multiple times.

Program Source Code: [redacted]

TABLE 14.1 1.1.2.J

Subject Disposition During the First 12 Weeks of Study by Enrollment Sample by Time Interval
(Enrolled Japan Subjects)

	Sample 1 (N=18) n (%)	Sample 2 (N=9) n (%)	All Subjects (N=27) n (%)
ABBV-951 prematurely discontinued within first 4 weeks of study	6 (33.3)	1 (11.1)	7 (25.9)
ABBV-951 ongoing within first 4 weeks of study	12 (66.7)	8 (88.9)	20 (74.1)
Primary reasons #			
Adverse event	3 (16.7)	0	3 (11.1)
Infusion site related infections	0	0	0
Infusion site related non infection reactions	1 (5.6)	0	1 (3.7)
Polyneuropathy	0	0	0
Weight loss	0	0	0
Hallucinations/psychosis	1 (5.6)	0	1 (3.7)
Somnolence	0	0	0
Falls and associated injuries	0	0	0
Withdrew consent	2 (11.1)	1 (11.1)	3 (11.1)
Lost to follow-up	0	0	0
Lack of efficacy	1 (5.6)	0	1 (3.7)
COVID-19 infection	0	0	0
COVID-19 logistical restrictions	0	0	0
Difficulty with drug delivery system	0	0	0
Other	0	0	0

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].
One subject can be only counted once.
$ All reasons that are contributing to the disposition event, including the primary reason. One subject can be counted multiple times.

Program Source Code: [redacted]

TABLE 14.1 1.1.2.J

Subject Disposition During the First 12 Weeks of Study by Enrollment Sample by Time Interval
(Enrolled Japan Subjects)

	Sample 1 (N=18) n (%)	Sample 2 (N=9) n (%)	All Subjects (N=27) n (%)
ABBV-951 prematurely discontinued within first 4 weeks of study (cont'd)			
All reasons $			
Adverse event	4 (22.2)	0	4 (14.8)
Infusion site related infections	0	0	0
Infusion site related non infection reactions	1 (5.6)	0	1 (3.7)
Polyneuropathy	0	0	0
Weight loss	0	0	0
Hallucinations/psychosis	1 (5.6)	0	1 (3.7)
Somnolence	0	0	0
Falls and associated injuries	0	0	0
Withdrew consent	2 (11.1)	1 (11.1)	3 (11.1)
Lost to follow-up	0	0	0
Lack of efficacy	3 (16.7)	0	3 (11.1)
COVID-19 infection	0	0	0
COVID-19 logistical restrictions	0	0	0
Difficulty with drug delivery system	0	0	0
Other	0	0	0

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].
One subject can be only counted once.
$ All reasons that are contributing to the disposition event, including the primary reason. One subject can be counted multiple times.

Program Source Code: [redacted]

TABLE 14.1 1.1.2.J

Subject Disposition During the First 12 Weeks of Study by Enrollment Sample by Time Interval
(Enrolled Japan Subjects)

	Sample 1 (N=18) n (%)	Sample 2 (N=9) n (%)	All Subjects (N=27) n (%)
ABBV-951 prematurely discontinued within first 2 weeks of study	1 (5.6)	1 (11.1)	2 (7.4)
ABBV-951 ongoing within first 2 weeks of study	17 (94.4)	8 (88.9)	25 (92.6)
Primary reasons #			
Adverse event	0	0	0
Infusion site related infections	0	0	0
Infusion site related non infection reactions	0	0	0
Polyneuropathy	0	0	0
Weight loss	0	0	0
Hallucinations/psychosis	0	0	0
Somnolence	0	0	0
Falls and associated injuries	0	0	0
Withdrew consent	1 (5.6)	1 (11.1)	2 (7.4)
Lost to follow-up	0	0	0
Lack of efficacy	0	0	0
COVID-19 infection	0	0	0
COVID-19 logistical restrictions	0	0	0
Difficulty with drug delivery system	0	0	0
Other	0	0	0

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].
One subject can be only counted once.
$ All reasons that are contributing to the disposition event, including the primary reason. One subject can be counted multiple times.

Program Source Code: [redacted]

TABLE 14.1 1.1.2.J

Subject Disposition During the First 12 Weeks of Study by Enrollment Sample by Time Interval
(Enrolled Japan Subjects)

	Sample 1 (N=18) n (%)	Sample 2 (N=9) n (%)	All Subjects (N=27) n (%)
ABBV-951 prematurely discontinued within first 2 weeks of study (cont'd)			
All reasons $			
Adverse event	0	0	0
Infusion site related infections	0	0	0
Infusion site related non infection reactions	0	0	0
Polyneuropathy	0	0	0
Weight loss	0	0	0
Hallucinations/psychosis	0	0	0
Somnolence	0	0	0
Falls and associated injuries	0	0	0
Withdrew consent	1 (5.6)	1 (11.1)	2 (7.4)
Lost to follow-up	0	0	0
Lack of efficacy	0	0	0
COVID-19 infection	0	0	0
COVID-19 logistical restrictions	0	0	0
Difficulty with drug delivery system	0	0	0
Other	0	0	0

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].
One subject can be only counted once.
$ All reasons that are contributing to the disposition event, including the primary reason. One subject can be counted multiple times.

Program Source Code: [redacted]

TABLE 14.1 1.1.2.J

Subject Disposition During the First 12 Weeks of Study by Enrollment Sample by Time Interval
(Enrolled Japan Subjects)

	Sample 1 (N=18) n (%)	Sample 2 (N=9) n (%)	All Subjects (N=27) n (%)
ABBV-951 prematurely discontinued within first 1 week of study	1 (5.6)	0	1 (3.7)
ABBV-951 ongoing within first 1 week of study	17 (94.4)	9 (100)	26 (96.3)
Primary reasons #			
Adverse event	0	0	0
Infusion site related infections	0	0	0
Infusion site related non infection reactions	0	0	0
Polyneuropathy	0	0	0
Weight loss	0	0	0
Hallucinations/psychosis	0	0	0
Somnolence	0	0	0
Falls and associated injuries	0	0	0
Withdrew consent	1 (5.6)	0	1 (3.7)
Lost to follow-up	0	0	0
Lack of efficacy	0	0	0
COVID-19 infection	0	0	0
COVID-19 logistical restrictions	0	0	0
Difficulty with drug delivery system	0	0	0
Other	0	0	0

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].
One subject can be only counted once.
$ All reasons that are contributing to the disposition event, including the primary reason. One subject can be counted multiple times.

Program Source Code: [redacted]

TABLE 14.1 1.1.2.J

Subject Disposition During the First 12 Weeks of Study by Enrollment Sample by Time Interval
(Enrolled Japan Subjects)

	Sample 1 (N=18) n (%)	Sample 2 (N=9) n (%)	All Subjects (N=27) n (%)
ABBV-951 prematurely discontinued within first 1 week of study (cont'd)			
All reasons $			
Adverse event	0	0	0
Infusion site related infections	0	0	0
Infusion site related non infection reactions	0	0	0
Polyneuropathy	0	0	0
Weight loss	0	0	0
Hallucinations/psychosis	0	0	0
Somnolence	0	0	0
Falls and associated injuries	0	0	0
Withdrew consent	1 (5.6)	0	1 (3.7)
Lost to follow-up	0	0	0
Lack of efficacy	0	0	0
COVID-19 infection	0	0	0
COVID-19 logistical restrictions	0	0	0
Difficulty with drug delivery system	0	0	0
Other	0	0	0

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].
One subject can be only counted once.
$ All reasons that are contributing to the disposition event, including the primary reason. One subject can be counted multiple times.

Program Source Code: [redacted]

表6　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

[redacted]20[redacted] 10:11 <[redacted]>
ABBV-951
STUDY M15-741 - SECOND INTERIM (CUTOFF [redacted]20[redacted])
R&D/20/1632 - CLINICAL/STATISTICAL

TABLE 14.1__2

Demographic and Baseline Characteristics
(Safety Analysis Set)

	Dose Category		
	Low Dose (N=132)	High Dose (N=112)	All Subjects (N=244)
Age (year)			
n	132	112	244
Mean (SD)	63.6 (8.89)	64.3 (9.53)	63.9 (9.18)
Median	65.0	64.0	65.0
Min, Max	34, 83	43, 86	34, 86
Age (year) - n (%)			
< 65	62 (47.0)	57 (50.9)	119 (48.8)
>= 65	70 (53.0)	55 (49.1)	125 (51.2)
Age (year) - n (%)			
< 75	121 (91.7)	96 (85.7)	217 (88.9)
>= 75	11 (8.3)	16 (14.3)	27 (11.1)
Weight (kg)			
n	132	112	244
Mean (SD)	68.28 (17.338)	76.59 (16.366)	72.10 (17.367)
Median	67.50	78.25	72.00
Min, Max	34.1, 120.7	41.4, 110.9	34.1, 120.7
Height (cm)			
n	130	111	241
Mean (SD)	166.38 (10.498)	172.45 (10.341)	169.18 (10.838)
Median	166.00	172.20	170.00
Min, Max	140.1, 189.0	142.2, 197.5	140.1, 197.5

Note: Percentages calculated on non-missing or non-unknown values.
For categorical variables, 'Missing' row is only presented when there are missing data presented.

Program Source Code: [redacted]

TABLE 14.1 2

Demographic and Baseline Characteristics
(Safety Analysis Set)

	Dose Category: Low Dose (N=132)	Dose Category: High Dose (N=112)	All Subjects (N=244)
BMI (kg/m^2)			
n	130	111	241
Mean (SD)	24.41 (5.031)	25.59 (4.485)	24.95 (4.814)
Median	23.55	25.24	24.41
Min, Max	14.1, 39.9	16.5, 35.1	14.1, 39.9
BMI (kg/m^2) - n (%)			
< 18.5	8 (6.2)	5 (4.5)	13 (5.4)
18.5 - < 25.0	72 (55.4)	46 (41.4)	118 (49.0)
25.0 - < 30.0	28 (21.5)	39 (35.1)	67 (27.8)
>= 30.0	22 (16.9)	21 (18.9)	43 (17.8)
Missing	2	1	3
Mini-Mental State Examination (MMSE) total score			
n	131	111	242
Mean (SD)	28.83 (1.575)	28.55 (1.877)	28.70 (1.722)
Median	29.00	29.00	29.00
Min, Max	20.0, 30.0	21.0, 30.0	20.0, 30.0

Note: Percentages calculated on non-missing or non-unknown values.
For categorical variables, 'Missing' row is only presented when there are missing data presented.

Program Source Code: [redacted]

TABLE 14.1 2

Demographic and Baseline Characteristics
(Safety Analysis Set)

	Dose Category		
	Low Dose (N=132)	High Dose (N=112)	All Subjects (N=244)
Country - n (%)			
AUSTRALIA	18 (13.6)	9 (8.0)	27 (11.1)
BELGIUM	4 (3.0)	3 (2.7)	7 (2.9)
CANADA	4 (3.0)	5 (4.5)	9 (3.7)
DENMARK	3 (2.3)	6 (5.4)	9 (3.7)
GERMANY	8 (6.1)	4 (3.6)	12 (4.9)
ITALY	5 (3.8)	1 (0.9)	6 (2.5)
JAPAN	22 (16.7)	5 (4.5)	27 (11.1)
NETHERLANDS	4 (3.0)	2 (1.8)	6 (2.5)
RUSSIA	6 (4.5)	2 (1.8)	8 (3.3)
SPAIN	12 (9.1)	16 (14.3)	28 (11.5)
SWEDEN	5 (3.8)	6 (5.4)	11 (4.5)
UNITED KINGDOM	5 (3.8)	8 (7.1)	13 (5.3)
UNITED STATES	36 (27.3)	45 (40.2)	81 (33.2)
Geographic region - n (%)			
North America	40 (30.3)	50 (44.6)	90 (36.9)
Europe and Australia	70 (53.0)	57 (50.9)	127 (52.0)
Japan	22 (16.7)	5 (4.5)	27 (11.1)
Sex - n (%)			
Female	66 (50.0)	32 (28.6)	98 (40.2)
Male	66 (50.0)	80 (71.4)	146 (59.8)
Ethnicity - n (%)			
Hispanic or Latino	8 (6.1)	12 (10.7)	20 (8.2)
Not Hispanic or Latino	124 (93.9)	100 (89.3)	224 (91.8)

Note: Percentages calculated on non-missing or non-unknown values.
For categorical variables, 'Missing' row is only presented when there are missing data presented.

Program Source Code: [redacted]

TABLE 14.1 2

Demographic and Baseline Characteristics
(Safety Analysis Set)

	Dose Category: Low Dose (N=132)	Dose Category: High Dose (N=112)	All Subjects (N=244)
Race - n (%)			
White	103 (78.0)	104 (92.9)	207 (84.8)
Black or African American	0	1 (0.9)	1 (0.4)
Asian	27 (20.5)	7 (6.3)	34 (13.9)
American Indian or Alaska Native	1 (0.8)	0	1 (0.4)
Native Hawaiian or Other Pacific Islander	0	0	0
Multiple	1 (0.8)	0	1 (0.4)
Tobacco - n (%)			
Current	10 (7.6)	5 (4.5)	15 (6.1)
Former	38 (28.8)	36 (32.1)	74 (30.3)
Never	84 (63.6)	71 (63.4)	155 (63.5)
Unknown	0	0	0
Alcohol - n (%)			
Current	86 (65.2)	65 (58.0)	151 (61.9)
Former	19 (14.4)	14 (12.5)	33 (13.5)
Never	27 (20.5)	33 (29.5)	60 (24.6)
Unknown	0	0	0
Brief neurological examination			
Mental status - n (%)			
Normal	130 (98.5)	108 (96.4)	238 (97.5)
Abnormal	2 (1.5)	4 (3.6)	6 (2.5)
Cranial nerves - n (%)			
Normal	122 (92.4)	102 (91.1)	224 (91.8)
Abnormal	10 (7.6)	10 (8.9)	20 (8.2)

Note: Percentages calculated on non-missing or non-unknown values.
For categorical variables, 'Missing' row is only presented when there are missing data presented.

Program Source Code: [redacted]

TABLE 14.1 2

Demographic and Baseline Characteristics
(Safety Analysis Set)

	Dose Category		
	Low Dose (N=132)	High Dose (N=112)	All Subjects (N=244)
Motor system - n (%)			
Normal	63 (47.7)	66 (58.9)	129 (52.9)
Abnormal	69 (52.3)	46 (41.1)	115 (47.1)
Sensory system - n (%)			
Normal	120 (92.3)	96 (85.7)	216 (89.3)
Abnormal	10 (7.7)	16 (14.3)	26 (10.7)
Missing	2	0	2
Reflexes - n (%)			
Normal	120 (92.3)	95 (84.8)	215 (88.8)
Abnormal	10 (7.7)	17 (15.2)	27 (11.2)
Missing	2	0	2
Coordination - n (%)			
Normal	110 (84.6)	96 (85.7)	206 (85.1)
Abnormal	20 (15.4)	16 (14.3)	36 (14.9)
Missing	2	0	2
Gait - n (%)			
Normal	51 (38.6)	52 (46.4)	103 (42.2)
Abnormal	81 (61.4)	60 (53.6)	141 (57.8)
Station - n (%)			
Normal	96 (74.4)	80 (74.1)	176 (74.3)
Abnormal	33 (25.6)	28 (25.9)	61 (25.7)
Missing	3	4	7

Note: Percentages calculated on non-missing or non-unknown values.
For categorical variables, 'Missing' row is only presented when there are missing data presented.

Program Source Code: [redacted]

表7　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

[redacted]20[redacted] 04:28 <[redacted]>
ABBV-951
STUDY M15-741 - SECOND INTERIM (CUTOFF [redacted]20[redacted])
R&D/20/1632 - CLINICAL/STATISTICAL

TABLE 14.1__2.1.J

Demographic and Baseline Characteristics by Dose Category
(Safety Analysis Set - Japan Subjects)

	Dose Category		
	Low Dose (N=22)	High Dose (N=5)	All Subjects (N=27)
Age (year)			
n	22	5	27
Mean (SD)	62.5 (9.43)	66.8 (6.10)	63.3 (8.97)
Median	62.0	69.0	62.0
Min, Max	46, 83	57, 72	46, 83
Age (year) - n (%)			
< 65	14 (63.6)	1 (20.0)	15 (55.6)
>= 65	8 (36.4)	4 (80.0)	12 (44.4)
Age (year) - n (%)			
< 75	20 (90.9)	5 (100)	25 (92.6)
>= 75	2 (9.1)	0	2 (7.4)
Weight (kg)			
n	22	5	27
Mean (SD)	53.32 (12.482)	69.06 (16.463)	56.23 (14.365)
Median	48.65	75.80	58.00
Min, Max	34.1, 73.0	41.4, 82.5	34.1, 82.5
Height (cm)			
n	22	5	27
Mean (SD)	159.73 (11.147)	161.98 (10.690)	160.15 (10.897)
Median	160.05	165.10	160.10
Min, Max	140.1, 177.4	149.6, 173.3	140.1, 177.4

Note: Percentages calculated on non-missing or non-unknown values.
For categorical variables, 'Missing' row is only presented when there are missing data presented.

Program Source Code: [redacted]

TABLE 14.1 2.1.J

Demographic and Baseline Characteristics by Dose Category
(Safety Analysis Set - Japan Subjects)

	Dose Category		
	Low Dose (N=22)	High Dose (N=5)	All Subjects (N=27)
BMI (kg/m^2)			
n	22	5	27
Mean (SD)	20.70 (3.347)	26.05 (4.634)	21.69 (4.103)
Median	20.43	27.16	20.70
Min, Max	14.1, 27.4	18.5, 30.3	14.1, 30.3
BMI (kg/m^2) - n (%)			
< 18.5	6 (27.3)	1 (20.0)	7 (25.9)
18.5 - < 25.0	13 (59.1)	0	13 (48.1)
25.0 - < 30.0	3 (13.6)	3 (60.0)	6 (22.2)
>= 30.0	0	1 (20.0)	1 (3.7)
Mini-Mental State Examination (MMSE) total score			
n	22	5	27
Mean (SD)	29.00 (1.024)	29.40 (0.548)	29.07 (0.958)
Median	29.00	29.00	29.00
Min, Max	27.0, 30.0	29.0, 30.0	27.0, 30.0
Country - n (%)			
JAPAN	22 (100)	5 (100)	27 (100)
Geographic region - n (%)			
Japan	22 (100)	5 (100)	27 (100)
Sex - n (%)			
Female	13 (59.1)	1 (20.0)	14 (51.9)
Male	9 (40.9)	4 (80.0)	13 (48.1)

Note: Percentages calculated on non-missing or non-unknown values.
For categorical variables, 'Missing' row is only presented when there are missing data presented.

Program Source Code: [redacted]

TABLE 14.1 2.1.J

Demographic and Baseline Characteristics by Dose Category
(Safety Analysis Set - Japan Subjects)

	Dose Category		
	Low Dose (N=22)	High Dose (N=5)	All Subjects (N=27)
Ethnicity - n (%)			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	22 (100)	5 (100)	27 (100)
Race - n (%)			
White	0	0	0
Black or African American	0	0	0
Asian	22 (100)	5 (100)	27 (100)
American Indian or Alaska Native	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Multiple	0	0	0
Tobacco - n (%)			
Current	1 (4.5)	0	1 (3.7)
Former	6 (27.3)	3 (60.0)	9 (33.3)
Never	15 (68.2)	2 (40.0)	17 (63.0)
Unknown	0	0	0
Alcohol - n (%)			
Current	11 (50.0)	4 (80.0)	15 (55.6)
Former	6 (27.3)	0	6 (22.2)
Never	5 (22.7)	1 (20.0)	6 (22.2)
Unknown	0	0	0
Brief neurological examination			
Mental status - n (%)			
Normal	22 (100)	4 (80.0)	26 (96.3)
Abnormal	0	1 (20.0)	1 (3.7)

Note: Percentages calculated on non-missing or non-unknown values.
For categorical variables, 'Missing' row is only presented when there are missing data presented.

Program Source Code: [redacted]

TABLE 14.1 2.1.J

Demographic and Baseline Characteristics by Dose Category
(Safety Analysis Set - Japan Subjects)

	Dose Category		
	Low Dose (N=22)	High Dose (N=5)	All Subjects (N=27)
Cranial nerves - n (%)			
Normal	21 (95.5)	5 (100)	26 (96.3)
Abnormal	1 (4.5)	0	1 (3.7)
Motor system - n (%)			
Normal	12 (54.5)	3 (60.0)	15 (55.6)
Abnormal	10 (45.5)	2 (40.0)	12 (44.4)
Sensory system - n (%)			
Normal	21 (95.5)	5 (100)	26 (96.3)
Abnormal	1 (4.5)	0	1 (3.7)
Reflexes - n (%)			
Normal	21 (95.5)	5 (100)	26 (96.3)
Abnormal	1 (4.5)	0	1 (3.7)
Coordination - n (%)			
Normal	15 (68.2)	3 (60.0)	18 (66.7)
Abnormal	7 (31.8)	2 (40.0)	9 (33.3)
Gait - n (%)			
Normal	9 (40.9)	1 (20.0)	10 (37.0)
Abnormal	13 (59.1)	4 (80.0)	17 (63.0)
Station - n (%)			
Normal	14 (63.6)	2 (40.0)	16 (59.3)
Abnormal	8 (36.4)	3 (60.0)	11 (40.7)

Note: Percentages calculated on non-missing or non-unknown values.
For categorical variables, 'Missing' row is only presented when there are missing data presented.

Program Source Code: [redacted]

表8　パーキンソン病の病歴（安全性解析対象集団）：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 14.1__3.1

Parkinson's Disease History
(Safety Analysis Set)

	Dose Category		
	Low Dose (N=132)	High Dose (N=112)	All Subjects (N=244)
Duration of PD since diagnosis - n (%)			
< 10 years	67 (50.8)	64 (57.1)	131 (53.7)
>= 10 years	65 (49.2)	48 (42.9)	113 (46.3)
History of levodopa induced dyskinesia - n (%)			
Yes	107 (81.1)	85 (75.9)	192 (78.7)
No	25 (18.9)	27 (24.1)	52 (21.3)
Levodopa response for more than 5 years - n (%)			
Yes	117 (88.6)	90 (80.4)	207 (84.8)
No	15 (11.4)	22 (19.6)	37 (15.2)
Baseline parkinson's disease Hoehn and Yahr Stage (MDS-UPDRS) - n (%)			
0	0	0	0
1	0	0	0
2	70 (53.4)	52 (46.8)	122 (50.4)
3	34 (26.0)	31 (27.9)	65 (26.9)
4	19 (14.5)	18 (16.2)	37 (15.3)
5	8 (6.1)	10 (9.0)	18 (7.4)
Missing	1	1	2
Age at PD onset (years)			
n	132	112	244
Mean (SD)	51.6 (9.12)	52.9 (9.70)	52.2 (9.40)
Median	53.0	53.0	53.0
Min, Max	21, 74	34, 77	21, 77

Note: Percentages calculated on non-missing or non-unknown values.

Program Source Code: [redacted]

TABLE 14.1 3.1

Parkinson's Disease History
(Safety Analysis Set)

	Dose Category		
	Low Dose (N=132)	High Dose (N=112)	All Subjects (N=244)
Duration of PD since onset (years)			
n	132	112	244
Mean (SD)	12.60 (5.477)	11.86 (5.112)	12.26 (5.315)
Median	11.85	10.20	11.33
Min, Max	2.7, 32.4	2.1, 25.0	2.1, 32.4
Age at first diagnosis by a physician (years)			
n	132	112	244
Mean (SD)	53.2 (9.02)	54.4 (9.25)	53.8 (9.13)
Median	55.0	54.2	54.9
Min, Max	27, 74	37, 79	27, 79
Duration of PD since first diagnosis by a physician (years)			
n	132	112	244
Mean (SD)	10.96 (5.395)	10.33 (5.007)	10.67 (5.219)
Median	9.92	9.07	9.56
Min, Max	1.6, 32.4	2.1, 23.7	1.6, 32.4
Age at onset of motor fluctuation (years)			
n	132	111	243
Mean (SD)	57.3 (9.63)	58.5 (10.12)	57.9 (9.85)
Median	58.1	58.1	58.1
Min, Max	31, 76	39, 80	31, 80
Duration since onset of motor fluctuation (years)			
n	132	111	243
Mean (SD)	6.84 (4.877)	6.30 (4.488)	6.59 (4.701)
Median	5.88	5.05	5.25
Min, Max	0.1, 31.4	0.4, 22.9	0.1, 31.4

Note: Percentages calculated on non-missing or non-unknown values.

Program Source Code: [redacted]

TABLE 14.1 3.1

Parkinson's Disease History
(Safety Analysis Set)

	Dose Category		
	Low Dose (N=132)	High Dose (N=112)	All Subjects (N=244)
MDS-UPDRS - Part III score during 'Off' state			
n	131	111	242
Mean (SD)	46.6 (14.25)	49.0 (15.20)	47.7 (14.71)
Median	45.0	49.0	47.0
Min, Max	7, 87	19, 95	7, 95

Note: Percentages calculated on non-missing or non-unknown values.

Program Source Code: [redacted]

表9　レボドパの1日あたりの規定投与量（安全性解析対象集団）：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 2

TABLE 14.1__6.1

Daily Prescribed Dose
(Safety Analysis Set)

	N	Mean	SD	25% Quantile	Median	75% Quantile	Min / Max
Oral loading dose on day 1 - levodopa (mg LD)	233	149.0	55.68	100.0	125.0	200.0	100.0 / 300.0
ABBV-951 continuous infusion rate ('base') - LD mg/HR							
Initial CSCI prescription	244	66.3	27.75	46.1	63.2	80.3	29.0 / 152.0
End of optimization	203	76.8	29.37	56.3	71.7	95.6	29.0 / 170.8
Final prescription in 48-week maintenance period	204	80.0	31.49	56.3	76.8	99.0	29.0 / 174.2
Final prescription in study	243	79.0	30.94	56.3	76.8	97.3	29.0 / 174.2
Change from initial to end of optimization	203	10.3	16.66	0.0	6.8	18.8	-29.0 / 88.8
Change from initial to end of maintenance	204	13.6	22.11	0.0	12.0	23.9	-71.7 / 88.8
Change from initial to final	243	12.7	22.06	0.0	12.0	23.9	-73.4 / 88.8
Change from end of optimization to final	203	3.4	14.72	0.0	1.7	10.2	-56.3 / 49.5
ABBV-951 continuous infusion rate ('high') & - LD mg/HR							
Initial CSCI prescription	198	74.7	30.84	51.2	68.3	88.8	30.7 / 177.6
End of optimization	177	84.2	31.82	59.8	78.5	102.5	30.7 / 177.6
Final prescription in 48-week maintenance period	182	87.6	33.10	61.5	82.8	107.6	34.2 / 177.6
Final prescription in study	214	87.3	32.39	63.2	83.7	107.6	34.2 / 177.6
Change from initial to end of optimization	166	10.1	18.88	0.0	6.8	20.5	-35.9 / 97.3
Change from initial to end of maintenance	163	13.1	23.09	0.0	8.5	25.6	-47.8 / 97.3
Change from initial to final	192	12.4	23.52	0.0	8.5	25.6	-83.7 / 97.3
Change from end of optimization to final	172	3.2	15.00	0.0	1.7	9.4	-52.9 / 58.1

& Only for subjects whose 'high' or 'low' flow rates are allowed, non-zero and different from 'base'.
$ Only for subjects whose extra dose function is allowed (volume > 0 mL).
# Calculated as 'base' (mL/HR) * 24 HR/day * 170.75 mg LD/mL.

Program Source Code: [redacted]

TABLE 14.1 6.1

Daily Prescribed Dose
(Safety Analysis Set)

	N	Mean	SD	25% Quantile	Median	75% Quantile	Min / Max
ABBV-951 continuous infusion rate ('low') & - LD mg/HR							
Initial CSCI prescription	188	56.4	23.36	37.6	51.2	71.7	22.2 / 128.1
End of optimization	177	68.9	28.34	44.4	64.9	85.4	27.3 / 162.2
Final prescription in 48-week maintenance period	182	71.6	29.74	47.8	66.6	90.5	25.6 / 170.8
Final prescription in study	213	70.8	28.88	47.8	66.6	90.5	25.6 / 170.8
Change from initial to end of optimization	157	12.2	16.88	0.0	10.2	20.5	-47.8 / 80.3
Change from initial to end of maintenance	155	15.1	20.39	1.7	13.7	27.3	-52.9 / 80.3
Change from initial to final	184	13.9	20.69	0.0	12.0	24.8	-63.2 / 80.3
Change from end of optimization to final	175	2.8	16.59	0.0	0.0	10.2	-70.0 / 51.2
Extra dose $ - LD mg/use							
Initial CSCI prescription	227	29.79	11.128	18.78	25.61	32.44	18.78 / 51.23
End of optimization	193	33.39	11.769	25.61	32.44	40.98	18.78 / 51.23
Final prescription in 48-week maintenance period	193	33.55	11.548	25.61	32.44	40.98	18.78 / 51.23
Final prescription in study	230	33.46	11.557	25.61	32.44	40.98	18.78 / 51.23
Change from initial to end of optimization	188	3.55	9.148	0.00	0.00	6.83	-25.61 / 32.44
Change from initial to end of maintenance	188	3.81	10.381	0.00	0.00	8.54	-32.44 / 32.44
Change from initial to final	225	3.83	9.985	0.00	0.00	8.54	-32.44 / 32.44
Change from end of optimization to final	191	0.41	7.729	0.00	0.00	0.00	-32.44 / 25.61
Total daily dose # - LD mg/day							
Initial CSCI prescription	244	1591.5	666.06	1106.5	1516.3	1926.1	696.7 / 3647.2
End of optimization	203	1844.1	704.93	1352.3	1721.2	2294.9	696.7 / 4098.0
Final prescription in 48-week maintenance period	204	1919.8	755.69	1352.3	1844.1	2376.8	696.7 / 4180.0
Final prescription in study	243	1896.0	742.51	1352.3	1844.1	2335.9	696.7 / 4180.0
Change from initial to end of optimization	203	246.1	399.87	0.0	163.9	450.8	-696.7 / 2131.0
Change from initial to end of maintenance	204	326.2	530.66	0.0	286.9	573.7	-1721.2 / 2131.0
Change from initial to final	243	304.7	529.52	0.0	286.9	573.7	-1762.1 / 2131.0
Change from end of optimization to final	203	81.8	353.19	0.0	41.0	245.9	-1352.3 / 1188.4

& Only for subjects whose 'high' or 'low' flow rates are allowed, non-zero and different from 'base'.
$ Only for subjects whose extra dose function is allowed (volume > 0 mL).
# Calculated as 'base' (mL/HR) * 24 HR/day * 170.75 mg LD/mL.

Program Source Code: [redacted]

表10　レボドパの1日あたりの規定投与量（安全性解析対象集団，日本人部分集団）：M15-741試験

[redacted]20[redacted] 04:27 <[redacted]>
ABBV-951
STUDY M15-741 - SECOND INTERIM (CUTOFF [redacted]20[redacted])
R&D/20/1632 - CLINICAL/STATISTICAL

TABLE 14.1__6.1.J

Daily Prescribed Dose
(Safety Analysis Set - Japan Subjects)

	N	Mean	SD	25% Quantile	Median	75% Quantile	Min / Max
Oral loading dose on day 1 - levodopa (mg LD)	27	114.8	29.63	100.0	100.0	125.0	100.0 / 200.0
ABBV-951 continuous infusion rate ('base') - LD mg/HR							
Initial CSCI prescription	27	45.0	12.26	34.2	44.4	51.2	29.0 / 71.7
End of optimization	19	55.4	16.96	42.7	51.2	68.3	29.0 / 85.4
Final prescription in 48-week maintenance period	20	55.9	18.06	46.1	50.4	70.0	29.0 / 88.8
Final prescription in study	27	56.9	18.35	46.1	51.2	76.8	29.0 / 88.8
Change from initial to end of optimization	19	7.6	14.05	0.0	5.1	15.4	-27.3 / 39.3
Change from initial to end of maintenance	20	9.0	17.89	0.0	6.0	16.2	-34.2 / 42.7
Change from initial to final	27	11.8	18.21	0.0	6.8	22.2	-34.2 / 46.1
Change from end of optimization to final	19	1.9	14.09	-5.1	0.0	6.8	-22.2 / 37.6
ABBV-951 continuous infusion rate ('high') & - LD mg/HR							
Initial CSCI prescription	25	54.3	14.58	46.1	52.9	61.5	34.2 / 82.0
End of optimization	19	63.5	19.99	47.8	54.6	75.1	34.2 / 102.5
Final prescription in 48-week maintenance period	20	61.9	18.94	51.2	54.6	76.0	34.2 / 95.6
Final prescription in study	25	63.7	21.26	51.2	54.6	83.7	34.2 / 102.5
Change from initial to end of optimization	19	6.7	16.48	0.0	0.0	13.7	-34.1 / 47.8
Change from initial to end of maintenance	20	6.2	19.76	-0.9	3.4	10.2	-41.0 / 42.7
Change from initial to final	25	9.4	21.42	0.0	3.4	13.7	-41.0 / 56.3
Change from end of optimization to final	19	-0.2	16.49	-8.5	-1.7	6.8	-27.3 / 41.0

& Only for subjects whose 'high' or 'low' flow rates are allowed, non-zero and different from 'base'.
$ Only for subjects whose extra dose function is allowed (volume > 0 mL).
# Calculated as 'base' (mL/HR) * 24 HR/day * 170.75 mg LD/mL.

Program Source Code: [redacted]

TABLE 14.1 6.1.J

Daily Prescribed Dose
(Safety Analysis Set - Japan Subjects)

	N	Mean	SD	25% Quantile	Median	75% Quantile	Min / Max
ABBV-951 continuous infusion rate ('low') & - LD mg/HR							
Initial CSCI prescription	24	38.2	8.63	31.6	37.6	41.0	23.9 / 54.6
End of optimization	18	47.5	13.59	37.6	42.7	56.3	29.0 / 73.4
Final prescription in 48-week maintenance period	18	46.8	14.61	35.9	41.8	58.1	29.0 / 80.3
Final prescription in study	24	47.7	14.27	37.6	41.8	59.8	29.0 / 80.3
Change from initial to end of optimization	18	8.1	11.08	0.0	5.1	18.8	-13.7 / 30.7
Change from initial to end of maintenance	18	7.3	14.56	-3.4	6.0	15.4	-20.5 / 34.2
Change from initial to final	23	9.4	14.77	0.0	8.5	18.8	-20.5 / 35.9
Change from end of optimization to final	18	-0.8	10.05	-5.1	-1.7	6.8	-20.5 / 17.1
Extra dose $ - LD mg/use							
Initial CSCI prescription	25	26.16	6.515	18.78	25.61	32.44	18.78 / 32.44
End of optimization	18	28.93	7.579	25.61	29.03	32.44	18.78 / 40.98
Final prescription in 48-week maintenance period	20	29.63	9.439	25.61	25.61	32.44	18.78 / 51.23
Final prescription in study	25	30.26	8.783	25.61	32.44	32.44	18.78 / 51.23
Change from initial to end of optimization	18	2.94	3.832	0.00	0.00	6.83	0.00 / 8.54
Change from initial to end of maintenance	20	4.01	6.025	0.00	0.00	6.83	0.00 / 18.78
Change from initial to final	25	4.10	5.956	0.00	0.00	6.83	0.00 / 18.78
Change from end of optimization to final	18	1.52	4.259	0.00	0.00	0.00	-6.83 / 10.25
Total daily dose # - LD mg/day							
Initial CSCI prescription	27	1080.7	294.23	819.6	1065.5	1229.4	696.7 / 1721.2
End of optimization	19	1330.8	407.14	1024.5	1229.4	1639.2	696.7 / 2049.0
Final prescription in 48-week maintenance period	20	1342.1	433.46	1106.5	1208.9	1680.2	696.7 / 2131.0
Final prescription in study	27	1364.5	440.32	1106.5	1229.4	1844.1	696.7 / 2131.0
Change from initial to end of optimization	19	183.3	337.20	0.0	122.9	368.8	-655.7 / 942.5
Change from initial to end of maintenance	20	217.2	429.41	0.0	143.4	389.3	-819.6 / 1024.5
Change from initial to final	27	283.8	436.94	0.0	163.9	532.7	-819.6 / 1106.5
Change from end of optimization to final	19	45.3	338.18	-122.9	0.0	163.9	-532.7 / 901.6

& Only for subjects whose 'high' or 'low' flow rates are allowed, non-zero and different from 'base'.
$ Only for subjects whose extra dose function is allowed (volume > 0 mL).
# Calculated as 'base' (mL/HR) * 24 HR/day * 170.75 mg LD/mL.

Program Source Code: [redacted]

表11　規定注入速度（安全性解析対象集団）：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 14.1__6.3

Prescribed Pump Infusion Flow Rate by Category
(Safety Analysis Set)

	Base n (%)	High n (%)	Low n (%)
Modal prescribed pump infusion flow rate	N=244	N=215	N=213
FLOW RATE < 0.17 mL/hr	0	0	0
0.17 <= FLOW RATE < 0.20 mL/hr	8 (3.3)	1 (0.5)	13 (6.1)
0.20 <= FLOW RATE < 0.23 mL/hr	9 (3.7)	8 (3.7)	15 (7.0)
0.23 <= FLOW RATE < 0.26 mL/hr	9 (3.7)	5 (2.3)	14 (6.6)
0.26 <= FLOW RATE < 0.29 mL/hr	17 (7.0)	9 (4.2)	13 (6.1)
0.29 <= FLOW RATE < 0.32 mL/hr	10 (4.1)	10 (4.7)	18 (8.5)
0.32 <= FLOW RATE < 0.35 mL/hr	18 (7.4)	10 (4.7)	22 (10.3)
0.35 <= FLOW RATE < 0.38 mL/hr	22 (9.0)	16 (7.4)	12 (5.6)
0.38 <= FLOW RATE < 0.41 mL/hr	14 (5.7)	17 (7.9)	15 (7.0)
0.41 <= FLOW RATE < 0.44 mL/hr	23 (9.4)	12 (5.6)	11 (5.2)
0.44 <= FLOW RATE < 0.47 mL/hr	11 (4.5)	17 (7.9)	15 (7.0)
0.47 <= FLOW RATE < 0.50 mL/hr	11 (4.5)	11 (5.1)	7 (3.3)
0.50 <= FLOW RATE < 0.53 mL/hr	14 (5.7)	12 (5.6)	9 (4.2)
0.53 <= FLOW RATE < 0.56 mL/hr	10 (4.1)	11 (5.1)	11 (5.2)

Note: High and low columns only contain subjects whose high/low prescription is not 0.

Program Source Code: [redacted]

TABLE 14.1 6.3

Prescribed Pump Infusion Flow Rate by Category
(Safety Analysis Set)

	Base n (%)	High n (%)	Low n (%)
0.56 <= FLOW RATE < 0.59 mL/hr	15 (6.1)	9 (4.2)	9 (4.2)
0.59 <= FLOW RATE < 0.62 mL/hr	13 (5.3)	15 (7.0)	3 (1.4)
0.62 <= FLOW RATE < 0.65 mL/hr	5 (2.0)	9 (4.2)	6 (2.8)
0.65 <= FLOW RATE < 0.68 mL/hr	9 (3.7)	3 (1.4)	4 (1.9)
0.68 <= FLOW RATE < 0.71 mL/hr	7 (2.9)	10 (4.7)	7 (3.3)
0.71 <= FLOW RATE < 0.74 mL/hr	1 (0.4)	7 (3.3)	1 (0.5)
0.74 <= FLOW RATE < 0.77 mL/hr	2 (0.8)	2 (0.9)	1 (0.5)
0.77 <= FLOW RATE < 0.80 mL/hr	2 (0.8)	2 (0.9)	1 (0.5)
0.80 <= FLOW RATE < 0.83 mL/hr	4 (1.6)	2 (0.9)	3 (1.4)
0.83 <= FLOW RATE < 0.86 mL/hr	5 (2.0)	5 (2.3)	1 (0.5)
0.86 <= FLOW RATE < 0.89 mL/hr	2 (0.8)	2 (0.9)	0
0.89 <= FLOW RATE < 0.92 mL/hr	1 (0.4)	5 (2.3)	1 (0.5)
0.92 <= FLOW RATE < 0.95 mL/hr	0	1 (0.5)	0
0.95 <= FLOW RATE < 0.98 mL/hr	1 (0.4)	1 (0.5)	1 (0.5)
0.98 <= FLOW RATE < 1.01 mL/hr	1 (0.4)	2 (0.9)	0
FLOW RATE >= 1.01 mL/hr	0	1 (0.5)	0

Note: High and low columns only contain subjects whose high/low prescription is not 0.

Program Source Code: [redacted]

表12　レボドパの1日あたりの投与量（安全性解析対象集団）：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 14.1__8.1

Daily Levodopa Dose (mg LD)
(Safety Analysis Set)

		ABBV-951 CSCI			Oral			
Week		Continuous Infusion	Extra Dose	Total	Rescue Dose	Loading Dose	Total	Overall Total
WEEK 1	n	220	138	220	28	4	30	220
	Mean	1573.7	76.8	1621.9	132.1	137.5	141.7	1641.2
	SD	653.80	62.36	657.31	62.68	47.87	63.09	667.22
	Median	1440.8	56.3	1501.4	100.0	125.0	100.0	1521.0
	Min	430.3	18.8	486.6	100.0	100.0	100.0	486.6
	Max	3524.3	327.8	3562.7	300.0	200.0	300.0	3710.4
WEEK 2	n	220	155	220	33	5	36	220
	Mean	1666.6	80.7	1723.4	171.2	135.0	175.7	1752.1
	SD	657.07	62.94	660.70	93.57	41.83	89.34	670.83
	Median	1572.8	61.5	1629.4	100.0	125.0	175.0	1646.2
	Min	630.1	18.8	668.5	100.0	100.0	100.0	668.5
	Max	4072.4	368.8	4136.4	450.0	200.0	450.0	4136.4
WEEK 3	n	200	139	200	23	3	26	200
	Mean	1711.5	73.7	1762.8	134.8	100.0	130.8	1779.8
	SD	663.38	54.70	669.51	61.12	0.00	58.44	673.67
	Median	1595.9	51.2	1657.6	100.0	100.0	100.0	1665.9
	Min	686.5	18.8	686.5	100.0	100.0	100.0	686.5
	Max	4021.2	333.0	4059.6	350.0	100.0	350.0	4059.6
WEEK 4	n	192	136	192	20	0	20	192
	Mean	1770.2	66.2	1817.1	155.0		155.0	1833.3
	SD	683.36	50.10	686.98	95.83		95.83	692.36
	Median	1687.1	51.2	1740.2	100.0		100.0	1752.0
	Min	672.0	18.8	696.7	100.0		100.0	696.7
	Max	4080.9	281.7	4106.5	400.0		400.0	4106.5

Program Source Code: [redacted]

TABLE 14.1 8.1

Daily Levodopa Dose (mg LD)
(Safety Analysis Set)

Week		ABBV-951 CSCI			Oral			Overall Total
		Continuous Infusion	Extra Dose	Total	Rescue Dose	Loading Dose	Total	
WEEK 6	n	183	129	183	26	4	29	183
	Mean	1788.7	61.9	1832.3	153.8	175.0	162.1	1858.0
	SD	682.20	40.92	689.68	119.10	86.60	115.46	695.38
	Median	1721.2	48.7	1762.1	100.0	175.0	100.0	1831.5
	Min	672.0	18.8	686.5	100.0	100.0	100.0	686.5
	Max	4055.3	204.9	4119.3	600.0	250.0	600.0	4119.3
WEEK 13	n	172	116	172	30	5	34	172
	Mean	1798.7	62.3	1840.6	148.3	190.0	158.8	1872.0
	SD	714.97	48.05	718.85	157.28	54.77	148.97	731.52
	Median	1720.2	51.2	1783.0	100.0	200.0	100.0	1820.3
	Min	682.1	18.8	697.3	100.0	100.0	100.0	697.3
	Max	4098.0	307.4	4116.8	950.0	250.0	950.0	4316.8
WEEK 26	n	152	98	152	30	10	35	152
	Mean	1775.8	59.6	1814.2	135.0	145.0	157.1	1850.4
	SD	718.19	40.88	722.29	90.16	72.46	105.12	737.12
	Median	1652.9	47.8	1720.7	100.0	100.0	100.0	1765.0
	Min	669.1	18.8	705.3	100.0	100.0	100.0	705.3
	Max	4098.0	230.5	4098.0	550.0	250.0	550.0	4098.0
WEEK 39	n	128	86	128	29	7	31	128
	Mean	1755.2	67.4	1800.6	144.8	164.3	172.6	1842.3
	SD	700.91	54.07	702.85	91.95	85.22	105.55	726.50
	Median	1677.4	51.2	1726.0	100.0	100.0	100.0	1751.2
	Min	657.0	18.8	657.0	100.0	100.0	100.0	657.0
	Max	3961.4	307.4	3987.0	550.0	300.0	550.0	3987.0

Program Source Code: [redacted]

TABLE 14.1 8.1

Daily Levodopa Dose (mg LD)
(Safety Analysis Set)

Week		ABBV-951 CSCI			Oral			Overall Total
		Continuous Infusion	Extra Dose	Total	Rescue Dose	Loading Dose	Total	
WEEK 52	n	109	64	109	22	6	27	109
	Mean	1808.0	66.4	1847.0	104.5	170.8	123.1	1877.5
	SD	711.67	54.82	713.09	21.32	71.44	55.87	722.73
	Median	1719.9	49.9	1762.1	100.0	162.5	100.0	1767.4
	Min	669.1	18.8	669.1	100.0	100.0	100.0	716.5
	Max	3682.7	266.4	3721.2	200.0	250.0	300.0	3721.2

Program Source Code: [redacted]

表13　レボドパの1日あたりの投与量（安全性解析対象集団，日本人部分集団）：M15-741試験

[redacted]20[redacted] 04:27 <[redacted]>
ABBV-951
STUDY M15-741 - SECOND INTERIM (CUTOFF [redacted]20[redacted])
R&D/20/1632 - CLINICAL/STATISTICAL

TABLE 14.1__8.1.J

Daily Levodopa Dose (mg LD)
(Safety Analysis Set - Japan Subjects)

Enrollment Sample Week		ABBV-951 CSCI: Continuous Infusion	ABBV-951 CSCI: Extra Dose	ABBV-951 CSCI: Total	Oral: Rescue Dose	Oral: Loading Dose	Oral: Total	Overall Total
Sample 1								
WEEK 1	n	18	8	18	1	0	1	18
	Mean	1255.4	77.9	1290.0	100.0		100.0	1295.5
	SD	363.89	42.18	380.69	NA		NA	380.06
	Median	1195.4	81.1	1227.9	100.0		100.0	1253.5
	Min	682.1	28.2	682.1	100.0		100.0	682.1
	Max	2213.3	153.7	2294.5	100.0		100.0	2294.5
WEEK 2	n	17	9	17	2	1	2	17
	Mean	1438.9	94.1	1488.7	100.0	100.0	150.0	1506.3
	SD	276.36	64.54	310.25	0.00	NA	70.71	311.71
	Median	1354.7	81.1	1494.9	100.0	100.0	150.0	1494.9
	Min	1030.5	32.4	1030.5	100.0	100.0	100.0	1030.5
	Max	1977.8	210.9	2162.2	100.0	100.0	200.0	2262.2
WEEK 3	n	15	9	15	3	1	4	15
	Mean	1467.0	63.4	1505.0	150.0	100.0	137.5	1541.7
	SD	379.74	23.74	392.72	50.00	NA	47.87	403.15
	Median	1338.0	61.5	1370.4	150.0	100.0	125.0	1520.4
	Min	1024.5	32.4	1056.6	100.0	100.0	100.0	1056.6
	Max	2345.3	97.3	2426.4	200.0	100.0	200.0	2426.4
WEEK 4	n	11	6	11	0	0	0	11
	Mean	1483.6	78.5	1526.5				1526.5
	SD	380.31	28.87	388.68				388.68
	Median	1423.7	81.1	1423.7				1423.7
	Min	1001.1	32.4	1001.1				1001.1
	Max	2099.9	112.7	2099.9				2099.9

Program Source Code: [redacted]

TABLE 14.1 8.1.J

Daily Levodopa Dose (mg LD)
(Safety Analysis Set - Japan Subjects)

Enrollment Sample Week		ABBV-951 CSCI: Continuous Infusion	ABBV-951 CSCI: Extra Dose	ABBV-951 CSCI: Total	Oral: Rescue Dose	Oral: Loading Dose	Oral: Total	Overall Total
Sample 1 (Cont.)								
WEEK 6	n	10	6	10	2	0	2	10
	Mean	1533.5	77.8	1580.2	350.0		350.0	1650.2
	SD	450.68	22.61	457.00	353.55		353.55	532.52
	Median	1716.7	81.1	1759.1	350.0		350.0	1809.0
	Min	800.8	41.0	800.8	100.0		100.0	800.8
	Max	2179.6	102.5	2179.6	600.0		600.0	2446.7
WEEK 13	n	10	8	10	2	1	3	10
	Mean	1519.2	68.5	1574.1	525.0	200.0	416.7	1699.1
	SD	415.30	28.98	415.51	601.04	NA	464.58	461.13
	Median	1654.6	62.8	1725.0	525.0	200.0	200.0	1913.6
	Min	937.2	32.4	1034.6	100.0	200.0	100.0	1034.6
	Max	1992.7	113.5	1993.4	950.0	200.0	950.0	2193.4
WEEK 26	n	9	7	9	1	0	1	9
	Mean	1426.6	55.0	1469.4	100.0		100.0	1480.5
	SD	386.50	31.97	389.38	NA		NA	390.74
	Median	1401.5	41.0	1467.3	100.0		100.0	1567.3
	Min	932.8	25.6	997.4	100.0		100.0	997.4
	Max	1919.0	97.3	1951.4	100.0		100.0	1951.4
WEEK 39	n	6	4	6	1	0	1	6
	Mean	1450.2	81.1	1504.2	150.0		150.0	1529.2
	SD	479.65	22.95	452.92	NA		NA	488.69
	Median	1539.8	73.4	1572.7	150.0		150.0	1572.7
	Min	837.5	64.0	951.1	150.0		150.0	951.1
	Max	1930.6	113.5	2003.1	150.0		150.0	2153.1

Program Source Code: [redacted]

TABLE 14.1 8.1.J

Daily Levodopa Dose (mg LD)
(Safety Analysis Set - Japan Subjects)

Enrollment Sample Week		ABBV-951 CSCI: Continuous Infusion	ABBV-951 CSCI: Extra Dose	ABBV-951 CSCI: Total	Oral: Rescue Dose	Oral: Loading Dose	Oral: Total	Overall Total
Sample 1 (Cont.)								
WEEK 52	n	5	4	5	1	0	1	5
	Mean	1558.2	82.6	1624.3	100.0		100.0	1644.3
	SD	419.36	33.56	407.70	NA		NA	423.80
	Median	1627.5	97.3	1660.2	100.0		100.0	1660.2
	Min	856.8	32.4	954.2	100.0		100.0	954.2
	Max	1930.2	103.3	2027.5	100.0		100.0	2027.5

Program Source Code: [redacted]

TABLE 14.1 8.1.J

Daily Levodopa Dose (mg LD)
(Safety Analysis Set - Japan Subjects)

Enrollment Sample		ABBV-951 CSCI			Oral			
Week		Continuous Infusion	Extra Dose	Total	Rescue Dose	Loading Dose	Total	Overall Total
Sample 2								
WEEK 1	n	9	7	9	1	0	1	9
	Mean	945.1	57.4	989.8	200.0		200.0	1012.0
	SD	196.29	25.89	198.52	NA		NA	221.28
	Median	1007.4	65.7	1078.6	200.0		200.0	1078.6
	Min	644.1	18.8	702.3	200.0		200.0	702.3
	Max	1183.3	84.5	1220.9	200.0		200.0	1291.9
WEEK 2	n	8	8	8	0	0	0	8
	Mean	1023.9	53.7	1077.6				1077.6
	SD	205.34	26.60	219.36				219.36
	Median	1068.1	49.5	1101.0				1101.0
	Min	683.6	18.8	721.2				721.2
	Max	1311.4	89.6	1386.5				1386.5
WEEK 3	n	8	7	8	1	1	2	8
	Mean	1070.6	67.9	1130.1	100.0	100.0	100.0	1155.1
	SD	258.37	32.71	274.68	NA	NA	0.00	291.86
	Median	1093.9	61.5	1122.0	100.0	100.0	100.0	1172.0
	Min	686.5	18.8	737.7	100.0	100.0	100.0	737.7
	Max	1413.8	122.9	1488.9	100.0	100.0	100.0	1488.9
WEEK 4	n	8	8	8	0	0	0	8
	Mean	1118.0	57.1	1175.1				1175.1
	SD	333.19	31.82	341.05				341.05
	Median	1174.2	53.8	1198.5				1198.5
	Min	672.0	18.8	709.6				709.6
	Max	1638.0	102.5	1694.4				1694.4

Program Source Code: [redacted]

TABLE 14.1 8.1.J

Daily Levodopa Dose (mg LD)
(Safety Analysis Set - Japan Subjects)

Enrollment Sample Week		ABBV-951 CSCI: Continuous Infusion	ABBV-951 CSCI: Extra Dose	ABBV-951 CSCI: Total	Oral: Rescue Dose	Oral: Loading Dose	Oral: Total	Overall Total
Sample 2 (Cont.)								
WEEK 6	n	8	7	8	1	0	1	8
	Mean	1133.9	55.9	1182.8	100.0		100.0	1195.3
	SD	349.28	39.18	357.13	NA		NA	338.73
	Median	1106.5	51.2	1148.2	100.0		100.0	1148.2
	Min	672.0	18.8	690.8	100.0		100.0	779.6
	Max	1617.9	122.9	1646.0	100.0		100.0	1646.0
WEEK 13	n	8	8	8	1	0	1	8
	Mean	1058.5	66.4	1124.9	100.0		100.0	1137.4
	SD	200.18	28.24	221.80	NA		NA	197.15
	Median	1083.1	64.0	1145.1	100.0		100.0	1145.1
	Min	682.1	37.6	719.7	100.0		100.0	819.7
	Max	1324.2	102.5	1426.6	100.0		100.0	1426.6
WEEK 26	n	8	7	8	3	0	3	8
	Mean	1083.3	91.2	1163.1	100.0		100.0	1200.6
	SD	290.92	56.78	343.02	0.00		0.00	383.06
	Median	1038.5	76.8	1102.5	100.0		100.0	1140.2
	Min	669.1	37.6	706.6	100.0		100.0	706.6
	Max	1610.5	179.3	1764.2	100.0		100.0	1864.2
WEEK 39	n	8	7	8	0	0	0	8
	Mean	1120.3	78.9	1189.4				1189.4
	SD	325.58	46.71	365.02				365.02
	Median	1053.4	64.0	1091.8				1091.8
	Min	672.0	18.8	690.8				690.8
	Max	1788.9	153.7	1917.0				1917.0

Program Source Code: [redacted]

TABLE 14.1 8.1.J

Daily Levodopa Dose (mg LD)
(Safety Analysis Set - Japan Subjects)

Enrollment Sample Week		ABBV-951 CSCI: Continuous Infusion	ABBV-951 CSCI: Extra Dose	ABBV-951 CSCI: Total	Oral: Rescue Dose	Oral: Loading Dose	Oral: Total	Overall Total
Sample 2 (Cont.)								
WEEK 52	n	7	5	7	0	0	0	7
	Mean	1150.2	115.1	1232.4				1232.4
	SD	302.98	77.58	360.00				360.00
	Median	1099.5	89.6	1099.5				1099.5
	Min	689.4	37.6	727.0				727.0
	Max	1686.0	230.5	1839.7				1839.7

Program Source Code: [redacted]

TABLE 14.1 8.1.J

Daily Levodopa Dose (mg LD)
(Safety Analysis Set - Japan Subjects)

Enrollment Sample	Week	ABBV-951 CSCI: Continuous Infusion	ABBV-951 CSCI: Extra Dose	ABBV-951 CSCI: Total	Oral: Rescue Dose	Oral: Loading Dose	Oral: Total	Overall Total
Both Enrollment Samples								
WEEK 1	n	27	15	27	2	0	2	27
	Mean	1151.9	68.4	1189.9	150.0		150.0	1201.0
	SD	347.35	35.90	357.33	70.71		70.71	357.86
	Median	1121.1	76.8	1162.2	150.0		150.0	1220.9
	Min	644.1	18.8	682.1	100.0		100.0	682.1
	Max	2213.3	153.7	2294.5	200.0		200.0	2294.5
WEEK 2	n	25	17	25	2	1	2	25
	Mean	1306.1	75.1	1357.1	100.0	100.0	150.0	1369.1
	SD	319.75	53.15	341.33	0.00	NA	70.71	347.09
	Median	1292.2	64.9	1343.5	100.0	100.0	150.0	1343.5
	Min	683.6	18.8	721.2	100.0	100.0	100.0	721.2
	Max	1977.8	210.9	2162.2	100.0	100.0	200.0	2262.2
WEEK 3	n	23	16	23	4	2	6	23
	Mean	1329.1	65.4	1374.6	137.5	100.0	125.0	1407.2
	SD	387.65	27.09	394.34	47.87	0.00	41.83	407.41
	Median	1221.7	61.5	1303.9	125.0	100.0	100.0	1403.9
	Min	686.5	18.8	737.7	100.0	100.0	100.0	737.7
	Max	2345.3	122.9	2426.4	200.0	100.0	200.0	2426.4
WEEK 4	n	19	14	19	0	0	0	19
	Mean	1329.7	66.3	1378.5				1378.5
	SD	397.39	31.42	401.15				401.15
	Median	1258.6	71.3	1329.5				1329.5
	Min	672.0	18.8	709.6				709.6
	Max	2099.9	112.7	2099.9				2099.9

Program Source Code: [redacted]

TABLE 14.1 8.1.J

Daily Levodopa Dose (mg LD)
(Safety Analysis Set - Japan Subjects)

Enrollment Sample	Week	ABBV-951 CSCI: Continuous Infusion	ABBV-951 CSCI: Extra Dose	ABBV-951 CSCI: Total	Oral: Rescue Dose	Oral: Loading Dose	Oral: Total	Overall Total
Both Enrollment Samples (Cont.)								
WEEK 6	n	18	13	18	3	0	3	18
	Mean	1355.9	66.0	1403.6	266.7		266.7	1448.0
	SD	446.68	33.32	452.09	288.68		288.68	501.49
	Median	1391.4	64.0	1468.8	100.0		100.0	1468.8
	Min	672.0	18.8	690.8	100.0		100.0	779.6
	Max	2179.6	122.9	2179.6	600.0		600.0	2446.7
WEEK 13	n	18	16	18	3	1	4	18
	Mean	1314.5	67.4	1374.4	383.3	200.0	337.5	1449.4
	SD	404.12	27.66	405.48	490.75	NA	411.05	459.42
	Median	1138.0	62.8	1213.8	100.0	200.0	150.0	1277.6
	Min	682.1	32.4	719.7	100.0	200.0	100.0	819.7
	Max	1992.7	113.5	1993.4	950.0	200.0	950.0	2193.4
WEEK 26	n	17	14	17	4	0	4	17
	Mean	1265.0	73.1	1325.3	100.0		100.0	1348.8
	SD	378.05	48.09	390.02	0.00		0.00	401.58
	Median	1065.5	58.5	1167.4	100.0		100.0	1192.1
	Min	669.1	25.6	706.6	100.0		100.0	706.6
	Max	1919.0	179.3	1951.4	100.0		100.0	1951.4
WEEK 39	n	14	11	14	1	0	1	14
	Mean	1261.7	79.7	1324.3	150.0		150.0	1335.0
	SD	417.44	38.32	420.46	NA		NA	440.52
	Median	1082.3	65.7	1144.2	150.0		150.0	1144.2
	Min	672.0	18.8	690.8	150.0		150.0	690.8
	Max	1930.6	153.7	2003.1	150.0		150.0	2153.1

Program Source Code: [redacted]

TABLE 14.1 8.1.J

Daily Levodopa Dose (mg LD)
(Safety Analysis Set - Japan Subjects)

Enrollment Sample	Week	ABBV-951 CSCI: Continuous Infusion	ABBV-951 CSCI: Extra Dose	ABBV-951 CSCI: Total	Oral: Rescue Dose	Oral: Loading Dose	Oral: Total	Overall Total
Both Enrollment Samples (Cont.)								
	WEEK 52 n	12	9	12	1	0	1	12
	Mean	1320.2	100.6	1395.7	100.0		100.0	1404.1
	SD	397.69	61.03	414.54	NA		NA	425.42
	Median	1245.9	97.3	1406.0	100.0		100.0	1406.0
	Min	689.4	32.4	727.0	100.0		100.0	727.0
	Max	1930.2	230.5	2027.5	100.0		100.0	2027.5

Program Source Code: [redacted]

表14　レボドパの1日あたりの最頻投与量（安全性解析対象集団）：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 2

TABLE 14.1__8.2

Modal Daily Levodopa Dose by Dose Range Category
(Safety Analysis Set)

Categories (mg LD)	CSCI + Extra (N=244) n (%)	CSCI + Extra + Rescue + Loading Oral (N=244) n (%)
< 500	0	0
500 - < 600	0	0
600 - < 700	7 (2.9)	7 (2.9)
700 - < 800	4 (1.6)	4 (1.6)
800 - < 900	7 (2.9)	7 (2.9)
900 - < 1000	12 (4.9)	12 (4.9)
1000 - < 1100	9 (3.7)	9 (3.7)
1100 - < 1200	14 (5.7)	13 (5.3)
1200 - < 1300	10 (4.1)	10 (4.1)
1300 - < 1400	17 (7.0)	17 (7.0)
1400 - < 1500	10 (4.1)	9 (3.7)
1500 - < 1600	14 (5.7)	16 (6.6)
1600 - < 1700	16 (6.6)	15 (6.1)
1700 - < 1800	12 (4.9)	13 (5.3)
1800 - < 1900	16 (6.6)	16 (6.6)
1900 - < 2000	11 (4.5)	8 (3.3)
2000 - < 2100	9 (3.7)	12 (4.9)
2100 - < 2200	11 (4.5)	11 (4.5)
2200 - < 2300	9 (3.7)	8 (3.3)
2300 - < 2400	5 (2.0)	6 (2.5)
2400 - < 2500	10 (4.1)	10 (4.1)
2500 - < 2600	5 (2.0)	5 (2.0)
2600 - < 2700	7 (2.9)	7 (2.9)
2700 - < 2800	7 (2.9)	7 (2.9)
2800 - < 2900	5 (2.0)	5 (2.0)
2900 - < 3000	1 (0.4)	1 (0.4)
3000 - < 3100	1 (0.4)	1 (0.4)
3100 - < 3200	3 (1.2)	3 (1.2)

Program Source Code: [redacted]

TABLE 14.1 8.2

Modal Daily Levodopa Dose by Dose Range Category
(Safety Analysis Set)

Categories (mg LD)	CSCI + Extra (N=244) n (%)	CSCI + Extra + Rescue + Loading Oral (N=244) n (%)
3200 - < 3300	4 (1.6)	4 (1.6)
3300 - < 3400	2 (0.8)	2 (0.8)
3400 - < 3500	1 (0.4)	1 (0.4)
3500 - < 3600	1 (0.4)	1 (0.4)
3600 - < 3700	2 (0.8)	2 (0.8)
3700 - < 3800	0	0
3800 - < 3900	0	0
3900 - < 4000	1 (0.4)	1 (0.4)
4000 - < 4100	1 (0.4)	1 (0.4)
4100 - < 4200	0	0
4200 - < 4300	0	0
>= 4300	0	0

Program Source Code: [redacted]

表15　ABBV-951及び併用薬のレボドパ換算1日投与量（安全性解析対象集団）：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 14.1__8.3

Daily Levodopa Equivalent Dose (mg) from ABBV-951 and All Concomitant Medications
(Safety Analysis Set)

Week		ABBV-951 (CSCI + Extra)	LED from Concomitant Medications	Total
WEEK 1	n	220	118	220
	Mean	1621.9	788.9	2045.0
	SD	657.31	853.77	1041.67
	Median	1501.4	564.0	1839.0
	Min	486.6	4.0	682.1
	Max	3562.7	5101.6	8346.9
WEEK 2	n	220	70	220
	Mean	1723.4	377.9	1843.6
	SD	660.70	313.75	693.63
	Median	1629.4	275.0	1765.8
	Min	668.5	2.0	668.5
	Max	4136.4	1620.0	4136.4
WEEK 3	n	200	55	200
	Mean	1762.8	416.1	1877.2
	SD	669.51	391.88	723.00
	Median	1657.6	300.0	1813.0
	Min	686.5	2.0	686.5
	Max	4059.6	2200.0	4308.2
WEEK 4	n	192	51	192
	Mean	1817.1	438.0	1933.5
	SD	686.98	437.97	743.82
	Median	1740.2	300.0	1865.1
	Min	696.7	2.0	696.7
	Max	4106.5	2200.0	4109.2

Program Source Code: [redacted]

TABLE 14.1 8.3

Daily Levodopa Equivalent Dose (mg) from ABBV-951 and All Concomitant Medications
(Safety Analysis Set)

Week		ABBV-951 (CSCI + Extra)	LED from Concomitant Medications	Total
WEEK 6	n	183	49	183
	Mean	1832.3	465.9	1957.0
	SD	689.68	435.81	743.13
	Median	1762.1	260.0	1916.0
	Min	686.5	80.0	686.5
	Max	4119.3	1720.0	4468.3
WEEK 13	n	172	44	172
	Mean	1840.6	807.3	2047.1
	SD	718.85	1096.42	1036.79
	Median	1783.0	372.5	1933.7
	Min	697.3	80.0	697.3
	Max	4116.8	6500.0	10616.8
WEEK 26	n	152	35	152
	Mean	1814.2	858.5	2011.9
	SD	722.29	1389.38	1009.62
	Median	1720.7	360.0	1823.5
	Min	705.3	100.0	705.3
	Max	4098.0	6745.0	7857.9
WEEK 39	n	128	22	128
	Mean	1800.6	864.7	1949.2
	SD	702.85	1342.38	967.95
	Median	1726.0	240.0	1767.2
	Min	657.0	100.0	657.0
	Max	3987.0	5320.0	7491.9

Program Source Code: [redacted]

TABLE 14.1 8.3

Daily Levodopa Equivalent Dose (mg) from ABBV-951 and All Concomitant Medications
(Safety Analysis Set)

Week		ABBV-951 (CSCI + Extra)	LED from Concomitant Medications	Total
WEEK 52	n	109	20	109
	Mean	1847.0	546.1	1947.2
	SD	713.09	539.99	801.57
	Median	1762.1	330.0	1830.1
	Min	669.1	40.0	669.1
	Max	3721.2	2150.0	4537.1

Program Source Code: [redacted]

表16　治験薬曝露期間（安全性解析対象集団）：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 14.1__10

Duration of Study Drug Exposure
(Safety Analysis Set)

	Dose Category		
	Low Dose (N=132)	High Dose (N=112)	All Subjects (N=244)
Duration of ABBV-951 exposure (days) &			
n	132	112	244
Mean (SD)	229.1 (151.37)	230.5 (146.68)	229.7 (148.93)
Median	328.0	281.5	307.5
Min, Max	3, 438	4, 389	3, 438
By time intervals - n(%) &			
1 - 7 Days	5 (3.8)	2 (1.8)	7 (2.9)
8 - 14 Days	3 (2.3)	7 (6.3)	10 (4.1)
15 - 21 Days	10 (7.6)	3 (2.7)	13 (5.3)
22 - 28 Days	3 (2.3)	5 (4.5)	8 (3.3)
29 - 42 Days	7 (5.3)	4 (3.6)	11 (4.5)
43 - 91 Days	10 (7.6)	10 (8.9)	20 (8.2)
92 - 182 Days	18 (13.6)	14 (12.5)	32 (13.1)
183 - 273 Days	7 (5.3)	10 (8.9)	17 (7.0)
>= 274 Days	69 (52.3)	57 (50.9)	126 (51.6)
At least 6 months (>= 180 days)	77 (58.3)	68 (60.7)	145 (59.4)
At least 1 year (>= 360 days)	61 (46.2)	51 (45.5)	112 (45.9)
Patient-years of exposure &	82.8	70.7	153.5

Note: Percentages calculated on non-missing values.
&: Duration of ABBV-951 exposure (days) = Date of ABBV-951 stopped - Date of ABBV-951 started + 1.
*: Duration of ABBV-951 exposure (days) excluding study drug interruption = Duration of ABBV-951 exposure (days) - Duration of interruption (days).

Program Source Code: [redacted]

TABLE 14.1 10

Duration of Study Drug Exposure
(Safety Analysis Set)

	Dose Category		
	Low Dose (N=132)	High Dose (N=112)	All Subjects (N=244)
Duration of ABBV-951 exposure (days) without interruption *			
n	132	112	244
Mean (SD)	221.6 (151.91)	226.0 (147.13)	223.6 (149.45)
Median	305.5	280.5	292.0
Min, Max	3, 438	4, 389	3, 438
By time intervals - n(%) *			
1 - 7 Days	7 (5.3)	2 (1.8)	9 (3.7)
8 - 14 Days	2 (1.5)	7 (6.3)	9 (3.7)
15 - 21 Days	9 (6.8)	4 (3.6)	13 (5.3)
22 - 28 Days	4 (3.0)	4 (3.6)	8 (3.3)
29 - 42 Days	9 (6.8)	4 (3.6)	13 (5.3)
43 - 91 Days	10 (7.6)	11 (9.8)	21 (8.6)
92 - 182 Days	19 (14.4)	17 (15.2)	36 (14.8)
183 - 273 Days	4 (3.0)	7 (6.3)	11 (4.5)
>= 274 Days	68 (51.5)	56 (50.0)	124 (50.8)
At least 6 months (>= 180 days)	73 (55.3)	64 (57.1)	137 (56.1)
At least 1 year (>= 360 days)	50 (37.9)	48 (42.9)	98 (40.2)
Patient-years of exposure *	80.1	69.3	149.4

Note: Percentages calculated on non-missing values.
&: Duration of ABBV-951 exposure (days) = Date of ABBV-951 stopped - Date of ABBV-951 started + 1.
*: Duration of ABBV-951 exposure (days) excluding study drug interruption = Duration of ABBV-951 exposure (days) - Duration of interruption (days).

Program Source Code: [redacted]

表17　治験薬曝露期間（安全性解析対象集団，日本人部分集団）：M15-741試験

[redacted]20[redacted] 04:28 <[redacted]>
ABBV-951
STUDY M15-741 - SECOND INTERIM (CUTOFF [redacted]20[redacted])
R&D/20/1632 - CLINICAL/STATISTICAL

TABLE 14.1__10.J

Duration of Study Drug Exposure
(Safety Analysis Set - Japan Subjects)

	Dose Category		
	Low Dose (N=22)	High Dose (N=5)	All Subjects (N=27)
Duration of ABBV-951 exposure (days) &			
n	22	5	27
Mean (SD)	193.0 (155.09)	226.4 (189.34)	199.2 (158.49)
Median	178.5	364.0	190.0
Min, Max	3, 366	17, 365	3, 366
By time intervals - n(%) &			
1 - 7 Days	1 (4.5)	0	1 (3.7)
8 - 14 Days	1 (4.5)	0	1 (3.7)
15 - 21 Days	2 (9.1)	2 (40.0)	4 (14.8)
22 - 28 Days	1 (4.5)	0	1 (3.7)
29 - 42 Days	2 (9.1)	0	2 (7.4)
43 - 91 Days	1 (4.5)	0	1 (3.7)
92 - 182 Days	3 (13.6)	0	3 (11.1)
183 - 273 Days	2 (9.1)	0	2 (7.4)
>= 274 Days	9 (40.9)	3 (60.0)	12 (44.4)
At least 6 months (>= 180 days)	11 (50.0)	3 (60.0)	14 (51.9)
At least 1 year (>= 360 days)	8 (36.4)	3 (60.0)	11 (40.7)
Patient-years of exposure &	11.6	3.1	14.7

Note: Percentages calculated on non-missing values.
&: Duration of ABBV-951 exposure (days) = Date of ABBV-951 stopped - Date of ABBV-951 started + 1.
*: Duration of ABBV-951 exposure (days) excluding study drug interruption = Duration of ABBV-951 exposure (days) - Duration of interruption (days).

Program Source Code: [redacted]

TABLE 14.1 10.J

Duration of Study Drug Exposure
(Safety Analysis Set - Japan Subjects)

	Dose Category		
	Low Dose (N=22)	High Dose (N=5)	All Subjects (N=27)
Duration of ABBV-951 exposure (days) without interruption *			
n	22	5	27
Mean (SD)	179.8 (152.13)	226.0 (188.97)	188.3 (156.59)
Median	143.0	363.0	167.0
Min, Max	3, 366	17, 365	3, 366
By time intervals - n(%) *			
1 - 7 Days	1 (4.5)	0	1 (3.7)
8 - 14 Days	1 (4.5)	0	1 (3.7)
15 - 21 Days	2 (9.1)	2 (40.0)	4 (14.8)
22 - 28 Days	1 (4.5)	0	1 (3.7)
29 - 42 Days	3 (13.6)	0	3 (11.1)
43 - 91 Days	1 (4.5)	0	1 (3.7)
92 - 182 Days	4 (18.2)	0	4 (14.8)
183 - 273 Days	0	0	0
>= 274 Days	9 (40.9)	3 (60.0)	12 (44.4)
At least 6 months (>= 180 days)	9 (40.9)	3 (60.0)	12 (44.4)
At least 1 year (>= 360 days)	6 (27.3)	3 (60.0)	9 (33.3)
Patient-years of exposure *	10.8	3.1	13.9

Note: Percentages calculated on non-missing values.
&: Duration of ABBV-951 exposure (days) = Date of ABBV-951 stopped - Date of ABBV-951 started + 1.
*: Duration of ABBV-951 exposure (days) excluding study drug interruption = Duration of ABBV-951 exposure (days) - Duration of interruption (days).

Program Source Code: [redacted]

表18　治験薬投与中断理由（安全性解析対象集団）：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 1

TABLE 14.1__12.1

All Reasons for Infusion Interruption
(Safety Analysis Set)

	Total
Total number of subjects with any interruptions	89
By all reasons	
COVID-19 infection	0
COVID-19 logistical restrictions	3
Pump malfunction	20
Adverse event (not COVID-19 infection)	38
Other	47

Note: One subject can be counted multiple times.

Program Source Code: [redacted]

表19　治験薬投与中断理由（安全性解析対象集団，日本人部分集団）：M15-741試験

[redacted]20[redacted] 04:27 <[redacted]>
ABBV-951
STUDY M15-741 - SECOND INTERIM (CUTOFF [redacted]20[redacted])
R&D/20/1632 - CLINICAL/STATISTICAL
TABLE PAGE 1 OF 1

TABLE 14.1__12.1.J

All Reasons for Infusion Interruption
(Safety Analysis Set - Japan Subjects)

	Total
Total number of subjects with any interruptions	9
By all reasons	
COVID-19 infection	0
COVID-19 logistical restrictions	0
Pump malfunction	1
Adverse event (not COVID-19 infection)	3
Other	6

Note: One subject can be counted multiple times.

Program Source Code: [redacted]

表20　治験薬投与中断期間（安全性解析対象集団）：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 14.1__12.2

Duration of Infusion Interruption
(Safety Analysis Set)

	Dose Category		
	Low Dose (N=132)	High Dose (N=112)	All Subjects (N=244)
Duration of ABBV-951 interruption (days)			
n	59	33	92
Mean (SD)	14.95 (37.096)	12.71 (29.245)	14.15 (34.336)
Median	1.20	0.88	1.00
Min, Max	0.0, 246.9	0.0, 121.0	0.0, 246.9
By time intervals - n(%)			
< 1 day	27 (45.8)	17 (51.5)	44 (47.8)
1 - < 2 days	8 (13.6)	6 (18.2)	14 (15.2)
2 - < 3 days	1 (1.7)	1 (3.0)	2 (2.2)
3 - < 4 days	1 (1.7)	2 (6.1)	3 (3.3)
4 - < 5 days	3 (5.1)	0	3 (3.3)
5 - < 10 days	4 (6.8)	1 (3.0)	5 (5.4)
10 - < 20 days	3 (5.1)	0	3 (3.3)
20 - < 30 days	4 (6.8)	1 (3.0)	5 (5.4)
>= 30 days	8 (13.6)	5 (15.2)	13 (14.1)

Program Source Code: [redacted]

表21　パーキンソン病日誌に基づく，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22　パーキンソン病日誌に基づく，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	Change from Baseline: 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	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	Change from Baseline: 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	Change from Baseline: 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	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	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	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	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	Change from Baseline: 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	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	Change from Baseline: 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	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	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	Change from Baseline: 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	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23　パーキンソン病日誌に基づく，早朝覚醒時状態の分布（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__1.5

Distribution of Early Morning First Non-Sleep Symptom in PD Diary
(FAS)

	N	Off n (%)	On without Dyskinesia n (%)	On with Non-Troublesome Dyskinesia n (%)	On with Troublesome Dyskinesia n (%)	Total n (%)
BASELINE	238	129 (77.7)	29 (17.5)	5 (3.0)	3 (1.8)	166 (100)
Low Dose	129	68 (76.4)	15 (16.9)	3 (3.4)	3 (3.4)	89 (100)
High Dose	109	61 (79.2)	14 (18.2)	2 (2.6)	0	77 (100)
WEEK 1	231	49 (31.0)	79 (50.0)	20 (12.7)	10 (6.3)	158 (100)
Low Dose	125	25 (29.1)	38 (44.2)	16 (18.6)	7 (8.1)	86 (100)
High Dose	106	24 (33.3)	41 (56.9)	4 (5.6)	3 (4.2)	72 (100)
WEEK 6	213	54 (30.9)	104 (59.4)	14 (8.0)	3 (1.7)	175 (100)
Low Dose	116	23 (23.5)	61 (62.2)	11 (11.2)	3 (3.1)	98 (100)
High Dose	97	31 (40.3)	43 (55.8)	3 (3.9)	0	77 (100)
WEEK 13	123	27 (28.4)	60 (63.2)	7 (7.4)	1 (1.1)	95 (100)
Low Dose	68	15 (28.3)	32 (60.4)	6 (11.3)	0	53 (100)
High Dose	55	12 (28.6)	28 (66.7)	1 (2.4)	1 (2.4)	42 (100)
WEEK 26	134	19 (19.4)	66 (67.3)	12 (12.2)	1 (1.0)	98 (100)
Low Dose	71	9 (18.0)	35 (70.0)	6 (12.0)	0	50 (100)
High Dose	63	10 (20.8)	31 (64.6)	6 (12.5)	1 (2.1)	48 (100)
WEEK 39	119	20 (24.1)	58 (69.9)	5 (6.0)	0	83 (100)
Low Dose	67	11 (24.4)	31 (68.9)	3 (6.7)	0	45 (100)
High Dose	52	9 (23.7)	27 (71.1)	2 (5.3)	0	38 (100)
WEEK 52	106	20 (27.0)	48 (64.9)	4 (5.4)	2 (2.7)	74 (100)
Low Dose	59	13 (31.0)	25 (59.5)	2 (4.8)	2 (4.8)	42 (100)
High Dose	47	7 (21.9)	23 (71.9)	2 (6.3)	0	32 (100)

Program Source Code: [redacted]

表24　パーキンソン病日誌に基づく，早朝覚醒時状態の分布（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__1.5.J

Distribution of Early Morning First Non-Sleep Symptom in PD Diary
(FAS - Japan Subjects)

	N	Off n (%)	On without Dyskinesia n (%)	On with Non-Troublesome Dyskinesia n (%)	On with Troublesome Dyskinesia n (%)	Total n (%)
BASELINE	27	14 (93.3)	0	0	1 (6.7)	15 (100)
Low Dose	22	11 (91.7)	0	0	1 (8.3)	12 (100)
High Dose	5	3 (100)	0	0	0	3 (100)
WEEK 1	26	5 (29.4)	7 (41.2)	4 (23.5)	1 (5.9)	17 (100)
Low Dose	21	4 (28.6)	5 (35.7)	4 (28.6)	1 (7.1)	14 (100)
High Dose	5	1 (33.3)	2 (66.7)	0	0	3 (100)
WEEK 6	24	10 (52.6)	7 (36.8)	2 (10.5)	0	19 (100)
Low Dose	19	7 (43.8)	7 (43.8)	2 (12.5)	0	16 (100)
High Dose	5	3 (100)	0	0	0	3 (100)
WEEK 13	10	5 (55.6)	4 (44.4)	0	0	9 (100)
Low Dose	10	5 (55.6)	4 (44.4)	0	0	9 (100)
High Dose	0	0	0	0	0	0
WEEK 26	15	3 (33.3)	4 (44.4)	2 (22.2)	0	9 (100)
Low Dose	12	3 (33.3)	4 (44.4)	2 (22.2)	0	9 (100)
High Dose	3	0	0	0	0	0
WEEK 39	14	3 (37.5)	5 (62.5)	0	0	8 (100)
Low Dose	11	3 (37.5)	5 (62.5)	0	0	8 (100)
High Dose	3	0	0	0	0	0
WEEK 52	12	5 (55.6)	4 (44.4)	0	0	9 (100)
Low Dose	9	3 (42.9)	4 (57.1)	0	0	7 (100)
High Dose	3	2 (100)	0	0	0	2 (100)

Program Source Code: [redacted]

表25　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	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	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26　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27　MDS-UPDRSスコア（Hoehn-Yahr 重症度分類，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__2.2

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 Hoehn and Yahr Stage
(FAS)

Parameter Time Point Dose Category	N	Baseline Mean	Visit Mean (SD)	Median	Min, Max	Change from Baseline Mean (SD)	Median	Min, Max	P-Value &
MDS-UPDRS Hoehn and Yahr Stage									
BASELINE	244		2.2 (0.68)	2.0	0, 5				
Low dose	132		2.2 (0.61)	2.0	1, 5				
High dose	112		2.2 (0.74)	2.0	0, 5				
DAY 2	222	2.2	2.2 (0.67)	2.0	0, 5	-0.0 (0.52)	0.0	-2, 2	0.4398
Low dose	121	2.2	2.2 (0.65)	2.0	0, 5	-0.0 (0.47)	0.0	-2, 2	0.5659
High dose	101	2.3	2.2 (0.69)	2.0	1, 4	-0.0 (0.57)	0.0	-2, 2	0.6040
WEEK 1	224	2.2	2.2 (0.73)	2.0	1, 5	0.0 (0.61)	0.0	-2, 3	0.3839
Low dose	119	2.2	2.2 (0.64)	2.0	1, 5	0.0 (0.58)	0.0	-2, 3	0.7533
High dose	105	2.2	2.3 (0.82)	2.0	1, 5	0.1 (0.65)	0.0	-2, 2	0.3682
WEEK 2	211	2.2	2.2 (0.74)	2.0	0, 5	0.1 (0.64)	0.0	-2, 3	0.2016
Low dose	118	2.2	2.3 (0.79)	2.0	0, 5	0.1 (0.70)	0.0	-2, 3	0.1155
High dose	93	2.2	2.2 (0.69)	2.0	0, 5	0.0 (0.57)	0.0	-2, 2	>0.999
WEEK 3	203	2.2	2.2 (0.69)	2.0	0, 5	-0.0 (0.64)	0.0	-3, 3	0.3783
Low dose	108	2.2	2.1 (0.72)	2.0	0, 5	-0.0 (0.68)	0.0	-3, 3	0.6703
High dose	95	2.2	2.2 (0.66)	2.0	1, 5	-0.1 (0.59)	0.0	-2, 1	0.3869
WEEK 4	201	2.2	2.2 (0.70)	2.0	0, 5	0.0 (0.69)	0.0	-2, 3	0.9186
Low dose	109	2.2	2.2 (0.78)	2.0	0, 5	0.0 (0.73)	0.0	-2, 3	0.6930
High dose	92	2.2	2.2 (0.58)	2.0	1, 4	-0.0 (0.65)	0.0	-2, 2	0.7475

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

Program Source Code: [redacted]

TABLE 14.2 2.2

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 Hoehn and Yahr Stage
(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 Hoehn and Yahr Stage									
WEEK 6	192	2.2	2.1 (0.76)	2.0	0, 5	-0.1 (0.68)	0.0	-2, 3	0.0747
Low dose	105	2.2	2.2 (0.81)	2.0	0, 5	0.0 (0.69)	0.0	-2, 3	>0.999
High dose	87	2.2	2.0 (0.70)	2.0	0, 4	-0.2 (0.66)	0.0	-2, 1	0.0072**
WEEK 13	160	2.2	2.1 (0.82)	2.0	0, 5	-0.1 (0.78)	0.0	-4, 2	0.1923
Low dose	90	2.1	2.1 (0.82)	2.0	0, 5	-0.1 (0.72)	0.0	-2, 2	0.4689
High dose	70	2.2	2.1 (0.84)	2.0	0, 5	-0.1 (0.86)	0.0	-4, 1	0.2703
WEEK 26	134	2.2	2.1 (0.88)	2.0	0, 5	-0.1 (0.86)	0.0	-4, 2	0.1623
Low dose	71	2.2	2.2 (0.97)	2.0	0, 5	-0.1 (0.81)	0.0	-2, 2	0.5591
High dose	63	2.2	2.0 (0.76)	2.0	0, 4	-0.2 (0.92)	0.0	-4, 2	0.1755
WEEK 39	116	2.2	2.1 (0.75)	2.0	0, 5	-0.0 (0.73)	0.0	-2, 2	0.5244
Low dose	68	2.1	2.2 (0.76)	2.0	0, 5	0.1 (0.62)	0.0	-2, 2	0.4368
High dose	48	2.3	2.1 (0.74)	2.0	0, 4	-0.2 (0.84)	0.0	-2, 1	0.1295
WEEK 52	108	2.1	2.1 (0.68)	2.0	0, 5	-0.0 (0.68)	0.0	-2, 1	0.7788
Low dose	60	2.1	2.1 (0.68)	2.0	0, 5	0.0 (0.61)	0.0	-2, 1	0.6735
High dose	48	2.2	2.1 (0.70)	2.0	0, 4	-0.1 (0.77)	0.0	-2, 1	0.4555

&: P-value is 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28　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	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	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29　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30　PDQ-39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__4

Change from Baseline to Each Planned Visit in Quality of Life as Assessed
by The PD Questionnaire-39 Items
(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 &
PDQ-39 Summary Index Total Score									
BASELINE	243		34.5 (15.01)	32.7	4.5, 79.5				
Low dose	132		34.2 (16.27)	31.4	4.5, 79.5				
High dose	111		34.8 (13.41)	34.0	6.4, 61.5				
WEEK 6	196	33.7	26.0 (15.09)	25.0	1.9, 76.3	-7.6 (12.81)	-8.3	-44.6, 42.9	<=0.001***
Low dose	106	33.0	26.1 (16.06)	26.0	1.9, 76.3	-6.9 (14.53)	-8.7	-44.6, 42.9	<=0.001***
High dose	90	34.5	25.9 (13.94)	24.7	1.9, 57.7	-8.5 (10.45)	-8.3	-29.5, 19.2	<=0.001***
WEEK 13	168	34.0	25.8 (15.04)	25.6	0.0, 69.9	-8.2 (13.61)	-8.3	-58.2, 42.9	<=0.001***
Low dose	92	33.0	24.8 (16.32)	21.2	0.0, 69.9	-8.1 (15.35)	-7.7	-58.2, 42.9	<=0.001***
High dose	76	35.3	27.1 (13.33)	27.2	1.9, 55.1	-8.3 (11.24)	-9.0	-26.9, 21.8	<=0.001***
WEEK 26	141	34.6	27.2 (14.85)	25.0	3.2, 61.5	-7.4 (12.15)	-7.7	-53.2, 27.6	<=0.001***
Low dose	75	33.5	26.3 (15.03)	24.4	3.2, 61.5	-7.1 (12.38)	-7.7	-41.0, 27.6	<=0.001***
High dose	66	35.9	28.3 (14.70)	28.2	3.2, 57.7	-7.6 (11.97)	-8.4	-53.2, 22.4	<=0.001***
WEEK 39	123	33.7	26.0 (15.90)	23.7	0.0, 65.4	-7.7 (13.88)	-7.7	-53.2, 34.0	<=0.001***
Low dose	69	33.0	25.2 (15.82)	23.7	1.3, 65.4	-7.7 (14.15)	-7.7	-48.7, 34.0	<=0.001***
High dose	54	34.6	27.1 (16.10)	25.0	0.0, 64.1	-7.6 (13.66)	-7.1	-53.2, 30.1	<=0.001***
WEEK 52	107	32.5	26.8 (16.85)	23.7	3.2, 76.9	-5.7 (13.17)	-5.8	-49.2, 25.0	<=0.001***
Low dose	60	32.1	26.7 (17.10)	23.7	3.2, 64.1	-5.4 (14.49)	-3.2	-49.2, 25.0	0.0052**
High dose	47	33.0	27.0 (16.71)	25.0	3.2, 76.9	-6.0 (11.41)	-6.9	-24.4, 20.5	<=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 4

Change from Baseline to Each Planned Visit in Quality of Life as Assessed
by The PD Questionnaire-39 Items
(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 &
PDQ-39 Mobility Domain Score									
BASELINE	243		45.9 (24.94)	45.0	2.5, 95.0				
Low dose	132		45.0 (25.73)	42.5	2.5, 95.0				
High dose	111		47.0 (24.03)	47.5	2.5, 92.5				
WEEK 6	196	45.3	33.5 (24.98)	27.5	0.0, 100.0	-11.8 (20.74)	-12.5	-77.5, 65.0	<=0.001***
Low dose	106	43.4	33.4 (25.51)	27.5	0.0, 100.0	-10.0 (23.28)	-11.3	-77.5, 65.0	<=0.001***
High dose	90	47.5	33.6 (24.47)	28.8	0.0, 87.5	-13.9 (17.16)	-12.5	-60.0, 30.0	<=0.001***
WEEK 13	168	45.1	32.5 (25.45)	27.5	0.0, 97.5	-12.6 (21.92)	-12.5	-82.5, 67.5	<=0.001***
Low dose	92	43.5	30.7 (25.47)	26.3	0.0, 97.5	-12.8 (23.90)	-12.5	-82.5, 67.5	<=0.001***
High dose	76	47.2	34.8 (25.39)	31.3	0.0, 90.0	-12.4 (19.41)	-10.0	-70.0, 25.0	<=0.001***
WEEK 26	141	45.7	34.0 (24.55)	30.0	0.0, 92.5	-11.7 (19.95)	-10.0	-67.5, 57.5	<=0.001***
Low dose	75	44.5	33.9 (24.00)	27.5	0.0, 87.5	-10.6 (20.83)	-10.0	-67.5, 57.5	<=0.001***
High dose	66	47.1	34.2 (25.33)	30.0	0.0, 92.5	-12.9 (18.99)	-10.0	-57.5, 57.5	<=0.001***
WEEK 39	123	43.9	31.6 (24.68)	25.0	0.0, 97.5	-12.3 (21.13)	-12.5	-67.5, 62.5	<=0.001***
Low dose	69	43.0	31.3 (24.29)	27.5	0.0, 97.5	-11.8 (21.52)	-12.5	-57.5, 62.5	<=0.001***
High dose	54	44.9	31.9 (25.39)	25.0	0.0, 85.0	-13.0 (20.79)	-11.3	-67.5, 30.0	<=0.001***
WEEK 52	107	42.5	33.8 (25.64)	27.5	0.0, 100.0	-8.7 (19.73)	-5.0	-67.5, 57.5	<=0.001***
Low dose	60	41.8	33.2 (25.65)	26.3	0.0, 92.5	-8.6 (21.08)	-5.0	-67.5, 57.5	0.0025**
High dose	47	43.5	34.5 (25.88)	32.5	0.0, 100.0	-8.9 (18.06)	-2.5	-45.0, 32.5	0.0014**

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

Program Source Code: [redacted]

TABLE 14.2 4

Change from Baseline to Each Planned Visit in Quality of Life as Assessed
by The PD Questionnaire-39 Items
(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 &
PDQ-39 Activities of Daily Living Domain Score									
BASELINE	243		40.7 (22.11)	37.5	0.0, 100.0				
Low dose	132		39.8 (23.33)	37.5	0.0, 100.0				
High dose	111		41.7 (20.62)	37.5	0.0, 91.7				
WEEK 6	196	39.7	30.2 (21.74)	29.2	0.0, 100.0	-9.5 (21.16)	-12.5	-70.8, 75.0	<=0.001***
Low dose	106	38.2	30.4 (22.04)	29.2	0.0, 100.0	-7.8 (22.53)	-6.3	-70.8, 75.0	<=0.001***
High dose	90	41.4	30.0 (21.49)	25.0	0.0, 100.0	-11.5 (19.36)	-12.5	-54.2, 58.3	<=0.001***
WEEK 13	168	40.4	30.3 (22.56)	25.0	0.0, 100.0	-10.2 (21.80)	-10.4	-75.0, 58.3	<=0.001***
Low dose	92	37.8	29.2 (23.08)	25.0	0.0, 91.7	-8.6 (24.24)	-4.2	-75.0, 58.3	0.0010**
High dose	76	43.6	31.5 (22.01)	27.1	4.2, 100.0	-12.1 (18.41)	-12.5	-50.0, 29.2	<=0.001***
WEEK 26	141	41.0	29.6 (20.52)	25.0	0.0, 100.0	-11.4 (18.97)	-8.3	-54.2, 37.5	<=0.001***
Low dose	75	39.2	29.4 (20.06)	25.0	0.0, 87.5	-9.8 (19.14)	-8.3	-54.2, 37.5	<=0.001***
High dose	66	43.1	29.7 (21.18)	25.0	0.0, 100.0	-13.3 (18.74)	-12.5	-54.2, 25.0	<=0.001***
WEEK 39	123	40.4	29.4 (20.82)	25.0	0.0, 87.5	-10.9 (21.76)	-8.3	-79.2, 41.7	<=0.001***
Low dose	69	39.4	29.0 (20.90)	25.0	0.0, 87.5	-10.4 (23.62)	-8.3	-79.2, 41.7	<=0.001***
High dose	54	41.7	30.0 (20.91)	25.0	0.0, 79.2	-11.7 (19.33)	-8.3	-58.3, 41.7	<=0.001***
WEEK 52	107	38.8	30.0 (22.02)	25.0	0.0, 87.5	-8.8 (20.01)	-8.3	-70.8, 37.5	<=0.001***
Low dose	60	37.3	30.6 (23.15)	29.2	0.0, 87.5	-6.7 (21.96)	-4.2	-70.8, 37.5	0.0220*
High dose	47	40.7	29.3 (20.70)	25.0	0.0, 87.5	-11.4 (17.06)	-12.5	-54.2, 25.0	<=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 4

Change from Baseline to Each Planned Visit in Quality of Life as Assessed
by The PD Questionnaire-39 Items
(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 &
PDQ-39 Emotional Well-being Domain Score									
BASELINE	243		30.3 (20.66)	25.0	0.0, 95.8				
Low dose	132		31.4 (21.68)	27.1	0.0, 95.8				
High dose	111		29.0 (19.39)	25.0	0.0, 87.5				
WEEK 6	196	29.4	26.4 (18.97)	25.0	0.0, 87.5	-3.0 (17.97)	-4.2	-58.3, 66.7	0.0206*
Low dose	106	30.0	26.5 (19.01)	25.0	0.0, 87.5	-3.6 (20.13)	-8.3	-58.3, 66.7	0.0702
High dose	90	28.7	26.4 (19.03)	20.8	0.0, 70.8	-2.3 (15.12)	-2.1	-37.5, 37.5	0.1500
WEEK 13	168	30.1	25.8 (17.95)	25.0	0.0, 83.3	-4.3 (17.43)	-4.2	-62.5, 50.0	0.0018**
Low dose	92	30.7	24.8 (19.11)	22.9	0.0, 83.3	-5.9 (17.64)	-4.2	-62.5, 41.7	0.0019**
High dose	76	29.4	27.1 (16.48)	25.0	0.0, 66.7	-2.3 (17.10)	-2.1	-54.2, 50.0	0.2441
WEEK 26	141	30.9	28.4 (20.37)	25.0	0.0, 91.7	-2.4 (16.45)	0.0	-66.7, 33.3	0.0825
Low dose	75	30.6	26.7 (20.11)	25.0	0.0, 91.7	-3.9 (18.04)	-4.2	-50.0, 33.3	0.0658
High dose	66	31.1	30.4 (20.63)	27.1	0.0, 75.0	-0.8 (14.40)	0.0	-66.7, 29.2	0.6704
WEEK 39	123	30.7	26.9 (19.73)	25.0	0.0, 75.0	-3.9 (18.69)	0.0	-66.7, 41.7	0.0236*
Low dose	69	31.0	26.3 (19.56)	20.8	0.0, 75.0	-4.6 (19.42)	-4.2	-62.5, 41.7	0.0507
High dose	54	30.4	27.5 (20.10)	25.0	0.0, 70.8	-2.9 (17.84)	0.0	-66.7, 37.5	0.2449
WEEK 52	107	29.1	26.7 (19.87)	25.0	0.0, 79.2	-2.4 (19.38)	0.0	-54.2, 50.0	0.2004
Low dose	60	30.3	26.8 (19.65)	27.1	0.0, 75.0	-3.5 (18.38)	0.0	-54.2, 45.8	0.1408
High dose	47	27.6	26.6 (20.35)	25.0	0.0, 79.2	-1.0 (20.71)	0.0	-50.0, 50.0	0.7483

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

Program Source Code: [redacted]

TABLE 14.2 4

Change from Baseline to Each Planned Visit in Quality of Life as Assessed
by The PD Questionnaire-39 Items
(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 &
PDQ-39 Stigma Domain Score									
BASELINE	243		24.7 (23.82)	18.8	0.0, 100.0				
Low dose	132		26.1 (24.61)	18.8	0.0, 100.0				
High dose	111		23.1 (22.84)	12.5	0.0, 75.0				
WEEK 6	196	23.5	17.1 (19.75)	12.5	0.0, 75.0	-6.4 (19.74)	-6.3	-68.8, 56.3	<=0.001***
Low dose	106	24.5	18.3 (21.43)	12.5	0.0, 75.0	-6.1 (21.02)	-6.3	-56.3, 56.3	0.0033**
High dose	90	22.3	15.6 (17.56)	12.5	0.0, 75.0	-6.7 (18.22)	0.0	-68.8, 56.3	<=0.001***
WEEK 13	168	23.7	15.9 (19.34)	12.5	0.0, 100.0	-7.8 (20.26)	-6.3	-87.5, 75.0	<=0.001***
Low dose	92	23.5	16.8 (20.12)	12.5	0.0, 100.0	-6.7 (20.88)	-6.3	-87.5, 56.3	0.0029**
High dose	76	23.9	14.7 (18.42)	9.4	0.0, 93.8	-9.2 (19.54)	-6.3	-62.5, 75.0	<=0.001***
WEEK 26	141	23.8	17.2 (20.56)	12.5	0.0, 87.5	-6.6 (19.89)	-6.3	-75.0, 68.8	<=0.001***
Low dose	75	21.8	16.1 (17.80)	12.5	0.0, 75.0	-5.8 (19.65)	-6.3	-50.0, 68.8	0.0134*
High dose	66	26.0	18.5 (23.37)	6.3	0.0, 87.5	-7.6 (20.26)	0.0	-75.0, 37.5	0.0034**
WEEK 39	123	22.6	15.8 (19.56)	12.5	0.0, 81.3	-6.8 (21.43)	-6.3	-75.0, 62.5	<=0.001***
Low dose	69	21.9	16.4 (17.55)	12.5	0.0, 62.5	-5.5 (20.21)	-6.3	-75.0, 50.0	0.0263*
High dose	54	23.5	15.0 (22.01)	6.3	0.0, 81.3	-8.4 (22.98)	-6.3	-75.0, 62.5	0.0092**
WEEK 52	107	22.0	15.5 (20.07)	6.3	0.0, 75.0	-6.4 (20.43)	0.0	-75.0, 50.0	0.0015**
Low dose	60	21.8	16.7 (18.44)	12.5	0.0, 62.5	-5.1 (23.23)	0.0	-75.0, 50.0	0.0940
High dose	47	22.2	14.1 (22.10)	0.0	0.0, 75.0	-8.1 (16.27)	-6.3	-50.0, 31.3	0.0013**

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

Program Source Code: [redacted]

TABLE 14.2 4

Change from Baseline to Each Planned Visit in Quality of Life as Assessed
by The PD Questionnaire-39 Items
(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 &
PDQ-39 Social Support Domain Score									
BASELINE	218		12.4 (16.94)	8.3	0.0, 83.3				
Low dose	118		12.6 (18.19)	8.3	0.0, 83.3				
High dose	100		12.2 (15.42)	8.3	0.0, 58.3				
WEEK 6	174	11.4	10.6 (15.14)	0.0	0.0, 83.3	-0.8 (14.19)	0.0	-41.7, 66.7	0.4500
Low dose	93	11.6	10.8 (15.43)	0.0	0.0, 66.7	-0.8 (13.35)	0.0	-33.3, 33.3	0.5616
High dose	81	11.2	10.4 (14.88)	0.0	0.0, 83.3	-0.8 (15.17)	0.0	-41.7, 66.7	0.6267
WEEK 13	151	12.4	10.8 (15.54)	0.0	0.0, 75.0	-1.5 (17.01)	0.0	-58.3, 58.3	0.2660
Low dose	80	12.4	13.5 (18.34)	8.3	0.0, 75.0	1.1 (18.22)	0.0	-58.3, 58.3	0.5753
High dose	71	12.3	7.7 (10.94)	0.0	0.0, 41.7	-4.6 (15.09)	0.0	-50.0, 33.3	0.0128*
WEEK 26	127	13.5	14.3 (16.99)	8.3	0.0, 75.0	0.8 (14.71)	0.0	-41.7, 41.7	0.5476
Low dose	66	13.6	14.1 (17.72)	8.3	0.0, 66.7	0.5 (14.46)	0.0	-33.3, 33.3	0.7775
High dose	61	13.4	14.5 (16.31)	8.3	0.0, 75.0	1.1 (15.10)	0.0	-41.7, 41.7	0.5739
WEEK 39	108	12.6	14.0 (18.57)	8.3	0.0, 66.7	1.5 (14.45)	0.0	-33.3, 41.7	0.2940
Low dose	59	13.6	13.8 (18.67)	8.3	0.0, 66.7	0.3 (13.40)	0.0	-33.3, 33.3	0.8719
High dose	49	11.4	14.3 (18.63)	8.3	0.0, 66.7	2.9 (15.64)	0.0	-33.3, 41.7	0.2019
WEEK 52	92	11.9	13.5 (18.57)	8.3	0.0, 75.0	1.6 (16.90)	0.0	-41.7, 66.7	0.3574
Low dose	49	12.8	14.6 (19.88)	8.3	0.0, 75.0	1.9 (15.89)	0.0	-41.7, 50.0	0.4140
High dose	43	10.9	12.2 (17.09)	0.0	0.0, 66.7	1.4 (18.18)	0.0	-33.3, 66.7	0.6271

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

Program Source Code: [redacted]

TABLE 14.2 4

Change from Baseline to Each Planned Visit in Quality of Life as Assessed
by The PD Questionnaire-39 Items
(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 &
PDQ-39 Cognition Domain Score									
BASELINE	243		26.8 (17.24)	25.0	0.0, 81.3				
Low dose	132		26.8 (17.75)	25.0	0.0, 81.3				
High dose	111		26.9 (16.68)	25.0	0.0, 68.8				
WEEK 6	196	26.3	21.8 (19.15)	18.8	0.0, 87.5	-4.5 (18.88)	-6.3	-50.0, 56.3	0.0011**
Low dose	106	25.9	22.1 (21.01)	12.5	0.0, 87.5	-3.9 (20.07)	-6.3	-50.0, 56.3	0.0485*
High dose	90	26.7	21.5 (16.82)	18.8	0.0, 81.3	-5.1 (17.47)	-6.3	-37.5, 56.3	0.0064**
WEEK 13	168	27.2	24.6 (18.68)	18.8	0.0, 75.0	-2.6 (17.11)	-6.3	-56.3, 50.0	0.0470*
Low dose	92	27.1	24.0 (20.24)	18.8	0.0, 75.0	-3.1 (17.93)	-6.3	-56.3, 50.0	0.1054
High dose	76	27.4	25.2 (16.72)	25.0	0.0, 75.0	-2.1 (16.16)	0.0	-37.5, 37.5	0.2522
WEEK 26	141	27.5	26.6 (17.72)	25.0	0.0, 75.0	-0.9 (16.76)	0.0	-50.0, 43.8	0.5311
Low dose	75	26.9	25.8 (18.94)	18.8	0.0, 75.0	-1.2 (16.69)	0.0	-43.8, 43.8	0.5467
High dose	66	28.2	27.7 (16.30)	25.0	0.0, 75.0	-0.6 (16.97)	0.0	-50.0, 37.5	0.7865
WEEK 39	123	27.2	25.6 (18.61)	25.0	0.0, 75.0	-1.6 (17.73)	0.0	-50.0, 68.8	0.3111
Low dose	69	26.3	23.0 (17.76)	18.8	0.0, 75.0	-3.3 (18.52)	0.0	-50.0, 68.8	0.1482
High dose	54	28.4	28.8 (19.33)	25.0	0.0, 68.8	0.5 (16.60)	0.0	-50.0, 37.5	0.8384
WEEK 52	107	26.1	24.9 (18.29)	25.0	0.0, 81.3	-1.2 (17.00)	0.0	-56.3, 56.3	0.4788
Low dose	60	25.7	23.9 (17.36)	18.8	0.0, 62.5	-1.9 (18.10)	0.0	-56.3, 56.3	0.4254
High dose	47	26.5	26.2 (19.53)	25.0	0.0, 81.3	-0.3 (15.64)	0.0	-50.0, 37.5	0.9077

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

Program Source Code: [redacted]

TABLE 14.2 4

Change from Baseline to Each Planned Visit in Quality of Life as Assessed
by The PD Questionnaire-39 Items
(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 &
PDQ-39 Communication Domain Score									
BASELINE	243		27.9 (21.82)	25.0	0.0, 100.0				
Low dose	132		26.3 (22.48)	25.0	0.0, 100.0				
High dose	111		29.9 (20.95)	25.0	0.0, 83.3				
WEEK 6	196	26.8	21.7 (20.52)	16.7	0.0, 83.3	-5.1 (19.58)	0.0	-83.3, 58.3	<=0.001***
Low dose	106	25.2	20.2 (21.82)	16.7	0.0, 83.3	-5.0 (20.30)	0.0	-83.3, 58.3	0.0122*
High dose	90	28.7	23.5 (18.85)	16.7	0.0, 66.7	-5.2 (18.80)	0.0	-58.3, 50.0	0.0105*
WEEK 13	168	27.3	21.8 (19.15)	16.7	0.0, 91.7	-5.5 (18.71)	0.0	-58.3, 41.7	<=0.001***
Low dose	92	24.5	17.3 (17.22)	12.5	0.0, 66.7	-7.2 (17.37)	-4.2	-58.3, 33.3	<=0.001***
High dose	76	30.8	27.3 (20.03)	25.0	0.0, 91.7	-3.5 (20.15)	0.0	-58.3, 41.7	0.1332
WEEK 26	141	28.6	22.2 (21.07)	16.7	0.0, 83.3	-6.4 (21.14)	0.0	-75.0, 50.0	<=0.001***
Low dose	75	26.0	18.3 (18.43)	16.7	0.0, 66.7	-7.7 (18.72)	-8.3	-75.0, 33.3	<=0.001***
High dose	66	31.6	26.6 (23.08)	20.8	0.0, 83.3	-4.9 (23.66)	0.0	-75.0, 50.0	0.0957
WEEK 39	123	29.4	24.7 (22.10)	16.7	0.0, 91.7	-4.7 (20.16)	0.0	-75.0, 50.0	0.0113*
Low dose	69	25.7	21.7 (22.10)	16.7	0.0, 91.7	-4.0 (18.45)	0.0	-66.7, 50.0	0.0772
High dose	54	34.1	28.5 (21.69)	25.0	0.0, 75.0	-5.6 (22.31)	0.0	-75.0, 33.3	0.0729
WEEK 52	107	27.9	26.0 (21.86)	25.0	0.0, 83.3	-1.9 (21.36)	0.0	-66.7, 41.7	0.3675
Low dose	60	25.8	24.0 (22.03)	16.7	0.0, 75.0	-1.8 (20.65)	0.0	-66.7, 41.7	0.5008
High dose	47	30.5	28.5 (21.62)	25.0	0.0, 83.3	-2.0 (22.47)	0.0	-66.7, 41.7	0.5547

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

Program Source Code: [redacted]

TABLE 14.2 4

Change from Baseline to Each Planned Visit in Quality of Life as Assessed
by The PD Questionnaire-39 Items
(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 &
PDQ-39 Bodily Discomfort Domain Score									
BASELINE	243		42.9 (22.42)	41.7	0.0, 100.0				
Low dose	132		41.9 (23.65)	41.7	0.0, 100.0				
High dose	111		44.1 (20.91)	41.7	0.0, 91.7				
WEEK 6	196	42.1	28.6 (21.63)	25.0	0.0, 100.0	-13.5 (23.84)	-16.7	-66.7, 66.7	<=0.001***
Low dose	106	41.5	29.2 (20.93)	25.0	0.0, 75.0	-12.3 (24.32)	-8.3	-66.7, 66.7	<=0.001***
High dose	90	42.8	28.0 (22.53)	25.0	0.0, 100.0	-14.8 (23.33)	-16.7	-66.7, 50.0	<=0.001***
WEEK 13	168	41.7	28.5 (21.20)	25.0	0.0, 91.7	-13.2 (24.27)	-16.7	-66.7, 50.0	<=0.001***
Low dose	92	40.9	28.0 (20.06)	33.3	0.0, 75.0	-12.9 (25.90)	-8.3	-66.7, 50.0	<=0.001***
High dose	76	42.8	29.1 (22.63)	25.0	0.0, 91.7	-13.7 (22.31)	-16.7	-66.7, 41.7	<=0.001***
WEEK 26	141	41.9	29.6 (22.04)	25.0	0.0, 91.7	-12.4 (20.76)	-8.3	-58.3, 41.7	<=0.001***
Low dose	75	41.8	29.3 (23.58)	25.0	0.0, 91.7	-12.4 (21.15)	-8.3	-50.0, 33.3	<=0.001***
High dose	66	42.0	29.8 (20.31)	25.0	0.0, 83.3	-12.2 (20.48)	-16.7	-58.3, 41.7	<=0.001***
WEEK 39	123	39.6	27.0 (20.84)	25.0	0.0, 100.0	-12.6 (21.13)	-16.7	-66.7, 58.3	<=0.001***
Low dose	69	40.3	26.3 (21.28)	25.0	0.0, 91.7	-14.0 (23.24)	-16.7	-66.7, 58.3	<=0.001***
High dose	54	38.7	27.9 (20.42)	25.0	0.0, 100.0	-10.8 (18.14)	-8.3	-41.7, 33.3	<=0.001***
WEEK 52	107	39.5	29.3 (23.24)	25.0	0.0, 91.7	-10.2 (21.45)	-8.3	-66.7, 50.0	<=0.001***
Low dose	60	39.6	29.2 (22.47)	25.0	0.0, 91.7	-10.4 (22.79)	-8.3	-66.7, 50.0	<=0.001***
High dose	47	39.4	29.4 (24.44)	25.0	0.0, 91.7	-9.9 (19.86)	-8.3	-41.7, 33.3	0.0013**

&: P-value is 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31　EQ-5D-5L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__5

Change from Baseline to Each Planned Visit in Health-Related Quality of Life as Assessed by EQ-5D-5L
(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 &
EQ-5D-5L Mobility									
BASELINE	229		2.8 (1.08)	3.0	1.0, 5.0				
Low dose	125		2.8 (1.11)	3.0	1.0, 5.0				
High dose	104		2.9 (1.03)	3.0	1.0, 5.0				
WEEK 6	175	2.8	2.0 (0.99)	2.0	1.0, 5.0	-0.7 (1.18)	-1.0	-4.0, 3.0	<=0.001***
Low dose	93	2.7	2.1 (1.05)	2.0	1.0, 5.0	-0.6 (1.21)	-1.0	-3.0, 3.0	<=0.001***
High dose	82	2.8	2.0 (0.92)	2.0	1.0, 5.0	-0.8 (1.15)	-1.0	-4.0, 2.0	<=0.001***
WEEK 13	144	2.7	2.1 (0.99)	2.0	1.0, 5.0	-0.7 (1.20)	-1.0	-4.0, 2.0	<=0.001***
Low dose	78	2.7	2.1 (1.04)	2.0	1.0, 5.0	-0.6 (1.16)	-1.0	-3.0, 2.0	<=0.001***
High dose	66	2.8	2.0 (0.93)	2.0	1.0, 4.0	-0.7 (1.25)	-1.0	-4.0, 2.0	<=0.001***
WEEK 26	122	2.7	2.0 (0.93)	2.0	1.0, 5.0	-0.8 (1.17)	-1.0	-3.0, 2.0	<=0.001***
Low dose	66	2.8	2.0 (0.98)	2.0	1.0, 5.0	-0.7 (1.17)	-1.0	-3.0, 1.0	<=0.001***
High dose	56	2.7	1.9 (0.87)	2.0	1.0, 4.0	-0.8 (1.17)	-1.0	-3.0, 2.0	<=0.001***
WEEK 39	108	2.7	2.1 (0.93)	2.0	1.0, 4.0	-0.6 (1.16)	-1.0	-3.0, 2.0	<=0.001***
Low dose	65	2.7	2.1 (1.00)	2.0	1.0, 4.0	-0.6 (1.25)	0.0	-3.0, 2.0	<=0.001***
High dose	43	2.8	2.0 (0.82)	2.0	1.0, 4.0	-0.7 (1.01)	-1.0	-3.0, 1.0	<=0.001***
WEEK 52	100	2.7	2.0 (1.01)	2.0	1.0, 5.0	-0.7 (1.28)	-1.0	-4.0, 2.0	<=0.001***
Low dose	57	2.6	2.0 (1.06)	2.0	1.0, 5.0	-0.6 (1.29)	-1.0	-4.0, 2.0	<=0.001***
High dose	43	2.7	2.0 (0.96)	2.0	1.0, 5.0	-0.7 (1.29)	-1.0	-4.0, 2.0	0.0013**

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

Program Source Code: [redacted]

TABLE 14.2 5

Change from Baseline to Each Planned Visit in Health-Related Quality of Life as Assessed by EQ-5D-5L
(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 &
EQ-5D-5L Self-care									
BASELINE	229		2.3 (1.03)	2.0	1.0, 5.0				
Low dose	125		2.3 (1.07)	2.0	1.0, 5.0				
High dose	104		2.3 (0.99)	2.0	1.0, 5.0				
WEEK 6	175	2.2	1.8 (0.86)	2.0	1.0, 5.0	-0.3 (1.09)	0.0	-4.0, 3.0	<=0.001***
Low dose	93	2.2	1.9 (0.94)	2.0	1.0, 5.0	-0.3 (1.12)	0.0	-3.0, 3.0	0.0234*
High dose	82	2.2	1.8 (0.77)	2.0	1.0, 4.0	-0.4 (1.06)	0.0	-4.0, 2.0	<=0.001***
WEEK 13	144	2.2	1.9 (0.92)	2.0	1.0, 5.0	-0.4 (1.07)	0.0	-4.0, 3.0	<=0.001***
Low dose	78	2.2	1.9 (0.94)	2.0	1.0, 5.0	-0.4 (1.05)	0.0	-3.0, 2.0	0.0024**
High dose	66	2.2	1.9 (0.89)	2.0	1.0, 4.0	-0.3 (1.10)	0.0	-4.0, 3.0	0.0165*
WEEK 26	122	2.3	1.7 (0.80)	2.0	1.0, 5.0	-0.5 (1.10)	0.0	-4.0, 2.0	<=0.001***
Low dose	66	2.3	1.8 (0.86)	2.0	1.0, 5.0	-0.5 (1.22)	0.0	-4.0, 2.0	0.0014**
High dose	56	2.3	1.7 (0.73)	2.0	1.0, 3.0	-0.6 (0.95)	-0.5	-3.0, 1.0	<=0.001***
WEEK 39	108	2.3	1.8 (0.80)	2.0	1.0, 4.0	-0.5 (1.11)	0.0	-4.0, 2.0	<=0.001***
Low dose	65	2.2	1.8 (0.78)	2.0	1.0, 4.0	-0.4 (1.13)	0.0	-3.0, 2.0	0.0058**
High dose	43	2.3	1.7 (0.83)	2.0	1.0, 4.0	-0.6 (1.10)	0.0	-4.0, 1.0	0.0012**
WEEK 52	100	2.2	1.7 (0.82)	2.0	1.0, 4.0	-0.4 (1.23)	0.0	-4.0, 3.0	<=0.001***
Low dose	57	2.2	1.8 (0.77)	2.0	1.0, 4.0	-0.4 (1.26)	0.0	-3.0, 3.0	0.0401*
High dose	43	2.2	1.7 (0.90)	1.0	1.0, 4.0	-0.5 (1.20)	0.0	-4.0, 2.0	0.0056**

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

Program Source Code: [redacted]

TABLE 14.2 5

Change from Baseline to Each Planned Visit in Health-Related Quality of Life as Assessed by EQ-5D-5L
(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 &
EQ-5D-5L Usual Activities									
BASELINE	229		2.8 (1.05)	3.0	1.0, 5.0				
Low dose	125		2.7 (1.11)	3.0	1.0, 5.0				
High dose	104		2.9 (0.96)	3.0	1.0, 5.0				
WEEK 6	175	2.7	2.2 (0.91)	2.0	1.0, 5.0	-0.6 (1.06)	0.0	-4.0, 2.0	<=0.001***
Low dose	93	2.6	2.2 (1.02)	2.0	1.0, 5.0	-0.4 (1.09)	0.0	-3.0, 2.0	<=0.001***
High dose	82	2.8	2.1 (0.78)	2.0	1.0, 4.0	-0.7 (1.01)	-1.0	-4.0, 1.0	<=0.001***
WEEK 13	144	2.7	2.1 (1.02)	2.0	1.0, 5.0	-0.6 (1.24)	-1.0	-4.0, 4.0	<=0.001***
Low dose	78	2.6	2.2 (1.09)	2.0	1.0, 5.0	-0.5 (1.27)	0.0	-3.0, 4.0	0.0019**
High dose	66	2.9	2.1 (0.94)	2.0	1.0, 4.0	-0.8 (1.19)	-1.0	-4.0, 3.0	<=0.001***
WEEK 26	122	2.8	2.1 (0.86)	2.0	1.0, 5.0	-0.7 (1.07)	-1.0	-3.0, 2.0	<=0.001***
Low dose	66	2.7	2.2 (0.92)	2.0	1.0, 5.0	-0.5 (1.14)	0.0	-3.0, 2.0	0.0014**
High dose	56	2.9	2.0 (0.79)	2.0	1.0, 4.0	-0.9 (0.94)	-1.0	-3.0, 1.0	<=0.001***
WEEK 39	108	2.8	2.0 (0.86)	2.0	1.0, 4.0	-0.8 (1.12)	-1.0	-3.0, 2.0	<=0.001***
Low dose	65	2.7	2.0 (0.83)	2.0	1.0, 4.0	-0.6 (1.13)	-1.0	-3.0, 2.0	<=0.001***
High dose	43	3.0	1.9 (0.92)	2.0	1.0, 4.0	-1.1 (1.08)	-1.0	-3.0, 1.0	<=0.001***
WEEK 52	100	2.8	2.1 (0.97)	2.0	1.0, 5.0	-0.6 (1.23)	-1.0	-4.0, 2.0	<=0.001***
Low dose	57	2.6	2.2 (0.99)	2.0	1.0, 5.0	-0.4 (1.19)	0.0	-3.0, 1.0	0.0101*
High dose	43	2.9	2.1 (0.96)	2.0	1.0, 5.0	-0.9 (1.25)	-1.0	-4.0, 2.0	<=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 5

Change from Baseline to Each Planned Visit in Health-Related Quality of Life as Assessed by EQ-5D-5L
(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 &
EQ-5D-5L Pain/Discomfort									
BASELINE	229		2.4 (1.04)	2.0	1.0, 5.0				
Low dose	125		2.3 (1.07)	2.0	1.0, 5.0				
High dose	104		2.5 (0.99)	3.0	1.0, 5.0				
WEEK 6	175	2.4	1.9 (0.85)	2.0	1.0, 5.0	-0.5 (1.14)	0.0	-4.0, 3.0	<=0.001***
Low dose	93	2.4	2.0 (0.88)	2.0	1.0, 5.0	-0.4 (1.20)	0.0	-4.0, 3.0	0.0032**
High dose	82	2.5	1.9 (0.81)	2.0	1.0, 4.0	-0.6 (1.08)	0.0	-3.0, 2.0	<=0.001***
WEEK 13	144	2.4	1.9 (0.88)	2.0	1.0, 4.0	-0.5 (1.21)	0.0	-4.0, 2.0	<=0.001***
Low dose	78	2.3	1.9 (0.89)	2.0	1.0, 4.0	-0.4 (1.17)	0.0	-4.0, 2.0	0.0065**
High dose	66	2.5	2.0 (0.88)	2.0	1.0, 4.0	-0.6 (1.24)	-0.5	-4.0, 2.0	<=0.001***
WEEK 26	122	2.3	1.9 (0.90)	2.0	1.0, 5.0	-0.5 (1.22)	0.0	-4.0, 2.0	<=0.001***
Low dose	66	2.3	1.9 (0.94)	2.0	1.0, 5.0	-0.4 (1.14)	0.0	-4.0, 2.0	0.0035**
High dose	56	2.4	1.9 (0.85)	2.0	1.0, 4.0	-0.5 (1.32)	-1.0	-4.0, 2.0	0.0085**
WEEK 39	108	2.3	1.9 (0.79)	2.0	1.0, 4.0	-0.4 (1.18)	0.0	-4.0, 2.0	<=0.001***
Low dose	65	2.2	1.9 (0.85)	2.0	1.0, 4.0	-0.3 (1.17)	0.0	-4.0, 2.0	0.0381*
High dose	43	2.3	1.8 (0.70)	2.0	1.0, 4.0	-0.5 (1.20)	0.0	-4.0, 2.0	0.0079**
WEEK 52	100	2.2	1.9 (0.90)	2.0	1.0, 5.0	-0.3 (1.23)	0.0	-4.0, 3.0	0.0107*
Low dose	57	2.2	1.9 (0.90)	2.0	1.0, 5.0	-0.3 (1.11)	0.0	-4.0, 1.0	0.0790
High dose	43	2.2	1.8 (0.91)	2.0	1.0, 4.0	-0.4 (1.38)	0.0	-4.0, 3.0	0.0677

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

Program Source Code: [redacted]

TABLE 14.2 5

Change from Baseline to Each Planned Visit in Health-Related Quality of Life as Assessed by EQ-5D-5L
(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 &
EQ-5D-5L Anxiety/Depression									
BASELINE	229		1.9 (0.91)	2.0	1.0, 4.0				
Low dose	125		1.8 (0.91)	2.0	1.0, 4.0				
High dose	104		2.0 (0.90)	2.0	1.0, 4.0				
WEEK 6	175	1.8	1.7 (0.83)	2.0	1.0, 5.0	-0.1 (1.02)	0.0	-2.0, 4.0	0.1853
Low dose	93	1.7	1.7 (0.88)	2.0	1.0, 5.0	0.0 (1.07)	0.0	-2.0, 4.0	0.7715
High dose	82	1.9	1.7 (0.77)	2.0	1.0, 4.0	-0.3 (0.95)	0.0	-2.0, 3.0	0.0172*
WEEK 13	144	1.9	1.7 (0.82)	2.0	1.0, 5.0	-0.1 (0.93)	0.0	-2.0, 4.0	0.0747
Low dose	78	1.8	1.8 (0.88)	2.0	1.0, 5.0	0.0 (0.90)	0.0	-2.0, 4.0	>0.999
High dose	66	1.9	1.6 (0.74)	1.5	1.0, 4.0	-0.3 (0.94)	0.0	-2.0, 2.0	0.0113*
WEEK 26	122	1.9	1.7 (0.87)	2.0	1.0, 5.0	-0.2 (0.88)	0.0	-2.0, 2.0	0.0256*
Low dose	66	1.8	1.8 (0.92)	2.0	1.0, 5.0	-0.0 (0.89)	0.0	-2.0, 2.0	0.7839
High dose	56	2.1	1.7 (0.81)	1.5	1.0, 4.0	-0.4 (0.84)	0.0	-2.0, 1.0	0.0024**
WEEK 39	108	1.8	1.7 (0.71)	2.0	1.0, 4.0	-0.1 (0.97)	0.0	-3.0, 2.0	0.2757
Low dose	65	1.8	1.7 (0.69)	2.0	1.0, 3.0	-0.1 (0.85)	0.0	-2.0, 2.0	0.4701
High dose	43	1.9	1.8 (0.74)	2.0	1.0, 4.0	-0.1 (1.13)	0.0	-3.0, 2.0	0.4206
WEEK 52	100	1.8	1.8 (0.74)	2.0	1.0, 4.0	-0.1 (0.90)	0.0	-2.0, 2.0	0.5051
Low dose	57	1.8	1.8 (0.75)	2.0	1.0, 4.0	0.0 (0.87)	0.0	-2.0, 1.0	0.7606
High dose	43	1.9	1.7 (0.74)	2.0	1.0, 4.0	-0.2 (0.93)	0.0	-2.0, 2.0	0.1978

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

Program Source Code: [redacted]

TABLE 14.2 5

Change from Baseline to Each Planned Visit in Health-Related Quality of Life as Assessed by EQ-5D-5L
(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 &
EQ-5D-5L VAS									
BASELINE	229		57.0 (22.21)	60.0	8.0, 100.0				
Low dose	125		57.9 (22.75)	60.0	8.0, 100.0				
High dose	104		55.9 (21.61)	59.0	9.0, 99.0				
WEEK 6	175	58.5	68.4 (18.20)	70.0	1.0, 99.0	9.9 (24.87)	10.0	-90.0, 79.0	<=0.001***
Low dose	93	58.9	66.3 (19.74)	70.0	1.0, 95.0	7.5 (26.35)	9.0	-90.0, 67.0	0.0076**
High dose	82	58.2	70.8 (16.08)	70.0	21.0, 99.0	12.6 (22.91)	11.0	-34.0, 79.0	<=0.001***
WEEK 13	144	58.6	69.5 (18.82)	74.0	10.0, 100.0	10.9 (24.33)	10.0	-65.0, 90.0	<=0.001***
Low dose	78	58.8	68.0 (20.09)	74.0	10.0, 97.0	9.2 (25.11)	8.5	-65.0, 70.0	0.0018**
High dose	66	58.5	71.3 (17.18)	74.0	28.0, 100.0	12.8 (23.41)	11.0	-40.0, 90.0	<=0.001***
WEEK 26	122	58.7	71.9 (16.20)	75.0	10.0, 99.0	13.2 (22.51)	10.0	-39.0, 72.0	<=0.001***
Low dose	66	58.5	70.8 (16.69)	73.0	10.0, 94.0	12.3 (22.51)	10.0	-35.0, 72.0	<=0.001***
High dose	56	58.9	73.2 (15.65)	76.5	29.0, 99.0	14.4 (22.67)	14.5	-39.0, 71.0	<=0.001***
WEEK 39	108	60.6	71.5 (16.31)	75.0	18.0, 96.0	10.9 (22.30)	9.0	-49.0, 77.0	<=0.001***
Low dose	65	59.8	71.8 (16.83)	75.0	35.0, 96.0	12.0 (22.37)	10.0	-24.0, 77.0	<=0.001***
High dose	43	61.8	71.2 (15.69)	74.0	18.0, 93.0	9.3 (22.37)	5.0	-49.0, 60.0	0.0091**
WEEK 52	100	59.5	72.0 (16.46)	75.0	20.0, 100.0	12.5 (25.03)	7.5	-60.0, 71.0	<=0.001***
Low dose	57	59.8	72.8 (16.02)	75.0	20.0, 96.0	13.0 (26.06)	8.0	-60.0, 71.0	<=0.001***
High dose	43	59.1	70.8 (17.15)	74.0	30.0, 100.0	11.7 (23.88)	7.0	-35.0, 68.0	0.0024**

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

Program Source Code: [redacted]

TABLE 14.2 5

Change from Baseline to Each Planned Visit in Health-Related Quality of Life as Assessed by EQ-5D-5L
(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 &
EQ-5D-5L Summary Index - Based on USA									
BASELINE	229		0.644 (0.1745)	0.666	-0.037, 1.000				
Low dose	125		0.654 (0.1854)	0.689	-0.024, 1.000				
High dose	104		0.631 (0.1604)	0.646	-0.037, 0.888				
WEEK 6	175	0.657	0.742 (0.1506)	0.748	0.145, 1.000	0.085 (0.1870)	0.073	-0.592, 0.769	<=0.001***
Low dose	93	0.673	0.732 (0.1689)	0.730	0.145, 1.000	0.060 (0.1921)	0.045	-0.592, 0.640	0.0035**
High dose	82	0.640	0.753 (0.1269)	0.754	0.163, 1.000	0.113 (0.1780)	0.089	-0.446, 0.769	<=0.001***
WEEK 13	144	0.656	0.747 (0.1688)	0.741	0.127, 1.000	0.091 (0.2104)	0.060	-0.683, 1.037	<=0.001***
Low dose	78	0.669	0.734 (0.1852)	0.743	0.127, 1.000	0.065 (0.2178)	0.047	-0.683, 0.753	0.0106*
High dose	66	0.640	0.762 (0.1468)	0.738	0.425, 1.000	0.122 (0.1984)	0.083	-0.242, 1.037	<=0.001***
WEEK 26	122	0.649	0.748 (0.1418)	0.770	0.178, 1.000	0.099 (0.1796)	0.081	-0.198, 0.836	<=0.001***
Low dose	66	0.658	0.737 (0.1533)	0.761	0.178, 1.000	0.079 (0.1752)	0.055	-0.198, 0.748	<=0.001***
High dose	56	0.639	0.761 (0.1270)	0.777	0.393, 1.000	0.122 (0.1835)	0.097	-0.178, 0.836	<=0.001***
WEEK 39	108	0.658	0.753 (0.1224)	0.756	0.461, 1.000	0.094 (0.1934)	0.038	-0.236, 0.890	<=0.001***
Low dose	65	0.667	0.749 (0.1207)	0.756	0.461, 1.000	0.082 (0.1884)	0.033	-0.236, 0.660	<=0.001***
High dose	43	0.645	0.758 (0.1262)	0.756	0.540, 1.000	0.113 (0.2016)	0.059	-0.144, 0.890	<=0.001***
WEEK 52	100	0.662	0.751 (0.1521)	0.756	0.126, 1.000	0.089 (0.2175)	0.056	-0.447, 1.037	<=0.001***
Low dose	57	0.669	0.739 (0.1389)	0.748	0.306, 1.000	0.070 (0.2061)	0.036	-0.234, 0.748	0.0125*
High dose	43	0.654	0.767 (0.1682)	0.778	0.126, 1.000	0.113 (0.2318)	0.097	-0.447, 1.037	0.0026**

&: P-value is 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32　PDQ-39スコア（FAS，日本人部分集団）：M15-741試験

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

TABLE 14.2__4.J

Change from Baseline to Each Planned Visit in Quality of Life as Assessed
by The PD Questionnaire-39 Items
(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 &
PDQ-39 Summary Index Total Score									
BASELINE	27		34.9 (13.29)	34.0	12.8, 57.7				
Low dose	22		32.0 (12.18)	34.0	12.8, 57.7				
High dose	5		47.7 (10.93)	52.6	31.4, 56.4				
WEEK 6	19	34.0	33.2 (20.18)	29.5	1.9, 76.3	-0.8 (14.14)	-5.8	-15.8, 34.0	0.8007
Low dose	16	32.3	32.8 (21.02)	28.8	1.9, 76.3	0.5 (14.89)	-4.8	-15.8, 34.0	0.8875
High dose	3	43.2	35.0 (18.58)	29.5	19.9, 55.8	-8.1 (6.48)	-11.5	-12.2, -0.6	0.1624
WEEK 13	17	33.9	34.9 (17.78)	42.3	5.1, 69.9	1.0 (15.83)	-4.5	-21.8, 42.9	0.7890
Low dose	14	31.9	35.7 (17.88)	42.3	5.1, 69.9	3.8 (15.80)	-0.3	-14.7, 42.9	0.3806
High dose	3	43.2	31.2 (20.60)	33.3	9.6, 50.6	-12.0 (8.61)	-8.3	-21.8, -5.8	0.1377
WEEK 26	15	35.2	31.9 (16.64)	33.6	3.2, 56.4	-3.3 (11.78)	-4.5	-20.5, 19.2	0.2961
Low dose	12	33.3	32.4 (15.83)	34.1	3.2, 56.4	-0.9 (11.00)	-2.9	-17.3, 19.2	0.7897
High dose	3	43.2	30.1 (23.56)	23.1	10.9, 56.4	-13.0 (11.33)	-18.6	-20.5, 0.0	0.1845
WEEK 39	12	33.3	29.1 (18.68)	27.0	1.9, 64.1	-4.2 (12.22)	-5.4	-23.7, 14.7	0.2602
Low dose	9	30.0	28.1 (16.30)	29.6	1.9, 50.6	-1.9 (10.61)	-3.8	-18.6, 14.7	0.6094
High dose	3	43.2	32.1 (28.98)	24.4	7.7, 64.1	-11.1 (16.60)	-17.3	-23.7, 7.7	0.3659
WEEK 52	11	35.2	32.8 (19.50)	34.6	3.2, 76.9	-2.4 (13.86)	0.0	-24.4, 20.5	0.5759
Low dose	8	32.2	30.1 (12.67)	31.1	3.2, 44.9	-2.1 (11.35)	2.6	-17.3, 9.0	0.6135
High dose	3	43.2	40.0 (35.11)	35.9	7.1, 76.9	-3.2 (22.55)	-5.8	-24.4, 20.5	0.8285

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

Program Source Code: [redacted]

TABLE 14.2 4.J

Change from Baseline to Each Planned Visit in Quality of Life as Assessed
by The PD Questionnaire-39 Items
(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 &
PDQ-39 Mobility Domain Score									
BASELINE	27		50.0 (19.99)	47.5	7.5, 82.5				
Low dose	22		47.0 (19.92)	46.3	7.5, 80.0				
High dose	5		63.0 (15.95)	60.0	40.0, 82.5				
WEEK 6	19	49.5	47.6 (30.75)	42.5	0.0, 100.0	-1.8 (21.13)	-7.5	-25.0, 52.5	0.7084
Low dose	16	47.3	46.7 (31.61)	37.5	0.0, 100.0	-0.6 (22.52)	-6.3	-25.0, 52.5	0.9131
High dose	3	60.8	52.5 (31.22)	42.5	27.5, 87.5	-8.3 (11.81)	-12.5	-17.5, 5.0	0.3463
WEEK 13	17	49.4	52.9 (29.70)	55.0	5.0, 95.0	3.5 (22.66)	-2.5	-22.5, 67.5	0.5298
Low dose	14	47.0	53.2 (29.68)	57.5	5.0, 95.0	6.3 (23.47)	0.0	-22.5, 67.5	0.3372
High dose	3	60.8	51.7 (36.43)	47.5	17.5, 90.0	-9.2 (15.28)	-12.5	-22.5, 7.5	0.4078
WEEK 26	15	51.0	48.8 (26.12)	55.0	5.0, 87.5	-2.2 (17.42)	-5.0	-32.5, 22.5	0.6374
Low dose	12	48.5	50.6 (26.20)	56.3	5.0, 87.5	2.1 (16.54)	5.0	-32.5, 22.5	0.6711
High dose	3	60.8	41.7 (30.03)	40.0	12.5, 72.5	-19.2 (8.78)	-20.0	-27.5, -10.0	0.0634
WEEK 39	12	46.9	43.1 (26.57)	37.5	5.0, 82.5	-3.8 (18.14)	-3.8	-32.5, 22.5	0.4888
Low dose	9	42.2	42.5 (26.19)	40.0	5.0, 80.0	0.3 (18.22)	0.0	-32.5, 22.5	0.9646
High dose	3	60.8	45.0 (33.63)	35.0	17.5, 82.5	-15.8 (13.77)	-22.5	-25.0, 0.0	0.1846
WEEK 52	11	49.5	45.2 (28.97)	42.5	5.0, 100.0	-4.3 (20.44)	-5.0	-35.0, 20.0	0.4994
Low dose	8	45.3	43.8 (23.15)	48.8	5.0, 75.0	-1.6 (18.99)	1.3	-32.5, 20.0	0.8226
High dose	3	60.8	49.2 (47.85)	42.5	5.0, 100.0	-11.7 (26.73)	-17.5	-35.0, 17.5	0.5286

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

Program Source Code: [redacted]

TABLE 14.2 4.J

Change from Baseline to Each Planned Visit in Quality of Life as Assessed
by The PD Questionnaire-39 Items
(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	Change from Baseline P-Value &
PDQ-39 Activities of Daily Living Domain Score									
BASELINE	27		38.7 (26.35)	29.2	0.0, 100.0				
Low dose	22		32.2 (24.34)	25.0	0.0, 100.0				
High dose	5		67.5 (11.56)	62.5	54.2, 83.3				
WEEK 6	19	34.6	41.0 (26.51)	37.5	0.0, 100.0	6.4 (23.99)	4.2	-29.2, 75.0	0.2630
Low dose	16	28.6	39.1 (27.76)	37.5	0.0, 100.0	10.4 (22.87)	6.2	-20.8, 75.0	0.0885
High dose	3	66.7	51.4 (18.79)	50.0	33.3, 70.8	-15.3 (20.55)	-25.0	-29.2, 8.3	0.3268
WEEK 13	17	36.3	42.4 (23.02)	41.7	4.2, 79.2	6.1 (26.73)	4.2	-50.0, 58.3	0.3585
Low dose	14	29.8	42.0 (21.89)	47.9	4.2, 75.0	12.2 (21.65)	8.3	-16.7, 58.3	0.0549
High dose	3	66.7	44.4 (33.42)	41.7	12.5, 79.2	-22.2 (34.69)	-33.3	-50.0, 16.7	0.3828
WEEK 26	15	39.4	35.0 (19.47)	37.5	8.3, 66.7	-4.4 (18.53)	0.0	-45.8, 20.8	0.3687
Low dose	12	32.6	33.0 (18.92)	35.4	8.3, 66.7	0.3 (14.70)	4.2	-29.2, 20.8	0.9363
High dose	3	66.7	43.1 (23.69)	50.0	16.7, 62.5	-23.6 (22.95)	-25.0	-45.8, 0.0	0.2167
WEEK 39	12	38.9	36.8 (25.43)	35.4	0.0, 79.2	-2.1 (28.29)	2.1	-58.3, 33.3	0.8033
Low dose	9	29.6	36.6 (22.90)	41.7	0.0, 62.5	6.9 (18.16)	4.2	-25.0, 33.3	0.2845
High dose	3	66.7	37.5 (38.19)	29.2	4.2, 79.2	-29.2 (40.18)	-45.8	-58.3, 16.7	0.3356
WEEK 52	11	41.3	42.0 (22.78)	45.8	4.2, 87.5	0.8 (27.18)	8.3	-54.2, 25.0	0.9282
Low dose	8	31.8	38.5 (15.23)	43.8	4.2, 54.2	6.8 (21.36)	16.7	-20.8, 25.0	0.3996
High dose	3	66.7	51.4 (40.04)	58.3	8.3, 87.5	-15.3 (39.60)	-16.7	-54.2, 25.0	0.5728

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

Program Source Code: [redacted]

TABLE 14.2 4.J

Change from Baseline to Each Planned Visit in Quality of Life as Assessed
by The PD Questionnaire-39 Items
(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 &
PDQ-39 Emotional Well-being Domain Score									
BASELINE	27		31.6 (19.03)	25.0	12.5, 87.5				
Low dose	22		31.8 (19.27)	25.0	12.5, 87.5				
High dose	5		30.8 (20.11)	25.0	12.5, 62.5				
WEEK 6	19	33.1	35.1 (23.25)	37.5	0.0, 87.5	2.0 (26.55)	0.0	-50.0, 66.7	0.7496
Low dose	16	34.6	35.4 (24.01)	37.5	0.0, 87.5	0.8 (28.15)	-4.2	-50.0, 66.7	0.9131
High dose	3	25.0	33.3 (23.20)	29.2	12.5, 58.3	8.3 (18.16)	16.7	-12.5, 20.8	0.5101
WEEK 13	17	33.3	33.1 (22.89)	20.8	0.0, 83.3	-0.2 (19.40)	0.0	-45.8, 41.7	0.9591
Low dose	14	35.1	34.8 (23.89)	27.1	0.0, 83.3	-0.3 (20.77)	0.0	-45.8, 41.7	0.9581
High dose	3	25.0	25.0 (19.09)	20.8	8.3, 45.8	0.0 (14.43)	8.3	-16.7, 8.3	>0.999
WEEK 26	15	33.3	30.0 (25.16)	29.2	0.0, 91.7	-3.3 (22.72)	-8.3	-50.0, 33.3	0.5789
Low dose	12	35.4	32.3 (26.24)	33.3	0.0, 91.7	-3.1 (25.20)	-6.2	-50.0, 33.3	0.6758
High dose	3	25.0	20.8 (22.05)	12.5	4.2, 45.8	-4.2 (11.02)	-8.3	-12.5, 8.3	0.5799
WEEK 39	12	33.0	22.2 (18.32)	16.7	0.0, 50.0	-10.8 (19.01)	-12.5	-45.8, 16.7	0.0756
Low dose	9	35.6	22.7 (17.32)	20.8	0.0, 50.0	-13.0 (20.14)	-12.5	-45.8, 16.7	0.0896
High dose	3	25.0	20.8 (25.34)	8.3	4.2, 50.0	-4.2 (16.67)	-4.2	-20.8, 12.5	0.7072
WEEK 52	11	34.5	31.8 (22.46)	25.0	0.0, 75.0	-2.7 (23.81)	4.2	-54.2, 33.3	0.7196
Low dose	8	38.0	29.7 (21.06)	25.0	0.0, 75.0	-8.3 (22.82)	-4.2	-54.2, 12.5	0.3361
High dose	3	25.0	37.5 (30.05)	29.2	12.5, 70.8	12.5 (23.20)	16.7	-12.5, 33.3	0.4492

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

Program Source Code: [redacted]

TABLE 14.2 4.J

Change from Baseline to Each Planned Visit in Quality of Life as Assessed
by The PD Questionnaire-39 Items
(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	Change from Baseline P-Value &
PDQ-39 Stigma Domain Score									
BASELINE	27		25.7 (19.87)	18.8	0.0, 75.0				
Low dose	22		21.9 (18.37)	18.8	0.0, 75.0				
High dose	5		42.5 (18.96)	50.0	12.5, 62.5				
WEEK 6	19	24.7	18.1 (18.39)	12.5	0.0, 75.0	-6.6 (21.09)	-6.3	-56.3, 50.0	0.1907
Low dose	16	22.3	16.8 (19.73)	12.5	0.0, 75.0	-5.5 (21.88)	-6.3	-56.3, 50.0	0.3332
High dose	3	37.5	25.0 (6.25)	25.0	18.8, 31.3	-12.5 (18.75)	-12.5	-31.3, 6.3	0.3675
WEEK 13	17	22.1	16.2 (20.14)	12.5	0.0, 75.0	-5.9 (27.82)	-6.3	-62.5, 56.3	0.3962
Low dose	14	18.8	17.9 (21.21)	12.5	0.0, 75.0	-0.9 (25.93)	-6.3	-56.3, 56.3	0.8994
High dose	3	37.5	8.3 (14.43)	0.0	0.0, 25.0	-29.2 (28.87)	-12.5	-62.5, -12.5	0.2222
WEEK 26	15	25.0	22.1 (25.32)	12.5	0.0, 87.5	-2.9 (22.89)	-6.3	-31.3, 50.0	0.6293
Low dose	12	21.9	19.8 (18.81)	15.6	0.0, 56.3	-2.1 (22.67)	-6.3	-31.3, 50.0	0.7561
High dose	3	37.5	31.3 (48.81)	6.3	0.0, 87.5	-6.3 (28.64)	-12.5	-31.3, 25.0	0.7418
WEEK 39	12	26.6	19.8 (22.43)	18.8	0.0, 81.3	-6.8 (17.57)	-6.3	-31.3, 25.0	0.2088
Low dose	9	22.9	16.7 (11.69)	18.8	0.0, 31.3	-6.3 (16.24)	-6.3	-31.3, 25.0	0.2815
High dose	3	37.5	29.2 (45.21)	6.3	0.0, 81.3	-8.3 (25.26)	-12.5	-31.3, 18.8	0.6254
WEEK 52	11	28.4	19.9 (20.69)	18.8	0.0, 75.0	-8.5 (14.60)	-6.3	-37.5, 12.5	0.0816
Low dose	8	25.0	16.4 (9.99)	18.8	0.0, 31.3	-8.6 (14.15)	-3.1	-37.5, 6.3	0.1295
High dose	3	37.5	29.2 (40.18)	12.5	0.0, 75.0	-8.3 (19.09)	-12.5	-25.0, 12.5	0.5286

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

Program Source Code: [redacted]

TABLE 14.2 4.J

Change from Baseline to Each Planned Visit in Quality of Life as Assessed
by The PD Questionnaire-39 Items
(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 &
PDQ-39 Social Support Domain Score									
BASELINE	23		11.6 (16.43)	0.0	0.0, 58.3				
Low dose	19		10.5 (17.09)	0.0	0.0, 58.3				
High dose	4		16.7 (13.61)	16.7	0.0, 33.3				
WEEK 6	18	12.0	8.3 (11.79)	0.0	0.0, 33.3	-3.7 (9.14)	0.0	-25.0, 8.3	0.1037
Low dose	15	12.2	8.9 (12.78)	0.0	0.0, 33.3	-3.3 (9.86)	0.0	-25.0, 8.3	0.2115
High dose	3	11.1	5.6 (4.81)	8.3	0.0, 8.3	-5.6 (4.81)	-8.3	-8.3, 0.0	0.1835
WEEK 13	16	13.5	14.1 (21.24)	0.0	0.0, 66.7	0.5 (16.52)	0.0	-16.7, 50.0	0.9013
Low dose	13	14.1	17.3 (22.43)	16.7	0.0, 66.7	3.2 (16.85)	0.0	-16.7, 50.0	0.5059
High dose	3	11.1	0.0 (0.00)	0.0	0.0, 0.0	-11.1 (9.62)	-16.7	-16.7, 0.0	0.1835
WEEK 26	14	13.1	11.3 (12.49)	8.3	0.0, 33.3	-1.8 (16.72)	0.0	-33.3, 33.3	0.6960
Low dose	11	13.6	12.9 (13.62)	8.3	0.0, 33.3	-0.8 (18.05)	0.0	-33.3, 33.3	0.8920
High dose	3	11.1	5.6 (4.81)	8.3	0.0, 8.3	-5.6 (12.73)	-8.3	-16.7, 8.3	0.5286
WEEK 39	11	9.1	6.8 (10.42)	0.0	0.0, 25.0	-2.3 (11.24)	0.0	-25.0, 16.7	0.5175
Low dose	8	8.3	6.3 (9.71)	0.0	0.0, 25.0	-2.1 (11.57)	0.0	-25.0, 16.7	0.6263
High dose	3	11.1	8.3 (14.43)	0.0	0.0, 25.0	-2.8 (12.73)	0.0	-16.7, 8.3	0.7418
WEEK 52	10	10.0	9.2 (9.17)	8.3	0.0, 25.0	-0.8 (12.70)	0.0	-25.0, 16.7	0.8402
Low dose	7	9.5	8.3 (8.33)	8.3	0.0, 16.7	-1.2 (13.11)	0.0	-25.0, 16.7	0.8182
High dose	3	11.1	11.1 (12.73)	8.3	0.0, 25.0	-0.0 (14.43)	8.3	-16.7, 8.3	>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]

TABLE 14.2 4.J

Change from Baseline to Each Planned Visit in Quality of Life as Assessed
by The PD Questionnaire-39 Items
(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 &
PDQ-39 Cognition Domain Score									
BASELINE	27		28.9 (14.10)	31.3	6.3, 62.5				
Low dose	22		26.7 (12.53)	25.0	6.3, 50.0				
High dose	5		38.8 (17.90)	37.5	12.5, 62.5				
WEEK 6	19	26.6	31.6 (23.52)	25.0	0.0, 81.3	4.9 (22.49)	-6.3	-25.0, 50.0	0.3517
Low dose	16	25.8	32.8 (25.46)	21.9	0.0, 81.3	7.0 (23.59)	-3.1	-25.0, 50.0	0.2517
High dose	3	31.3	25.0 (6.25)	25.0	18.8, 31.3	-6.3 (12.50)	-6.3	-18.8, 6.3	0.4778
WEEK 13	17	27.6	34.9 (21.20)	25.0	12.5, 75.0	7.4 (20.76)	6.3	-25.0, 50.0	0.1635
Low dose	14	26.8	38.4 (21.77)	31.3	18.8, 75.0	11.6 (20.04)	9.4	-25.0, 50.0	0.0494*
High dose	3	31.3	18.8 (6.25)	18.8	12.5, 25.0	-12.5 (10.83)	-18.8	-18.8, 0.0	0.1835
WEEK 26	15	26.3	30.4 (19.46)	25.0	6.3, 75.0	4.2 (16.14)	0.0	-18.8, 43.8	0.3343
Low dose	12	25.0	31.3 (21.49)	25.0	6.3, 75.0	6.3 (16.64)	3.1	-12.5, 43.8	0.2199
High dose	3	31.3	27.1 (9.55)	25.0	18.8, 37.5	-4.2 (13.01)	0.0	-18.8, 6.3	0.6349
WEEK 39	12	24.5	27.6 (16.09)	25.0	6.3, 62.5	3.1 (10.15)	3.1	-12.5, 25.0	0.3089
Low dose	9	22.2	22.9 (9.38)	25.0	6.3, 37.5	0.7 (8.53)	0.0	-12.5, 12.5	0.8131
High dose	3	31.3	41.7 (26.02)	50.0	12.5, 62.5	10.4 (13.01)	6.3	0.0, 25.0	0.2999
WEEK 52	11	25.0	26.7 (12.53)	25.0	12.5, 50.0	1.7 (7.95)	0.0	-6.3, 12.5	0.4933
Low dose	8	22.7	23.4 (8.01)	21.9	12.5, 37.5	0.8 (8.48)	-3.1	-6.3, 12.5	0.8018
High dose	3	31.3	35.4 (20.09)	43.8	12.5, 50.0	4.2 (7.22)	0.0	0.0, 12.5	0.4226

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

Program Source Code: [redacted]

TABLE 14.2 4.J

Change from Baseline to Each Planned Visit in Quality of Life as Assessed
by The PD Questionnaire-39 Items
(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 &
PDQ-39 Communication Domain Score									
BASELINE	27		23.5 (21.06)	16.7	0.0, 66.7				
Low dose	22		20.8 (19.54)	16.7	0.0, 66.7				
High dose	5		35.0 (25.95)	25.0	8.3, 66.7				
WEEK 6	19	25.0	21.5 (26.40)	16.7	0.0, 75.0	-3.5 (23.29)	0.0	-66.7, 41.7	0.5197
Low dose	16	24.0	21.4 (27.38)	12.5	0.0, 75.0	-2.6 (25.41)	0.0	-66.7, 41.7	0.6876
High dose	3	30.6	22.2 (25.46)	16.7	0.0, 50.0	-8.3 (0.00)	-8.3	-8.3, -8.3	<=0.001***
WEEK 13	17	25.0	18.6 (21.15)	16.7	0.0, 75.0	-6.4 (20.94)	0.0	-58.3, 25.0	0.2277
Low dose	14	23.8	14.3 (16.16)	12.5	0.0, 58.3	-9.5 (20.11)	0.0	-58.3, 25.0	0.0998
High dose	3	30.6	38.9 (33.68)	33.3	8.3, 75.0	8.3 (22.05)	16.7	-16.7, 25.0	0.5799
WEEK 26	15	27.2	17.8 (20.38)	8.3	0.0, 66.7	-9.4 (21.56)	-8.3	-66.7, 25.0	0.1119
Low dose	12	26.4	16.0 (16.46)	12.5	0.0, 58.3	-10.4 (23.60)	-8.3	-66.7, 25.0	0.1546
High dose	3	30.6	25.0 (36.32)	8.3	0.0, 66.7	-5.6 (12.73)	-8.3	-16.7, 8.3	0.5286
WEEK 39	12	27.1	22.9 (27.55)	12.5	0.0, 91.7	-4.2 (23.70)	0.0	-66.7, 33.3	0.5549
Low dose	9	25.9	22.2 (28.87)	16.7	0.0, 91.7	-3.7 (27.36)	0.0	-66.7, 33.3	0.6953
High dose	3	30.6	25.0 (28.87)	8.3	8.3, 58.3	-5.6 (9.62)	0.0	-16.7, 0.0	0.4226
WEEK 52	11	29.5	29.5 (28.95)	16.7	0.0, 83.3	-0.0 (26.87)	0.0	-66.7, 33.3	>0.999
Low dose	8	29.2	26.0 (26.52)	16.7	0.0, 66.7	-3.1 (29.19)	0.0	-66.7, 33.3	0.7708
High dose	3	30.6	38.9 (39.38)	25.0	8.3, 83.3	8.3 (22.05)	16.7	-16.7, 25.0	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 4.J

Change from Baseline to Each Planned Visit in Quality of Life as Assessed
by The PD Questionnaire-39 Items
(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 &
PDQ-39 Bodily Discomfort Domain Score									
BASELINE	27		37.0 (24.93)	33.3	0.0, 100.0				
Low dose	22		34.1 (25.96)	33.3	0.0, 100.0				
High dose	5		50.0 (15.59)	50.0	33.3, 75.0				
WEEK 6	19	35.1	24.1 (21.50)	25.0	0.0, 66.7	-11.0 (20.61)	-8.3	-50.0, 25.0	0.0324*
Low dose	16	33.9	25.5 (22.66)	25.0	0.0, 66.7	-8.3 (21.30)	0.0	-50.0, 25.0	0.1385
High dose	3	41.7	16.7 (14.43)	8.3	8.3, 33.3	-25.0 (8.33)	-25.0	-33.3, -16.7	0.0351*
WEEK 13	17	30.9	25.5 (23.47)	16.7	0.0, 66.7	-5.4 (31.31)	0.0	-50.0, 50.0	0.4879
Low dose	14	28.6	26.8 (23.61)	25.0	0.0, 66.7	-1.8 (30.87)	0.0	-50.0, 50.0	0.8320
High dose	3	41.7	19.4 (26.79)	8.3	0.0, 50.0	-22.2 (33.68)	-41.7	-41.7, 16.7	0.3715
WEEK 26	15	32.8	23.3 (18.15)	25.0	0.0, 58.3	-9.4 (18.06)	-16.7	-41.7, 16.7	0.0623
Low dose	12	30.6	25.0 (18.80)	25.0	0.0, 58.3	-5.6 (17.16)	0.0	-33.3, 16.7	0.2861
High dose	3	41.7	16.7 (16.67)	16.7	0.0, 33.3	-25.0 (14.43)	-16.7	-41.7, -16.7	0.0955
WEEK 39	12	27.1	23.6 (23.79)	25.0	0.0, 75.0	-3.5 (27.17)	-12.5	-41.7, 58.3	0.6665
Low dose	9	22.2	24.1 (25.83)	25.0	0.0, 75.0	1.9 (26.93)	-8.3	-25.0, 58.3	0.8417
High dose	3	41.7	22.2 (20.97)	25.0	0.0, 41.7	-19.4 (25.46)	-25.0	-41.7, 8.3	0.3169
WEEK 52	11	28.0	26.5 (24.39)	25.0	0.0, 75.0	-1.5 (25.23)	0.0	-41.7, 33.3	0.8461
Low dose	8	22.9	20.8 (17.25)	20.8	0.0, 41.7	-2.1 (23.04)	0.0	-41.7, 33.3	0.8055
High dose	3	41.7	41.7 (38.19)	50.0	0.0, 75.0	0.0 (36.32)	16.7	-41.7, 25.0	>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33　EQ-5D-5L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__5.J

Change from Baseline to Each Planned Visit in Health-Related Quality of Life as Assessed
by EQ-5D-5L
(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 &
EQ-5D-5L Mobility									
BASELINE	26		3.5 (1.14)	4.0	1.0, 5.0				
Low dose	21		3.6 (1.08)	4.0	1.0, 5.0				
High dose	5		3.2 (1.48)	3.0	1.0, 5.0				
WEEK 6	18	3.4	2.6 (1.09)	3.0	1.0, 5.0	-0.8 (1.34)	-1.0	-3.0, 1.0	0.0172*
Low dose	15	3.7	2.7 (1.18)	3.0	1.0, 5.0	-1.0 (1.36)	-1.0	-3.0, 1.0	0.0131*
High dose	3	2.3	2.3 (0.58)	2.0	2.0, 3.0	0.0 (1.00)	0.0	-1.0, 1.0	>0.999
WEEK 13	17	3.5	2.8 (1.03)	3.0	1.0, 5.0	-0.8 (1.39)	-1.0	-3.0, 2.0	0.0379*
Low dose	14	3.8	2.9 (1.03)	3.0	1.0, 5.0	-0.9 (1.49)	-1.5	-3.0, 2.0	0.0366*
High dose	3	2.3	2.3 (1.15)	3.0	1.0, 3.0	0.0 (0.00)	0.0	0.0, 0.0	
WEEK 26	15	3.7	2.2 (0.86)	2.0	1.0, 4.0	-1.5 (1.30)	-2.0	-3.0, 1.0	<=0.001***
Low dose	12	4.0	2.2 (0.94)	2.0	1.0, 4.0	-1.8 (1.11)	-2.0	-3.0, 0.0	<=0.001***
High dose	3	2.3	2.3 (0.58)	2.0	2.0, 3.0	0.0 (1.00)	0.0	-1.0, 1.0	>0.999
WEEK 39	12	3.7	2.6 (1.24)	2.5	1.0, 4.0	-1.1 (1.62)	-1.5	-3.0, 1.0	0.0410*
Low dose	9	4.1	2.4 (1.13)	2.0	1.0, 4.0	-1.7 (1.41)	-2.0	-3.0, 1.0	0.0077**
High dose	3	2.3	3.0 (1.73)	4.0	1.0, 4.0	0.7 (0.58)	1.0	0.0, 1.0	0.1835
WEEK 52	11	3.6	2.4 (1.36)	2.0	1.0, 5.0	-1.3 (1.79)	-1.0	-4.0, 2.0	0.0404*
Low dose	8	4.1	2.3 (1.16)	2.5	1.0, 4.0	-1.9 (1.55)	-2.0	-4.0, 1.0	0.0112*
High dose	3	2.3	2.7 (2.08)	2.0	1.0, 5.0	0.3 (1.53)	0.0	-1.0, 2.0	0.7418

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

Program Source Code: [redacted]

TABLE 14.2 5.J

Change from Baseline to Each Planned Visit in Health-Related Quality of Life as Assessed by EQ-5D-5L
(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 &
EQ-5D-5L Self-care									
BASELINE	26		3.0 (1.31)	3.0	1.0, 5.0				
Low dose	21		3.0 (1.32)	3.0	1.0, 5.0				
High dose	5		3.0 (1.41)	3.0	1.0, 5.0				
WEEK 6	18	2.9	2.3 (1.13)	2.0	1.0, 5.0	-0.6 (1.58)	0.0	-3.0, 2.0	0.1185
Low dose	15	3.0	2.3 (1.23)	2.0	1.0, 5.0	-0.7 (1.68)	0.0	-3.0, 2.0	0.1458
High dose	3	2.3	2.0 (0.00)	2.0	2.0, 2.0	-0.3 (1.15)	-1.0	-1.0, 1.0	0.6667
WEEK 13	17	3.0	2.6 (1.06)	3.0	1.0, 4.0	-0.4 (1.54)	0.0	-3.0, 2.0	0.2876
Low dose	14	3.1	2.6 (1.02)	2.5	1.0, 4.0	-0.6 (1.65)	-0.5	-3.0, 2.0	0.2178
High dose	3	2.3	2.7 (1.53)	3.0	1.0, 4.0	0.3 (0.58)	0.0	0.0, 1.0	0.4226
WEEK 26	15	3.2	1.9 (0.59)	2.0	1.0, 3.0	-1.3 (1.53)	-1.0	-4.0, 1.0	0.0064**
Low dose	12	3.4	1.8 (0.58)	2.0	1.0, 3.0	-1.6 (1.51)	-1.5	-4.0, 1.0	0.0039**
High dose	3	2.3	2.3 (0.58)	2.0	2.0, 3.0	0.0 (1.00)	0.0	-1.0, 1.0	>0.999
WEEK 39	12	3.4	2.3 (1.06)	2.0	1.0, 4.0	-1.2 (1.40)	-1.5	-3.0, 1.0	0.0150*
Low dose	9	3.8	2.1 (0.93)	2.0	1.0, 4.0	-1.7 (1.22)	-2.0	-3.0, 1.0	0.0035**
High dose	3	2.3	2.7 (1.53)	3.0	1.0, 4.0	0.3 (0.58)	0.0	0.0, 1.0	0.4226
WEEK 52	11	3.5	2.2 (0.98)	2.0	1.0, 4.0	-1.3 (1.49)	-1.0	-3.0, 1.0	0.0177*
Low dose	8	3.9	2.1 (0.83)	2.0	1.0, 3.0	-1.8 (1.39)	-2.0	-3.0, 1.0	0.0092**
High dose	3	2.3	2.3 (1.53)	2.0	1.0, 4.0	0.0 (1.00)	0.0	-1.0, 1.0	>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]

TABLE 14.2 5.J

Change from Baseline to Each Planned Visit in Health-Related Quality of Life as Assessed by EQ-5D-5L
(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 &
EQ-5D-5L Usual Activities									
BASELINE	26		3.5 (1.21)	4.0	1.0, 5.0				
Low dose	21		3.4 (1.28)	4.0	1.0, 5.0				
High dose	5		4.0 (0.71)	4.0	3.0, 5.0				
WEEK 6	18	3.6	2.6 (1.20)	2.0	1.0, 5.0	-1.0 (1.24)	-1.0	-3.0, 1.0	0.0032**
Low dose	15	3.5	2.5 (1.25)	2.0	1.0, 5.0	-0.9 (1.33)	-1.0	-3.0, 1.0	0.0170*
High dose	3	4.0	2.7 (1.15)	2.0	2.0, 4.0	-1.3 (0.58)	-1.0	-2.0, -1.0	0.0572
WEEK 13	17	3.6	2.6 (1.32)	2.0	1.0, 5.0	-1.0 (1.66)	-1.0	-3.0, 3.0	0.0243*
Low dose	14	3.6	2.6 (1.34)	2.0	1.0, 5.0	-0.9 (1.82)	-1.0	-3.0, 3.0	0.0782
High dose	3	4.0	2.7 (1.53)	3.0	1.0, 4.0	-1.3 (0.58)	-1.0	-2.0, -1.0	0.0572
WEEK 26	15	3.8	2.6 (1.06)	3.0	1.0, 4.0	-1.2 (1.37)	-1.0	-3.0, 2.0	0.0044**
Low dose	12	3.8	2.5 (1.17)	2.5	1.0, 4.0	-1.3 (1.48)	-1.0	-3.0, 2.0	0.0140*
High dose	3	4.0	3.0 (0.00)	3.0	3.0, 3.0	-1.0 (1.00)	-1.0	-2.0, 0.0	0.2254
WEEK 39	12	4.0	2.3 (0.97)	2.0	1.0, 4.0	-1.8 (0.97)	-2.0	-3.0, 0.0	<=0.001***
Low dose	9	4.0	2.2 (0.83)	2.0	1.0, 3.0	-1.8 (1.09)	-2.0	-3.0, 0.0	0.0012**
High dose	3	4.0	2.3 (1.53)	2.0	1.0, 4.0	-1.7 (0.58)	-2.0	-2.0, -1.0	0.0377*
WEEK 52	11	4.0	2.5 (1.21)	2.0	1.0, 5.0	-1.5 (1.29)	-2.0	-3.0, 1.0	0.0027**
Low dose	8	4.0	2.4 (0.92)	2.0	1.0, 4.0	-1.6 (1.41)	-1.5	-3.0, 1.0	0.0138*
High dose	3	4.0	2.7 (2.08)	2.0	1.0, 5.0	-1.3 (1.15)	-2.0	-2.0, 0.0	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 5.J

Change from Baseline to Each Planned Visit in Health-Related Quality of Life as Assessed by EQ-5D-5L
(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 &
EQ-5D-5L Pain/Discomfort									
BASELINE	26		2.8 (1.13)	3.0	1.0, 5.0				
Low dose	21		2.9 (1.15)	3.0	1.0, 5.0				
High dose	5		2.6 (1.14)	3.0	1.0, 4.0				
WEEK 6	18	3.0	2.0 (0.84)	2.0	1.0, 3.0	-1.0 (1.08)	-1.0	-4.0, 1.0	0.0011**
Low dose	15	3.1	1.9 (0.80)	2.0	1.0, 3.0	-1.2 (1.01)	-1.0	-4.0, 0.0	<=0.001***
High dose	3	2.3	2.3 (1.15)	3.0	1.0, 3.0	0.0 (1.00)	0.0	-1.0, 1.0	>0.999
WEEK 13	17	3.1	2.3 (1.10)	2.0	1.0, 4.0	-0.8 (1.64)	-1.0	-4.0, 2.0	0.0726
Low dose	14	3.2	2.2 (1.05)	2.0	1.0, 4.0	-1.0 (1.62)	-1.0	-4.0, 2.0	0.0377*
High dose	3	2.3	2.7 (1.53)	3.0	1.0, 4.0	0.3 (1.53)	0.0	-1.0, 2.0	0.7418
WEEK 26	15	3.2	2.4 (0.99)	2.0	1.0, 5.0	-0.8 (1.47)	-1.0	-4.0, 1.0	0.0541
Low dose	12	3.4	2.5 (1.00)	2.0	1.0, 5.0	-0.9 (1.31)	-1.0	-4.0, 1.0	0.0339*
High dose	3	2.3	2.0 (1.00)	2.0	1.0, 3.0	-0.3 (2.31)	1.0	-3.0, 1.0	0.8259
WEEK 39	12	3.3	2.2 (0.72)	2.0	1.0, 3.0	-1.2 (1.47)	-1.0	-4.0, 2.0	0.0187*
Low dose	9	3.7	2.1 (0.78)	2.0	1.0, 3.0	-1.6 (1.13)	-1.0	-4.0, 0.0	0.0033**
High dose	3	2.3	2.3 (0.58)	2.0	2.0, 3.0	0.0 (2.00)	0.0	-2.0, 2.0	>0.999
WEEK 52	11	3.3	2.2 (0.87)	2.0	1.0, 4.0	-1.1 (1.81)	-1.0	-4.0, 3.0	0.0741
Low dose	8	3.6	2.1 (0.64)	2.0	1.0, 3.0	-1.5 (1.41)	-1.0	-4.0, 0.0	0.0199*
High dose	3	2.3	2.3 (1.53)	2.0	1.0, 4.0	0.0 (2.65)	-1.0	-2.0, 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]

TABLE 14.2 5.J

Change from Baseline to Each Planned Visit in Health-Related Quality of Life as Assessed by EQ-5D-5L
(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 &
EQ-5D-5L Anxiety/Depression									
BASELINE	26		1.7 (0.96)	1.0	1.0, 4.0				
Low dose	21		1.8 (1.00)	1.0	1.0, 4.0				
High dose	5		1.6 (0.89)	1.0	1.0, 3.0				
WEEK 6	18	1.8	1.7 (1.08)	1.0	1.0, 5.0	-0.1 (1.60)	0.0	-2.0, 4.0	0.7725
Low dose	15	1.9	1.8 (1.15)	1.0	1.0, 5.0	-0.1 (1.77)	0.0	-2.0, 4.0	0.7744
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 13	17	1.8	1.9 (1.05)	2.0	1.0, 4.0	0.1 (0.97)	0.0	-2.0, 1.0	0.8050
Low dose	14	2.0	2.1 (1.07)	2.0	1.0, 4.0	0.1 (1.07)	0.0	-2.0, 1.0	0.8069
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 26	15	1.8	2.0 (1.07)	2.0	1.0, 4.0	0.2 (1.08)	0.0	-2.0, 2.0	0.4860
Low dose	12	2.0	2.1 (1.16)	2.0	1.0, 4.0	0.1 (1.16)	0.0	-2.0, 2.0	0.8088
High dose	3	1.0	1.7 (0.58)	2.0	1.0, 2.0	0.7 (0.58)	1.0	0.0, 1.0	0.1835
WEEK 39	12	1.7	1.5 (0.52)	1.5	1.0, 2.0	-0.2 (1.27)	0.0	-2.0, 1.0	0.6576
Low dose	9	1.9	1.3 (0.50)	1.0	1.0, 2.0	-0.6 (1.24)	0.0	-2.0, 1.0	0.2145
High dose	3	1.0	2.0 (0.00)	2.0	2.0, 2.0	1.0 (0.00)	1.0	1.0, 1.0	<=0.001***
WEEK 52	11	1.7	1.7 (0.79)	2.0	1.0, 3.0	0.0 (1.34)	0.0	-2.0, 2.0	>0.999
Low dose	8	2.0	1.6 (0.74)	1.5	1.0, 3.0	-0.4 (1.30)	-0.5	-2.0, 1.0	0.4423
High dose	3	1.0	2.0 (1.00)	2.0	1.0, 3.0	1.0 (1.00)	1.0	0.0, 2.0	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 5.J

Change from Baseline to Each Planned Visit in Health-Related Quality of Life as Assessed by EQ-5D-5L
(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 &
EQ-5D-5L VAS									
BASELINE	26		43.7 (23.08)	39.5	8.0, 80.0				
Low dose	21		44.2 (23.26)	40.0	8.0, 80.0				
High dose	5		41.2 (24.75)	35.0	10.0, 78.0				
WEEK 6	18	42.7	60.4 (26.48)	65.0	8.0, 91.0	17.8 (29.10)	10.5	-20.0, 67.0	0.0190*
Low dose	15	40.5	60.0 (28.14)	70.0	8.0, 91.0	19.5 (31.69)	13.0	-20.0, 67.0	0.0316*
High dose	3	53.7	62.7 (20.23)	52.0	50.0, 86.0	9.0 (5.57)	8.0	4.0, 15.0	0.1074
WEEK 13	17	41.1	60.6 (23.41)	60.0	13.0, 95.0	19.5 (27.72)	17.0	-23.0, 70.0	0.0103*
Low dose	14	38.4	59.3 (23.89)	66.5	13.0, 88.0	20.9 (30.32)	15.0	-23.0, 70.0	0.0227*
High dose	3	53.7	66.7 (24.66)	55.0	50.0, 95.0	13.0 (9.64)	17.0	2.0, 20.0	0.1447
WEEK 26	15	39.9	64.9 (24.14)	70.0	10.0, 90.0	24.9 (32.93)	25.0	-39.0, 72.0	0.0109*
Low dose	12	36.5	67.0 (25.19)	73.0	10.0, 90.0	30.5 (29.84)	27.5	-20.0, 72.0	0.0046**
High dose	3	53.7	56.3 (21.22)	50.0	39.0, 80.0	2.7 (42.00)	2.0	-39.0, 45.0	0.9225
WEEK 39	12	39.9	70.9 (18.89)	75.0	35.0, 95.0	31.0 (31.78)	21.5	-15.0, 77.0	0.0062**
Low dose	9	35.3	72.0 (20.65)	75.0	35.0, 95.0	36.7 (33.43)	28.0	-15.0, 77.0	0.0110*
High dose	3	53.7	67.7 (15.37)	75.0	50.0, 78.0	14.0 (22.54)	2.0	0.0, 40.0	0.3945
WEEK 52	11	39.9	70.1 (21.11)	79.0	40.0, 96.0	30.2 (33.61)	12.0	-8.0, 71.0	0.0138*
Low dose	8	34.8	75.1 (17.09)	79.5	46.0, 96.0	40.4 (33.89)	56.5	-4.0, 71.0	0.0119*
High dose	3	53.7	56.7 (28.87)	40.0	40.0, 90.0	3.0 (10.15)	5.0	-8.0, 12.0	0.6596

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

Program Source Code: [redacted]

TABLE 14.2 5.J

Change from Baseline to Each Planned Visit in Health-Related Quality of Life as Assessed by EQ-5D-5L
(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 &
EQ-5D-5L Summary Index - Based on USA									
BASELINE	26		0.515 (0.2449)	0.540	-0.024, 1.000				
Low dose	21		0.514 (0.2510)	0.540	-0.024, 1.000				
High dose	5		0.520 (0.2445)	0.540	0.142, 0.825				
WEEK 6	18	0.529	0.680 (0.1879)	0.721	0.145, 0.888	0.151 (0.2480)	0.107	-0.202, 0.640	0.0192*
Low dose	15	0.506	0.671 (0.2060)	0.717	0.145, 0.888	0.165 (0.2641)	0.067	-0.202, 0.640	0.0298*
High dose	3	0.639	0.722 (0.0023)	0.723	0.719, 0.723	0.082 (0.1622)	0.146	-0.102, 0.203	0.4719
WEEK 13	17	0.512	0.636 (0.2050)	0.630	0.320, 1.000	0.123 (0.3250)	0.057	-0.301, 0.753	0.1371
Low dose	14	0.485	0.619 (0.2003)	0.638	0.320, 1.000	0.133 (0.3579)	0.041	-0.301, 0.753	0.1864
High dose	3	0.639	0.716 (0.2526)	0.630	0.517, 1.000	0.076 (0.0906)	0.057	-0.003, 0.175	0.2817
WEEK 26	15	0.478	0.668 (0.1459)	0.647	0.446, 1.000	0.190 (0.2655)	0.180	-0.178, 0.748	0.0151*
Low dose	12	0.438	0.661 (0.1606)	0.608	0.446, 1.000	0.223 (0.2732)	0.199	-0.171, 0.748	0.0163*
High dose	3	0.639	0.694 (0.0760)	0.654	0.647, 0.782	0.055 (0.2211)	0.081	-0.178, 0.262	0.7086
WEEK 39	12	0.450	0.705 (0.1258)	0.729	0.540, 0.880	0.255 (0.2646)	0.260	-0.113, 0.660	0.0066**
Low dose	9	0.386	0.725 (0.1181)	0.729	0.561, 0.880	0.339 (0.2535)	0.286	-0.113, 0.660	0.0039**
High dose	3	0.639	0.643 (0.1537)	0.570	0.540, 0.820	0.004 (0.0422)	-0.005	-0.033, 0.050	0.8848
WEEK 52	11	0.445	0.694 (0.2356)	0.718	0.126, 1.000	0.249 (0.3560)	0.220	-0.447, 0.748	0.0425*
Low dose	8	0.372	0.729 (0.1356)	0.728	0.559, 1.000	0.357 (0.3107)	0.286	-0.145, 0.748	0.0140*
High dose	3	0.639	0.601 (0.4420)	0.678	0.126, 1.000	-0.038 (0.3543)	0.158	-0.447, 0.175	0.8698

&: P-value is 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34　有害事象の概要（安全性解析対象集団）：M15-741試験

[redacted]20[redacted] 06:16 <[redacted]>
ABBV-951
STUDY M15-741 - SECOND INTERIM (CUTOFF [redacted]20[redacted])
R&D/20/1632 - CLINICAL/STATISTICAL

TABLE 14.3__1.1

Overview of Treatment-Emergent Adverse Events and All Deaths by Time Interval
(Safety Analysis Set)

	Dose Category: Low Dose n (%)	Dose Category: High Dose n (%)	All Subjects n (%)
Entire study period	N=132	N=112	N=244
Subjects with:			
Any TEAE	122 (92.4)	108 (96.4)	230 (94.3)
Any severe TEAE	26 (19.7)	36 (32.1)	62 (25.4)
Any TEAE that is considered associated with study drug$	118 (89.4)	106 (94.6)	224 (91.8)
Any TEAE that is considered associated with product complaint$	91 (68.9)	80 (71.4)	171 (70.1)
ABBV-951	52 (39.4)	43 (38.4)	95 (38.9)
Infusion pump	9 (6.8)	8 (7.1)	17 (7.0)
Vial adapter	0	1 (0.9)	1 (0.4)
Syringes	0	0	0
[redacted] infusion set (total)	51 (38.6)	40 (35.7)	91 (37.3)
[redacted] infusion set 6 mm	37 (28.0)	26 (23.2)	63 (25.8)
[redacted] infusion set 9 mm	25 (18.9)	23 (20.5)	48 (19.7)
Neria guard infusion set (total)	14 (10.6)	16 (14.3)	30 (12.3)
Neria guard infusion set 6 mm	8 (6.1)	9 (8.0)	17 (7.0)
Neria guard infusion set 9 mm	9 (6.8)	12 (10.7)	21 (8.6)
[redacted]	3 (2.3)	4 (3.6)	7 (2.9)
Any TEAE that is considered associated with loading dose$	2 (1.5)	5 (4.5)	7 (2.9)
Any TEAE that is considered associated with rescue dose$	4 (3.0)	8 (7.1)	12 (4.9)
Any TEAE that is considered associated with COVID-19 infection	2 (1.5)	1 (0.9)	3 (1.2)
Any TEAE leading to prematurely discontinuation of study drug	32 (24.2)	30 (26.8)	62 (25.4)
Any TEAE leading to death (fatal TEAE)	0	3 (2.7)	3 (1.2)
Any serious TEAE	31 (23.5)	30 (26.8)	61 (25.0)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
$ As assessed by investigator.

Program Source Code: [redacted]

TABLE 14.3 1.1

Overview of Treatment-Emergent Adverse Events and All Deaths by Time Interval
(Safety Analysis Set)

	Dose Category		
	Low Dose n (%)	High Dose n (%)	All Subjects n (%)
Any SAE that is considered associated with infusion pump$	14 (10.6)	8 (7.1)	22 (9.0)
Possible	6 (4.5)	5 (4.5)	11 (4.5)
Probable	5 (3.8)	3 (2.7)	8 (3.3)
Causal relationship	7 (5.3)	2 (1.8)	9 (3.7)
Any SAE that is considered associated with [redacted] infusion set$	1 (0.8)	1 (0.9)	2 (0.8)
Possible	1 (0.8)	1 (0.9)	2 (0.8)
Probable	0	0	0
Causal relationship	0	0	0
Any SAE that is considered associated with neria guards infusion set$	2 (1.5)	1 (0.9)	3 (1.2)
Possible	1 (0.8)	1 (0.9)	2 (0.8)
Probable	0	0	0
Causal relationship	1 (0.8)	0	1 (0.4)
Any SAE that is considered associated with product complaint$	11 (8.3)	7 (6.3)	18 (7.4)
ABBV-951	4 (3.0)	3 (2.7)	7 (2.9)
Infusion pump	2 (1.5)	1 (0.9)	3 (1.2)
Vial adapter	0	0	0
Syringes	0	0	0
[redacted] infusion set (total)	3 (2.3)	2 (1.8)	5 (2.0)
[redacted] infusion set 6 mm	2 (1.5)	1 (0.9)	3 (1.2)
[redacted] infusion set 9 mm	1 (0.8)	1 (0.9)	2 (0.8)
Neria guard infusion set (total)	2 (1.5)	1 (0.9)	3 (1.2)
Neria guard infusion set 6 mm	2 (1.5)	1 (0.9)	3 (1.2)
Neria guard infusion set 9 mm	0	0	0
[redacted]	0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
$ As assessed by investigator.

Program Source Code: [redacted]

TABLE 14.3 1.1

Overview of Treatment-Emergent Adverse Events and All Deaths by Time Interval
(Safety Analysis Set)

	Dose Category		
	Low Dose n (%)	High Dose n (%)	All Subjects n (%)
All deaths#	0	5 (4.5)	5 (2.0)
All TE-deaths	0	3 (2.7)	3 (1.2)
Deaths related to COVID-19 infection	0	0	0
AESI: polyneuropathy (narrow)	2 (1.5)	6 (5.4)	8 (3.3)
AESI: weight loss	12 (9.1)	13 (11.6)	25 (10.2)
AESI: hallucinations/psychosis	32 (24.2)	27 (24.1)	59 (24.2)
AESI: somnolence	9 (6.8)	3 (2.7)	12 (4.9)
AESI: infusion site related infections	41 (31.1)	43 (38.4)	84 (34.4)
AESI: infusion site related non infection reactions	103 (78.0)	96 (85.7)	199 (81.6)
AESI: falls and associated injuries	35 (26.5)	36 (32.1)	71 (29.1)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Includes non treatment-emergent deaths.

Program Source Code: [redacted]

TABLE 14.3 1.1

Overview of Treatment-Emergent Adverse Events and All Deaths by Time Interval
(Safety Analysis Set)

	Dose Category		
	Low Dose n (%)	High Dose n (%)	All Subjects n (%)
Optimization period	N=132	N=112	N=244
Subjects with:			
Any TEAE	105 (79.5)	97 (86.6)	202 (82.8)
Any severe TEAE	11 (8.3)	10 (8.9)	21 (8.6)
Any TEAE that is considered associated with study drug$	96 (72.7)	95 (84.8)	191 (78.3)
Any TEAE that is considered associated with product complaint$	67 (50.8)	63 (56.3)	130 (53.3)
ABBV-951	38 (28.8)	32 (28.6)	70 (28.7)
Infusion pump	3 (2.3)	2 (1.8)	5 (2.0)
Vial adapter	0	1 (0.9)	1 (0.4)
Syringes	0	0	0
[redacted] infusion set (total)	37 (28.0)	31 (27.7)	68 (27.9)
[redacted] infusion set 6 mm	27 (20.5)	15 (13.4)	42 (17.2)
[redacted] infusion set 9 mm	15 (11.4)	17 (15.2)	32 (13.1)
Neria guard infusion set (total)	6 (4.5)	7 (6.3)	13 (5.3)
Neria guard infusion set 6 mm	3 (2.3)	5 (4.5)	8 (3.3)
Neria guard infusion set 9 mm	3 (2.3)	4 (3.6)	7 (2.9)
[redacted]	2 (1.5)	2 (1.8)	4 (1.6)
Any TEAE that is considered associated with loading dose$	2 (1.5)	3 (2.7)	5 (2.0)
Any TEAE that is considered associated with rescue dose$	2 (1.5)	2 (1.8)	4 (1.6)
Any TEAE that is considered associated with COVID-19 infection	0	0	0
Any TEAE leading to prematurely discontinuation of study drug	16 (12.1)	10 (8.9)	26 (10.7)
Any TEAE leading to death (fatal TEAE)	0	0	0
Any serious TEAE	11 (8.3)	6 (5.4)	17 (7.0)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
$ As assessed by investigator.

Program Source Code: [redacted]

TABLE 14.3 1.1

Overview of Treatment-Emergent Adverse Events and All Deaths by Time Interval
(Safety Analysis Set)

	Dose Category		
	Low Dose n (%)	High Dose n (%)	All Subjects n (%)
Any SAE that is considered associated with infusion pump$	6 (4.5)	2 (1.8)	8 (3.3)
Possible	3 (2.3)	1 (0.9)	4 (1.6)
Probable	0	1 (0.9)	1 (0.4)
Causal relationship	3 (2.3)	0	3 (1.2)
Any SAE that is considered associated with [redacted] infusion set$	0	0	0
Possible	0	0	0
Probable	0	0	0
Causal relationship	0	0	0
Any SAE that is considered associated with neria guards infusion set$	0	0	0
Possible	0	0	0
Probable	0	0	0
Causal relationship	0	0	0
Any SAE that is considered associated with product complaint$	3 (2.3)	2 (1.8)	5 (2.0)
ABBV-951	2 (1.5)	0	2 (0.8)
Infusion pump	1 (0.8)	0	1 (0.4)
Vial adapter	0	0	0
Syringes	0	0	0
[redacted] infusion set (total)	0	2 (1.8)	2 (0.8)
[redacted] infusion set 6 mm	0	1 (0.9)	1 (0.4)
[redacted] infusion set 9 mm	0	1 (0.9)	1 (0.4)
Neria guard infusion set (total)	0	0	0
Neria guard infusion set 6 mm	0	0	0
Neria guard infusion set 9 mm	0	0	0
[redacted]	0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
$ As assessed by investigator.

Program Source Code: [redacted]

TABLE 14.3 1.1

Overview of Treatment-Emergent Adverse Events and All Deaths by Time Interval
(Safety Analysis Set)

	Dose Category		
	Low Dose n (%)	High Dose n (%)	All Subjects n (%)
All deaths#	0	0	0
All TE-deaths	0	0	0
Deaths related to COVID-19 infection	0	0	0
AESI: polyneuropathy (narrow)	0	0	0
AESI: weight loss	1 (0.8)	1 (0.9)	2 (0.8)
AESI: hallucinations/psychosis	17 (12.9)	8 (7.1)	25 (10.2)
AESI: somnolence	2 (1.5)	2 (1.8)	4 (1.6)
AESI: infusion site related infections	11 (8.3)	18 (16.1)	29 (11.9)
AESI: infusion site related non infection reactions	87 (65.9)	82 (73.2)	169 (69.3)
AESI: falls and associated injuries	19 (14.4)	19 (17.0)	38 (15.6)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Includes non treatment-emergent deaths.

Program Source Code: [redacted]

TABLE 14.3 1.1

Overview of Treatment-Emergent Adverse Events and All Deaths by Time Interval
(Safety Analysis Set)

	Dose Category		
	Low Dose n (%)	High Dose n (%)	All Subjects n (%)
Maintenance period	N=111	N=95	N=206
Subjects with:			
Any TEAE	98 (88.3)	88 (92.6)	186 (90.3)
Any severe TEAE	18 (16.2)	28 (29.5)	46 (22.3)
Any TEAE that is considered associated with study drug$	89 (80.2)	83 (87.4)	172 (83.5)
Any TEAE that is considered associated with product complaint$	65 (58.6)	62 (65.3)	127 (61.7)
ABBV-951	31 (27.9)	35 (36.8)	66 (32.0)
Infusion pump	6 (5.4)	6 (6.3)	12 (5.8)
Vial adapter	0	0	0
Syringes	0	0	0
[redacted] infusion set (total)	33 (29.7)	28 (29.5)	61 (29.6)
[redacted] infusion set 6 mm	20 (18.0)	16 (16.8)	36 (17.5)
[redacted] infusion set 9 mm	18 (16.2)	16 (16.8)	34 (16.5)
Neria guard infusion set (total)	13 (11.7)	13 (13.7)	26 (12.6)
Neria guard infusion set 6 mm	6 (5.4)	7 (7.4)	13 (6.3)
Neria guard infusion set 9 mm	8 (7.2)	10 (10.5)	18 (8.7)
[redacted]	1 (0.9)	2 (2.1)	3 (1.5)
Any TEAE that is considered associated with loading dose$	0	2 (2.1)	2 (1.0)
Any TEAE that is considered associated with rescue dose$	2 (1.8)	6 (6.3)	8 (3.9)
Any TEAE that is considered associated with COVID-19 infection	2 (1.8)	1 (1.1)	3 (1.5)
Any TEAE leading to prematurely discontinuation of study drug	16 (14.4)	20 (21.1)	36 (17.5)
Any TEAE leading to death (fatal TEAE)	0	3 (3.2)	3 (1.5)
Any serious TEAE	21 (18.9)	26 (27.4)	47 (22.8)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
$ As assessed by investigator.

Program Source Code: [redacted]

TABLE 14.3 1.1

Overview of Treatment-Emergent Adverse Events and All Deaths by Time Interval
(Safety Analysis Set)

	Dose Category		
	Low Dose n (%)	High Dose n (%)	All Subjects n (%)
Any SAE that is considered associated with infusion pump$	8 (7.2)	7 (7.4)	15 (7.3)
Possible	3 (2.7)	4 (4.2)	7 (3.4)
Probable	5 (4.5)	2 (2.1)	7 (3.4)
Causal relationship	4 (3.6)	2 (2.1)	6 (2.9)
Any SAE that is considered associated with [redacted] infusion set$	1 (0.9)	1 (1.1)	2 (1.0)
Possible	1 (0.9)	1 (1.1)	2 (1.0)
Probable	0	0	0
Causal relationship	0	0	0
Any SAE that is considered associated with neria guards infusion set$	2 (1.8)	1 (1.1)	3 (1.5)
Possible	1 (0.9)	1 (1.1)	2 (1.0)
Probable	0	0	0
Causal relationship	1 (0.9)	0	1 (0.5)
Any SAE that is considered associated with product complaint$	8 (7.2)	5 (5.3)	13 (6.3)
ABBV-951	2 (1.8)	3 (3.2)	5 (2.4)
Infusion pump	1 (0.9)	1 (1.1)	2 (1.0)
Vial adapter	0	0	0
Syringes	0	0	0
[redacted] infusion set (total)	3 (2.7)	0	3 (1.5)
[redacted] infusion set 6 mm	2 (1.8)	0	2 (1.0)
[redacted] infusion set 9 mm	1 (0.9)	0	1 (0.5)
Neria guard infusion set (total)	2 (1.8)	1 (1.1)	3 (1.5)
Neria guard infusion set 6 mm	2 (1.8)	1 (1.1)	3 (1.5)
Neria guard infusion set 9 mm	0	0	0
[redacted]	0	0	0

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
$ As assessed by investigator.

Program Source Code: [redacted]

TABLE 14.3 1.1

Overview of Treatment-Emergent Adverse Events and All Deaths by Time Interval
(Safety Analysis Set)

	Dose Category		
	Low Dose n (%)	High Dose n (%)	All Subjects n (%)
All deaths#	0	3 (3.2)	3 (1.5)
All TE-deaths	0	3 (3.2)	3 (1.5)
Deaths related to COVID-19 infection	0	0	0
AESI: polyneuropathy (narrow)	2 (1.8)	6 (6.3)	8 (3.9)
AESI: weight loss	11 (9.9)	12 (12.6)	23 (11.2)
AESI: hallucinations/psychosis	23 (20.7)	21 (22.1)	44 (21.4)
AESI: somnolence	8 (7.2)	1 (1.1)	9 (4.4)
AESI: infusion site related infections	33 (29.7)	33 (34.7)	66 (32.0)
AESI: infusion site related non infection reactions	64 (57.7)	70 (73.7)	134 (65.0)
AESI: falls and associated injuries	21 (18.9)	24 (25.3)	45 (21.8)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.
Includes non treatment-emergent deaths.

Program Source Code: [redacted]

表35　すべての有害事象（安全性解析対象集団）：M15-741試験

[redacted]20[redacted] 04:28 <[redacted]>
ABBV-951
STUDY M15-741 - SECOND INTERIM (CUTOFF [redacted]20[redacted])
R&D/20/1632 - CLINICAL/STATISTICAL

TABLE 14.3__1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period	N=132	N=112	N=244
Any adverse event	122 (92.4)	108 (96.4)	230 (94.3)
血液およびリンパ系障害	1 (0.8)	3 (2.7)	4 (1.6)
大球性貧血	0	1 (0.9)	1 (0.4)
凝血異常	0	1 (0.9)	1 (0.4)
リンパ節症	1 (0.8)	0	1 (0.4)
縦隔リンパ節腫脹	0	1 (0.9)	1 (0.4)
心臓障害	4 (3.0)	7 (6.3)	11 (4.5)
急性心筋梗塞	1 (0.8)	0	1 (0.4)
狭心症	1 (0.8)	0	1 (0.4)
心房細動	0	1 (0.9)	1 (0.4)
徐脈	0	1 (0.9)	1 (0.4)
心停止	1 (0.8)	0	1 (0.4)
心肺停止	0	1 (0.9)	1 (0.4)
冠動脈疾患	1 (0.8)	1 (0.9)	2 (0.8)
冠動脈狭窄	1 (0.8)	0	1 (0.4)
期外収縮	0	1 (0.9)	1 (0.4)
左室肥大	0	1 (0.9)	1 (0.4)
心筋梗塞	1 (0.8)	0	1 (0.4)
動悸	0	2 (1.8)	2 (0.8)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
耳および迷路障害	4 (3.0)	4 (3.6)	8 (3.3)
感音性難聴	1 (0.8)	0	1 (0.4)
乗物酔い	0	1 (0.9)	1 (0.4)
回転性めまい	3 (2.3)	2 (1.8)	5 (2.0)
頭位性回転性めまい	0	1 (0.9)	1 (0.4)
眼障害	7 (5.3)	8 (7.1)	15 (6.1)
白内障	2 (1.5)	2 (1.8)	4 (1.6)
複視	2 (1.5)	1 (0.9)	3 (1.2)
ドライアイ	1 (0.8)	3 (2.7)	4 (1.6)
緑内障	1 (0.8)	1 (0.9)	2 (0.8)
眼窩周囲痛	0	1 (0.9)	1 (0.4)
眼窩周囲腫脹	0	2 (1.8)	2 (0.8)
網膜裂孔	2 (1.5)	0	2 (0.8)
霧視	1 (0.8)	0	1 (0.4)
視野欠損	0	1 (0.9)	1 (0.4)
胃腸障害	27 (20.5)	29 (25.9)	56 (23.0)
腹部膨満	1 (0.8)	3 (2.7)	4 (1.6)
腹痛	2 (1.5)	1 (0.9)	3 (1.2)
上腹部痛	1 (0.8)	1 (0.9)	2 (0.8)
アフタ性潰瘍	1 (0.8)	0	1 (0.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
胃腸障害 (Cont.)			
呼気臭	2 (1.5)	1 (0.9)	3 (1.2)
虚血性大腸炎	1 (0.8)	0	1 (0.4)
便秘	8 (6.1)	12 (10.7)	20 (8.2)
齲歯	1 (0.8)	0	1 (0.4)
下痢	6 (4.5)	3 (2.7)	9 (3.7)
口内乾燥	3 (2.3)	5 (4.5)	8 (3.3)
消化不良	1 (0.8)	0	1 (0.4)
嚥下障害	0	1 (0.9)	1 (0.4)
糞塊	0	1 (0.9)	1 (0.4)
排便回数増加	0	1 (0.9)	1 (0.4)
胃食道逆流性疾患	1 (0.8)	1 (0.9)	2 (0.8)
舌炎	1 (0.8)	0	1 (0.4)
舌痛	1 (0.8)	0	1 (0.4)
吐血	1 (0.8)	0	1 (0.4)
痔核	1 (0.8)	0	1 (0.4)
裂孔ヘルニア	1 (0.8)	0	1 (0.4)
胃排出不全	1 (0.8)	0	1 (0.4)
腸出血	1 (0.8)	0	1 (0.4)
過敏性腸症候群	1 (0.8)	1 (0.9)	2 (0.8)
大腸ポリープ	0	1 (0.9)	1 (0.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
胃腸障害 (Cont.)			
口唇乾燥	1 (0.8)	0	1 (0.4)
メレナ	2 (1.5)	0	2 (0.8)
口腔腫脹	1 (0.8)	0	1 (0.4)
悪心	8 (6.1)	11 (9.8)	19 (7.8)
口腔内不快感	1 (0.8)	0	1 (0.4)
口腔内痛	1 (0.8)	0	1 (0.4)
口の錯感覚	1 (0.8)	1 (0.9)	2 (0.8)
直腸出血	1 (0.8)	1 (0.9)	2 (0.8)
歯痛	0	1 (0.9)	1 (0.4)
嘔吐	3 (2.3)	3 (2.7)	6 (2.5)
一般・全身障害および投与部位の状態	106 (80.3)	96 (85.7)	202 (82.8)
投与部位内出血	0	1 (0.9)	1 (0.4)
投与部位紅斑	1 (0.8)	0	1 (0.4)
投与部位漏出	0	2 (1.8)	2 (0.8)
無力症	3 (2.3)	0	3 (1.2)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
一般・全身障害および投与部位の状態 (Cont.)			
カテーテル留置部位紅斑	1 (0.8)	1 (0.9)	2 (0.8)
カテーテル留置部位漏出	1 (0.8)	0	1 (0.4)
カテーテル留置部位出血	0	1 (0.9)	1 (0.4)
カテーテル留置部位炎症	0	1 (0.9)	1 (0.4)
カテーテル留置部位刺激感	0	1 (0.9)	1 (0.4)
カテーテル留置部位浮腫	0	1 (0.9)	1 (0.4)
カテーテル留置部位疼痛	0	2 (1.8)	2 (0.8)
胸部不快感	0	1 (0.9)	1 (0.4)
胸痛	1 (0.8)	1 (0.9)	2 (0.8)
泣き	1 (0.8)	0	1 (0.4)
不快感	1 (0.8)	0	1 (0.4)
薬効欠如	0	1 (0.9)	1 (0.4)
薬剤離脱症候群	1 (0.8)	1 (0.9)	2 (0.8)
疲労	6 (4.5)	3 (2.7)	9 (3.7)
異常感	1 (0.8)	1 (0.9)	2 (0.8)
冷感	0	1 (0.9)	1 (0.4)
熱感	1 (0.8)	0	1 (0.4)
歩行障害	0	2 (1.8)	2 (0.8)
歩行不能	1 (0.8)	0	1 (0.4)
低体温	1 (0.8)	1 (0.9)	2 (0.8)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
一般・全身障害および投与部位の状態 (Cont.)			
インフルエンザ様疾患	1 (0.8)	2 (1.8)	3 (1.2)
注入部位内出血	10 (7.6)	8 (7.1)	18 (7.4)
注入部位皮膚炎	2 (1.5)	2 (1.8)	4 (1.6)
注入部位分泌物	1 (0.8)	1 (0.9)	2 (0.8)
注入部位変色	2 (1.5)	0	2 (0.8)
注入部位不快感	3 (2.3)	1 (0.9)	4 (1.6)
注入部位びらん	1 (0.8)	1 (0.9)	2 (0.8)
注入部位紅斑	65 (49.2)	60 (53.6)	125 (51.2)
注入部位皮膚剥脱	3 (2.3)	3 (2.7)	6 (2.5)
注入部位血管外漏出	8 (6.1)	12 (10.7)	20 (8.2)
注入部位血腫	8 (6.1)	8 (7.1)	16 (6.6)
注入部位出血	4 (3.0)	5 (4.5)	9 (3.7)
注入部位硬結	7 (5.3)	3 (2.7)	10 (4.1)
注入部位炎症	3 (2.3)	6 (5.4)	9 (3.7)
注入部位損傷	1 (0.8)	2 (1.8)	3 (1.2)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
一般・全身障害および投与部位の状態 (Cont.)			
注入部位刺激感	1 (0.8)	4 (3.6)	5 (2.0)
注入部位腫瘤	5 (3.8)	3 (2.7)	8 (3.3)
注入部位壊死	0	1 (0.9)	1 (0.4)
注入部位結節	34 (25.8)	34 (30.4)	68 (27.9)
注入部位浮腫	19 (14.4)	28 (25.0)	47 (19.3)
注入部位疼痛	18 (13.6)	20 (17.9)	38 (15.6)
注入部位蒼白	3 (2.3)	1 (0.9)	4 (1.6)
注入部位丘疹	7 (5.3)	11 (9.8)	18 (7.4)
注入部位異常感覚	0	2 (1.8)	2 (0.8)
注入部位そう痒感	5 (3.8)	2 (1.8)	7 (2.9)
注入部位発疹	3 (2.3)	4 (3.6)	7 (2.9)
注入部位反応	13 (9.8)	18 (16.1)	31 (12.7)
注入部位痂皮	0	1 (0.9)	1 (0.4)
注入部位腫脹	4 (3.0)	2 (1.8)	6 (2.5)
注入部位小水疱	0	2 (1.8)	2 (0.8)
注入部位熱感	0	1 (0.9)	1 (0.4)
注射部位内出血	2 (1.5)	1 (0.9)	3 (1.2)
注射部位変色	1 (0.8)	0	1 (0.4)
注射部位紅斑	6 (4.5)	8 (7.1)	14 (5.7)
注射部位漏出	1 (0.8)	1 (0.9)	2 (0.8)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
一般・全身障害および投与部位の状態 (Cont.)			
注射部位血腫	0	1 (0.9)	1 (0.4)
注射部位出血	0	1 (0.9)	1 (0.4)
注射部位炎症	2 (1.5)	4 (3.6)	6 (2.5)
注射部位結節	3 (2.3)	6 (5.4)	9 (3.7)
注射部位浮腫	2 (1.5)	3 (2.7)	5 (2.0)
注射部位疼痛	2 (1.5)	6 (5.4)	8 (3.3)
注射部位丘疹	0	1 (0.9)	1 (0.4)
注射部位反応	1 (0.8)	1 (0.9)	2 (0.8)
注射部位腫脹	2 (1.5)	2 (1.8)	4 (1.6)
注射部位蕁麻疹	0	1 (0.9)	1 (0.4)
滴下投与部位熱傷	0	1 (0.9)	1 (0.4)
滴下投与部位痛	0	1 (0.9)	1 (0.4)
限局性浮腫	0	1 (0.9)	1 (0.4)
適用部位からの吸収不良	0	1 (0.9)	1 (0.4)
倦怠感	1 (0.8)	2 (1.8)	3 (1.2)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
一般・全身障害および投与部位の状態 (Cont.)			
医療機器使用部位刺激感	1 (0.8)	2 (1.8)	3 (1.2)
医療機器使用部位そう痒感	1 (0.8)	0	1 (0.4)
医療機器使用部位発疹	0	2 (1.8)	2 (0.8)
小結節	1 (0.8)	0	1 (0.4)
非心臓性胸痛	0	2 (1.8)	2 (0.8)
末梢性浮腫	5 (3.8)	4 (3.6)	9 (3.7)
疼痛	2 (1.5)	0	2 (0.8)
末梢腫脹	0	4 (3.6)	4 (1.6)
穿刺部位内出血	1 (0.8)	0	1 (0.4)
穿刺部位紅斑	0	3 (2.7)	3 (1.2)
穿刺部位出血	1 (0.8)	0	1 (0.4)
穿刺部位硬結	2 (1.5)	0	2 (0.8)
穿刺部位浮腫	0	1 (0.9)	1 (0.4)
穿刺部位腫脹	0	1 (0.9)	1 (0.4)
発熱	2 (1.5)	2 (1.8)	4 (1.6)
口渇	1 (0.8)	0	1 (0.4)
血管穿刺部位硬結	1 (0.8)	0	1 (0.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
肝胆道系障害	2 (1.5)	1 (0.9)	3 (1.2)
肝嚢胞	1 (0.8)	0	1 (0.4)
脂肪肝	0	1 (0.9)	1 (0.4)
門脈血栓症	1 (0.8)	0	1 (0.4)
感染症および寄生虫症	58 (43.9)	56 (50.0)	114 (46.7)
無症候性COVID-19	0	1 (0.9)	1 (0.4)
細菌性疾患キャリアー	0	1 (0.9)	1 (0.4)
ボレリア感染	1 (0.8)	0	1 (0.4)
ウイルス性気管支炎	0	1 (0.9)	1 (0.4)
COVID-19	1 (0.8)	0	1 (0.4)
COVID-19肺炎	1 (0.8)	0	1 (0.4)
カテーテル留置部位感染	1 (0.8)	0	1 (0.4)
蜂巣炎	1 (0.8)	1 (0.9)	2 (0.8)
結膜炎	2 (1.5)	0	2 (0.8)
膀胱炎	0	1 (0.9)	1 (0.4)
爪の皮膚糸状菌症	0	1 (0.9)	1 (0.4)
真菌感染	1 (0.8)	0	1 (0.4)
胃腸炎	0	1 (0.9)	1 (0.4)
歯肉炎	1 (0.8)	0	1 (0.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
感染症および寄生虫症 (Cont.)			
麦粒腫	1 (0.8)	0	1 (0.4)
感染性皮膚潰瘍	0	1 (0.9)	1 (0.4)
インフルエンザ	0	1 (0.9)	1 (0.4)
注入部位膿瘍	13 (9.8)	13 (11.6)	26 (10.7)
注入部位蜂巣炎	29 (22.0)	27 (24.1)	56 (23.0)
注入部位感染	6 (4.5)	11 (9.8)	17 (7.0)
注入部位膿疱	0	1 (0.9)	1 (0.4)
注射部位蜂巣炎	0	3 (2.7)	3 (1.2)
上咽頭炎	5 (3.8)	5 (4.5)	10 (4.1)
爪真菌症	0	1 (0.9)	1 (0.4)
耳下腺膿瘍	0	1 (0.9)	1 (0.4)
肺炎	3 (2.3)	1 (0.9)	4 (1.6)
術後膿瘍	1 (0.8)	0	1 (0.4)
シュードモナス感染	0	1 (0.9)	1 (0.4)
膿疱性皮疹	1 (0.8)	0	1 (0.4)
気道感染	0	1 (0.9)	1 (0.4)
敗血症	3 (2.3)	1 (0.9)	4 (1.6)
敗血症性ショック	1 (0.8)	0	1 (0.4)
副鼻腔炎	1 (0.8)	0	1 (0.4)
ブドウ球菌感染	1 (0.8)	1 (0.9)	2 (0.8)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
感染症および寄生虫症 (Cont.)			
歯感染	1 (0.8)	1 (0.9)	2 (0.8)
上気道感染	1 (0.8)	0	1 (0.4)
尿路感染	8 (6.1)	11 (9.8)	19 (7.8)
水痘帯状疱疹ウイルス感染	1 (0.8)	0	1 (0.4)
傷害、中毒および処置合併症	21 (15.9)	26 (23.2)	47 (19.3)
足関節部骨折	0	1 (0.9)	1 (0.4)
節足動物咬傷	0	1 (0.9)	1 (0.4)
骨挫傷	1 (0.8)	1 (0.9)	2 (0.8)
脳挫傷	1 (0.8)	0	1 (0.4)
挫傷	2 (1.5)	6 (5.4)	8 (3.3)
医療機器設置の問題	1 (0.8)	0	1 (0.4)
医療機器による投与の欠落	1 (0.8)	0	1 (0.4)
期限切れの製品使用	1 (0.8)	0	1 (0.4)
眼挫傷	0	1 (0.9)	1 (0.4)
顔面損傷	0	1 (0.9)	1 (0.4)
顔面骨骨折	0	2 (1.8)	2 (0.8)
転倒	16 (12.1)	23 (20.5)	39 (16.0)
頭部損傷	2 (1.5)	2 (1.8)	4 (1.6)
注入に伴う反応	1 (0.8)	0	1 (0.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
傷害、中毒および処置合併症 (Cont.)			
関節脱臼	0	1 (0.9)	1 (0.4)
靭帯捻挫	1 (0.8)	1 (0.9)	2 (0.8)
腰椎骨折	0	1 (0.9)	1 (0.4)
過量投与	0	1 (0.9)	1 (0.4)
処置後挫傷	1 (0.8)	0	1 (0.4)
処置によるめまい	0	1 (0.9)	1 (0.4)
肋骨骨折	1 (0.8)	2 (1.8)	3 (1.2)
皮膚擦過傷	1 (0.8)	2 (1.8)	3 (1.2)
皮膚損傷	1 (0.8)	0	1 (0.4)
皮膚裂傷	1 (0.8)	6 (5.4)	7 (2.9)
ストレス骨折	1 (0.8)	0	1 (0.4)
硬膜下血腫	0	1 (0.9)	1 (0.4)
サンバーン	0	1 (0.9)	1 (0.4)
腱断裂	1 (0.8)	1 (0.9)	2 (0.8)
過少量投与	0	1 (0.9)	1 (0.4)
創傷	1 (0.8)	0	1 (0.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
臨床検査	23 (17.4)	22 (19.6)	45 (18.4)
血中クレアチンホスホキナーゼ増加	1 (0.8)	1 (0.9)	2 (0.8)
血中クレアチニン減少	0	1 (0.9)	1 (0.4)
血中葉酸減少	1 (0.8)	2 (1.8)	3 (1.2)
血中ホモシステイン増加	1 (0.8)	2 (1.8)	3 (1.2)
血中リン減少	0	1 (0.9)	1 (0.4)
血圧上昇	1 (0.8)	1 (0.9)	2 (0.8)
起立血圧低下	1 (0.8)	0	1 (0.4)
血中ナトリウム減少	1 (0.8)	0	1 (0.4)
C-反応性蛋白増加	0	1 (0.9)	1 (0.4)
握力低下	1 (0.8)	0	1 (0.4)
ヘモグロビン減少	1 (0.8)	1 (0.9)	2 (0.8)
リンパ球数減少	0	1 (0.9)	1 (0.4)
単球数増加	0	1 (0.9)	1 (0.4)
好中球数増加	0	2 (1.8)	2 (0.8)
プロトロンビン時間延長	0	1 (0.9)	1 (0.4)
赤血球数減少	0	1 (0.9)	1 (0.4)
ビタミンB12減少	1 (0.8)	1 (0.9)	2 (0.8)
ビタミンB6減少	5 (3.8)	6 (5.4)	11 (4.5)
ビタミンD減少	0	1 (0.9)	1 (0.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
臨床検査 (Cont.)			
体重減少	10 (7.6)	12 (10.7)	22 (9.0)
体重増加	2 (1.5)	0	2 (0.8)
白血球数増加	0	2 (1.8)	2 (0.8)
代謝および栄養障害	11 (8.3)	17 (15.2)	28 (11.5)
悪液質	1 (0.8)	0	1 (0.4)
食欲減退	3 (2.3)	2 (1.8)	5 (2.0)
脱水	1 (0.8)	3 (2.7)	4 (1.6)
糖尿病	0	1 (0.9)	1 (0.4)
水分過負荷	0	1 (0.9)	1 (0.4)
体液貯留	1 (0.8)	1 (0.9)	2 (0.8)
葉酸欠乏	1 (0.8)	1 (0.9)	2 (0.8)
耐糖能障害	0	1 (0.9)	1 (0.4)
高コレステロール血症	0	1 (0.9)	1 (0.4)
高血糖	0	1 (0.9)	1 (0.4)
高ホモシステイン血症	0	1 (0.9)	1 (0.4)
低カリウム血症	0	3 (2.7)	3 (1.2)
低ナトリウム血症	2 (1.5)	0	2 (0.8)
栄養障害	0	1 (0.9)	1 (0.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
代謝および栄養障害 (Cont.)			
ビタミンB群欠乏	1 (0.8)	1 (0.9)	2 (0.8)
ビタミンB12欠乏	0	2 (1.8)	2 (0.8)
ビタミンB6欠乏	3 (2.3)	5 (4.5)	8 (3.3)
筋骨格系および結合組織障害	24 (18.2)	20 (17.9)	44 (18.0)
関節痛	3 (2.3)	3 (2.7)	6 (2.5)
反応性関節炎	1 (0.8)	1 (0.9)	2 (0.8)
背部痛	8 (6.1)	4 (3.6)	12 (4.9)
骨痛	0	1 (0.9)	1 (0.4)
滑液包炎	2 (1.5)	0	2 (0.8)
外骨腫	0	1 (0.9)	1 (0.4)
椎間関節症候群	0	1 (0.9)	1 (0.4)
椎間板変性症	1 (0.8)	0	1 (0.4)
椎間板突出	0	1 (0.9)	1 (0.4)
関節滲出液	0	2 (1.8)	2 (0.8)
関節腫脹	0	1 (0.9)	1 (0.4)
四肢不快感	0	1 (0.9)	1 (0.4)
筋萎縮	0	1 (0.9)	1 (0.4)
筋痙縮	2 (1.5)	3 (2.7)	5 (2.0)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
筋骨格系および結合組織障害 (Cont.)			
筋力低下	4 (3.0)	1 (0.9)	5 (2.0)
筋骨格硬直	0	1 (0.9)	1 (0.4)
筋肉痛	2 (1.5)	1 (0.9)	3 (1.2)
頚部痛	2 (1.5)	0	2 (0.8)
骨炎	0	1 (0.9)	1 (0.4)
変形性関節症	1 (0.8)	4 (3.6)	5 (2.0)
骨減少症	1 (0.8)	0	1 (0.4)
四肢痛	3 (2.3)	3 (2.7)	6 (2.5)
関節周囲炎	0	1 (0.9)	1 (0.4)
姿勢異常	0	1 (0.9)	1 (0.4)
横紋筋融解症	2 (1.5)	0	2 (0.8)
肩回旋筋腱板症候群	0	1 (0.9)	1 (0.4)
仙腸関節機能障害	1 (0.8)	0	1 (0.4)
変形性脊椎症	1 (0.8)	0	1 (0.4)
腱障害	0	1 (0.9)	1 (0.4)
腱炎	1 (0.8)	0	1 (0.4)
斜頚	0	1 (0.9)	1 (0.4)
弾発指	1 (0.8)	0	1 (0.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	4 (3.6)	4 (1.6)
基底細胞癌	0	2 (1.8)	2 (0.8)
脂漏性角化症	0	1 (0.9)	1 (0.4)
皮膚有棘細胞癌	0	1 (0.9)	1 (0.4)
神経系障害	62 (47.0)	48 (42.9)	110 (45.1)
アカシジア	1 (0.8)	0	1 (0.4)
健忘	1 (0.8)	0	1 (0.4)
失語症	0	1 (0.9)	1 (0.4)
運動失調	1 (0.8)	0	1 (0.4)
平衡障害	0	4 (3.6)	4 (1.6)
運動緩慢	1 (0.8)	1 (0.9)	2 (0.8)
手根管症候群	0	1 (0.9)	1 (0.4)
大脳萎縮	0	1 (0.9)	1 (0.4)
脳出血	0	1 (0.9)	1 (0.4)
脳圧排効果	0	1 (0.9)	1 (0.4)
脳血管発作	0	1 (0.9)	1 (0.4)
認知障害	4 (3.0)	2 (1.8)	6 (2.5)
振動覚低下	1 (0.8)	0	1 (0.4)
注意力障害	0	1 (0.9)	1 (0.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
神経系障害 (Cont.)			
浮動性めまい	15 (11.4)	10 (8.9)	25 (10.2)
体位性めまい	5 (3.8)	0	5 (2.0)
構語障害	0	3 (2.7)	3 (1.2)
味覚不全	2 (1.5)	1 (0.9)	3 (1.2)
ジスキネジア	12 (9.1)	6 (5.4)	18 (7.4)
起立障害	1 (0.8)	0	1 (0.4)
ジストニア	2 (1.5)	5 (4.5)	7 (2.9)
脳症	0	1 (0.9)	1 (0.4)
てんかん	0	1 (0.9)	1 (0.4)
本態性振戦	0	1 (0.9)	1 (0.4)
伸展性足底反応	1 (0.8)	0	1 (0.4)
すくみ現象	4 (3.0)	0	4 (1.6)
全身性強直性間代性発作	0	1 (0.9)	1 (0.4)
頭部不快感	1 (0.8)	0	1 (0.4)
頭痛	7 (5.3)	7 (6.3)	14 (5.7)
片側感覚消失	0	1 (0.9)	1 (0.4)
不全片麻痺	0	1 (0.9)	1 (0.4)
感覚鈍麻	1 (0.8)	2 (1.8)	3 (1.2)
反射減弱	2 (1.5)	1 (0.9)	3 (1.2)
不規則睡眠覚醒リズム障害	1 (0.8)	0	1 (0.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
神経系障害 (Cont.)			
嗜眠	1 (0.8)	1 (0.9)	2 (0.8)
意識消失	1 (0.8)	1 (0.9)	2 (0.8)
腰仙部神経根障害	0	1 (0.9)	1 (0.4)
記憶障害	0	2 (1.8)	2 (0.8)
代謝性脳症	1 (0.8)	1 (0.9)	2 (0.8)
神経痛	0	1 (0.9)	1 (0.4)
末梢性ニューロパチー	1 (0.8)	1 (0.9)	2 (0.8)
オンオフ現象	4 (3.0)	4 (3.6)	8 (3.3)
錯感覚	4 (3.0)	3 (2.7)	7 (2.9)
パーキンソン病	12 (9.1)	5 (4.5)	17 (7.0)
パーキンソニズム	0	3 (2.7)	3 (1.2)
側反弓	1 (0.8)	2 (1.8)	3 (1.2)
多発ニューロパチー	0	2 (1.8)	2 (0.8)
失神寸前の状態	0	1 (0.9)	1 (0.4)
心因性発作	0	1 (0.9)	1 (0.4)
精神運動亢進	1 (0.8)	1 (0.9)	2 (0.8)
反射異常	0	1 (0.9)	1 (0.4)
安静時振戦	0	1 (0.9)	1 (0.4)
坐骨神経痛	0	3 (2.7)	3 (1.2)
痙攣発作	0	1 (0.9)	1 (0.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
神経系障害 (Cont.)			
感覚障害	0	1 (0.9)	1 (0.4)
感覚消失	0	1 (0.9)	1 (0.4)
睡眠時麻痺	1 (0.8)	0	1 (0.4)
傾眠	9 (6.8)	3 (2.7)	12 (4.9)
失神	0	3 (2.7)	3 (1.2)
振戦	1 (0.8)	2 (1.8)	3 (1.2)
製品の問題	2 (1.5)	1 (0.9)	3 (1.2)
医療機器送達システムの問題	1 (0.8)	0	1 (0.4)
医療機器位置異常	1 (0.8)	0	1 (0.4)
医療機器機能不良	0	1 (0.9)	1 (0.4)
精神障害	50 (37.9)	54 (48.2)	104 (42.6)
異常な夢	0	1 (0.9)	1 (0.4)
感情不安定	1 (0.8)	1 (0.9)	2 (0.8)
激越	0	1 (0.9)	1 (0.4)
不安	10 (7.6)	18 (16.1)	28 (11.5)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
精神障害 (Cont.)			
不安障害	0	1 (0.9)	1 (0.4)
無感情	1 (0.8)	0	1 (0.4)
歯ぎしり	2 (1.5)	0	2 (0.8)
強迫行為	0	1 (0.9)	1 (0.4)
強迫性性行動	1 (0.8)	0	1 (0.4)
錯乱状態	4 (3.0)	4 (3.6)	8 (3.3)
譫妄	1 (0.8)	4 (3.6)	5 (2.0)
妄想	8 (6.1)	2 (1.8)	10 (4.1)
寄生虫妄想	1 (0.8)	0	1 (0.4)
妄想性障害、詳細不明	0	1 (0.9)	1 (0.4)
抑うつ気分	2 (1.5)	1 (0.9)	3 (1.2)
うつ病	2 (1.5)	2 (1.8)	4 (1.6)
抑うつ症状	2 (1.5)	0	2 (0.8)
ドーパミン調節障害症候群	1 (0.8)	0	1 (0.4)
ディスフェミア	0	1 (0.9)	1 (0.4)
睡眠異常	1 (0.8)	0	1 (0.4)
情動障害	1 (0.8)	1 (0.9)	2 (0.8)
注射恐怖	0	1 (0.9)	1 (0.4)
幻覚	20 (15.2)	21 (18.8)	41 (16.8)
幻聴	3 (2.3)	3 (2.7)	6 (2.5)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
精神障害 (Cont.)			
幻嗅	0	1 (0.9)	1 (0.4)
幻視	10 (7.6)	5 (4.5)	15 (6.1)
混合性幻覚	1 (0.8)	0	1 (0.4)
性欲過剰	1 (0.8)	0	1 (0.4)
錯覚	1 (0.8)	0	1 (0.4)
衝動制御障害	0	4 (3.6)	4 (1.6)
衝動行為	0	1 (0.9)	1 (0.4)
不眠症	9 (6.8)	9 (8.0)	18 (7.4)
易刺激性	1 (0.8)	1 (0.9)	2 (0.8)
嫉妬妄想	1 (0.8)	0	1 (0.4)
躁病	0	1 (0.9)	1 (0.4)
気分変化	1 (0.8)	0	1 (0.4)
気分動揺	0	1 (0.9)	1 (0.4)
悪夢	1 (0.8)	1 (0.9)	2 (0.8)
強迫観念	1 (0.8)	0	1 (0.4)
パニック発作	0	3 (2.7)	3 (1.2)
パニック反応	0	1 (0.9)	1 (0.4)
妄想症	2 (1.5)	0	2 (0.8)
睡眠の質低下	1 (0.8)	0	1 (0.4)
処置に対する不安	0	1 (0.9)	1 (0.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
精神障害 (Cont.)			
精神病性障害	4 (3.0)	2 (1.8)	6 (2.5)
精神病症状	1 (0.8)	0	1 (0.4)
レム睡眠行動障害	1 (0.8)	1 (0.9)	2 (0.8)
レム睡眠異常	1 (0.8)	0	1 (0.4)
睡眠障害	2 (1.5)	1 (0.9)	3 (1.2)
ねごと	1 (0.8)	1 (0.9)	2 (0.8)
常同症	0	1 (0.9)	1 (0.4)
ストレス	0	1 (0.9)	1 (0.4)
自殺念慮	1 (0.8)	2 (1.8)	3 (1.2)
自殺企図	1 (0.8)	0	1 (0.4)
腎および尿路障害	11 (8.3)	7 (6.3)	18 (7.4)
膀胱痙縮	1 (0.8)	0	1 (0.4)
膀胱結石	1 (0.8)	0	1 (0.4)
排尿困難	1 (0.8)	2 (1.8)	3 (1.2)
緊張性膀胱	1 (0.8)	0	1 (0.4)
夜間頻尿	0	1 (0.9)	1 (0.4)
多尿	0	1 (0.9)	1 (0.4)
腎機能障害	0	1 (0.9)	1 (0.4)
尿管結石症	0	1 (0.9)	1 (0.4)
切迫性尿失禁	3 (2.3)	0	3 (1.2)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
腎および尿路障害 (Cont.)			
尿失禁	3 (2.3)	2 (1.8)	5 (2.0)
尿閉	0	3 (2.7)	3 (1.2)
尿路障害	1 (0.8)	0	1 (0.4)
尿異常	0	1 (0.9)	1 (0.4)
尿臭異常	0	1 (0.9)	1 (0.4)
生殖系および乳房障害	2 (1.5)	4 (3.6)	6 (2.5)
良性前立腺肥大症	1 (0.8)	0	1 (0.4)
勃起不全	1 (0.8)	1 (0.9)	2 (0.8)
ペイロニー病	0	1 (0.9)	1 (0.4)
前立腺腫大	0	1 (0.9)	1 (0.4)
腟脱	0	1 (0.9)	1 (0.4)
呼吸器、胸郭および縦隔障害	6 (4.5)	19 (17.0)	25 (10.2)
急性呼吸不全	0	1 (0.9)	1 (0.4)
気管支拡張症	1 (0.8)	0	1 (0.4)
咳嗽	1 (0.8)	2 (1.8)	3 (1.2)
発声障害	0	2 (1.8)	2 (0.8)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
呼吸器、胸郭および縦隔障害 (Cont.)			
呼吸困難	2 (1.5)	6 (5.4)	8 (3.3)
労作性呼吸困難	1 (0.8)	0	1 (0.4)
鼻出血	0	1 (0.9)	1 (0.4)
過換気	0	2 (1.8)	2 (0.8)
口腔咽頭痛	1 (0.8)	1 (0.9)	2 (0.8)
誤嚥性肺炎	0	1 (0.9)	1 (0.4)
湿性咳嗽	0	1 (0.9)	1 (0.4)
肺塞栓症	0	2 (1.8)	2 (0.8)
ラ音	0	1 (0.9)	1 (0.4)
鼻痛	0	1 (0.9)	1 (0.4)
鼻漏	0	2 (1.8)	2 (0.8)
咽喉刺激感	0	1 (0.9)	1 (0.4)
皮膚および皮下組織障害	14 (10.6)	14 (12.5)	28 (11.5)
脱毛症	2 (1.5)	0	2 (0.8)
褥瘡性潰瘍	0	1 (0.9)	1 (0.4)
皮膚嚢腫	1 (0.8)	1 (0.9)	2 (0.8)
皮膚炎	0	1 (0.9)	1 (0.4)
接触皮膚炎	2 (1.5)	0	2 (0.8)
おむつ皮膚炎	1 (0.8)	0	1 (0.4)
薬疹	1 (0.8)	0	1 (0.4)
皮膚乾燥	1 (0.8)	1 (0.9)	2 (0.8)
斑状出血	1 (0.8)	0	1 (0.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
皮膚および皮下組織障害 (Cont.)			
紅斑	1 (0.8)	3 (2.7)	4 (1.6)
爪の障害	1 (0.8)	0	1 (0.4)
脂肪織炎	0	1 (0.9)	1 (0.4)
丘疹	0	2 (1.8)	2 (0.8)
光線過敏性反応	0	1 (0.9)	1 (0.4)
そう痒症	2 (1.5)	1 (0.9)	3 (1.2)
乾癬	0	1 (0.9)	1 (0.4)
発疹	2 (1.5)	1 (0.9)	3 (1.2)
紅斑性皮疹	0	1 (0.9)	1 (0.4)
そう痒性皮疹	2 (1.5)	1 (0.9)	3 (1.2)
皮膚刺激	0	1 (0.9)	1 (0.4)
皮膚病変	0	1 (0.9)	1 (0.4)
皮膚潰瘍	1 (0.8)	1 (0.9)	2 (0.8)
蕁麻疹	2 (1.5)	0	2 (0.8)
社会環境	1 (0.8)	0	1 (0.4)
運動不能	1 (0.8)	0	1 (0.4)
外科および内科処置	0	1 (0.9)	1 (0.4)
抜歯	0	1 (0.9)	1 (0.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
血管障害	11 (8.3)	15 (13.4)	26 (10.7)
深部静脈血栓症	0	1 (0.9)	1 (0.4)
血腫	0	1 (0.9)	1 (0.4)
出血	0	1 (0.9)	1 (0.4)
ほてり	0	1 (0.9)	1 (0.4)
高血圧	3 (2.3)	3 (2.7)	6 (2.5)
高血圧クリーゼ	1 (0.8)	0	1 (0.4)
低血圧	2 (1.5)	4 (3.6)	6 (2.5)
不安定血圧	0	1 (0.9)	1 (0.4)
起立性高血圧	0	1 (0.9)	1 (0.4)
起立性低血圧	6 (4.5)	6 (5.4)	12 (4.9)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Optimization period	N=132	N=112	N=244
Any adverse event	105 (79.5)	97 (86.6)	202 (82.8)
心臓障害	0	2 (1.8)	2 (0.8)
徐脈	0	1 (0.9)	1 (0.4)
動悸	0	1 (0.9)	1 (0.4)
耳および迷路障害	2 (1.5)	2 (1.8)	4 (1.6)
乗物酔い	0	1 (0.9)	1 (0.4)
回転性めまい	2 (1.5)	1 (0.9)	3 (1.2)
眼障害	1 (0.8)	2 (1.8)	3 (1.2)
複視	0	1 (0.9)	1 (0.4)
眼窩周囲腫脹	0	1 (0.9)	1 (0.4)
霧視	1 (0.8)	0	1 (0.4)
胃腸障害	13 (9.8)	15 (13.4)	28 (11.5)
腹部膨満	0	2 (1.8)	2 (0.8)
腹痛	1 (0.8)	0	1 (0.4)
上腹部痛	0	1 (0.9)	1 (0.4)
アフタ性潰瘍	1 (0.8)	0	1 (0.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
胃腸障害 (Cont.)			
呼気臭	2 (1.5)	0	2 (0.8)
便秘	2 (1.5)	2 (1.8)	4 (1.6)
下痢	2 (1.5)	2 (1.8)	4 (1.6)
口内乾燥	2 (1.5)	3 (2.7)	5 (2.0)
消化不良	1 (0.8)	0	1 (0.4)
胃食道逆流性疾患	0	1 (0.9)	1 (0.4)
痔核	1 (0.8)	0	1 (0.4)
過敏性腸症候群	0	1 (0.9)	1 (0.4)
悪心	5 (3.8)	5 (4.5)	10 (4.1)
嘔吐	2 (1.5)	1 (0.9)	3 (1.2)
一般・全身障害および投与部位の状態	90 (68.2)	82 (73.2)	172 (70.5)
投与部位紅斑	1 (0.8)	0	1 (0.4)
無力症	1 (0.8)	0	1 (0.4)
カテーテル留置部位紅斑	0	1 (0.9)	1 (0.4)
カテーテル留置部位炎症	0	1 (0.9)	1 (0.4)
カテーテル留置部位疼痛	0	2 (1.8)	2 (0.8)
不快感	1 (0.8)	0	1 (0.4)
薬剤離脱症候群	1 (0.8)	0	1 (0.4)
疲労	3 (2.3)	2 (1.8)	5 (2.0)
異常感	1 (0.8)	0	1 (0.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
一般・全身障害および投与部位の状態 (Cont.)			
熱感	1 (0.8)	0	1 (0.4)
歩行障害	0	1 (0.9)	1 (0.4)
歩行不能	1 (0.8)	0	1 (0.4)
低体温	1 (0.8)	0	1 (0.4)
インフルエンザ様疾患	1 (0.8)	1 (0.9)	2 (0.8)
注入部位内出血	3 (2.3)	7 (6.3)	10 (4.1)
注入部位分泌物	1 (0.8)	1 (0.9)	2 (0.8)
注入部位変色	2 (1.5)	0	2 (0.8)
注入部位不快感	2 (1.5)	1 (0.9)	3 (1.2)
注入部位びらん	0	1 (0.9)	1 (0.4)
注入部位紅斑	50 (37.9)	45 (40.2)	95 (38.9)
注入部位皮膚剥脱	0	1 (0.9)	1 (0.4)
注入部位血管外漏出	4 (3.0)	7 (6.3)	11 (4.5)
注入部位血腫	4 (3.0)	4 (3.6)	8 (3.3)
注入部位出血	0	3 (2.7)	3 (1.2)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
一般・全身障害および投与部位の状態 (Cont.)			
注入部位硬結	4 (3.0)	1 (0.9)	5 (2.0)
注入部位炎症	1 (0.8)	3 (2.7)	4 (1.6)
注入部位腫瘤	4 (3.0)	1 (0.9)	5 (2.0)
注入部位壊死	0	1 (0.9)	1 (0.4)
注入部位結節	20 (15.2)	18 (16.1)	38 (15.6)
注入部位浮腫	14 (10.6)	16 (14.3)	30 (12.3)
注入部位疼痛	13 (9.8)	14 (12.5)	27 (11.1)
注入部位蒼白	2 (1.5)	0	2 (0.8)
注入部位丘疹	1 (0.8)	4 (3.6)	5 (2.0)
注入部位異常感覚	0	1 (0.9)	1 (0.4)
注入部位そう痒感	2 (1.5)	1 (0.9)	3 (1.2)
注入部位発疹	2 (1.5)	1 (0.9)	3 (1.2)
注入部位反応	9 (6.8)	12 (10.7)	21 (8.6)
注入部位腫脹	3 (2.3)	1 (0.9)	4 (1.6)
注射部位内出血	1 (0.8)	0	1 (0.4)
注射部位紅斑	5 (3.8)	5 (4.5)	10 (4.1)
注射部位漏出	1 (0.8)	1 (0.9)	2 (0.8)
注射部位血腫	0	1 (0.9)	1 (0.4)
注射部位炎症	1 (0.8)	2 (1.8)	3 (1.2)
注射部位結節	1 (0.8)	2 (1.8)	3 (1.2)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
一般・全身障害および投与部位の状態 (Cont.)			
注射部位浮腫	2 (1.5)	2 (1.8)	4 (1.6)
注射部位疼痛	2 (1.5)	4 (3.6)	6 (2.5)
注射部位反応	0	1 (0.9)	1 (0.4)
注射部位腫脹	1 (0.8)	0	1 (0.4)
滴下投与部位熱傷	0	1 (0.9)	1 (0.4)
限局性浮腫	0	1 (0.9)	1 (0.4)
適用部位からの吸収不良	0	1 (0.9)	1 (0.4)
倦怠感	1 (0.8)	1 (0.9)	2 (0.8)
医療機器使用部位刺激感	0	1 (0.9)	1 (0.4)
医療機器使用部位そう痒感	1 (0.8)	0	1 (0.4)
医療機器使用部位発疹	0	1 (0.9)	1 (0.4)
小結節	1 (0.8)	0	1 (0.4)
末梢性浮腫	1 (0.8)	3 (2.7)	4 (1.6)
末梢腫脹	0	2 (1.8)	2 (0.8)
穿刺部位内出血	1 (0.8)	0	1 (0.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
一般・全身障害および投与部位の状態 (Cont.)			
穿刺部位紅斑	0	1 (0.9)	1 (0.4)
穿刺部位出血	1 (0.8)	0	1 (0.4)
穿刺部位硬結	1 (0.8)	0	1 (0.4)
穿刺部位浮腫	0	1 (0.9)	1 (0.4)
穿刺部位腫脹	0	1 (0.9)	1 (0.4)
発熱	2 (1.5)	1 (0.9)	3 (1.2)
口渇	1 (0.8)	0	1 (0.4)
肝胆道系障害	1 (0.8)	0	1 (0.4)
門脈血栓症	1 (0.8)	0	1 (0.4)
感染症および寄生虫症	17 (12.9)	27 (24.1)	44 (18.0)
ボレリア感染	1 (0.8)	0	1 (0.4)
膀胱炎	0	1 (0.9)	1 (0.4)
真菌感染	1 (0.8)	0	1 (0.4)
胃腸炎	0	1 (0.9)	1 (0.4)
注入部位膿瘍	3 (2.3)	5 (4.5)	8 (3.3)
注入部位蜂巣炎	10 (7.6)	13 (11.6)	23 (9.4)
注入部位感染	1 (0.8)	3 (2.7)	4 (1.6)
注射部位蜂巣炎	0	1 (0.9)	1 (0.4)
上咽頭炎	0	3 (2.7)	3 (1.2)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
感染症および寄生虫症 (Cont.)			
爪真菌症	0	1 (0.9)	1 (0.4)
肺炎	1 (0.8)	1 (0.9)	2 (0.8)
膿疱性皮疹	1 (0.8)	0	1 (0.4)
敗血症	1 (0.8)	0	1 (0.4)
敗血症性ショック	1 (0.8)	0	1 (0.4)
尿路感染	3 (2.3)	3 (2.7)	6 (2.5)
傷害、中毒および処置合併症	10 (7.6)	11 (9.8)	21 (8.6)
挫傷	1 (0.8)	0	1 (0.4)
医療機器設置の問題	1 (0.8)	0	1 (0.4)
医療機器による投与の欠落	1 (0.8)	0	1 (0.4)
顔面骨骨折	0	2 (1.8)	2 (0.8)
転倒	7 (5.3)	9 (8.0)	16 (6.6)
頭部損傷	1 (0.8)	0	1 (0.4)
注入に伴う反応	1 (0.8)	0	1 (0.4)
腰椎骨折	0	1 (0.9)	1 (0.4)
処置後挫傷	1 (0.8)	0	1 (0.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
傷害、中毒および処置合併症 (Cont.)			
処置によるめまい	0	1 (0.9)	1 (0.4)
肋骨骨折	0	1 (0.9)	1 (0.4)
皮膚擦過傷	1 (0.8)	0	1 (0.4)
皮膚裂傷	0	2 (1.8)	2 (0.8)
臨床検査	3 (2.3)	5 (4.5)	8 (3.3)
血圧上昇	1 (0.8)	1 (0.9)	2 (0.8)
起立血圧低下	1 (0.8)	0	1 (0.4)
リンパ球数減少	0	1 (0.9)	1 (0.4)
単球数増加	0	1 (0.9)	1 (0.4)
好中球数増加	0	1 (0.9)	1 (0.4)
ビタミンB12減少	1 (0.8)	0	1 (0.4)
ビタミンB6減少	0	2 (1.8)	2 (0.8)
体重減少	0	1 (0.9)	1 (0.4)
白血球数増加	0	1 (0.9)	1 (0.4)
代謝および栄養障害	1 (0.8)	5 (4.5)	6 (2.5)
食欲減退	1 (0.8)	1 (0.9)	2 (0.8)
脱水	0	1 (0.9)	1 (0.4)
耐糖能障害	0	1 (0.9)	1 (0.4)
高血糖	0	1 (0.9)	1 (0.4)
低カリウム血症	0	1 (0.9)	1 (0.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
筋骨格系および結合組織障害	10 (7.6)	8 (7.1)	18 (7.4)
関節痛	2 (1.5)	2 (1.8)	4 (1.6)
反応性関節炎	0	1 (0.9)	1 (0.4)
背部痛	3 (2.3)	1 (0.9)	4 (1.6)
関節腫脹	0	1 (0.9)	1 (0.4)
筋力低下	2 (1.5)	0	2 (0.8)
筋骨格硬直	0	1 (0.9)	1 (0.4)
筋肉痛	2 (1.5)	1 (0.9)	3 (1.2)
四肢痛	0	1 (0.9)	1 (0.4)
姿勢異常	0	1 (0.9)	1 (0.4)
横紋筋融解症	1 (0.8)	0	1 (0.4)
仙腸関節機能障害	1 (0.8)	0	1 (0.4)
斜頚	0	1 (0.9)	1 (0.4)
神経系障害	36 (27.3)	26 (23.2)	62 (25.4)
運動失調	1 (0.8)	0	1 (0.4)
平衡障害	0	1 (0.9)	1 (0.4)
運動緩慢	1 (0.8)	0	1 (0.4)
認知障害	2 (1.5)	0	2 (0.8)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
神経系障害 (Cont.)			
浮動性めまい	10 (7.6)	8 (7.1)	18 (7.4)
体位性めまい	3 (2.3)	0	3 (1.2)
構語障害	0	1 (0.9)	1 (0.4)
味覚不全	2 (1.5)	0	2 (0.8)
ジスキネジア	6 (4.5)	3 (2.7)	9 (3.7)
起立障害	1 (0.8)	0	1 (0.4)
ジストニア	1 (0.8)	1 (0.9)	2 (0.8)
本態性振戦	0	1 (0.9)	1 (0.4)
すくみ現象	3 (2.3)	0	3 (1.2)
頭部不快感	1 (0.8)	0	1 (0.4)
頭痛	4 (3.0)	2 (1.8)	6 (2.5)
片側感覚消失	0	1 (0.9)	1 (0.4)
不全片麻痺	0	1 (0.9)	1 (0.4)
代謝性脳症	0	1 (0.9)	1 (0.4)
オンオフ現象	3 (2.3)	3 (2.7)	6 (2.5)
錯感覚	0	1 (0.9)	1 (0.4)
パーキンソン病	5 (3.8)	3 (2.7)	8 (3.3)
パーキンソニズム	0	1 (0.9)	1 (0.4)
精神運動亢進	1 (0.8)	1 (0.9)	2 (0.8)
安静時振戦	0	1 (0.9)	1 (0.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
神経系障害 (Cont.)			
坐骨神経痛	0	2 (1.8)	2 (0.8)
傾眠	2 (1.5)	2 (1.8)	4 (1.6)
振戦	0	2 (1.8)	2 (0.8)
製品の問題	0	1 (0.9)	1 (0.4)
医療機器機能不良	0	1 (0.9)	1 (0.4)
精神障害	31 (23.5)	24 (21.4)	55 (22.5)
異常な夢	0	1 (0.9)	1 (0.4)
感情不安定	1 (0.8)	0	1 (0.4)
不安	2 (1.5)	8 (7.1)	10 (4.1)
歯ぎしり	2 (1.5)	0	2 (0.8)
錯乱状態	1 (0.8)	1 (0.9)	2 (0.8)
譫妄	1 (0.8)	2 (1.8)	3 (1.2)
妄想	1 (0.8)	1 (0.9)	2 (0.8)
抑うつ気分	1 (0.8)	1 (0.9)	2 (0.8)
抑うつ症状	2 (1.5)	0	2 (0.8)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
精神障害 (Cont.)			
睡眠異常	1 (0.8)	0	1 (0.4)
情動障害	0	1 (0.9)	1 (0.4)
幻覚	13 (9.8)	5 (4.5)	18 (7.4)
幻聴	0	1 (0.9)	1 (0.4)
幻視	4 (3.0)	1 (0.9)	5 (2.0)
不眠症	7 (5.3)	3 (2.7)	10 (4.1)
易刺激性	1 (0.8)	0	1 (0.4)
嫉妬妄想	1 (0.8)	0	1 (0.4)
気分変化	1 (0.8)	0	1 (0.4)
強迫観念	1 (0.8)	0	1 (0.4)
パニック発作	0	3 (2.7)	3 (1.2)
精神病性障害	2 (1.5)	0	2 (0.8)
レム睡眠行動障害	1 (0.8)	0	1 (0.4)
睡眠障害	0	1 (0.9)	1 (0.4)
ねごと	0	1 (0.9)	1 (0.4)
腎および尿路障害	6 (4.5)	1 (0.9)	7 (2.9)
排尿困難	1 (0.8)	1 (0.9)	2 (0.8)
切迫性尿失禁	2 (1.5)	0	2 (0.8)
尿失禁	2 (1.5)	0	2 (0.8)
尿路障害	1 (0.8)	0	1 (0.4)
尿異常	0	1 (0.9)	1 (0.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
生殖系および乳房障害	0	1 (0.9)	1 (0.4)
勃起不全	0	1 (0.9)	1 (0.4)
呼吸器、胸郭および縦隔障害	1 (0.8)	7 (6.3)	8 (3.3)
急性呼吸不全	0	1 (0.9)	1 (0.4)
咳嗽	1 (0.8)	1 (0.9)	2 (0.8)
呼吸困難	0	1 (0.9)	1 (0.4)
過換気	0	1 (0.9)	1 (0.4)
口腔咽頭痛	0	1 (0.9)	1 (0.4)
鼻痛	0	1 (0.9)	1 (0.4)
鼻漏	0	1 (0.9)	1 (0.4)
皮膚および皮下組織障害	6 (4.5)	5 (4.5)	11 (4.5)
脱毛症	1 (0.8)	0	1 (0.4)
接触皮膚炎	1 (0.8)	0	1 (0.4)
皮膚乾燥	0	1 (0.9)	1 (0.4)
斑状出血	1 (0.8)	0	1 (0.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
皮膚および皮下組織障害 (Cont.)			
紅斑	0	1 (0.9)	1 (0.4)
光線過敏性反応	0	1 (0.9)	1 (0.4)
発疹	1 (0.8)	0	1 (0.4)
そう痒性皮疹	1 (0.8)	0	1 (0.4)
皮膚刺激	0	1 (0.9)	1 (0.4)
皮膚病変	0	1 (0.9)	1 (0.4)
皮膚潰瘍	1 (0.8)	0	1 (0.4)
社会環境	1 (0.8)	0	1 (0.4)
運動不能	1 (0.8)	0	1 (0.4)
血管障害	3 (2.3)	7 (6.3)	10 (4.1)
ほてり	0	1 (0.9)	1 (0.4)
高血圧	2 (1.5)	1 (0.9)	3 (1.2)
低血圧	0	2 (1.8)	2 (0.8)
不安定血圧	0	1 (0.9)	1 (0.4)
起立性低血圧	1 (0.8)	4 (3.6)	5 (2.0)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Maintenance period	N=111	N=95	N=206
Any adverse event	98 (88.3)	88 (92.6)	186 (90.3)
血液およびリンパ系障害	1 (0.9)	3 (3.2)	4 (1.9)
大球性貧血	0	1 (1.1)	1 (0.5)
凝血異常	0	1 (1.1)	1 (0.5)
リンパ節症	1 (0.9)	0	1 (0.5)
縦隔リンパ節腫脹	0	1 (1.1)	1 (0.5)
心臓障害	4 (3.6)	5 (5.3)	9 (4.4)
急性心筋梗塞	1 (0.9)	0	1 (0.5)
狭心症	1 (0.9)	0	1 (0.5)
心房細動	0	1 (1.1)	1 (0.5)
心停止	1 (0.9)	0	1 (0.5)
心肺停止	0	1 (1.1)	1 (0.5)
冠動脈疾患	1 (0.9)	1 (1.1)	2 (1.0)
冠動脈狭窄	1 (0.9)	0	1 (0.5)
期外収縮	0	1 (1.1)	1 (0.5)
左室肥大	0	1 (1.1)	1 (0.5)
心筋梗塞	1 (0.9)	0	1 (0.5)
動悸	0	1 (1.1)	1 (0.5)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Maintenance period (Cont.)	N=111	N=95	N=206
耳および迷路障害	2 (1.8)	2 (2.1)	4 (1.9)
感音性難聴	1 (0.9)	0	1 (0.5)
回転性めまい	1 (0.9)	1 (1.1)	2 (1.0)
頭位性回転性めまい	0	1 (1.1)	1 (0.5)
眼障害	7 (6.3)	6 (6.3)	13 (6.3)
白内障	2 (1.8)	2 (2.1)	4 (1.9)
複視	2 (1.8)	0	2 (1.0)
ドライアイ	1 (0.9)	3 (3.2)	4 (1.9)
緑内障	1 (0.9)	1 (1.1)	2 (1.0)
眼窩周囲痛	0	1 (1.1)	1 (0.5)
眼窩周囲腫脹	0	1 (1.1)	1 (0.5)
網膜裂孔	2 (1.8)	0	2 (1.0)
視野欠損	0	1 (1.1)	1 (0.5)
胃腸障害	17 (15.3)	21 (22.1)	38 (18.4)
腹部膨満	1 (0.9)	2 (2.1)	3 (1.5)
腹痛	1 (0.9)	1 (1.1)	2 (1.0)
上腹部痛	1 (0.9)	0	1 (0.5)
呼気臭	0	1 (1.1)	1 (0.5)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Maintenance period (Cont.)	N=111	N=95	N=206
胃腸障害 (Cont.)			
虚血性大腸炎	1 (0.9)	0	1 (0.5)
便秘	6 (5.4)	10 (10.5)	16 (7.8)
齲歯	1 (0.9)	0	1 (0.5)
下痢	4 (3.6)	1 (1.1)	5 (2.4)
口内乾燥	1 (0.9)	3 (3.2)	4 (1.9)
嚥下障害	0	1 (1.1)	1 (0.5)
糞塊	0	1 (1.1)	1 (0.5)
排便回数増加	0	1 (1.1)	1 (0.5)
胃食道逆流性疾患	1 (0.9)	0	1 (0.5)
舌炎	1 (0.9)	0	1 (0.5)
舌痛	1 (0.9)	0	1 (0.5)
吐血	1 (0.9)	0	1 (0.5)
裂孔ヘルニア	1 (0.9)	0	1 (0.5)
胃排出不全	1 (0.9)	0	1 (0.5)
腸出血	1 (0.9)	0	1 (0.5)
過敏性腸症候群	1 (0.9)	1 (1.1)	2 (1.0)
大腸ポリープ	0	1 (1.1)	1 (0.5)
口唇乾燥	1 (0.9)	0	1 (0.5)
メレナ	2 (1.8)	0	2 (1.0)
口腔腫脹	1 (0.9)	0	1 (0.5)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Maintenance period (Cont.)	N=111	N=95	N=206
胃腸障害 (Cont.)			
悪心	4 (3.6)	7 (7.4)	11 (5.3)
口腔内不快感	1 (0.9)	0	1 (0.5)
口腔内痛	1 (0.9)	0	1 (0.5)
口の錯感覚	1 (0.9)	1 (1.1)	2 (1.0)
直腸出血	1 (0.9)	1 (1.1)	2 (1.0)
歯痛	0	1 (1.1)	1 (0.5)
嘔吐	1 (0.9)	2 (2.1)	3 (1.5)
一般・全身障害および投与部位の状態	66 (59.5)	71 (74.7)	137 (66.5)
投与部位内出血	0	1 (1.1)	1 (0.5)
投与部位漏出	0	2 (2.1)	2 (1.0)
無力症	2 (1.8)	0	2 (1.0)
カテーテル留置部位紅斑	1 (0.9)	1 (1.1)	2 (1.0)
カテーテル留置部位漏出	1 (0.9)	0	1 (0.5)
カテーテル留置部位出血	0	1 (1.1)	1 (0.5)
カテーテル留置部位刺激感	0	1 (1.1)	1 (0.5)
カテーテル留置部位浮腫	0	1 (1.1)	1 (0.5)
カテーテル留置部位疼痛	0	1 (1.1)	1 (0.5)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Maintenance period (Cont.)	N=111	N=95	N=206
一般・全身障害および投与部位の状態 (Cont.)			
胸部不快感	0	1 (1.1)	1 (0.5)
胸痛	1 (0.9)	1 (1.1)	2 (1.0)
泣き	1 (0.9)	0	1 (0.5)
薬効欠如	0	1 (1.1)	1 (0.5)
薬剤離脱症候群	0	1 (1.1)	1 (0.5)
疲労	3 (2.7)	1 (1.1)	4 (1.9)
異常感	0	1 (1.1)	1 (0.5)
冷感	0	1 (1.1)	1 (0.5)
歩行障害	0	1 (1.1)	1 (0.5)
低体温	1 (0.9)	1 (1.1)	2 (1.0)
インフルエンザ様疾患	1 (0.9)	2 (2.1)	3 (1.5)
注入部位内出血	7 (6.3)	2 (2.1)	9 (4.4)
注入部位皮膚炎	2 (1.8)	2 (2.1)	4 (1.9)
注入部位分泌物	0	1 (1.1)	1 (0.5)
注入部位不快感	1 (0.9)	0	1 (0.5)
注入部位びらん	1 (0.9)	0	1 (0.5)
注入部位紅斑	35 (31.5)	43 (45.3)	78 (37.9)
注入部位皮膚剥脱	3 (2.7)	2 (2.1)	5 (2.4)
注入部位血管外漏出	5 (4.5)	6 (6.3)	11 (5.3)
注入部位血腫	4 (3.6)	4 (4.2)	8 (3.9)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Maintenance period (Cont.)	N=111	N=95	N=206
一般・全身障害および投与部位の状態 (Cont.)			
注入部位出血	4 (3.6)	2 (2.1)	6 (2.9)
注入部位硬結	5 (4.5)	2 (2.1)	7 (3.4)
注入部位炎症	2 (1.8)	6 (6.3)	8 (3.9)
注入部位損傷	1 (0.9)	2 (2.1)	3 (1.5)
注入部位刺激感	1 (0.9)	4 (4.2)	5 (2.4)
注入部位腫瘤	1 (0.9)	2 (2.1)	3 (1.5)
注入部位結節	20 (18.0)	25 (26.3)	45 (21.8)
注入部位浮腫	8 (7.2)	18 (18.9)	26 (12.6)
注入部位疼痛	8 (7.2)	11 (11.6)	19 (9.2)
注入部位蒼白	1 (0.9)	1 (1.1)	2 (1.0)
注入部位丘疹	6 (5.4)	8 (8.4)	14 (6.8)
注入部位異常感覚	0	2 (2.1)	2 (1.0)
注入部位そう痒感	3 (2.7)	1 (1.1)	4 (1.9)
注入部位発疹	1 (0.9)	3 (3.2)	4 (1.9)
注入部位反応	8 (7.2)	11 (11.6)	19 (9.2)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Maintenance period (Cont.)	N=111	N=95	N=206
一般・全身障害および投与部位の状態 (Cont.)			
注入部位痂皮	0	1 (1.1)	1 (0.5)
注入部位腫脹	2 (1.8)	1 (1.1)	3 (1.5)
注入部位小水疱	0	2 (2.1)	2 (1.0)
注入部位熱感	0	1 (1.1)	1 (0.5)
注射部位内出血	1 (0.9)	1 (1.1)	2 (1.0)
注射部位変色	1 (0.9)	0	1 (0.5)
注射部位紅斑	5 (4.5)	5 (5.3)	10 (4.9)
注射部位出血	0	1 (1.1)	1 (0.5)
注射部位炎症	2 (1.8)	4 (4.2)	6 (2.9)
注射部位結節	3 (2.7)	5 (5.3)	8 (3.9)
注射部位浮腫	1 (0.9)	1 (1.1)	2 (1.0)
注射部位疼痛	0	2 (2.1)	2 (1.0)
注射部位丘疹	0	1 (1.1)	1 (0.5)
注射部位反応	1 (0.9)	0	1 (0.5)
注射部位腫脹	1 (0.9)	2 (2.1)	3 (1.5)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Maintenance period (Cont.)	N=111	N=95	N=206
一般・全身障害および投与部位の状態 (Cont.)			
注射部位蕁麻疹	0	1 (1.1)	1 (0.5)
滴下投与部位痛	0	1 (1.1)	1 (0.5)
倦怠感	0	1 (1.1)	1 (0.5)
医療機器使用部位刺激感	1 (0.9)	1 (1.1)	2 (1.0)
医療機器使用部位発疹	0	1 (1.1)	1 (0.5)
非心臓性胸痛	0	2 (2.1)	2 (1.0)
末梢性浮腫	4 (3.6)	1 (1.1)	5 (2.4)
疼痛	2 (1.8)	0	2 (1.0)
末梢腫脹	0	3 (3.2)	3 (1.5)
穿刺部位紅斑	0	2 (2.1)	2 (1.0)
穿刺部位硬結	2 (1.8)	0	2 (1.0)
発熱	0	1 (1.1)	1 (0.5)
血管穿刺部位硬結	1 (0.9)	0	1 (0.5)
肝胆道系障害	1 (0.9)	1 (1.1)	2 (1.0)
肝嚢胞	1 (0.9)	0	1 (0.5)
脂肪肝	0	1 (1.1)	1 (0.5)
感染症および寄生虫症	46 (41.4)	45 (47.4)	91 (44.2)
無症候性COVID-19	0	1 (1.1)	1 (0.5)
細菌性疾患キャリアー	0	1 (1.1)	1 (0.5)
ウイルス性気管支炎	0	1 (1.1)	1 (0.5)
COVID-19	1 (0.9)	0	1 (0.5)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Maintenance period (Cont.)	N=111	N=95	N=206
感染症および寄生虫症 (Cont.)			
COVID-19肺炎	1 (0.9)	0	1 (0.5)
カテーテル留置部位感染	1 (0.9)	0	1 (0.5)
蜂巣炎	1 (0.9)	1 (1.1)	2 (1.0)
結膜炎	2 (1.8)	0	2 (1.0)
爪の皮膚糸状菌症	0	1 (1.1)	1 (0.5)
歯肉炎	1 (0.9)	0	1 (0.5)
麦粒腫	1 (0.9)	0	1 (0.5)
感染性皮膚潰瘍	0	1 (1.1)	1 (0.5)
インフルエンザ	0	1 (1.1)	1 (0.5)
注入部位膿瘍	10 (9.0)	9 (9.5)	19 (9.2)
注入部位蜂巣炎	21 (18.9)	19 (20.0)	40 (19.4)
注入部位感染	5 (4.5)	9 (9.5)	14 (6.8)
注入部位膿疱	0	1 (1.1)	1 (0.5)
注射部位蜂巣炎	0	2 (2.1)	2 (1.0)
上咽頭炎	5 (4.5)	2 (2.1)	7 (3.4)
耳下腺膿瘍	0	1 (1.1)	1 (0.5)
肺炎	2 (1.8)	1 (1.1)	3 (1.5)
術後膿瘍	1 (0.9)	0	1 (0.5)
シュードモナス感染	0	1 (1.1)	1 (0.5)
気道感染	0	1 (1.1)	1 (0.5)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Maintenance period (Cont.)	N=111	N=95	N=206
感染症および寄生虫症 (Cont.)			
敗血症	2 (1.8)	1 (1.1)	3 (1.5)
副鼻腔炎	1 (0.9)	0	1 (0.5)
ブドウ球菌感染	1 (0.9)	1 (1.1)	2 (1.0)
歯感染	1 (0.9)	1 (1.1)	2 (1.0)
上気道感染	1 (0.9)	0	1 (0.5)
尿路感染	5 (4.5)	11 (11.6)	16 (7.8)
水痘帯状疱疹ウイルス感染	1 (0.9)	0	1 (0.5)
傷害、中毒および処置合併症	13 (11.7)	20 (21.1)	33 (16.0)
足関節部骨折	0	1 (1.1)	1 (0.5)
節足動物咬傷	0	1 (1.1)	1 (0.5)
骨挫傷	1 (0.9)	1 (1.1)	2 (1.0)
脳挫傷	1 (0.9)	0	1 (0.5)
挫傷	1 (0.9)	6 (6.3)	7 (3.4)
期限切れの製品使用	1 (0.9)	0	1 (0.5)
眼挫傷	0	1 (1.1)	1 (0.5)
顔面損傷	0	1 (1.1)	1 (0.5)
転倒	11 (9.9)	17 (17.9)	28 (13.6)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Maintenance period (Cont.)	N=111	N=95	N=206
傷害、中毒および処置合併症 (Cont.)			
頭部損傷	1 (0.9)	2 (2.1)	3 (1.5)
関節脱臼	0	1 (1.1)	1 (0.5)
靭帯捻挫	1 (0.9)	1 (1.1)	2 (1.0)
過量投与	0	1 (1.1)	1 (0.5)
肋骨骨折	1 (0.9)	1 (1.1)	2 (1.0)
皮膚擦過傷	0	2 (2.1)	2 (1.0)
皮膚損傷	1 (0.9)	0	1 (0.5)
皮膚裂傷	1 (0.9)	4 (4.2)	5 (2.4)
ストレス骨折	1 (0.9)	0	1 (0.5)
硬膜下血腫	0	1 (1.1)	1 (0.5)
サンバーン	0	1 (1.1)	1 (0.5)
腱断裂	1 (0.9)	1 (1.1)	2 (1.0)
過少量投与	0	1 (1.1)	1 (0.5)
創傷	1 (0.9)	0	1 (0.5)
臨床検査	20 (18.0)	17 (17.9)	37 (18.0)
血中クレアチンホスホキナーゼ増加	1 (0.9)	1 (1.1)	2 (1.0)
血中クレアチニン減少	0	1 (1.1)	1 (0.5)
血中葉酸減少	1 (0.9)	2 (2.1)	3 (1.5)
血中ホモシステイン増加	1 (0.9)	2 (2.1)	3 (1.5)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Maintenance period (Cont.)	N=111	N=95	N=206
臨床検査 (Cont.)			
血中リン減少	0	1 (1.1)	1 (0.5)
血中ナトリウム減少	1 (0.9)	0	1 (0.5)
C-反応性蛋白増加	0	1 (1.1)	1 (0.5)
握力低下	1 (0.9)	0	1 (0.5)
ヘモグロビン減少	1 (0.9)	1 (1.1)	2 (1.0)
好中球数増加	0	1 (1.1)	1 (0.5)
プロトロンビン時間延長	0	1 (1.1)	1 (0.5)
赤血球数減少	0	1 (1.1)	1 (0.5)
ビタミンB12減少	0	1 (1.1)	1 (0.5)
ビタミンB6減少	5 (4.5)	4 (4.2)	9 (4.4)
ビタミンD減少	0	1 (1.1)	1 (0.5)
体重減少	10 (9.0)	11 (11.6)	21 (10.2)
体重増加	2 (1.8)	0	2 (1.0)
白血球数増加	0	1 (1.1)	1 (0.5)
代謝および栄養障害	10 (9.0)	14 (14.7)	24 (11.7)
悪液質	1 (0.9)	0	1 (0.5)
食欲減退	2 (1.8)	1 (1.1)	3 (1.5)
脱水	1 (0.9)	2 (2.1)	3 (1.5)
糖尿病	0	1 (1.1)	1 (0.5)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Maintenance period (Cont.)	N=111	N=95	N=206
代謝および栄養障害 (Cont.)			
水分過負荷	0	1 (1.1)	1 (0.5)
体液貯留	1 (0.9)	1 (1.1)	2 (1.0)
葉酸欠乏	1 (0.9)	1 (1.1)	2 (1.0)
高コレステロール血症	0	1 (1.1)	1 (0.5)
高ホモシステイン血症	0	1 (1.1)	1 (0.5)
低カリウム血症	0	2 (2.1)	2 (1.0)
低ナトリウム血症	2 (1.8)	0	2 (1.0)
栄養障害	0	1 (1.1)	1 (0.5)
ビタミンB群欠乏	1 (0.9)	1 (1.1)	2 (1.0)
ビタミンB12欠乏	0	2 (2.1)	2 (1.0)
ビタミンB6欠乏	3 (2.7)	5 (5.3)	8 (3.9)
筋骨格系および結合組織障害	17 (15.3)	14 (14.7)	31 (15.0)
関節痛	1 (0.9)	1 (1.1)	2 (1.0)
反応性関節炎	1 (0.9)	0	1 (0.5)
背部痛	5 (4.5)	3 (3.2)	8 (3.9)
骨痛	0	1 (1.1)	1 (0.5)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Maintenance period (Cont.)	N=111	N=95	N=206
筋骨格系および結合組織障害 (Cont.)			
滑液包炎	2 (1.8)	0	2 (1.0)
外骨腫	0	1 (1.1)	1 (0.5)
椎間関節症候群	0	1 (1.1)	1 (0.5)
椎間板変性症	1 (0.9)	0	1 (0.5)
椎間板突出	0	1 (1.1)	1 (0.5)
関節滲出液	0	2 (2.1)	2 (1.0)
四肢不快感	0	1 (1.1)	1 (0.5)
筋萎縮	0	1 (1.1)	1 (0.5)
筋痙縮	2 (1.8)	3 (3.2)	5 (2.4)
筋力低下	2 (1.8)	1 (1.1)	3 (1.5)
頚部痛	2 (1.8)	0	2 (1.0)
骨炎	0	1 (1.1)	1 (0.5)
変形性関節症	1 (0.9)	4 (4.2)	5 (2.4)
骨減少症	1 (0.9)	0	1 (0.5)
四肢痛	3 (2.7)	2 (2.1)	5 (2.4)
関節周囲炎	0	1 (1.1)	1 (0.5)
横紋筋融解症	1 (0.9)	0	1 (0.5)
肩回旋筋腱板症候群	0	1 (1.1)	1 (0.5)
変形性脊椎症	1 (0.9)	0	1 (0.5)
腱障害	0	1 (1.1)	1 (0.5)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Maintenance period (Cont.)	N=111	N=95	N=206
筋骨格系および結合組織障害 (Cont.)			
腱炎	1 (0.9)	0	1 (0.5)
弾発指	1 (0.9)	0	1 (0.5)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	4 (4.2)	4 (1.9)
基底細胞癌	0	2 (2.1)	2 (1.0)
脂漏性角化症	0	1 (1.1)	1 (0.5)
皮膚有棘細胞癌	0	1 (1.1)	1 (0.5)
神経系障害	37 (33.3)	34 (35.8)	71 (34.5)
アカシジア	1 (0.9)	0	1 (0.5)
健忘	1 (0.9)	0	1 (0.5)
失語症	0	1 (1.1)	1 (0.5)
平衡障害	0	4 (4.2)	4 (1.9)
運動緩慢	0	1 (1.1)	1 (0.5)
手根管症候群	0	1 (1.1)	1 (0.5)
大脳萎縮	0	1 (1.1)	1 (0.5)
脳出血	0	1 (1.1)	1 (0.5)
脳圧排効果	0	1 (1.1)	1 (0.5)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Maintenance period (Cont.)	N=111	N=95	N=206
神経系障害 (Cont.)			
脳血管発作	0	1 (1.1)	1 (0.5)
認知障害	2 (1.8)	2 (2.1)	4 (1.9)
振動覚低下	1 (0.9)	0	1 (0.5)
注意力障害	0	1 (1.1)	1 (0.5)
浮動性めまい	6 (5.4)	2 (2.1)	8 (3.9)
体位性めまい	3 (2.7)	0	3 (1.5)
構語障害	0	2 (2.1)	2 (1.0)
味覚不全	0	1 (1.1)	1 (0.5)
ジスキネジア	7 (6.3)	3 (3.2)	10 (4.9)
ジストニア	1 (0.9)	4 (4.2)	5 (2.4)
脳症	0	1 (1.1)	1 (0.5)
てんかん	0	1 (1.1)	1 (0.5)
伸展性足底反応	1 (0.9)	0	1 (0.5)
すくみ現象	1 (0.9)	0	1 (0.5)
全身性強直性間代性発作	0	1 (1.1)	1 (0.5)
頭痛	3 (2.7)	6 (6.3)	9 (4.4)
感覚鈍麻	1 (0.9)	2 (2.1)	3 (1.5)
反射減弱	2 (1.8)	1 (1.1)	3 (1.5)
不規則睡眠覚醒リズム障害	1 (0.9)	0	1 (0.5)
嗜眠	1 (0.9)	1 (1.1)	2 (1.0)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Maintenance period (Cont.)	N=111	N=95	N=206
神経系障害 (Cont.)			
意識消失	1 (0.9)	1 (1.1)	2 (1.0)
腰仙部神経根障害	0	1 (1.1)	1 (0.5)
記憶障害	0	2 (2.1)	2 (1.0)
代謝性脳症	1 (0.9)	0	1 (0.5)
神経痛	0	1 (1.1)	1 (0.5)
末梢性ニューロパチー	1 (0.9)	1 (1.1)	2 (1.0)
オンオフ現象	1 (0.9)	1 (1.1)	2 (1.0)
錯感覚	4 (3.6)	2 (2.1)	6 (2.9)
パーキンソン病	7 (6.3)	2 (2.1)	9 (4.4)
パーキンソニズム	0	2 (2.1)	2 (1.0)
側反弓	1 (0.9)	2 (2.1)	3 (1.5)
多発ニューロパチー	0	2 (2.1)	2 (1.0)
失神寸前の状態	0	1 (1.1)	1 (0.5)
心因性発作	0	1 (1.1)	1 (0.5)
反射異常	0	1 (1.1)	1 (0.5)
坐骨神経痛	0	3 (3.2)	3 (1.5)
痙攣発作	0	1 (1.1)	1 (0.5)
感覚障害	0	1 (1.1)	1 (0.5)
感覚消失	0	1 (1.1)	1 (0.5)
睡眠時麻痺	1 (0.9)	0	1 (0.5)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Maintenance period (Cont.)	N=111	N=95	N=206
神経系障害 (Cont.)			
傾眠	8 (7.2)	1 (1.1)	9 (4.4)
失神	0	3 (3.2)	3 (1.5)
振戦	1 (0.9)	0	1 (0.5)
製品の問題	2 (1.8)	0	2 (1.0)
医療機器送達システムの問題	1 (0.9)	0	1 (0.5)
医療機器位置異常	1 (0.9)	0	1 (0.5)
精神障害	36 (32.4)	39 (41.1)	75 (36.4)
感情不安定	0	1 (1.1)	1 (0.5)
激越	0	1 (1.1)	1 (0.5)
不安	9 (8.1)	12 (12.6)	21 (10.2)
不安障害	0	1 (1.1)	1 (0.5)
無感情	1 (0.9)	0	1 (0.5)
強迫行為	0	1 (1.1)	1 (0.5)
強迫性性行動	1 (0.9)	0	1 (0.5)
錯乱状態	4 (3.6)	3 (3.2)	7 (3.4)
譫妄	0	2 (2.1)	2 (1.0)
妄想	7 (6.3)	1 (1.1)	8 (3.9)
寄生虫妄想	1 (0.9)	0	1 (0.5)
妄想性障害、詳細不明	0	1 (1.1)	1 (0.5)
抑うつ気分	2 (1.8)	0	2 (1.0)
うつ病	2 (1.8)	2 (2.1)	4 (1.9)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Maintenance period (Cont.)	N=111	N=95	N=206
精神障害 (Cont.)			
ドーパミン調節障害症候群	1 (0.9)	0	1 (0.5)
ディスフェミア	0	1 (1.1)	1 (0.5)
睡眠異常	1 (0.9)	0	1 (0.5)
情動障害	1 (0.9)	0	1 (0.5)
注射恐怖	0	1 (1.1)	1 (0.5)
幻覚	12 (10.8)	18 (18.9)	30 (14.6)
幻聴	3 (2.7)	2 (2.1)	5 (2.4)
幻嗅	0	1 (1.1)	1 (0.5)
幻視	6 (5.4)	4 (4.2)	10 (4.9)
混合性幻覚	1 (0.9)	0	1 (0.5)
性欲過剰	1 (0.9)	0	1 (0.5)
錯覚	1 (0.9)	0	1 (0.5)
衝動制御障害	0	4 (4.2)	4 (1.9)
衝動行為	0	1 (1.1)	1 (0.5)
不眠症	2 (1.8)	6 (6.3)	8 (3.9)
易刺激性	0	1 (1.1)	1 (0.5)
躁病	0	1 (1.1)	1 (0.5)
気分動揺	0	1 (1.1)	1 (0.5)
悪夢	1 (0.9)	1 (1.1)	2 (1.0)
パニック発作	0	1 (1.1)	1 (0.5)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Maintenance period (Cont.)	N=111	N=95	N=206
精神障害 (Cont.)			
パニック反応	0	1 (1.1)	1 (0.5)
妄想症	2 (1.8)	0	2 (1.0)
睡眠の質低下	1 (0.9)	0	1 (0.5)
処置に対する不安	0	1 (1.1)	1 (0.5)
精神病性障害	3 (2.7)	2 (2.1)	5 (2.4)
精神病症状	1 (0.9)	0	1 (0.5)
レム睡眠行動障害	0	1 (1.1)	1 (0.5)
レム睡眠異常	1 (0.9)	0	1 (0.5)
睡眠障害	2 (1.8)	0	2 (1.0)
ねごと	1 (0.9)	0	1 (0.5)
常同症	0	1 (1.1)	1 (0.5)
ストレス	0	1 (1.1)	1 (0.5)
自殺念慮	1 (0.9)	2 (2.1)	3 (1.5)
自殺企図	1 (0.9)	0	1 (0.5)
腎および尿路障害	5 (4.5)	7 (7.4)	12 (5.8)
膀胱痙縮	1 (0.9)	0	1 (0.5)
膀胱結石	1 (0.9)	0	1 (0.5)
排尿困難	0	1 (1.1)	1 (0.5)
緊張性膀胱	1 (0.9)	0	1 (0.5)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Maintenance period (Cont.)	N=111	N=95	N=206
腎および尿路障害 (Cont.)			
夜間頻尿	0	1 (1.1)	1 (0.5)
多尿	0	1 (1.1)	1 (0.5)
腎機能障害	0	1 (1.1)	1 (0.5)
尿管結石症	0	1 (1.1)	1 (0.5)
切迫性尿失禁	1 (0.9)	0	1 (0.5)
尿失禁	1 (0.9)	2 (2.1)	3 (1.5)
尿閉	0	3 (3.2)	3 (1.5)
尿臭異常	0	1 (1.1)	1 (0.5)
生殖系および乳房障害	2 (1.8)	3 (3.2)	5 (2.4)
良性前立腺肥大症	1 (0.9)	0	1 (0.5)
勃起不全	1 (0.9)	0	1 (0.5)
ペイロニー病	0	1 (1.1)	1 (0.5)
前立腺腫大	0	1 (1.1)	1 (0.5)
腟脱	0	1 (1.1)	1 (0.5)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Maintenance period (Cont.)	N=111	N=95	N=206
呼吸器、胸郭および縦隔障害	5 (4.5)	13 (13.7)	18 (8.7)
気管支拡張症	1 (0.9)	0	1 (0.5)
咳嗽	0	1 (1.1)	1 (0.5)
発声障害	0	2 (2.1)	2 (1.0)
呼吸困難	2 (1.8)	5 (5.3)	7 (3.4)
労作性呼吸困難	1 (0.9)	0	1 (0.5)
鼻出血	0	1 (1.1)	1 (0.5)
過換気	0	1 (1.1)	1 (0.5)
口腔咽頭痛	1 (0.9)	0	1 (0.5)
誤嚥性肺炎	0	1 (1.1)	1 (0.5)
湿性咳嗽	0	1 (1.1)	1 (0.5)
肺塞栓症	0	2 (2.1)	2 (1.0)
ラ音	0	1 (1.1)	1 (0.5)
鼻漏	0	1 (1.1)	1 (0.5)
咽喉刺激感	0	1 (1.1)	1 (0.5)
皮膚および皮下組織障害	10 (9.0)	10 (10.5)	20 (9.7)
脱毛症	1 (0.9)	0	1 (0.5)
褥瘡性潰瘍	0	1 (1.1)	1 (0.5)
皮膚嚢腫	1 (0.9)	1 (1.1)	2 (1.0)
皮膚炎	0	1 (1.1)	1 (0.5)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Maintenance period (Cont.)	N=111	N=95	N=206
皮膚および皮下組織障害 (Cont.)			
接触皮膚炎	1 (0.9)	0	1 (0.5)
おむつ皮膚炎	1 (0.9)	0	1 (0.5)
薬疹	1 (0.9)	0	1 (0.5)
皮膚乾燥	1 (0.9)	0	1 (0.5)
紅斑	1 (0.9)	2 (2.1)	3 (1.5)
爪の障害	1 (0.9)	0	1 (0.5)
脂肪織炎	0	1 (1.1)	1 (0.5)
丘疹	0	2 (2.1)	2 (1.0)
そう痒症	2 (1.8)	1 (1.1)	3 (1.5)
乾癬	0	1 (1.1)	1 (0.5)
発疹	1 (0.9)	1 (1.1)	2 (1.0)
紅斑性皮疹	0	1 (1.1)	1 (0.5)
そう痒性皮疹	1 (0.9)	1 (1.1)	2 (1.0)
皮膚潰瘍	0	1 (1.1)	1 (0.5)
蕁麻疹	2 (1.8)	0	2 (1.0)
外科および内科処置	0	1 (1.1)	1 (0.5)
抜歯	0	1 (1.1)	1 (0.5)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.2

Subjects with Treatment-Emergent Adverse Events
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Maintenance period (Cont.)	N=111	N=95	N=206
血管障害	10 (9.0)	9 (9.5)	19 (9.2)
深部静脈血栓症	0	1 (1.1)	1 (0.5)
血腫	0	1 (1.1)	1 (0.5)
出血	0	1 (1.1)	1 (0.5)
高血圧	1 (0.9)	2 (2.1)	3 (1.5)
高血圧クリーゼ	1 (0.9)	0	1 (0.5)
低血圧	2 (1.8)	2 (2.1)	4 (1.9)
起立性高血圧	0	1 (1.1)	1 (0.5)
起立性低血圧	6 (5.4)	3 (3.2)	9 (4.4)

Note: Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

表36　治験薬との因果関係別の有害事象（安全性解析対象集団）：M15-741試験

[redacted]20[redacted] 04:29 <[redacted]>
ABBV-951
STUDY M15-741 - SECOND INTERIM (CUTOFF [redacted]20[redacted])
R&D/20/1632 - CLINICAL/STATISTICAL

TABLE 14.3__1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period	N=132	N=112	N=244
Any adverse event	122 (92.4)	108 (96.4)	230 (94.3)
No reasonable possibility	4 (3.0)	2 (1.8)	6 (2.5)
Reasonable possibility	118 (89.4)	106 (94.6)	224 (91.8)
血液およびリンパ系障害	1 (0.8)	3 (2.7)	4 (1.6)
No reasonable possibility	1 (0.8)	3 (2.7)	4 (1.6)
大球性貧血	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
凝血異常	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
リンパ節症	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
血液およびリンパ系障害 (Cont.)			
縦隔リンパ節腫脹	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
心臓障害	4 (3.0)	7 (6.3)	11 (4.5)
No reasonable possibility	4 (3.0)	5 (4.5)	9 (3.7)
Reasonable possibility	0	2 (1.8)	2 (0.8)
急性心筋梗塞	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
狭心症	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
心房細動	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
心臓障害 (Cont.)			
徐脈	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
心停止	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
心肺停止	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
冠動脈疾患	1 (0.8)	1 (0.9)	2 (0.8)
No reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
冠動脈狭窄	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
心臓障害 (Cont.)			
期外収縮	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
左室肥大	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
心筋梗塞	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
動悸	0	2 (1.8)	2 (0.8)
No reasonable possibility	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
耳および迷路障害	4 (3.0)	4 (3.6)	8 (3.3)
No reasonable possibility	2 (1.5)	2 (1.8)	4 (1.6)
Reasonable possibility	2 (1.5)	2 (1.8)	4 (1.6)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
耳および迷路障害 (Cont.)			
感音性難聴	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
乗物酔い	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
回転性めまい	3 (2.3)	2 (1.8)	5 (2.0)
No reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
Reasonable possibility	2 (1.5)	1 (0.9)	3 (1.2)
頭位性回転性めまい	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
眼障害	7 (5.3)	8 (7.1)	15 (6.1)
No reasonable possibility	7 (5.3)	7 (6.3)	14 (5.7)
Reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
眼障害 (Cont.)			
白内障	2 (1.5)	2 (1.8)	4 (1.6)
No reasonable possibility	2 (1.5)	2 (1.8)	4 (1.6)
複視	2 (1.5)	1 (0.9)	3 (1.2)
No reasonable possibility	2 (1.5)	1 (0.9)	3 (1.2)
ドライアイ	1 (0.8)	3 (2.7)	4 (1.6)
No reasonable possibility	1 (0.8)	3 (2.7)	4 (1.6)
緑内障	1 (0.8)	1 (0.9)	2 (0.8)
No reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
眼窩周囲痛	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
眼障害 (Cont.)			
眼窩周囲腫脹	0	2 (1.8)	2 (0.8)
No reasonable possibility	0	2 (1.8)	2 (0.8)
網膜裂孔	2 (1.5)	0	2 (0.8)
No reasonable possibility	2 (1.5)	0	2 (0.8)
霧視	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
視野欠損	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
胃腸障害	27 (20.5)	29 (25.9)	56 (23.0)
No reasonable possibility	17 (12.9)	14 (12.5)	31 (12.7)
Reasonable possibility	10 (7.6)	15 (13.4)	25 (10.2)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
胃腸障害 (Cont.)			
腹部膨満	1 (0.8)	3 (2.7)	4 (1.6)
No reasonable possibility	0	2 (1.8)	2 (0.8)
Reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
腹痛	2 (1.5)	1 (0.9)	3 (1.2)
No reasonable possibility	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
上腹部痛	1 (0.8)	1 (0.9)	2 (0.8)
No reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
アフタ性潰瘍	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
呼気臭	2 (1.5)	1 (0.9)	3 (1.2)
No reasonable possibility	0	1 (0.9)	1 (0.4)
Reasonable possibility	2 (1.5)	0	2 (0.8)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
胃腸障害 (Cont.)			
虚血性大腸炎	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
便秘	8 (6.1)	12 (10.7)	20 (8.2)
No reasonable possibility	8 (6.1)	9 (8.0)	17 (7.0)
Reasonable possibility	0	3 (2.7)	3 (1.2)
齲歯	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
下痢	6 (4.5)	3 (2.7)	9 (3.7)
No reasonable possibility	6 (4.5)	3 (2.7)	9 (3.7)
口内乾燥	3 (2.3)	5 (4.5)	8 (3.3)
No reasonable possibility	0	3 (2.7)	3 (1.2)
Reasonable possibility	3 (2.3)	2 (1.8)	5 (2.0)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
胃腸障害 (Cont.)			
消化不良	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
嚥下障害	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
糞塊	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
排便回数増加	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
胃食道逆流性疾患	1 (0.8)	1 (0.9)	2 (0.8)
No reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
胃腸障害 (Cont.)			
舌炎	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
舌痛	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
吐血	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
痔核	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
裂孔ヘルニア	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
胃腸障害 (Cont.)			
胃排出不全	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
腸出血	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
過敏性腸症候群	1 (0.8)	1 (0.9)	2 (0.8)
No reasonable possibility	1 (0.8)	0	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
大腸ポリープ	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
口唇乾燥	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
胃腸障害 (Cont.)			
メレナ	2 (1.5)	0	2 (0.8)
No reasonable possibility	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
口腔腫脹	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
悪心	8 (6.1)	11 (9.8)	19 (7.8)
No reasonable possibility	2 (1.5)	4 (3.6)	6 (2.5)
Reasonable possibility	6 (4.5)	7 (6.3)	13 (5.3)
口腔内不快感	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
口腔内痛	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
胃腸障害 (Cont.)			
口の錯感覚	1 (0.8)	1 (0.9)	2 (0.8)
Reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
直腸出血	1 (0.8)	1 (0.9)	2 (0.8)
No reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
歯痛	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
嘔吐	3 (2.3)	3 (2.7)	6 (2.5)
No reasonable possibility	1 (0.8)	2 (1.8)	3 (1.2)
Reasonable possibility	2 (1.5)	1 (0.9)	3 (1.2)
一般・全身障害および投与部位の状態	106 (80.3)	96 (85.7)	202 (82.8)
No reasonable possibility	6 (4.5)	1 (0.9)	7 (2.9)
Reasonable possibility	100 (75.8)	95 (84.8)	195 (79.9)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
一般・全身障害および投与部位の状態 (Cont.)			
投与部位内出血	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
投与部位紅斑	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
投与部位漏出	0	2 (1.8)	2 (0.8)
Reasonable possibility	0	2 (1.8)	2 (0.8)
無力症	3 (2.3)	0	3 (1.2)
No reasonable possibility	2 (1.5)	0	2 (0.8)
Reasonable possibility	1 (0.8)	0	1 (0.4)
カテーテル留置部位紅斑	1 (0.8)	1 (0.9)	2 (0.8)
Reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
一般・全身障害および投与部位の状態 (Cont.)			
カテーテル留置部位漏出	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
カテーテル留置部位出血	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
カテーテル留置部位炎症	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
カテーテル留置部位刺激感	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
カテーテル留置部位浮腫	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
一般・全身障害および投与部位の状態 (Cont.)			
カテーテル留置部位疼痛	0	2 (1.8)	2 (0.8)
Reasonable possibility	0	2 (1.8)	2 (0.8)
胸部不快感	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
胸痛	1 (0.8)	1 (0.9)	2 (0.8)
No reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
泣き	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
不快感	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
一般・全身障害および投与部位の状態 (Cont.)			
薬効欠如	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
薬剤離脱症候群	1 (0.8)	1 (0.9)	2 (0.8)
No reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
疲労	6 (4.5)	3 (2.7)	9 (3.7)
No reasonable possibility	2 (1.5)	0	2 (0.8)
Reasonable possibility	4 (3.0)	3 (2.7)	7 (2.9)
異常感	1 (0.8)	1 (0.9)	2 (0.8)
No reasonable possibility	0	1 (0.9)	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
冷感	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
一般・全身障害および投与部位の状態 (Cont.)			
熱感	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
歩行障害	0	2 (1.8)	2 (0.8)
No reasonable possibility	0	2 (1.8)	2 (0.8)
歩行不能	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
低体温	1 (0.8)	1 (0.9)	2 (0.8)
No reasonable possibility	0	1 (0.9)	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
インフルエンザ様疾患	1 (0.8)	2 (1.8)	3 (1.2)
No reasonable possibility	1 (0.8)	2 (1.8)	3 (1.2)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
一般・全身障害および投与部位の状態 (Cont.)			
注入部位内出血	10 (7.6)	8 (7.1)	18 (7.4)
No reasonable possibility	2 (1.5)	1 (0.9)	3 (1.2)
Reasonable possibility	8 (6.1)	7 (6.3)	15 (6.1)
注入部位皮膚炎	2 (1.5)	2 (1.8)	4 (1.6)
Reasonable possibility	2 (1.5)	2 (1.8)	4 (1.6)
注入部位分泌物	1 (0.8)	1 (0.9)	2 (0.8)
Reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
注入部位変色	2 (1.5)	0	2 (0.8)
Reasonable possibility	2 (1.5)	0	2 (0.8)
注入部位不快感	3 (2.3)	1 (0.9)	4 (1.6)
Reasonable possibility	3 (2.3)	1 (0.9)	4 (1.6)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
一般・全身障害および投与部位の状態 (Cont.)			
注入部位びらん	1 (0.8)	1 (0.9)	2 (0.8)
No reasonable possibility	1 (0.8)	0	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
注入部位紅斑	65 (49.2)	60 (53.6)	125 (51.2)
No reasonable possibility	6 (4.5)	1 (0.9)	7 (2.9)
Reasonable possibility	59 (44.7)	59 (52.7)	118 (48.4)
注入部位皮膚剥脱	3 (2.3)	3 (2.7)	6 (2.5)
Reasonable possibility	3 (2.3)	3 (2.7)	6 (2.5)
注入部位血管外漏出	8 (6.1)	12 (10.7)	20 (8.2)
Reasonable possibility	8 (6.1)	12 (10.7)	20 (8.2)
注入部位血腫	8 (6.1)	8 (7.1)	16 (6.6)
No reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
Reasonable possibility	7 (5.3)	7 (6.3)	14 (5.7)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
一般・全身障害および投与部位の状態 (Cont.)			
注入部位出血	4 (3.0)	5 (4.5)	9 (3.7)
No reasonable possibility	2 (1.5)	1 (0.9)	3 (1.2)
Reasonable possibility	2 (1.5)	4 (3.6)	6 (2.5)
注入部位硬結	7 (5.3)	3 (2.7)	10 (4.1)
Reasonable possibility	7 (5.3)	3 (2.7)	10 (4.1)
注入部位炎症	3 (2.3)	6 (5.4)	9 (3.7)
No reasonable possibility	0	1 (0.9)	1 (0.4)
Reasonable possibility	3 (2.3)	5 (4.5)	8 (3.3)
注入部位損傷	1 (0.8)	2 (1.8)	3 (1.2)
Reasonable possibility	1 (0.8)	2 (1.8)	3 (1.2)
注入部位刺激感	1 (0.8)	4 (3.6)	5 (2.0)
No reasonable possibility	0	1 (0.9)	1 (0.4)
Reasonable possibility	1 (0.8)	3 (2.7)	4 (1.6)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
一般・全身障害および投与部位の状態 (Cont.)			
注入部位腫瘤	5 (3.8)	3 (2.7)	8 (3.3)
Reasonable possibility	5 (3.8)	3 (2.7)	8 (3.3)
注入部位壊死	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
注入部位結節	34 (25.8)	34 (30.4)	68 (27.9)
Reasonable possibility	34 (25.8)	34 (30.4)	68 (27.9)
注入部位浮腫	19 (14.4)	28 (25.0)	47 (19.3)
No reasonable possibility	0	1 (0.9)	1 (0.4)
Reasonable possibility	19 (14.4)	27 (24.1)	46 (18.9)
注入部位疼痛	18 (13.6)	20 (17.9)	38 (15.6)
No reasonable possibility	2 (1.5)	2 (1.8)	4 (1.6)
Reasonable possibility	16 (12.1)	18 (16.1)	34 (13.9)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
一般・全身障害および投与部位の状態 (Cont.)			
注入部位蒼白	3 (2.3)	1 (0.9)	4 (1.6)
No reasonable possibility	1 (0.8)	0	1 (0.4)
Reasonable possibility	2 (1.5)	1 (0.9)	3 (1.2)
注入部位丘疹	7 (5.3)	11 (9.8)	18 (7.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
Reasonable possibility	7 (5.3)	10 (8.9)	17 (7.0)
注入部位異常感覚	0	2 (1.8)	2 (0.8)
Reasonable possibility	0	2 (1.8)	2 (0.8)
注入部位そう痒感	5 (3.8)	2 (1.8)	7 (2.9)
No reasonable possibility	0	1 (0.9)	1 (0.4)
Reasonable possibility	5 (3.8)	1 (0.9)	6 (2.5)
注入部位発疹	3 (2.3)	4 (3.6)	7 (2.9)
No reasonable possibility	0	2 (1.8)	2 (0.8)
Reasonable possibility	3 (2.3)	2 (1.8)	5 (2.0)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
一般・全身障害および投与部位の状態 (Cont.)			
注入部位反応	13 (9.8)	18 (16.1)	31 (12.7)
Reasonable possibility	13 (9.8)	18 (16.1)	31 (12.7)
注入部位痂皮	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
注入部位腫脹	4 (3.0)	2 (1.8)	6 (2.5)
Reasonable possibility	4 (3.0)	2 (1.8)	6 (2.5)
注入部位小水疱	0	2 (1.8)	2 (0.8)
Reasonable possibility	0	2 (1.8)	2 (0.8)
注入部位熱感	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
一般・全身障害および投与部位の状態 (Cont.)			
注射部位内出血	2 (1.5)	1 (0.9)	3 (1.2)
Reasonable possibility	2 (1.5)	1 (0.9)	3 (1.2)
注射部位変色	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
注射部位紅斑	6 (4.5)	8 (7.1)	14 (5.7)
Reasonable possibility	6 (4.5)	8 (7.1)	14 (5.7)
注射部位漏出	1 (0.8)	1 (0.9)	2 (0.8)
Reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
注射部位血腫	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
一般・全身障害および投与部位の状態 (Cont.)			
注射部位出血	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
注射部位炎症	2 (1.5)	4 (3.6)	6 (2.5)
Reasonable possibility	2 (1.5)	4 (3.6)	6 (2.5)
注射部位結節	3 (2.3)	6 (5.4)	9 (3.7)
Reasonable possibility	3 (2.3)	6 (5.4)	9 (3.7)
注射部位浮腫	2 (1.5)	3 (2.7)	5 (2.0)
Reasonable possibility	2 (1.5)	3 (2.7)	5 (2.0)
注射部位疼痛	2 (1.5)	6 (5.4)	8 (3.3)
No reasonable possibility	0	2 (1.8)	2 (0.8)
Reasonable possibility	2 (1.5)	4 (3.6)	6 (2.5)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
一般・全身障害および投与部位の状態 (Cont.)			
注射部位丘疹	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
注射部位反応	1 (0.8)	1 (0.9)	2 (0.8)
Reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
注射部位腫脹	2 (1.5)	2 (1.8)	4 (1.6)
Reasonable possibility	2 (1.5)	2 (1.8)	4 (1.6)
注射部位蕁麻疹	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
滴下投与部位熱傷	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
一般・全身障害および投与部位の状態 (Cont.)			
滴下投与部位痛	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
限局性浮腫	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
適用部位からの吸収不良	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
倦怠感	1 (0.8)	2 (1.8)	3 (1.2)
No reasonable possibility	1 (0.8)	0	1 (0.4)
Reasonable possibility	0	2 (1.8)	2 (0.8)
医療機器使用部位刺激感	1 (0.8)	2 (1.8)	3 (1.2)
No reasonable possibility	1 (0.8)	2 (1.8)	3 (1.2)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
一般・全身障害および投与部位の状態 (Cont.)			
医療機器使用部位そう痒感	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
医療機器使用部位発疹	0	2 (1.8)	2 (0.8)
No reasonable possibility	0	2 (1.8)	2 (0.8)
小結節	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
非心臓性胸痛	0	2 (1.8)	2 (0.8)
No reasonable possibility	0	2 (1.8)	2 (0.8)
末梢性浮腫	5 (3.8)	4 (3.6)	9 (3.7)
No reasonable possibility	4 (3.0)	3 (2.7)	7 (2.9)
Reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
一般・全身障害および投与部位の状態 (Cont.)			
疼痛	2 (1.5)	0	2 (0.8)
No reasonable possibility	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
末梢腫脹	0	4 (3.6)	4 (1.6)
No reasonable possibility	0	2 (1.8)	2 (0.8)
Reasonable possibility	0	2 (1.8)	2 (0.8)
穿刺部位内出血	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
穿刺部位紅斑	0	3 (2.7)	3 (1.2)
No reasonable possibility	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	2 (1.8)	2 (0.8)
穿刺部位出血	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
一般・全身障害および投与部位の状態 (Cont.)			
穿刺部位硬結	2 (1.5)	0	2 (0.8)
Reasonable possibility	2 (1.5)	0	2 (0.8)
穿刺部位浮腫	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
穿刺部位腫脹	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
発熱	2 (1.5)	2 (1.8)	4 (1.6)
No reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
Reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
口渇	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
一般・全身障害および投与部位の状態 (Cont.)			
血管穿刺部位硬結	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
肝胆道系障害	2 (1.5)	1 (0.9)	3 (1.2)
No reasonable possibility	2 (1.5)	1 (0.9)	3 (1.2)
肝嚢胞	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
脂肪肝	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
門脈血栓症	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
感染症および寄生虫症	58 (43.9)	56 (50.0)	114 (46.7)
No reasonable possibility	18 (13.6)	16 (14.3)	34 (13.9)
Reasonable possibility	40 (30.3)	40 (35.7)	80 (32.8)
無症候性COVID-19	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
細菌性疾患キャリアー	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
ボレリア感染	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
ウイルス性気管支炎	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
感染症および寄生虫症 (Cont.)			
COVID-19	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
COVID-19肺炎	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
カテーテル留置部位感染	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
蜂巣炎	1 (0.8)	1 (0.9)	2 (0.8)
No reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
結膜炎	2 (1.5)	0	2 (0.8)
No reasonable possibility	2 (1.5)	0	2 (0.8)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
感染症および寄生虫症 (Cont.)			
膀胱炎	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
爪の皮膚糸状菌症	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
真菌感染	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
胃腸炎	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
歯肉炎	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
感染症および寄生虫症 (Cont.)			
麦粒腫	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
感染性皮膚潰瘍	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
インフルエンザ	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
注入部位膿瘍	13 (9.8)	13 (11.6)	26 (10.7)
No reasonable possibility	0	2 (1.8)	2 (0.8)
Reasonable possibility	13 (9.8)	11 (9.8)	24 (9.8)
注入部位蜂巣炎	29 (22.0)	27 (24.1)	56 (23.0)
No reasonable possibility	2 (1.5)	2 (1.8)	4 (1.6)
Reasonable possibility	27 (20.5)	25 (22.3)	52 (21.3)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
感染症および寄生虫症 (Cont.)			
注入部位感染	6 (4.5)	11 (9.8)	17 (7.0)
No reasonable possibility	2 (1.5)	1 (0.9)	3 (1.2)
Reasonable possibility	4 (3.0)	10 (8.9)	14 (5.7)
注入部位膿疱	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
注射部位蜂巣炎	0	3 (2.7)	3 (1.2)
No reasonable possibility	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	2 (1.8)	2 (0.8)
上咽頭炎	5 (3.8)	5 (4.5)	10 (4.1)
No reasonable possibility	5 (3.8)	5 (4.5)	10 (4.1)
爪真菌症	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
感染症および寄生虫症 (Cont.)			
耳下腺膿瘍	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
肺炎	3 (2.3)	1 (0.9)	4 (1.6)
No reasonable possibility	3 (2.3)	1 (0.9)	4 (1.6)
術後膿瘍	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
シュードモナス感染	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
膿疱性皮疹	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
感染症および寄生虫症 (Cont.)			
気道感染	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
敗血症	3 (2.3)	1 (0.9)	4 (1.6)
No reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
Reasonable possibility	2 (1.5)	0	2 (0.8)
敗血症性ショック	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
副鼻腔炎	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
ブドウ球菌感染	1 (0.8)	1 (0.9)	2 (0.8)
No reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
感染症および寄生虫症 (Cont.)			
歯感染	1 (0.8)	1 (0.9)	2 (0.8)
No reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
上気道感染	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
尿路感染	8 (6.1)	11 (9.8)	19 (7.8)
No reasonable possibility	8 (6.1)	11 (9.8)	19 (7.8)
水痘帯状疱疹ウイルス感染	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
傷害、中毒および処置合併症	21 (15.9)	26 (23.2)	47 (19.3)
No reasonable possibility	12 (9.1)	19 (17.0)	31 (12.7)
Reasonable possibility	9 (6.8)	7 (6.3)	16 (6.6)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
傷害、中毒および処置合併症 (Cont.)			
足関節部骨折	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
節足動物咬傷	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
骨挫傷	1 (0.8)	1 (0.9)	2 (0.8)
No reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
脳挫傷	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
挫傷	2 (1.5)	6 (5.4)	8 (3.3)
No reasonable possibility	2 (1.5)	4 (3.6)	6 (2.5)
Reasonable possibility	0	2 (1.8)	2 (0.8)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
傷害、中毒および処置合併症 (Cont.)			
医療機器設置の問題	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
医療機器による投与の欠落	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
期限切れの製品使用	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
眼挫傷	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
顔面損傷	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
傷害、中毒および処置合併症 (Cont.)			
顔面骨骨折	0	2 (1.8)	2 (0.8)
No reasonable possibility	0	2 (1.8)	2 (0.8)
転倒	16 (12.1)	23 (20.5)	39 (16.0)
No reasonable possibility	11 (8.3)	18 (16.1)	29 (11.9)
Reasonable possibility	5 (3.8)	5 (4.5)	10 (4.1)
頭部損傷	2 (1.5)	2 (1.8)	4 (1.6)
No reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
Reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
注入に伴う反応	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
関節脱臼	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
傷害、中毒および処置合併症 (Cont.)			
靭帯捻挫	1 (0.8)	1 (0.9)	2 (0.8)
No reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
腰椎骨折	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
過量投与	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
処置後挫傷	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
処置によるめまい	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
傷害、中毒および処置合併症 (Cont.)			
肋骨骨折	1 (0.8)	2 (1.8)	3 (1.2)
No reasonable possibility	1 (0.8)	2 (1.8)	3 (1.2)
皮膚擦過傷	1 (0.8)	2 (1.8)	3 (1.2)
No reasonable possibility	1 (0.8)	2 (1.8)	3 (1.2)
皮膚損傷	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
皮膚裂傷	1 (0.8)	6 (5.4)	7 (2.9)
No reasonable possibility	1 (0.8)	6 (5.4)	7 (2.9)
ストレス骨折	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
傷害、中毒および処置合併症 (Cont.)			
硬膜下血腫	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
サンバーン	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
腱断裂	1 (0.8)	1 (0.9)	2 (0.8)
No reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
過少量投与	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
創傷	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
臨床検査	23 (17.4)	22 (19.6)	45 (18.4)
No reasonable possibility	12 (9.1)	6 (5.4)	18 (7.4)
Reasonable possibility	11 (8.3)	16 (14.3)	27 (11.1)
血中クレアチンホスホキナーゼ増加	1 (0.8)	1 (0.9)	2 (0.8)
No reasonable possibility	0	1 (0.9)	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
血中クレアチニン減少	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
血中葉酸減少	1 (0.8)	2 (1.8)	3 (1.2)
No reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
Reasonable possibility	0	1 (0.9)	1 (0.4)
血中ホモシステイン増加	1 (0.8)	2 (1.8)	3 (1.2)
No reasonable possibility	0	1 (0.9)	1 (0.4)
Reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
臨床検査 (Cont.)			
血中リン減少	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
血圧上昇	1 (0.8)	1 (0.9)	2 (0.8)
No reasonable possibility	1 (0.8)	0	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
起立血圧低下	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
血中ナトリウム減少	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
C-反応性蛋白増加	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
臨床検査 (Cont.)			
握力低下	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
ヘモグロビン減少	1 (0.8)	1 (0.9)	2 (0.8)
No reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
リンパ球数減少	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
単球数増加	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
好中球数増加	0	2 (1.8)	2 (0.8)
No reasonable possibility	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
臨床検査 (Cont.)			
プロトロンビン時間延長	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
赤血球数減少	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
ビタミンB12減少	1 (0.8)	1 (0.9)	2 (0.8)
No reasonable possibility	1 (0.8)	0	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
ビタミンB6減少	5 (3.8)	6 (5.4)	11 (4.5)
No reasonable possibility	1 (0.8)	4 (3.6)	5 (2.0)
Reasonable possibility	4 (3.0)	2 (1.8)	6 (2.5)
ビタミンD減少	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
臨床検査 (Cont.)			
体重減少	10 (7.6)	12 (10.7)	22 (9.0)
No reasonable possibility	6 (4.5)	1 (0.9)	7 (2.9)
Reasonable possibility	4 (3.0)	11 (9.8)	15 (6.1)
体重増加	2 (1.5)	0	2 (0.8)
No reasonable possibility	2 (1.5)	0	2 (0.8)
白血球数増加	0	2 (1.8)	2 (0.8)
No reasonable possibility	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
代謝および栄養障害	11 (8.3)	17 (15.2)	28 (11.5)
No reasonable possibility	7 (5.3)	10 (8.9)	17 (7.0)
Reasonable possibility	4 (3.0)	7 (6.3)	11 (4.5)
悪液質	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
代謝および栄養障害 (Cont.)			
食欲減退	3 (2.3)	2 (1.8)	5 (2.0)
No reasonable possibility	2 (1.5)	1 (0.9)	3 (1.2)
Reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
脱水	1 (0.8)	3 (2.7)	4 (1.6)
No reasonable possibility	1 (0.8)	3 (2.7)	4 (1.6)
糖尿病	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
水分過負荷	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
体液貯留	1 (0.8)	1 (0.9)	2 (0.8)
No reasonable possibility	1 (0.8)	0	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
代謝および栄養障害 (Cont.)			
葉酸欠乏	1 (0.8)	1 (0.9)	2 (0.8)
No reasonable possibility	1 (0.8)	0	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
耐糖能障害	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
高コレステロール血症	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
高血糖	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
高ホモシステイン血症	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
代謝および栄養障害 (Cont.)			
低カリウム血症	0	3 (2.7)	3 (1.2)
No reasonable possibility	0	3 (2.7)	3 (1.2)
低ナトリウム血症	2 (1.5)	0	2 (0.8)
No reasonable possibility	2 (1.5)	0	2 (0.8)
栄養障害	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
ビタミンB群欠乏	1 (0.8)	1 (0.9)	2 (0.8)
Reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
ビタミンB12欠乏	0	2 (1.8)	2 (0.8)
Reasonable possibility	0	2 (1.8)	2 (0.8)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
代謝および栄養障害 (Cont.)			
ビタミンB6欠乏	3 (2.3)	5 (4.5)	8 (3.3)
No reasonable possibility	1 (0.8)	2 (1.8)	3 (1.2)
Reasonable possibility	2 (1.5)	3 (2.7)	5 (2.0)
筋骨格系および結合組織障害	24 (18.2)	20 (17.9)	44 (18.0)
No reasonable possibility	17 (12.9)	17 (15.2)	34 (13.9)
Reasonable possibility	7 (5.3)	3 (2.7)	10 (4.1)
関節痛	3 (2.3)	3 (2.7)	6 (2.5)
No reasonable possibility	2 (1.5)	3 (2.7)	5 (2.0)
Reasonable possibility	1 (0.8)	0	1 (0.4)
反応性関節炎	1 (0.8)	1 (0.9)	2 (0.8)
No reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
背部痛	8 (6.1)	4 (3.6)	12 (4.9)
No reasonable possibility	7 (5.3)	4 (3.6)	11 (4.5)
Reasonable possibility	1 (0.8)	0	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
筋骨格系および結合組織障害 (Cont.)			
骨痛	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
滑液包炎	2 (1.5)	0	2 (0.8)
No reasonable possibility	2 (1.5)	0	2 (0.8)
外骨腫	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
椎間関節症候群	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
椎間板変性症	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
筋骨格系および結合組織障害 (Cont.)			
椎間板突出	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
関節滲出液	0	2 (1.8)	2 (0.8)
No reasonable possibility	0	2 (1.8)	2 (0.8)
関節腫脹	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
四肢不快感	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
筋萎縮	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
筋骨格系および結合組織障害 (Cont.)			
筋痙縮	2 (1.5)	3 (2.7)	5 (2.0)
No reasonable possibility	2 (1.5)	3 (2.7)	5 (2.0)
筋力低下	4 (3.0)	1 (0.9)	5 (2.0)
No reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
Reasonable possibility	3 (2.3)	0	3 (1.2)
筋骨格硬直	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
筋肉痛	2 (1.5)	1 (0.9)	3 (1.2)
No reasonable possibility	2 (1.5)	1 (0.9)	3 (1.2)
頚部痛	2 (1.5)	0	2 (0.8)
No reasonable possibility	2 (1.5)	0	2 (0.8)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
筋骨格系および結合組織障害 (Cont.)			
骨炎	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
変形性関節症	1 (0.8)	4 (3.6)	5 (2.0)
No reasonable possibility	1 (0.8)	4 (3.6)	5 (2.0)
骨減少症	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
四肢痛	3 (2.3)	3 (2.7)	6 (2.5)
No reasonable possibility	2 (1.5)	2 (1.8)	4 (1.6)
Reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
関節周囲炎	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
筋骨格系および結合組織障害 (Cont.)			
姿勢異常	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
横紋筋融解症	2 (1.5)	0	2 (0.8)
No reasonable possibility	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
肩回旋筋腱板症候群	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
仙腸関節機能障害	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
変形性脊椎症	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
筋骨格系および結合組織障害 (Cont.)			
腱障害	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
腱炎	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
斜頚	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
弾発指	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	4 (3.6)	4 (1.6)
No reasonable possibility	0	4 (3.6)	4 (1.6)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）(Cont.)			
基底細胞癌	0	2 (1.8)	2 (0.8)
No reasonable possibility	0	2 (1.8)	2 (0.8)
脂漏性角化症	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
皮膚有棘細胞癌	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
神経系障害	62 (47.0)	48 (42.9)	110 (45.1)
No reasonable possibility	17 (12.9)	17 (15.2)	34 (13.9)
Reasonable possibility	45 (34.1)	31 (27.7)	76 (31.1)
アカシジア	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
神経系障害 (Cont.)			
健忘	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
失語症	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
運動失調	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
平衡障害	0	4 (3.6)	4 (1.6)
No reasonable possibility	0	3 (2.7)	3 (1.2)
Reasonable possibility	0	1 (0.9)	1 (0.4)
運動緩慢	1 (0.8)	1 (0.9)	2 (0.8)
Reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
神経系障害 (Cont.)			
手根管症候群	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
大脳萎縮	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
脳出血	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
脳圧排効果	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
脳血管発作	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
神経系障害 (Cont.)			
認知障害	4 (3.0)	2 (1.8)	6 (2.5)
No reasonable possibility	3 (2.3)	2 (1.8)	5 (2.0)
Reasonable possibility	1 (0.8)	0	1 (0.4)
振動覚低下	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
注意力障害	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
浮動性めまい	15 (11.4)	10 (8.9)	25 (10.2)
No reasonable possibility	3 (2.3)	2 (1.8)	5 (2.0)
Reasonable possibility	12 (9.1)	8 (7.1)	20 (8.2)
体位性めまい	5 (3.8)	0	5 (2.0)
Reasonable possibility	5 (3.8)	0	5 (2.0)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
神経系障害 (Cont.)			
構語障害	0	3 (2.7)	3 (1.2)
No reasonable possibility	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	2 (1.8)	2 (0.8)
味覚不全	2 (1.5)	1 (0.9)	3 (1.2)
Reasonable possibility	2 (1.5)	1 (0.9)	3 (1.2)
ジスキネジア	12 (9.1)	6 (5.4)	18 (7.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
Reasonable possibility	11 (8.3)	6 (5.4)	17 (7.0)
起立障害	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
ジストニア	2 (1.5)	5 (4.5)	7 (2.9)
No reasonable possibility	1 (0.8)	3 (2.7)	4 (1.6)
Reasonable possibility	1 (0.8)	2 (1.8)	3 (1.2)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
神経系障害 (Cont.)			
脳症	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
てんかん	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
本態性振戦	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
伸展性足底反応	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
すくみ現象	4 (3.0)	0	4 (1.6)
No reasonable possibility	1 (0.8)	0	1 (0.4)
Reasonable possibility	3 (2.3)	0	3 (1.2)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
神経系障害 (Cont.)			
全身性強直性間代性発作	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
頭部不快感	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
頭痛	7 (5.3)	7 (6.3)	14 (5.7)
No reasonable possibility	3 (2.3)	5 (4.5)	8 (3.3)
Reasonable possibility	4 (3.0)	2 (1.8)	6 (2.5)
片側感覚消失	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
不全片麻痺	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
神経系障害 (Cont.)			
感覚鈍麻	1 (0.8)	2 (1.8)	3 (1.2)
Reasonable possibility	1 (0.8)	2 (1.8)	3 (1.2)
反射減弱	2 (1.5)	1 (0.9)	3 (1.2)
No reasonable possibility	2 (1.5)	1 (0.9)	3 (1.2)
不規則睡眠覚醒リズム障害	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
嗜眠	1 (0.8)	1 (0.9)	2 (0.8)
No reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
意識消失	1 (0.8)	1 (0.9)	2 (0.8)
No reasonable possibility	0	1 (0.9)	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
神経系障害 (Cont.)			
腰仙部神経根障害	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
記憶障害	0	2 (1.8)	2 (0.8)
No reasonable possibility	0	2 (1.8)	2 (0.8)
代謝性脳症	1 (0.8)	1 (0.9)	2 (0.8)
No reasonable possibility	1 (0.8)	0	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
神経痛	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
末梢性ニューロパチー	1 (0.8)	1 (0.9)	2 (0.8)
No reasonable possibility	0	1 (0.9)	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
神経系障害 (Cont.)			
オンオフ現象	4 (3.0)	4 (3.6)	8 (3.3)
No reasonable possibility	2 (1.5)	0	2 (0.8)
Reasonable possibility	2 (1.5)	4 (3.6)	6 (2.5)
錯感覚	4 (3.0)	3 (2.7)	7 (2.9)
No reasonable possibility	1 (0.8)	0	1 (0.4)
Reasonable possibility	3 (2.3)	3 (2.7)	6 (2.5)
パーキンソン病	12 (9.1)	5 (4.5)	17 (7.0)
No reasonable possibility	6 (4.5)	0	6 (2.5)
Reasonable possibility	6 (4.5)	5 (4.5)	11 (4.5)
パーキンソニズム	0	3 (2.7)	3 (1.2)
No reasonable possibility	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	2 (1.8)	2 (0.8)
側反弓	1 (0.8)	2 (1.8)	3 (1.2)
No reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
Reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
神経系障害 (Cont.)			
多発ニューロパチー	0	2 (1.8)	2 (0.8)
Reasonable possibility	0	2 (1.8)	2 (0.8)
失神寸前の状態	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
心因性発作	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
精神運動亢進	1 (0.8)	1 (0.9)	2 (0.8)
Reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
反射異常	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
神経系障害 (Cont.)			
安静時振戦	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
坐骨神経痛	0	3 (2.7)	3 (1.2)
No reasonable possibility	0	2 (1.8)	2 (0.8)
Reasonable possibility	0	1 (0.9)	1 (0.4)
痙攣発作	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
感覚障害	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
感覚消失	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
神経系障害 (Cont.)			
睡眠時麻痺	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
傾眠	9 (6.8)	3 (2.7)	12 (4.9)
No reasonable possibility	4 (3.0)	0	4 (1.6)
Reasonable possibility	5 (3.8)	3 (2.7)	8 (3.3)
失神	0	3 (2.7)	3 (1.2)
No reasonable possibility	0	2 (1.8)	2 (0.8)
Reasonable possibility	0	1 (0.9)	1 (0.4)
振戦	1 (0.8)	2 (1.8)	3 (1.2)
No reasonable possibility	0	1 (0.9)	1 (0.4)
Reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
製品の問題	2 (1.5)	1 (0.9)	3 (1.2)
No reasonable possibility	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
製品の問題 (Cont.)			
医療機器送達システムの問題	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
医療機器位置異常	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
医療機器機能不良	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
精神障害	50 (37.9)	54 (48.2)	104 (42.6)
No reasonable possibility	8 (6.1)	17 (15.2)	25 (10.2)
Reasonable possibility	42 (31.8)	37 (33.0)	79 (32.4)
異常な夢	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
精神障害 (Cont.)			
感情不安定	1 (0.8)	1 (0.9)	2 (0.8)
No reasonable possibility	0	1 (0.9)	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
激越	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
不安	10 (7.6)	18 (16.1)	28 (11.5)
No reasonable possibility	7 (5.3)	11 (9.8)	18 (7.4)
Reasonable possibility	3 (2.3)	7 (6.3)	10 (4.1)
不安障害	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
無感情	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
精神障害 (Cont.)			
歯ぎしり	2 (1.5)	0	2 (0.8)
No reasonable possibility	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
強迫行為	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
強迫性性行動	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
錯乱状態	4 (3.0)	4 (3.6)	8 (3.3)
No reasonable possibility	0	1 (0.9)	1 (0.4)
Reasonable possibility	4 (3.0)	3 (2.7)	7 (2.9)
譫妄	1 (0.8)	4 (3.6)	5 (2.0)
No reasonable possibility	1 (0.8)	2 (1.8)	3 (1.2)
Reasonable possibility	0	2 (1.8)	2 (0.8)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
精神障害 (Cont.)			
妄想	8 (6.1)	2 (1.8)	10 (4.1)
No reasonable possibility	0	1 (0.9)	1 (0.4)
Reasonable possibility	8 (6.1)	1 (0.9)	9 (3.7)
寄生虫妄想	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
妄想性障害、詳細不明	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
抑うつ気分	2 (1.5)	1 (0.9)	3 (1.2)
No reasonable possibility	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
うつ病	2 (1.5)	2 (1.8)	4 (1.6)
No reasonable possibility	2 (1.5)	1 (0.9)	3 (1.2)
Reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
精神障害 (Cont.)			
抑うつ症状	2 (1.5)	0	2 (0.8)
No reasonable possibility	2 (1.5)	0	2 (0.8)
ドーパミン調節障害症候群	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
ディスフェミア	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
睡眠異常	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
情動障害	1 (0.8)	1 (0.9)	2 (0.8)
No reasonable possibility	0	1 (0.9)	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
精神障害 (Cont.)			
注射恐怖	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
幻覚	20 (15.2)	21 (18.8)	41 (16.8)
No reasonable possibility	1 (0.8)	4 (3.6)	5 (2.0)
Reasonable possibility	19 (14.4)	17 (15.2)	36 (14.8)
幻聴	3 (2.3)	3 (2.7)	6 (2.5)
No reasonable possibility	0	1 (0.9)	1 (0.4)
Reasonable possibility	3 (2.3)	2 (1.8)	5 (2.0)
幻嗅	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
幻視	10 (7.6)	5 (4.5)	15 (6.1)
No reasonable possibility	0	1 (0.9)	1 (0.4)
Reasonable possibility	10 (7.6)	4 (3.6)	14 (5.7)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
精神障害 (Cont.)			
混合性幻覚	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
性欲過剰	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
錯覚	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
衝動制御障害	0	4 (3.6)	4 (1.6)
No reasonable possibility	0	2 (1.8)	2 (0.8)
Reasonable possibility	0	2 (1.8)	2 (0.8)
衝動行為	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
精神障害 (Cont.)			
不眠症	9 (6.8)	9 (8.0)	18 (7.4)
No reasonable possibility	2 (1.5)	3 (2.7)	5 (2.0)
Reasonable possibility	7 (5.3)	6 (5.4)	13 (5.3)
易刺激性	1 (0.8)	1 (0.9)	2 (0.8)
No reasonable possibility	0	1 (0.9)	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
嫉妬妄想	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
躁病	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
気分変化	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
精神障害 (Cont.)			
気分動揺	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
悪夢	1 (0.8)	1 (0.9)	2 (0.8)
Reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
強迫観念	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
パニック発作	0	3 (2.7)	3 (1.2)
Reasonable possibility	0	3 (2.7)	3 (1.2)
パニック反応	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
精神障害 (Cont.)			
妄想症	2 (1.5)	0	2 (0.8)
Reasonable possibility	2 (1.5)	0	2 (0.8)
睡眠の質低下	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
処置に対する不安	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
精神病性障害	4 (3.0)	2 (1.8)	6 (2.5)
Reasonable possibility	4 (3.0)	2 (1.8)	6 (2.5)
精神病症状	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
精神障害 (Cont.)			
レム睡眠行動障害	1 (0.8)	1 (0.9)	2 (0.8)
Reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
レム睡眠異常	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
睡眠障害	2 (1.5)	1 (0.9)	3 (1.2)
Reasonable possibility	2 (1.5)	1 (0.9)	3 (1.2)
ねごと	1 (0.8)	1 (0.9)	2 (0.8)
Reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
精神障害 (Cont.)			
常同症	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
ストレス	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
自殺念慮	1 (0.8)	2 (1.8)	3 (1.2)
No reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
Reasonable possibility	0	1 (0.9)	1 (0.4)
自殺企図	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
腎および尿路障害	11 (8.3)	7 (6.3)	18 (7.4)
No reasonable possibility	11 (8.3)	5 (4.5)	16 (6.6)
Reasonable possibility	0	2 (1.8)	2 (0.8)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
腎および尿路障害 (Cont.)			
膀胱痙縮	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
膀胱結石	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
排尿困難	1 (0.8)	2 (1.8)	3 (1.2)
No reasonable possibility	1 (0.8)	2 (1.8)	3 (1.2)
緊張性膀胱	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
夜間頻尿	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
腎および尿路障害 (Cont.)			
多尿	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
腎機能障害	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
尿管結石症	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
切迫性尿失禁	3 (2.3)	0	3 (1.2)
No reasonable possibility	3 (2.3)	0	3 (1.2)
尿失禁	3 (2.3)	2 (1.8)	5 (2.0)
No reasonable possibility	3 (2.3)	1 (0.9)	4 (1.6)
Reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
腎および尿路障害 (Cont.)			
尿閉	0	3 (2.7)	3 (1.2)
No reasonable possibility	0	3 (2.7)	3 (1.2)
尿路障害	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
尿異常	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
尿臭異常	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
生殖系および乳房障害	2 (1.5)	4 (3.6)	6 (2.5)
No reasonable possibility	1 (0.8)	3 (2.7)	4 (1.6)
Reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
生殖系および乳房障害 (Cont.)			
良性前立腺肥大症	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
勃起不全	1 (0.8)	1 (0.9)	2 (0.8)
Reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
ペイロニー病	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
前立腺腫大	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
腟脱	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
呼吸器、胸郭および縦隔障害	6 (4.5)	19 (17.0)	25 (10.2)
No reasonable possibility	6 (4.5)	16 (14.3)	22 (9.0)
Reasonable possibility	0	3 (2.7)	3 (1.2)
急性呼吸不全	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
気管支拡張症	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
咳嗽	1 (0.8)	2 (1.8)	3 (1.2)
No reasonable possibility	1 (0.8)	2 (1.8)	3 (1.2)
発声障害	0	2 (1.8)	2 (0.8)
No reasonable possibility	0	2 (1.8)	2 (0.8)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
呼吸器、胸郭および縦隔障害 (Cont.)			
呼吸困難	2 (1.5)	6 (5.4)	8 (3.3)
No reasonable possibility	2 (1.5)	4 (3.6)	6 (2.5)
Reasonable possibility	0	2 (1.8)	2 (0.8)
労作性呼吸困難	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
鼻出血	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
過換気	0	2 (1.8)	2 (0.8)
No reasonable possibility	0	2 (1.8)	2 (0.8)
口腔咽頭痛	1 (0.8)	1 (0.9)	2 (0.8)
No reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
呼吸器、胸郭および縦隔障害 (Cont.)			
誤嚥性肺炎	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
湿性咳嗽	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
肺塞栓症	0	2 (1.8)	2 (0.8)
No reasonable possibility	0	2 (1.8)	2 (0.8)
ラ音	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
鼻痛	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
呼吸器、胸郭および縦隔障害 (Cont.)			
鼻漏	0	2 (1.8)	2 (0.8)
No reasonable possibility	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
咽喉刺激感	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
皮膚および皮下組織障害	14 (10.6)	14 (12.5)	28 (11.5)
No reasonable possibility	8 (6.1)	12 (10.7)	20 (8.2)
Reasonable possibility	6 (4.5)	2 (1.8)	8 (3.3)
脱毛症	2 (1.5)	0	2 (0.8)
Reasonable possibility	2 (1.5)	0	2 (0.8)
褥瘡性潰瘍	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
皮膚および皮下組織障害 (Cont.)			
皮膚嚢腫	1 (0.8)	1 (0.9)	2 (0.8)
No reasonable possibility	0	1 (0.9)	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
皮膚炎	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
接触皮膚炎	2 (1.5)	0	2 (0.8)
No reasonable possibility	2 (1.5)	0	2 (0.8)
おむつ皮膚炎	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
薬疹	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
皮膚および皮下組織障害 (Cont.)			
皮膚乾燥	1 (0.8)	1 (0.9)	2 (0.8)
No reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
斑状出血	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
紅斑	1 (0.8)	3 (2.7)	4 (1.6)
No reasonable possibility	1 (0.8)	3 (2.7)	4 (1.6)
爪の障害	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
脂肪織炎	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
皮膚および皮下組織障害 (Cont.)			
丘疹	0	2 (1.8)	2 (0.8)
No reasonable possibility	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
光線過敏性反応	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
そう痒症	2 (1.5)	1 (0.9)	3 (1.2)
No reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
Reasonable possibility	1 (0.8)	0	1 (0.4)
乾癬	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
発疹	2 (1.5)	1 (0.9)	3 (1.2)
No reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
Reasonable possibility	1 (0.8)	0	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
皮膚および皮下組織障害 (Cont.)			
紅斑性皮疹	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
そう痒性皮疹	2 (1.5)	1 (0.9)	3 (1.2)
No reasonable possibility	0	1 (0.9)	1 (0.4)
Reasonable possibility	2 (1.5)	0	2 (0.8)
皮膚刺激	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
皮膚病変	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
皮膚潰瘍	1 (0.8)	1 (0.9)	2 (0.8)
No reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
皮膚および皮下組織障害 (Cont.)			
蕁麻疹	2 (1.5)	0	2 (0.8)
Reasonable possibility	2 (1.5)	0	2 (0.8)
社会環境	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
運動不能	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
外科および内科処置	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
抜歯	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
血管障害	11 (8.3)	15 (13.4)	26 (10.7)
No reasonable possibility	5 (3.8)	7 (6.3)	12 (4.9)
Reasonable possibility	6 (4.5)	8 (7.1)	14 (5.7)
深部静脈血栓症	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
血腫	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
出血	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
ほてり	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
血管障害 (Cont.)			
高血圧	3 (2.3)	3 (2.7)	6 (2.5)
No reasonable possibility	3 (2.3)	2 (1.8)	5 (2.0)
Reasonable possibility	0	1 (0.9)	1 (0.4)
高血圧クリーゼ	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
低血圧	2 (1.5)	4 (3.6)	6 (2.5)
No reasonable possibility	0	2 (1.8)	2 (0.8)
Reasonable possibility	2 (1.5)	2 (1.8)	4 (1.6)
不安定血圧	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
起立性高血圧	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Entire study period (Cont.)	N=132	N=112	N=244
血管障害 (Cont.)			
起立性低血圧	6 (4.5)	6 (5.4)	12 (4.9)
No reasonable possibility	2 (1.5)	1 (0.9)	3 (1.2)
Reasonable possibility	4 (3.0)	5 (4.5)	9 (3.7)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Optimization period	N=132	N=112	N=244
Any adverse event	105 (79.5)	97 (86.6)	202 (82.8)
No reasonable possibility	9 (6.8)	2 (1.8)	11 (4.5)
Reasonable possibility	96 (72.7)	95 (84.8)	191 (78.3)
心臓障害	0	2 (1.8)	2 (0.8)
Reasonable possibility	0	2 (1.8)	2 (0.8)
徐脈	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
動悸	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
耳および迷路障害	2 (1.5)	2 (1.8)	4 (1.6)
No reasonable possibility	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	2 (1.8)	3 (1.2)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
耳および迷路障害 (Cont.)			
乗物酔い	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
回転性めまい	2 (1.5)	1 (0.9)	3 (1.2)
No reasonable possibility	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
眼障害	1 (0.8)	2 (1.8)	3 (1.2)
No reasonable possibility	1 (0.8)	2 (1.8)	3 (1.2)
複視	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
眼窩周囲腫脹	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
眼障害 (Cont.)			
霧視	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
胃腸障害	13 (9.8)	15 (13.4)	28 (11.5)
No reasonable possibility	5 (3.8)	8 (7.1)	13 (5.3)
Reasonable possibility	8 (6.1)	7 (6.3)	15 (6.1)
腹部膨満	0	2 (1.8)	2 (0.8)
No reasonable possibility	0	2 (1.8)	2 (0.8)
腹痛	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
上腹部痛	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
胃腸障害 (Cont.)			
アフタ性潰瘍	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
呼気臭	2 (1.5)	0	2 (0.8)
Reasonable possibility	2 (1.5)	0	2 (0.8)
便秘	2 (1.5)	2 (1.8)	4 (1.6)
No reasonable possibility	2 (1.5)	1 (0.9)	3 (1.2)
Reasonable possibility	0	1 (0.9)	1 (0.4)
下痢	2 (1.5)	2 (1.8)	4 (1.6)
No reasonable possibility	2 (1.5)	2 (1.8)	4 (1.6)
口内乾燥	2 (1.5)	3 (2.7)	5 (2.0)
No reasonable possibility	0	2 (1.8)	2 (0.8)
Reasonable possibility	2 (1.5)	1 (0.9)	3 (1.2)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
胃腸障害 (Cont.)			
消化不良	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
胃食道逆流性疾患	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
痔核	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
過敏性腸症候群	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
悪心	5 (3.8)	5 (4.5)	10 (4.1)
No reasonable possibility	0	1 (0.9)	1 (0.4)
Reasonable possibility	5 (3.8)	4 (3.6)	9 (3.7)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
胃腸障害 (Cont.)			
嘔吐	2 (1.5)	1 (0.9)	3 (1.2)
Reasonable possibility	2 (1.5)	1 (0.9)	3 (1.2)
一般・全身障害および投与部位の状態	90 (68.2)	82 (73.2)	172 (70.5)
No reasonable possibility	8 (6.1)	3 (2.7)	11 (4.5)
Reasonable possibility	82 (62.1)	79 (70.5)	161 (66.0)
投与部位紅斑	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
無力症	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
カテーテル留置部位紅斑	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
一般・全身障害および投与部位の状態 (Cont.)			
カテーテル留置部位炎症	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
カテーテル留置部位疼痛	0	2 (1.8)	2 (0.8)
No reasonable possibility	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
不快感	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
薬剤離脱症候群	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
疲労	3 (2.3)	2 (1.8)	5 (2.0)
No reasonable possibility	2 (1.5)	0	2 (0.8)
Reasonable possibility	1 (0.8)	2 (1.8)	3 (1.2)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
一般・全身障害および投与部位の状態 (Cont.)			
異常感	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
熱感	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
歩行障害	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
歩行不能	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
低体温	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
一般・全身障害および投与部位の状態 (Cont.)			
インフルエンザ様疾患	1 (0.8)	1 (0.9)	2 (0.8)
No reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
注入部位内出血	3 (2.3)	7 (6.3)	10 (4.1)
No reasonable possibility	2 (1.5)	2 (1.8)	4 (1.6)
Reasonable possibility	1 (0.8)	5 (4.5)	6 (2.5)
注入部位分泌物	1 (0.8)	1 (0.9)	2 (0.8)
Reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
注入部位変色	2 (1.5)	0	2 (0.8)
Reasonable possibility	2 (1.5)	0	2 (0.8)
注入部位不快感	2 (1.5)	1 (0.9)	3 (1.2)
Reasonable possibility	2 (1.5)	1 (0.9)	3 (1.2)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
一般・全身障害および投与部位の状態 (Cont.)			
注入部位びらん	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
注入部位紅斑	50 (37.9)	45 (40.2)	95 (38.9)
No reasonable possibility	4 (3.0)	0	4 (1.6)
Reasonable possibility	46 (34.8)	45 (40.2)	91 (37.3)
注入部位皮膚剥脱	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
注入部位血管外漏出	4 (3.0)	7 (6.3)	11 (4.5)
Reasonable possibility	4 (3.0)	7 (6.3)	11 (4.5)
注入部位血腫	4 (3.0)	4 (3.6)	8 (3.3)
No reasonable possibility	0	1 (0.9)	1 (0.4)
Reasonable possibility	4 (3.0)	3 (2.7)	7 (2.9)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
一般・全身障害および投与部位の状態 (Cont.)			
注入部位出血	0	3 (2.7)	3 (1.2)
Reasonable possibility	0	3 (2.7)	3 (1.2)
注入部位硬結	4 (3.0)	1 (0.9)	5 (2.0)
Reasonable possibility	4 (3.0)	1 (0.9)	5 (2.0)
注入部位炎症	1 (0.8)	3 (2.7)	4 (1.6)
Reasonable possibility	1 (0.8)	3 (2.7)	4 (1.6)
注入部位腫瘤	4 (3.0)	1 (0.9)	5 (2.0)
Reasonable possibility	4 (3.0)	1 (0.9)	5 (2.0)
注入部位壊死	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
一般・全身障害および投与部位の状態 (Cont.)			
注入部位結節	20 (15.2)	18 (16.1)	38 (15.6)
Reasonable possibility	20 (15.2)	18 (16.1)	38 (15.6)
注入部位浮腫	14 (10.6)	16 (14.3)	30 (12.3)
Reasonable possibility	14 (10.6)	16 (14.3)	30 (12.3)
注入部位疼痛	13 (9.8)	14 (12.5)	27 (11.1)
No reasonable possibility	1 (0.8)	2 (1.8)	3 (1.2)
Reasonable possibility	12 (9.1)	12 (10.7)	24 (9.8)
注入部位蒼白	2 (1.5)	0	2 (0.8)
No reasonable possibility	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
注入部位丘疹	1 (0.8)	4 (3.6)	5 (2.0)
Reasonable possibility	1 (0.8)	4 (3.6)	5 (2.0)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
一般・全身障害および投与部位の状態 (Cont.)			
注入部位異常感覚	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
注入部位そう痒感	2 (1.5)	1 (0.9)	3 (1.2)
Reasonable possibility	2 (1.5)	1 (0.9)	3 (1.2)
注入部位発疹	2 (1.5)	1 (0.9)	3 (1.2)
Reasonable possibility	2 (1.5)	1 (0.9)	3 (1.2)
注入部位反応	9 (6.8)	12 (10.7)	21 (8.6)
Reasonable possibility	9 (6.8)	12 (10.7)	21 (8.6)
注入部位腫脹	3 (2.3)	1 (0.9)	4 (1.6)
Reasonable possibility	3 (2.3)	1 (0.9)	4 (1.6)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
一般・全身障害および投与部位の状態 (Cont.)			
注射部位内出血	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
注射部位紅斑	5 (3.8)	5 (4.5)	10 (4.1)
Reasonable possibility	5 (3.8)	5 (4.5)	10 (4.1)
注射部位漏出	1 (0.8)	1 (0.9)	2 (0.8)
Reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
注射部位血腫	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
注射部位炎症	1 (0.8)	2 (1.8)	3 (1.2)
Reasonable possibility	1 (0.8)	2 (1.8)	3 (1.2)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
一般・全身障害および投与部位の状態 (Cont.)			
注射部位結節	1 (0.8)	2 (1.8)	3 (1.2)
Reasonable possibility	1 (0.8)	2 (1.8)	3 (1.2)
注射部位浮腫	2 (1.5)	2 (1.8)	4 (1.6)
Reasonable possibility	2 (1.5)	2 (1.8)	4 (1.6)
注射部位疼痛	2 (1.5)	4 (3.6)	6 (2.5)
No reasonable possibility	0	2 (1.8)	2 (0.8)
Reasonable possibility	2 (1.5)	2 (1.8)	4 (1.6)
注射部位反応	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
注射部位腫脹	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
一般・全身障害および投与部位の状態 (Cont.)			
滴下投与部位熱傷	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
限局性浮腫	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
適用部位からの吸収不良	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
倦怠感	1 (0.8)	1 (0.9)	2 (0.8)
No reasonable possibility	1 (0.8)	0	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
医療機器使用部位刺激感	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
一般・全身障害および投与部位の状態 (Cont.)			
医療機器使用部位そう痒感	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
医療機器使用部位発疹	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
小結節	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
末梢性浮腫	1 (0.8)	3 (2.7)	4 (1.6)
No reasonable possibility	1 (0.8)	2 (1.8)	3 (1.2)
Reasonable possibility	0	1 (0.9)	1 (0.4)
末梢腫脹	0	2 (1.8)	2 (0.8)
No reasonable possibility	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
一般・全身障害および投与部位の状態 (Cont.)			
穿刺部位内出血	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
穿刺部位紅斑	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
穿刺部位出血	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
穿刺部位硬結	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
穿刺部位浮腫	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
一般・全身障害および投与部位の状態 (Cont.)			
穿刺部位腫脹	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
発熱	2 (1.5)	1 (0.9)	3 (1.2)
No reasonable possibility	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
口渇	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
肝胆道系障害	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
門脈血栓症	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
感染症および寄生虫症	17 (12.9)	27 (24.1)	44 (18.0)
No reasonable possibility	7 (5.3)	12 (10.7)	19 (7.8)
Reasonable possibility	10 (7.6)	15 (13.4)	25 (10.2)
ボレリア感染	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
膀胱炎	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
真菌感染	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
胃腸炎	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
感染症および寄生虫症 (Cont.)			
注入部位膿瘍	3 (2.3)	5 (4.5)	8 (3.3)
No reasonable possibility	0	1 (0.9)	1 (0.4)
Reasonable possibility	3 (2.3)	4 (3.6)	7 (2.9)
注入部位蜂巣炎	10 (7.6)	13 (11.6)	23 (9.4)
No reasonable possibility	2 (1.5)	1 (0.9)	3 (1.2)
Reasonable possibility	8 (6.1)	12 (10.7)	20 (8.2)
注入部位感染	1 (0.8)	3 (2.7)	4 (1.6)
No reasonable possibility	0	1 (0.9)	1 (0.4)
Reasonable possibility	1 (0.8)	2 (1.8)	3 (1.2)
注射部位蜂巣炎	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
上咽頭炎	0	3 (2.7)	3 (1.2)
No reasonable possibility	0	3 (2.7)	3 (1.2)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
感染症および寄生虫症 (Cont.)			
爪真菌症	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
肺炎	1 (0.8)	1 (0.9)	2 (0.8)
No reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
膿疱性皮疹	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
敗血症	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
敗血症性ショック	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
感染症および寄生虫症 (Cont.)			
尿路感染	3 (2.3)	3 (2.7)	6 (2.5)
No reasonable possibility	3 (2.3)	3 (2.7)	6 (2.5)
傷害、中毒および処置合併症	10 (7.6)	11 (9.8)	21 (8.6)
No reasonable possibility	5 (3.8)	8 (7.1)	13 (5.3)
Reasonable possibility	5 (3.8)	3 (2.7)	8 (3.3)
挫傷	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
医療機器設置の問題	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
医療機器による投与の欠落	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
傷害、中毒および処置合併症 (Cont.)			
顔面骨骨折	0	2 (1.8)	2 (0.8)
No reasonable possibility	0	2 (1.8)	2 (0.8)
転倒	7 (5.3)	9 (8.0)	16 (6.6)
No reasonable possibility	5 (3.8)	6 (5.4)	11 (4.5)
Reasonable possibility	2 (1.5)	3 (2.7)	5 (2.0)
頭部損傷	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
注入に伴う反応	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
腰椎骨折	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
傷害、中毒および処置合併症 (Cont.)			
処置後挫傷	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
処置によるめまい	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
肋骨骨折	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
皮膚擦過傷	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
皮膚裂傷	0	2 (1.8)	2 (0.8)
No reasonable possibility	0	2 (1.8)	2 (0.8)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
臨床検査	3 (2.3)	5 (4.5)	8 (3.3)
No reasonable possibility	3 (2.3)	2 (1.8)	5 (2.0)
Reasonable possibility	0	3 (2.7)	3 (1.2)
血圧上昇	1 (0.8)	1 (0.9)	2 (0.8)
No reasonable possibility	1 (0.8)	0	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
起立血圧低下	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
リンパ球数減少	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
単球数増加	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
臨床検査 (Cont.)			
好中球数増加	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
ビタミンB12減少	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
ビタミンB6減少	0	2 (1.8)	2 (0.8)
No reasonable possibility	0	2 (1.8)	2 (0.8)
体重減少	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
白血球数増加	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
代謝および栄養障害	1 (0.8)	5 (4.5)	6 (2.5)
No reasonable possibility	0	4 (3.6)	4 (1.6)
Reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
食欲減退	1 (0.8)	1 (0.9)	2 (0.8)
Reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
脱水	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
耐糖能障害	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
高血糖	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
代謝および栄養障害 (Cont.)			
低カリウム血症	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
筋骨格系および結合組織障害	10 (7.6)	8 (7.1)	18 (7.4)
No reasonable possibility	6 (4.5)	6 (5.4)	12 (4.9)
Reasonable possibility	4 (3.0)	2 (1.8)	6 (2.5)
関節痛	2 (1.5)	2 (1.8)	4 (1.6)
No reasonable possibility	1 (0.8)	2 (1.8)	3 (1.2)
Reasonable possibility	1 (0.8)	0	1 (0.4)
反応性関節炎	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
背部痛	3 (2.3)	1 (0.9)	4 (1.6)
No reasonable possibility	2 (1.5)	1 (0.9)	3 (1.2)
Reasonable possibility	1 (0.8)	0	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
筋骨格系および結合組織障害 (Cont.)			
関節腫脹	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
筋力低下	2 (1.5)	0	2 (0.8)
No reasonable possibility	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
筋骨格硬直	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
筋肉痛	2 (1.5)	1 (0.9)	3 (1.2)
No reasonable possibility	2 (1.5)	1 (0.9)	3 (1.2)
四肢痛	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
筋骨格系および結合組織障害 (Cont.)			
姿勢異常	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
横紋筋融解症	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
仙腸関節機能障害	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
斜頚	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
神経系障害	36 (27.3)	26 (23.2)	62 (25.4)
No reasonable possibility	6 (4.5)	7 (6.3)	13 (5.3)
Reasonable possibility	30 (22.7)	19 (17.0)	49 (20.1)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
神経系障害 (Cont.)			
運動失調	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
平衡障害	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
運動緩慢	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
認知障害	2 (1.5)	0	2 (0.8)
No reasonable possibility	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
浮動性めまい	10 (7.6)	8 (7.1)	18 (7.4)
No reasonable possibility	0	2 (1.8)	2 (0.8)
Reasonable possibility	10 (7.6)	6 (5.4)	16 (6.6)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
神経系障害 (Cont.)			
体位性めまい	3 (2.3)	0	3 (1.2)
Reasonable possibility	3 (2.3)	0	3 (1.2)
構語障害	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
味覚不全	2 (1.5)	0	2 (0.8)
Reasonable possibility	2 (1.5)	0	2 (0.8)
ジスキネジア	6 (4.5)	3 (2.7)	9 (3.7)
Reasonable possibility	6 (4.5)	3 (2.7)	9 (3.7)
起立障害	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
神経系障害 (Cont.)			
ジストニア	1 (0.8)	1 (0.9)	2 (0.8)
No reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
本態性振戦	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
すくみ現象	3 (2.3)	0	3 (1.2)
Reasonable possibility	3 (2.3)	0	3 (1.2)
頭部不快感	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
頭痛	4 (3.0)	2 (1.8)	6 (2.5)
No reasonable possibility	2 (1.5)	2 (1.8)	4 (1.6)
Reasonable possibility	2 (1.5)	0	2 (0.8)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
神経系障害 (Cont.)			
片側感覚消失	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
不全片麻痺	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
代謝性脳症	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
オンオフ現象	3 (2.3)	3 (2.7)	6 (2.5)
No reasonable possibility	1 (0.8)	0	1 (0.4)
Reasonable possibility	2 (1.5)	3 (2.7)	5 (2.0)
錯感覚	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
神経系障害 (Cont.)			
パーキンソン病	5 (3.8)	3 (2.7)	8 (3.3)
No reasonable possibility	2 (1.5)	0	2 (0.8)
Reasonable possibility	3 (2.3)	3 (2.7)	6 (2.5)
パーキンソニズム	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
精神運動亢進	1 (0.8)	1 (0.9)	2 (0.8)
Reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
安静時振戦	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
坐骨神経痛	0	2 (1.8)	2 (0.8)
No reasonable possibility	0	2 (1.8)	2 (0.8)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
神経系障害 (Cont.)			
傾眠	2 (1.5)	2 (1.8)	4 (1.6)
Reasonable possibility	2 (1.5)	2 (1.8)	4 (1.6)
振戦	0	2 (1.8)	2 (0.8)
No reasonable possibility	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
製品の問題	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
医療機器機能不良	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
精神障害	31 (23.5)	24 (21.4)	55 (22.5)
No reasonable possibility	6 (4.5)	9 (8.0)	15 (6.1)
Reasonable possibility	25 (18.9)	15 (13.4)	40 (16.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
精神障害 (Cont.)			
異常な夢	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
感情不安定	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
不安	2 (1.5)	8 (7.1)	10 (4.1)
No reasonable possibility	1 (0.8)	5 (4.5)	6 (2.5)
Reasonable possibility	1 (0.8)	3 (2.7)	4 (1.6)
歯ぎしり	2 (1.5)	0	2 (0.8)
No reasonable possibility	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
錯乱状態	1 (0.8)	1 (0.9)	2 (0.8)
Reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
精神障害 (Cont.)			
譫妄	1 (0.8)	2 (1.8)	3 (1.2)
No reasonable possibility	1 (0.8)	2 (1.8)	3 (1.2)
妄想	1 (0.8)	1 (0.9)	2 (0.8)
Reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
抑うつ気分	1 (0.8)	1 (0.9)	2 (0.8)
No reasonable possibility	1 (0.8)	0	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
抑うつ症状	2 (1.5)	0	2 (0.8)
No reasonable possibility	2 (1.5)	0	2 (0.8)
睡眠異常	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
精神障害 (Cont.)			
情動障害	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
幻覚	13 (9.8)	5 (4.5)	18 (7.4)
No reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
Reasonable possibility	12 (9.1)	4 (3.6)	16 (6.6)
幻聴	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
幻視	4 (3.0)	1 (0.9)	5 (2.0)
No reasonable possibility	0	1 (0.9)	1 (0.4)
Reasonable possibility	4 (3.0)	0	4 (1.6)
不眠症	7 (5.3)	3 (2.7)	10 (4.1)
No reasonable possibility	2 (1.5)	0	2 (0.8)
Reasonable possibility	5 (3.8)	3 (2.7)	8 (3.3)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
精神障害 (Cont.)			
易刺激性	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
嫉妬妄想	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
気分変化	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
強迫観念	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
パニック発作	0	3 (2.7)	3 (1.2)
No reasonable possibility	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	2 (1.8)	2 (0.8)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
精神障害 (Cont.)			
精神病性障害	2 (1.5)	0	2 (0.8)
Reasonable possibility	2 (1.5)	0	2 (0.8)
レム睡眠行動障害	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
睡眠障害	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
ねごと	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
腎および尿路障害	6 (4.5)	1 (0.9)	7 (2.9)
No reasonable possibility	6 (4.5)	1 (0.9)	7 (2.9)
排尿困難	1 (0.8)	1 (0.9)	2 (0.8)
No reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
切迫性尿失禁	2 (1.5)	0	2 (0.8)
No reasonable possibility	2 (1.5)	0	2 (0.8)
尿失禁	2 (1.5)	0	2 (0.8)
No reasonable possibility	2 (1.5)	0	2 (0.8)
尿路障害	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
腎および尿路障害 (Cont.)			
尿異常	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
生殖系および乳房障害	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
勃起不全	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
呼吸器、胸郭および縦隔障害	1 (0.8)	7 (6.3)	8 (3.3)
No reasonable possibility	1 (0.8)	6 (5.4)	7 (2.9)
Reasonable possibility	0	1 (0.9)	1 (0.4)
急性呼吸不全	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
呼吸器、胸郭および縦隔障害 (Cont.)			
咳嗽	1 (0.8)	1 (0.9)	2 (0.8)
No reasonable possibility	1 (0.8)	1 (0.9)	2 (0.8)
呼吸困難	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
過換気	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
口腔咽頭痛	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
鼻痛	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
呼吸器、胸郭および縦隔障害 (Cont.)			
鼻漏	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
皮膚および皮下組織障害	6 (4.5)	5 (4.5)	11 (4.5)
No reasonable possibility	4 (3.0)	5 (4.5)	9 (3.7)
Reasonable possibility	2 (1.5)	0	2 (0.8)
脱毛症	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
接触皮膚炎	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
皮膚乾燥	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
皮膚および皮下組織障害 (Cont.)			
斑状出血	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
紅斑	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
光線過敏性反応	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
発疹	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
そう痒性皮疹	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
皮膚および皮下組織障害 (Cont.)			
皮膚刺激	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
皮膚病変	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)
皮膚潰瘍	1 (0.8)	0	1 (0.4)
No reasonable possibility	1 (0.8)	0	1 (0.4)
社会環境	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)
運動不能	1 (0.8)	0	1 (0.4)
Reasonable possibility	1 (0.8)	0	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
血管障害	3 (2.3)	7 (6.3)	10 (4.1)
No reasonable possibility	2 (1.5)	2 (1.8)	4 (1.6)
Reasonable possibility	1 (0.8)	5 (4.5)	6 (2.5)
ほてり	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
高血圧	2 (1.5)	1 (0.9)	3 (1.2)
No reasonable possibility	2 (1.5)	1 (0.9)	3 (1.2)
低血圧	0	2 (1.8)	2 (0.8)
No reasonable possibility	0	1 (0.9)	1 (0.4)
Reasonable possibility	0	1 (0.9)	1 (0.4)
不安定血圧	0	1 (0.9)	1 (0.4)
No reasonable possibility	0	1 (0.9)	1 (0.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Optimization period (Cont.)	N=132	N=112	N=244
血管障害 (Cont.)			
起立性低血圧	1 (0.8)	4 (3.6)	5 (2.0)
No reasonable possibility	0	1 (0.9)	1 (0.4)
Reasonable possibility	1 (0.8)	3 (2.7)	4 (1.6)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Maintenance period	N=111	N=95	N=206
Any adverse event	98 (88.3)	88 (92.6)	186 (90.3)
No reasonable possibility	9 (8.1)	5 (5.3)	14 (6.8)
Reasonable possibility	89 (80.2)	83 (87.4)	172 (83.5)
血液およびリンパ系障害	1 (0.9)	3 (3.2)	4 (1.9)
No reasonable possibility	1 (0.9)	3 (3.2)	4 (1.9)
大球性貧血	0	1 (1.1)	1 (0.5)
No reasonable possibility	0	1 (1.1)	1 (0.5)
凝血異常	0	1 (1.1)	1 (0.5)
No reasonable possibility	0	1 (1.1)	1 (0.5)
リンパ節症	1 (0.9)	0	1 (0.5)
No reasonable possibility	1 (0.9)	0	1 (0.5)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Maintenance period (Cont.)	N=111	N=95	N=206
血液およびリンパ系障害 (Cont.)			
縦隔リンパ節腫脹	0	1 (1.1)	1 (0.5)
No reasonable possibility	0	1 (1.1)	1 (0.5)
心臓障害	4 (3.6)	5 (5.3)	9 (4.4)
No reasonable possibility	4 (3.6)	5 (5.3)	9 (4.4)
急性心筋梗塞	1 (0.9)	0	1 (0.5)
No reasonable possibility	1 (0.9)	0	1 (0.5)
狭心症	1 (0.9)	0	1 (0.5)
No reasonable possibility	1 (0.9)	0	1 (0.5)
心房細動	0	1 (1.1)	1 (0.5)
No reasonable possibility	0	1 (1.1)	1 (0.5)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Maintenance period (Cont.)	N=111	N=95	N=206
心臓障害 (Cont.)			
心停止	1 (0.9)	0	1 (0.5)
No reasonable possibility	1 (0.9)	0	1 (0.5)
心肺停止	0	1 (1.1)	1 (0.5)
No reasonable possibility	0	1 (1.1)	1 (0.5)
冠動脈疾患	1 (0.9)	1 (1.1)	2 (1.0)
No reasonable possibility	1 (0.9)	1 (1.1)	2 (1.0)
冠動脈狭窄	1 (0.9)	0	1 (0.5)
No reasonable possibility	1 (0.9)	0	1 (0.5)
期外収縮	0	1 (1.1)	1 (0.5)
No reasonable possibility	0	1 (1.1)	1 (0.5)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Maintenance period (Cont.)	N=111	N=95	N=206
心臓障害 (Cont.)			
左室肥大	0	1 (1.1)	1 (0.5)
No reasonable possibility	0	1 (1.1)	1 (0.5)
心筋梗塞	1 (0.9)	0	1 (0.5)
No reasonable possibility	1 (0.9)	0	1 (0.5)
動悸	0	1 (1.1)	1 (0.5)
No reasonable possibility	0	1 (1.1)	1 (0.5)
耳および迷路障害	2 (1.8)	2 (2.1)	4 (1.9)
No reasonable possibility	1 (0.9)	2 (2.1)	3 (1.5)
Reasonable possibility	1 (0.9)	0	1 (0.5)
感音性難聴	1 (0.9)	0	1 (0.5)
No reasonable possibility	1 (0.9)	0	1 (0.5)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Maintenance period (Cont.)	N=111	N=95	N=206
耳および迷路障害 (Cont.)			
回転性めまい	1 (0.9)	1 (1.1)	2 (1.0)
No reasonable possibility	0	1 (1.1)	1 (0.5)
Reasonable possibility	1 (0.9)	0	1 (0.5)
頭位性回転性めまい	0	1 (1.1)	1 (0.5)
No reasonable possibility	0	1 (1.1)	1 (0.5)
眼障害	7 (6.3)	6 (6.3)	13 (6.3)
No reasonable possibility	7 (6.3)	5 (5.3)	12 (5.8)
Reasonable possibility	0	1 (1.1)	1 (0.5)
白内障	2 (1.8)	2 (2.1)	4 (1.9)
No reasonable possibility	2 (1.8)	2 (2.1)	4 (1.9)
複視	2 (1.8)	0	2 (1.0)
No reasonable possibility	2 (1.8)	0	2 (1.0)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Maintenance period (Cont.)	N=111	N=95	N=206
眼障害 (Cont.)			
ドライアイ	1 (0.9)	3 (3.2)	4 (1.9)
No reasonable possibility	1 (0.9)	3 (3.2)	4 (1.9)
緑内障	1 (0.9)	1 (1.1)	2 (1.0)
No reasonable possibility	1 (0.9)	1 (1.1)	2 (1.0)
眼窩周囲痛	0	1 (1.1)	1 (0.5)
No reasonable possibility	0	1 (1.1)	1 (0.5)
眼窩周囲腫脹	0	1 (1.1)	1 (0.5)
No reasonable possibility	0	1 (1.1)	1 (0.5)
網膜裂孔	2 (1.8)	0	2 (1.0)
No reasonable possibility	2 (1.8)	0	2 (1.0)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Maintenance period (Cont.)	N=111	N=95	N=206
眼障害 (Cont.)			
視野欠損	0	1 (1.1)	1 (0.5)
Reasonable possibility	0	1 (1.1)	1 (0.5)
胃腸障害	17 (15.3)	21 (22.1)	38 (18.4)
No reasonable possibility	14 (12.6)	12 (12.6)	26 (12.6)
Reasonable possibility	3 (2.7)	9 (9.5)	12 (5.8)
腹部膨満	1 (0.9)	2 (2.1)	3 (1.5)
No reasonable possibility	0	1 (1.1)	1 (0.5)
Reasonable possibility	1 (0.9)	1 (1.1)	2 (1.0)
腹痛	1 (0.9)	1 (1.1)	2 (1.0)
Reasonable possibility	1 (0.9)	1 (1.1)	2 (1.0)
上腹部痛	1 (0.9)	0	1 (0.5)
No reasonable possibility	1 (0.9)	0	1 (0.5)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Maintenance period (Cont.)	N=111	N=95	N=206
胃腸障害 (Cont.)			
呼気臭	0	1 (1.1)	1 (0.5)
No reasonable possibility	0	1 (1.1)	1 (0.5)
虚血性大腸炎	1 (0.9)	0	1 (0.5)
No reasonable possibility	1 (0.9)	0	1 (0.5)
便秘	6 (5.4)	10 (10.5)	16 (7.8)
No reasonable possibility	6 (5.4)	8 (8.4)	14 (6.8)
Reasonable possibility	0	2 (2.1)	2 (1.0)
齲歯	1 (0.9)	0	1 (0.5)
No reasonable possibility	1 (0.9)	0	1 (0.5)
下痢	4 (3.6)	1 (1.1)	5 (2.4)
No reasonable possibility	4 (3.6)	1 (1.1)	5 (2.4)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Maintenance period (Cont.)	N=111	N=95	N=206
胃腸障害 (Cont.)			
口内乾燥	1 (0.9)	3 (3.2)	4 (1.9)
No reasonable possibility	0	1 (1.1)	1 (0.5)
Reasonable possibility	1 (0.9)	2 (2.1)	3 (1.5)
嚥下障害	0	1 (1.1)	1 (0.5)
No reasonable possibility	0	1 (1.1)	1 (0.5)
糞塊	0	1 (1.1)	1 (0.5)
No reasonable possibility	0	1 (1.1)	1 (0.5)
排便回数増加	0	1 (1.1)	1 (0.5)
No reasonable possibility	0	1 (1.1)	1 (0.5)
胃食道逆流性疾患	1 (0.9)	0	1 (0.5)
No reasonable possibility	1 (0.9)	0	1 (0.5)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Maintenance period (Cont.)	N=111	N=95	N=206
胃腸障害 (Cont.)			
舌炎	1 (0.9)	0	1 (0.5)
Reasonable possibility	1 (0.9)	0	1 (0.5)
舌痛	1 (0.9)	0	1 (0.5)
Reasonable possibility	1 (0.9)	0	1 (0.5)
吐血	1 (0.9)	0	1 (0.5)
No reasonable possibility	1 (0.9)	0	1 (0.5)
裂孔ヘルニア	1 (0.9)	0	1 (0.5)
No reasonable possibility	1 (0.9)	0	1 (0.5)
胃排出不全	1 (0.9)	0	1 (0.5)
No reasonable possibility	1 (0.9)	0	1 (0.5)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Maintenance period (Cont.)	N=111	N=95	N=206
胃腸障害 (Cont.)			
腸出血	1 (0.9)	0	1 (0.5)
No reasonable possibility	1 (0.9)	0	1 (0.5)
過敏性腸症候群	1 (0.9)	1 (1.1)	2 (1.0)
No reasonable possibility	1 (0.9)	1 (1.1)	2 (1.0)
大腸ポリープ	0	1 (1.1)	1 (0.5)
No reasonable possibility	0	1 (1.1)	1 (0.5)
口唇乾燥	1 (0.9)	0	1 (0.5)
No reasonable possibility	1 (0.9)	0	1 (0.5)
メレナ	2 (1.8)	0	2 (1.0)
No reasonable possibility	1 (0.9)	0	1 (0.5)
Reasonable possibility	1 (0.9)	0	1 (0.5)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Maintenance period (Cont.)	N=111	N=95	N=206
胃腸障害 (Cont.)			
口腔腫脹	1 (0.9)	0	1 (0.5)
Reasonable possibility	1 (0.9)	0	1 (0.5)
悪心	4 (3.6)	7 (7.4)	11 (5.3)
No reasonable possibility	2 (1.8)	4 (4.2)	6 (2.9)
Reasonable possibility	2 (1.8)	3 (3.2)	5 (2.4)
口腔内不快感	1 (0.9)	0	1 (0.5)
Reasonable possibility	1 (0.9)	0	1 (0.5)
口腔内痛	1 (0.9)	0	1 (0.5)
Reasonable possibility	1 (0.9)	0	1 (0.5)
口の錯感覚	1 (0.9)	1 (1.1)	2 (1.0)
Reasonable possibility	1 (0.9)	1 (1.1)	2 (1.0)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	 High Dose n (%)	 All Subjects n (%)
Maintenance period (Cont.)	N=111	N=95	N=206
胃腸障害 (Cont.)			
直腸出血	1 (0.9)	1 (1.1)	2 (1.0)
No reasonable possibility	1 (0.9)	1 (1.1)	2 (1.0)
歯痛	0	1 (1.1)	1 (0.5)
No reasonable possibility	0	1 (1.1)	1 (0.5)
嘔吐	1 (0.9)	2 (2.1)	3 (1.5)
No reasonable possibility	1 (0.9)	2 (2.1)	3 (1.5)
一般・全身障害および投与部位の状態	66 (59.5)	71 (74.7)	137 (66.5)
No reasonable possibility	3 (2.7)	2 (2.1)	5 (2.4)
Reasonable possibility	63 (56.8)	69 (72.6)	132 (64.1)
投与部位内出血	0	1 (1.1)	1 (0.5)
Reasonable possibility	0	1 (1.1)	1 (0.5)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Maintenance period (Cont.)	N=111	N=95	N=206
一般・全身障害および投与部位の状態 (Cont.)			
投与部位漏出	0	2 (2.1)	2 (1.0)
Reasonable possibility	0	2 (2.1)	2 (1.0)
無力症	2 (1.8)	0	2 (1.0)
No reasonable possibility	2 (1.8)	0	2 (1.0)
カテーテル留置部位紅斑	1 (0.9)	1 (1.1)	2 (1.0)
Reasonable possibility	1 (0.9)	1 (1.1)	2 (1.0)
カテーテル留置部位漏出	1 (0.9)	0	1 (0.5)
Reasonable possibility	1 (0.9)	0	1 (0.5)
カテーテル留置部位出血	0	1 (1.1)	1 (0.5)
No reasonable possibility	0	1 (1.1)	1 (0.5)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Maintenance period (Cont.)	N=111	N=95	N=206
一般・全身障害および投与部位の状態 (Cont.)			
カテーテル留置部位刺激感	0	1 (1.1)	1 (0.5)
Reasonable possibility	0	1 (1.1)	1 (0.5)
カテーテル留置部位浮腫	0	1 (1.1)	1 (0.5)
Reasonable possibility	0	1 (1.1)	1 (0.5)
カテーテル留置部位疼痛	0	1 (1.1)	1 (0.5)
Reasonable possibility	0	1 (1.1)	1 (0.5)
胸部不快感	0	1 (1.1)	1 (0.5)
Reasonable possibility	0	1 (1.1)	1 (0.5)
胸痛	1 (0.9)	1 (1.1)	2 (1.0)
No reasonable possibility	1 (0.9)	1 (1.1)	2 (1.0)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]

TABLE 14.3 1.6

Subjects with Treatment-Emergent Adverse Events
by Maximum Relationship to Study Drug as Assessed by the Investigator
by Primary System Organ Class and Preferred Term by Time Interval
(Safety Analysis Set)

System Organ Class MedDRA 24.0 Preferred Term Relationship	Dose Category Low Dose n (%)	Dose Category High Dose n (%)	All Subjects n (%)
Maintenance period (Cont.)	N=111	N=95	N=206
一般・全身障害および投与部位の状態 (Cont.)			
泣き	1 (0.9)	0	1 (0.5)
Reasonable possibility	1 (0.9)	0	1 (0.5)
薬効欠如	0	1 (1.1)	1 (0.5)
Reasonable possibility	0	1 (1.1)	1 (0.5)
薬剤離脱症候群	0	1 (1.1)	1 (0.5)
No reasonable possibility	0	1 (1.1)	1 (0.5)
疲労	3 (2.7)	1 (1.1)	4 (1.9)
Reasonable possibility	3 (2.7)	1 (1.1)	4 (1.9)
異常感	0	1 (1.1)	1 (0.5)
No reasonable possibility	0	1 (1.1)	1 (0.5)

Note: Table depicts the most related adverse event for each preferred term as assessed by the investigator for each subject.
Subjects are counted once in each row, regardless of the number of events they may have had.

Program Source Code: [redacted]